Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0667

## THE RELEVANCE OF DOT BLOT TECHNIQUE IN THE DIAGNOSIS OF AUTOIMMUNE HEPATITIS

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### BACKGROUND-AIM

Autoimmune hepatitis (AIH) is an inflammatory chronic liver disease that affects individuals of all ages, with progression to cirrhosis in about 33% of adults.
The diagnosis of AIH is a complex challenge, requiring advanced diagnostic approaches for accurate identification. Traditionally, indirect immunofluorescence (IFI) is used to detect the presence of antinuclear antibodies (Abs), anti-smooth muscle Abs (SMA), Abs to liver-kidney microsome type 1 (anti-LKM1) in children and other specific Abs that may suggest AIH. However, techniques like dot blot offer significant advantages in diagnosing autoimmune liver diseases, as they allow for the identification of more specific Abs with greater precision, reducing the overlap with other liver diseases.

### METHODS

Dot blot is particularly useful for detecting Abs against liver microsomal antigens (LKM), anti-mitochondrial Abs (AMA), and anti-LKM1 Abs, which are essential for diagnosing AIH, especially in atypical cases or in AIH subtypes with distinctive features, such as type 2 AIH. Furthermore, dot blot provides better differentiation between various autoimmune liver diseases due to its ability to identify specific protein epitopes. For example, anti-LKM1 antibodies are associated with type 2 AIH, while anti-AMA Abs are more frequently detected in primary biliary cirrhosis (PBC).

### RESULTS

Statistical data on the concordance between IFI and dot blot show promising results. Recent studies indicate superior sensitivity and specificity of dot blot compared to IFI, particularly for detecting anti-LKM1 and anti-AMA Abs, with diagnostic concordance exceeding 90% in selected cases. A comparative analysis showed that dot blot has a sensitivity of 92% for detecting anti-LKM1 Abs, compared to 75% for IFI. Additionally, dot blot has a specificity of approximately 95% for anti-AMA Abs, compared to 85% for IFI.

### CONCLUSIONS

In our laboratory we have introduced the use of dot blot to confirm positive and doubtful results in IFI, observing that it represents a useful complement to IFI in the diagnosis of autoimmune liver diseases. Actually, dot blot enhances diagnostic accuracy, particularly in complex and atypical cases. Thus, the adoption of both techniques enables a more accurate and targeted diagnosis, facilitating timely and personalized treatment for patients.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0668

## GOODPASTURE SYNDROME: A RARE AND SEVERE FORM OF RENOPULMONARY SYNDROME

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### BACKGROUND-AIM

Renopulmonary syndrome is a severe clinical entity that combines rapidly progressive glomerulonephritis and pulmonary hemorrhage. Its primary etiologies include antineutrophil cytoplasmic antibody (ANCA)-associated vasculitides (60% of cases) and anti-glomerular basement membrane (anti-GBM) disease (15% of cases).
In anti-GBM disease, antibodies targeting type IV collagen damage glomerular and alveolar basement membranes, leading to progressive glomerulonephritis, alveolar hemorrhage, or both. The term Goodpasture Syndrome is used when both renal and pulmonary involvement are observed.

### METHODS

A 31-year-old male presented to the emergency department with oral ulcers, asthenia, non-hemoptysis cough, and progressively worsening dyspnea over one week. Personal history: former smoker and Huntington's disease. Physical examination: BP 140/70 mmHg, cleft tongue.

### RESULTS

Laboratory tests: hemoglobin 5.6 g/dL (13.0-16.5), urea 203 mg/dL (74-100), creatinine 14.07 mg/dL (0.73-1.18), glomerular filtration rate 4 mL/min (>90), Na 121 mmol/L (135-150), LDH 427 U/L (125-220), CRP 12.98 mg/dL (<0.5), procalcitonin 1.91 ng/mL (<0.5). The patient was admitted to the ICU due to suspected vasculitis.
A chest CT scan showed bilateral alveolar hemorrhage, suggesting renopulmonary syndrome secondary to vasculitis. Anti-GBM antibodies >680 U/mL were requested (<7 negative; 7-10 doubtful; >10 positive). The rest of the antibodies were negative. The patient was diagnosed with Goodpasture syndrome. He was treated with plasmapheresis, glucocorticoids and dialysis. The patient is currently on dialysis and is being monitored by the Nephrology Department.

### CONCLUSIONS

Goodpasture Syndrome is a rare and severe form of renopulmonary syndrome, with a mortality rate approaching 50%. Patients often require ICU admission due to the severity of organ dysfunction.
Early diagnosis and appropriate intervention are essential to improving outcomes, as the condition can progress rapidly to fatality. Laboratory findings play a pivotal role in both initial diagnosis and follow-up, emphasizing the importance of a comprehensive diagnostic approach in these autoimmune diseases.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0669

**TUMOUR MARKERS IN OVARIAN CANCER: A CASE REPORT.**

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**BACKGROUND-AIM**

Ovarian cancer is the third most common gynaecological tumour worldwide and the leading cause of death in gynaecological cancer. The lack of specific symptoms, effective screening and diagnostic techniques makes it challenging to diagnose in the early stages so late-stage diagnosis with metastasis results in a low survival rate. One of the most widely used screening test is the estimation of CA 125 serum antigen and Human epididymis protein 4 (HE-4), combined together in an algorithm known as Risk of Ovarian Malignancy Algorithm (ROMA) which classified patients as presenting a high or low risk for epithelial ovarian cancer (EOC), considering the menopausal status.

**METHODS**

We present the case of a 39 years-old woman who attended the emergency department for abdominal pain and swelling. The patient was referred to gynaecology and imaging techniques revealed the presence of a large adnexal mass in the left ovary. In the laboratory we received a blood sample for ROMA calculation (Cobas e 801, Roche Diagnostics).

**RESULTS**

ROMA algorithm resulted in a low risk of EOC as HE-4 value was 51.0 pmol/L (0 – 70) and CA 125 was 58.3 U/mL (5 – 35). Nevertheless, the laboratory performed complementary measurements of other tumor markers: CEA, CA 19.9 and Alfa-fetoprotein. The latter turned out to be pathologically high: 618 ng/mL (0.1 – 10) in a context of no pregnancy or hepatic disease (main false positives). In light of the results, the laboratory recommends to discard an endodermal sinus tumor which tends to have this pattern of markers expression. The patient went for a diagnostic/therapeutic laparotomy and the malignancy was confirmed.

**CONCLUSIONS**

In the context of ovarian cancer, the presence of an adnexal mass raises anxiety of patients and multiple resources and money are usually spent in characterising these lesions. Many of them result even in unnecessary surgery. In this report we validate the usefulness of serum tumour markers as a non-invasive, rapid and low-cost screening test even in situations where the tumour histology is not conventional or majority, as is the case here. it is important to choose the most appropriate combination of markers, as well as to ensure correct interpretation by the clinical laboratory, who plays a key role.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0670

**THE EFFECT OF CISPLATIN TREATMENT ON TRIPLE-NEGATIVE BREAST CANCER CELLS USING CELL-BASED ASSAY**

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**BACKGROUND-AIM**

Breast cancer is the fifth leading cause of cancer mortality in women. Breast cancer is classified molecularly into three main subtypes: luminal, Her2+, and basal-like tumors. The latter is also known as triple-negative breast cancer cells, in which only around 20% respond well to the standard chemotherapy. Cisplatin is a platinum-based drug used to treat TNBC, however, the development of drug resistances has limited its application. Cell-based assay is an important system for studying the physiological processes of cells growth and to analyze the relationship between cellular dysfunction and disease. It has been an essential base for drug discovery process in order to provide fast, simple and cost effective tool to avoid the cost intensive animal testing. This study aims to investigate and compare between the traditional 2D and a newly evolving 3D cell culture systems in testing drug efficacy on breast cancer cells.

**METHODS**

Triple-Negative Breast cancer; MDA-MB-231 cell line were cultured using both the 2D and 3D cell culture approaches. Both cultured cells were treated in parallel with 20 μM cisplatin for 24 hours and monitored by CytoSMART™ System. Subsequently, the effect of cisplatin treatment on the morphological features were examined using phase contrast microscope, Hematoxylin and Eosin stain, Scanning Electron Microscope while cell proliferation and apoptosis induction were assessed using AlamarBlue and flow cytometry and immunofluorescence respectively.

**RESULTS**

Untreated cells cultured on the 2D, grew in an elongated form with centered nucleus connecting to each other by the presence of lamellipodia. The 3D cells grew in a spherical form, each form containing groups of cells that was significantly increase in its size day by day. Once treated, both 2D and 3D cells strongly exhibited the apoptotic features of the nuclear shrinkage, cellular fragmentation and loss of intracellular connections but the effect of cisplatin was higher in the 2D. The detection of Cleaved caspase-3, a down-stream protein of apoptosis induction, using IF was specific and significant in the 2D and poorly detected in the 3D.

**CONCLUSIONS**

Our findings suggest the existence of morphological differences between 2D and 3D cell and the hydrogel matrix can be a useful tool in monitoring cell proliferation and death.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0671

## CHANGES IN SERUM PROSTATE SPECIFIC ANTIGEN LEVELS AMONG PROSTATE CANCER PATIENTS ON HORMONAL TREATMENT FOR PROSTATE CANCER AT THE KENYATTA NATIONAL HOSPITAL, KENYA

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### BACKGROUND-AIM

Serum prostatic-specific antigen (PSA) levels are recommended for prostate cancer response monitoring. The patterns of increase or decrease in serum PSA are used to assess treatment effectiveness and the likelihood of cancer recurrence. The mainstay of treatment for advanced prostate cancer is hormone therapy, which typically alters PSA levels. The purpose of this study was to examine the trends in serum PSA levels among patients with hormone-treated prostate cancer and relate it with selected clinical variables.

### METHODS

This was a retrospective study conducted at the KNH Central Health Records and Information Department. Records of 103 prostate cancer patients who received hormone therapy from January 2020 to December 2023 were reviewed. Data on age, nature of the disease, as well as the baseline and follow-up PSA levels, were abstracted from the patient records.

### RESULTS

The patient's ages ranged from 42 years to 97 years with mean (SD) of 71.9 years (9.9). Most of the study participants (90.29%) were aged 61 years and above. Most of the study participants (86.34 %) had metastatic prostate cancer at the time hormonal treatment was initiated. Majority of the participants with metastatic disease were in the 61 -70-year age bracket. The baseline serum PSA ranged from 7.885ng/ml to 6308ng/ml with a median (IQR) of 279.184 (601.67) ng/ml. Only 10 patients (9.71%) had baseline PSA values below 20 ng/ml. Following treatment, most of the patients showed a declining pattern in their PSA values. The highest reduction was at the first follow up visit. Most of the study participants (40.78%) had final PSA values above 10ng/ml, 36.89% had final values between 0.2 to 4.0ng/ml. Only 10 patients (9.70%) had final PSA values below 0.2 ng/ml.

### CONCLUSIONS

Most prostate cancer cases in this study presented with metastatic disease. The median baseline PSA was higher for patients with metastatic cancer than for those with localized prostate cancer. Although most of the participants showed a reduction in serum PSA following treatment, less than half had post treatment PSA values below the reference range.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0672

## PROSTATE CANCER EXHIBITS INHIBITED EXPRESSIONS OF EXTRACELLULAR NTCP ASSOCIATED WITH REDUCED BILE ACIDS UPTAKE

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### BACKGROUND-AIM

Bile acids (BAs) are cholesterol derivatives synthesized in the liver and then secreted into the intestine for lipid absorption. However, it remains unclear, how bile acids are transported inside prostate cancer cells and what pathways could be mediated though modulating cancer cell phenotype. In this study we aimed to study the impact of bile acid uptake on modulating prostate cancer cells phenotypic activity using primary prostate cancer cells (PC-3) through assessing expressions of bile acid transporter; Sodium+/taurocholate co-transporting polypeptide (NTCP).

### METHODS

We assessed NTCP surface and gene expressions in prostate cancer cells using flow cytometry and RT-PCR, respectively. Bile acids impact on: NTCP expressions and its functional role in mediating bile acid were studied. Intracellular IL-6 from prostate cancer cells as survival, angiogenesis, proliferation, and metastasis marker was evaluated. In all methods we used normal prostate tissue cells (HPrEC) and the results were presented as averages ±SD. Student t-test equal or below 0.05 were considered statistically significant.

### RESULTS

PC-3 cells exhibit no NTCP extracellular expressions as indicated by the flow cytometry. Moreover, these cells showed no bile acid uptake as compared to the normal prostate cells as similar concentrations of cytoplasmic NTCP were obtained. RT-PCR displayed reduced mRNA of NTCP gene expressions of 2.3 folds in the PC-3 while an increase of 2.3-fold in the HPrEC cells (P=0.0001) were obtained. ELISA results indicated an elevated concentrations of IL-6 of 270±82 pg/ml in PC-3 cells as compared to the normal cells HPrEC with IL-6 of 55±12 pg/ml (P=0.001). Flow cytometry analysis assessment demonstrated a basal level of 10±2.6 % of apoptotic cells of the PC-3 cells as compared to 18±3.1 % in normal tissue cells (P=0.02). Following TCA insults, PC-3 cells showed unchanged expressions in their apoptosis rate while an increase of 2.3-fold in the HPrEC cells (P=0.0001).

### CONCLUSIONS

Inhibited surface expressions of NTCP in PC-3 could indicate an escape mechanism of these cells via protecting themselves against apoptosis and restored their metastatic potentials. In highlight of the above data, modulatory therapies targeting IL-6 could be a potential approach to prevent complications to prostate cancer.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0673

**FLAVONOIDS AS POTENTIAL TREATMENTS FOR COLORECTAL CANCER**

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**BACKGROUND-AIM**

Colorectal cancer (CRC) is a significant global health concern, ranking as the third most common cancer and the fourth leading cause of cancer-related deaths worldwide. The search for effective anticancer agents has highlighted flavonoids as promising candidates due to their anti-inflammatory and anticancer properties. This study investigates the anti-proliferative and anti-inflammatory effects of three flavonoids—chrysin, xanthomicrol, and 3-hydroxyflavone—on Caco-2 human colon cancer cells, with comparisons to celecoxib, a conventional drug.

**METHODS**

Cytotoxicity was assessed using the MTT assay, and molecular mechanisms were explored through RT-PCR to measure the expression of GSK-3β, Cox-2, TNF-α, and IL-6 genes. Levels of inflammatory mediators (Cox-2 and p-GSK3β) and cytokines (TNF-α, IL-6, and IL-10) were quantified using ELISA.

**RESULTS**

All three flavonoids demonstrated time- and dose-dependent anti-proliferative effects, with 3-hydroxyflavone exhibiting the highest activity. Chrysin's growth inhibitory effects were linked to reduced Cox-2 and GSK-3β gene expression and lower p-GSK3β (S9) protein levels. Similar molecular effects were observed with 3-hydroxyflavone. Xanthomicrol inhibited GSK-3β gene expression, reduced Cox-2 protein levels, and suppressed IL-6 release.

**CONCLUSIONS**

These findings reveal that chrysin, xanthomicrol, and 3-hydroxyflavone inhibit CRC cell growth by targeting key molecular pathways, suggesting their potential as chemopreventive and chemotherapeutic agents for colorectal cancer.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0675

**TITLE: TLR4 GENE POLYMORPHISM AND BIOCHEMICAL MARKERS AS A TOOL TO IDENTIFY RISK OF OSTEOPOROSIS IN WOMEN FROM KARACHI**

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**BACKGROUND-AIM**

Background: Osteoporosis, characterized by low bone mineral density, poses a global health concern. Diagnosis increases the likelihood of developing osteoporosis, a multifactorial disorder marked by low bone mass, elevating the risk of fractures in the lumbar spine, femoral neck, hip, vertebras, and distal forearm, particularly in postmenopausal women due to bone loss influenced by various pathophysiological factors.
Objectives: To investigate the association of serum cytokine, bone turnover marker, bone mineral density and TLR4 gene polymorphism in pre and post-menopausal women and to find if any of these can be the potential predictor of osteoporosis in postmenopausal women.

**METHODS**

Material and methods: Study participants were consisting of Group A (n=91) healthy pre-menopausal women and Group B (n= 102) healthy postmenopausal women having ≥ 5 years' history of menopause. ELISA was performed for cytokine (TNFα) and bone turnover marker (carboxytelopeptides), respectively. Bone Mineral Density (BMD)was measured through dual X-ray absorptiometry (DEXA) scan. Toll-like Receptors 4 (TLR4) gene polymorphisms (A896G; Asp299Gly) and (C1196T; Thr399Ile) were investigated by PCR and Sanger sequencing.

**RESULTS**

Results: Statistical analysis reveals positive correlation of age and BMI with T scores in premenopausal group whereas in post-menopausal group found a significant negative correlation between age and T-score at hip (r = - 0.352**), spine (r = - .306**), and femoral neck (r = - 0.344**) and a significant negative correlation of BMI with TNF-α (- 0.316**).No association and significant differences were observed for TLR4 genotype and allele frequencies among studied groups However, both SNPs exhibited significant association with each other.

**CONCLUSIONS**

Conclusions: This study concludes that BMI, BMD and TNF-α are the potential predictors of osteoporosis in post-menopausal women. However, CTX and TLR4 gene polymorphism did not appear as potential predictors of bone loss in this study and apparently cannot help in predicting bone loss in post-menopausal women.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0676

## CAN SEX HORMON BINDING GLOBULIN PREDICT GESTATIONAL DIABETES MELLITUS IN EARLY PREGNANCY?

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### BACKGROUND-AIM

The most common complication during pregnancy is gestational diabetes mellitus (GDM). The aim of this study was to evaluate the role of sex hormone binding globulin (SHBG) in predicting GDM in early pregnancy.

### METHODS

A prospective study was conducted between May 2022 and December 2022. Blood samples were taken from pregnant women under prenatal follow-up at 11-14th weeks of gestation. Among the participants (n = 74), 20 cases subsequently developed GDM. At 24–28 weeks of gestation, screening for GDM was performed with a non-fasting 50 g glucose challenge test. Women with abnormal plasma glucose values (≥ 140 mg/dL) after the 50 g screening test underwent further testing with a 3-hour 100 g oral glucose tolerance test (OGTT). Pregnant women who had at least two abnormal values (fasting, ≥95 mg/dL; 1 hour, >180 mg/dL; 2 hours, >155 mg/dL; or 3 hours, >140 mg/dL) were diagnosed with GDM. Plasma glucose and serum SHBG concentrations were measured using Cobas c702 analyser and Cobas c802 analyser, respectively (Roche-Diagnostics®).

### RESULTS

SHBG level was lower in women with GDM (n = 20) than in women without GDM (n = 54) (271.59 ± 83.08 nmol/L vs 215.64 ± 70.18 nmol/L; p = 0.011). SHBG cut-off value was calculated, and ≤197 was the optimal threshold for the screening of GDM (Sensitivity:83%; Specificity:45%). In logistic regression analysis that was adjusted for body weight and age, SHBG levels remained independently associated with gestational diabetes mellitus (p=0.027).

### CONCLUSIONS

Decreased SHBG concentrations in early pregnancy may predict GDM development.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0677

**IS HASHIMOTO'S THYROIDITIS ASSOCIATED WITH INSULIN RESISTANCE MARKERS?**

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**BACKGROUND-AIM**

Hashimoto's thyroiditis (HT) is characterized by the progressive increase of anti-thyroid peroxidase and anti-thyroglobulin antibodies, leading to thyroid cell destruction, resulting hypothyroidism, insulin resistance (IR). Cocaine and amphetamine-regulated transcript (CART), orexin A and cholecystokinin (CCK) play important roles in the regulation of food intake and a number of endocrine and autonomic functions. In our study, we aimed to determine the levels of CART, orexin A and CCK in HT patients and to investigate their relationship with the metabolic parameters of HT.

**METHODS**

Our study was conducted with 44 HT patients and 40 healthy controls. The serum levels of CART, Orexin A, and CCK were measured by using an ELISA technique.

**RESULTS**

The CART levels ($p<0.05$) and BMI ($p<0.05$) were significantly higher in HT patients compared to the controls. The orexin A levels were lower in HT patients than in the controls ($p<0.05$). The CCK levels and HOMA-IR were similar between the two groups. A negative correlation was observed between the orexin A levels, and the CART and CKK levels (respectively, $r = -,365$, $p < 0.05$; $r = -,297$, $p < 0.05$). A positive correlation was observed between the CART levels, and BMI, insulin levels and HOMA-IR ( respectively, $r = ,448$, $p < 0.01$; $r = ,489$, $p < 0.01$; $r = ,492$, $p < 0.01$).

**CONCLUSIONS**

The increased CART and decreased orexin A levels may be involved in the pathogenesis of HT by controlling the thyroid-dependent immune system, IR, appetite and body weight. We believe that our findings will lead to new developments in the diagnosis and treatment of this disease.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0678

## TOTAL P-CRESYLSULPHATE , INDOXYL SULPHATE AND TMAO ARE ASSOCIATED WITH DIABETIC FOOT ULCERS IN DIABETES MELLITUS

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### BACKGROUND-AIM

Studies have shown that p-cresol sulfate (p-CS) and indoxyl sulfate (IS) are associated with cardiovascular diseases and mortality in diabetes mellitus. High Trimethylamine N-oxide (TMAO) levels increase the risk of retinopathy, kidney failure, and cardiovascular disease in type 2 diabetes mellitus (T2DM). This study investigates the relationship between p-CS, IS, and TMAO levels as blood microbiota indicators in diabetic patients with complications.

### METHODS

p-CS, IS, and TMAO were measured using LC-MS/MS. Chitothyroidase activity was manually determined, and vascular endothelial growth factor (VEGF) and Anti-Chitinase-3-like protein 1 (YKL-40) levels were measured using ELISA kits. The study included 30 controls and 86 T2DM patients, 60 of whom had various grades of diabetic foot ulcers (DFU).

### RESULTS

CRP and IS levels ($p<0.05$) were significantly higher in diabetic patients than controls. CRP, p-CS, and VEGF levels ($p<0.05$) were significantly higher in DFU patients than in controls. CRP levels increased with severity according to the Wagner classification. Fasting glucose, Advanced Glycation End Products (AGE), and TMAO levels were highest in Wagner-4 patients, while p-CS, IS, and VEGF levels peaked in Wagner-3 patients.

### CONCLUSIONS

TMAO, p-CS, and IS are associated with complications such as neuropathy and retinopathy in diabetic patients. These indicators were 2-3 times higher in patients with complications compared to controls, highlighting the importance of microbiota in complication development. The highest levels in Wagner-3 wounds suggest a role in peripheral circulatory disorders. Reducing IS, p-CS, and TMAO levels may be beneficial for systemic treatment of diabetic foot ulcers.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0679

**WHEN MORE IS LESS ! AN INTERESTING CASE OF ANTIGEN EXCESS.**

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**BACKGROUND-AIM**

Antigen excess and antibody excess are known causes of interference in immunoassays. Our lab came across this case of Multiple myeloma, Light chain disease. Unfortunately, the characteristic of the Monoclonal Band (M-band) had gotten reversed due to a false low concentration of one of the light chains.

**METHODS**

Discrepancy was observed in the quantification of Immunoglobins, done on Binding Site's Optilite and Immunosubtraction, done on Sebia Minicap. This led to further evaluation with quantification of total Immunoglobin concentrations done on Beckman Image 800 and Immunofixation electrophoresis (sIFE) done on Sebia Hydrasys in another laboratory.

**RESULTS**

Our laboratory had detected a light chain lambda disease based on an abnormal FLC ratio of 0.04 (Normal range: 0.26-1.65), with free kappa levels of 0.54 mg/L and free lambda level of 13.51 mg/dl
From the sIFE done in the second laboratory it was observed that there was a monoclonal band in Kappa. Thereby suggesting a false low reading of free kappa in the first laboratory. The immunoglobulin levels were subsequently quantified with dilution and free kappa was found to be 16,000 mg/L.
Serum total Kappa from the second lab was 1857 mg/dL and serum total lambda was 212 mg/dL, with an abnormal total kappa/lambda ratio of 8.8

**CONCLUSIONS**

It is essential to be alert for potential interferences leading to lab errors. Antigen excess and antibody excess are common causes of interferences in immunoassays. Hence it is advisable to investigate a sample through different methods to reduce such errors in estimation. Our case highlights the limitations as well as the need to incorporate diverse techniques like capillary and gel based electrophoresis, measuring free as well as total light chains so as to not misdiagnose/ mislabel cases due to interferences.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0680

## SALIVARY LYMPHOCYTES: POTENTIAL NON-INVASIVE DIAGNOSTIC BIOMARKER FOR PEDIATRIC INFLAMMATORY BOWEL DISEASE

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### BACKGROUND-AIM

Pediatric Inflammatory Bowel Disease (PIBD) is a chronic condition marked by a lifelong cycle of flare-ups and remissions, requiring frequent monitoring through invasive procedures. There is a growing need for non-invasive biomarkers to monitor disease activity and reduce patient burden. The aim was to investigate the presence of salivary lymphocytes as a potential non-invasive biomarker for diagnosing and monitoring PIBD.

### METHODS

Thirty-seven PIBD patients [15 females (F), median age 15.2 years] and 23 pediatric controls [C, 12 F, median age 12.3 years] were enrolled and asked to collect saliva sample using E-saliva device. Flow cytometry analysis was performed to characterize the presence (positive/negative) of lymphocyte population (CD3, CD4, CD8, CD19, CD45, CD16/56) and their activation state through HLA-DR expression by DXFlex cytometer (Beckman Coulter, Brea, CA, USA) and ESR (Test One, Alifax, Padova, Italy).

### RESULTS

Thirteen PIBD patients (35%) were positive for salivary lymphocytes (pL+), while 24 (65%) were negative (pL–). None of C were positive for salivary lymphocytes. A significantly higher proportion of Crohn's Disease (CD) patients was found in the pL+ group compared to the pL– (84% vs 50%, p=0.004). A higher proportion of CD4+ lymphocytes relative to CD8+ lymphocytes in saliva, with a median CD4/CD8 ratio of 2.25, was found. CD4+ and CD8+ lymphocytes exhibited a marked activation state, with a median HLA-DR expression of 57.4% in CD3+ HLA-DR cells. Among pL+ group, 30% of PIBD had active disease, while 70% were in remission; of those in remission, 50% had experienced active disease within the three months preceding saliva collection. Salivary lymphocyte counts were significantly correlated with erythrocyte sedimentation rate (ESR) (r=0.786, p=0.036) and clinical disease activity scores (r=0.575, p=0.040).

### CONCLUSIONS

Salivary lymphocytes were detected in CD patients, with a predominance of activated CD4+ cells. Lymphocyte counts correlated with disease activity and ESR, and their presence in patients during clinical remission suggests a potential role in monitoring immune responses throughout all disease phases. These results highlight a promising role of salivary lymphocytes as non-invasive biomarkers, although further studies are needed.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0681

## PANCREATIC CANCER WITH NEGATIVE CA 19.9 IN PATIENTS WITH LEWIS ANTIGEN (A-B-): A CASE REPORT

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### BACKGROUND-AIM

Lewis (Le) antigens are part of the erythrocyte membrane surface. The Le (a-b-) phenotype is present in individuals who are homozygous for the Le gene (5-10% of the caucasian population), and they are unable to express Le A or Le B antigens. The serum expression of the tumor marker Ca 19.9, used in the detection and monitoring of pancreatic cancer, requires the presence of Le antigens; therefore, patients with the Le (a-b-) phenotype will not express this marker.

### METHODS

Case presentation: A 91-year-old patient was admitted to the cardiology department for congestive heart failure. The patient presented with dyspnea accompanied by severe pleural effusion, and a sample was sent to the laboratory for analysis.

### RESULTS

In the laboratory, we performed cell counting and measured total proteins, glucose, ADA, and tumor markers. We calculated the tumor marker ratio in fluid/serum, which, when greater than 1.2 and combined with ADA <45 U/L and polymorphonuclear cells <90%, confirmed a high likelihood of malignancy in the effusion. The Ca 19.9 serum level was notably below the detection limit of the instrument, so we performed an antibody test against Le A and B antigens to detect Le antigens, which returned negative. We contacted the cardiology team to inform them of the suspected malignancy and the patient's double-negative Le phenotype, which prevents the expression of the Ca 19.9 marker. After a CT scan and biopsy, pancreatic neoplasia was confirmed, a diagnosis that had not been suspected due to the negative Ca 19.9 result in serum.

### CONCLUSIONS

This case highlights the importance of considering the Le (a-b-) phenotype in patients with suspected pancreatic neoplasia. Although the Ca 19.9 marker was negative in serum, the identification of the negative Le phenotype raised suspicion of underlying malignancy and prompted further studies, ultimately leading to the diagnosis of pancreatic neoplasia. It is crucial to account for genetic variability when interpreting tumor marker results and to adopt a comprehensive approach to cancer diagnosis.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0682

**DIAGNOSIS OF CEREBROSPINAL FLUID FISTULA: SIGNIFICANCE OF BETA-TRACE PROTEIN - A CASE REPORT.**

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**BACKGROUND-AIM**

Cerebrospinal fluid fistula (CSFF) is defined as the anomalous outflow of cerebrospinal fluid (CSF) out of the subarachnoid space through a pathologic communication with a lower pressure cavity. One of the main limitations for the accurate diagnosis of this condition is the possible contamination of secretions, which may be associated with mucus, tears or inflammatory exudates. Therefore, classical CSF markers, such as glucose or β2-transferrin determination, present notable limitations in identifying the presence of CRPF. In this context, the detection of beta-trace protein (PBT), also known as prostaglandin D2 synthase, has proven to be a more sensitive and early diagnostic tool for this pathology.

**METHODS**

We present the case of a 30-year-old male with a personal history of head trauma due to a traffic accident, who underwent intervention by transnasal transsphenoidal endoscopic approach for the treatment of a CRPF. Thirteen years later, the patient was admitted to the emergency department with low level of consciousness, intracranial hypertension and signs of severe encephalopathy.

**RESULTS**

CSF analysis shows a pleocytosis of 317 leukocytes/uL (reference values <15/uL), predominantly neutrophils, protein of 1,24 g/L (0,15-0,45 g/L), glucose of 32 mg/dL (50-80 mg/dL) and a positive culture for Streptococcus pneumoniae. During his hospitalization, the patient referred the outflow of fluid through the nostril, which was analyzed, revealing elevated levels of PBT. In view of the diagnosis of recurrent CRPF, a new surgical intervention was decided.
The recurrence of FLCR explains the origin of meningitis, since one of the risks associated with this pathology is the entry of microorganisms, particularly S. pneumoniae and N. meningitidis, into the central nervous system.

**CONCLUSIONS**

Laboratory detection of PBT in CSF is fundamental in the management of this pathology. The prevention of associated complications, such as meningitis, hydrocephalus or loss of neurological function, is crucial to reduce mortality and morbidity in these patients.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0683

## MEMED®BV AS A BIOMARKER OF INFECTION IN THE EMERGENCY DEPARTMENT. IS IT AFFECTED BY THE NUMBER OF DAYS OF PREVIOUS CLINICAL PRESENTATION?

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### BACKGROUND-AIM

The high workload of emergency services makes it essential to have rapid diagnostic biomarkers that can differentiate whether an infection is bacterial in origin or not, as sometimes the clinical presentation may be ambiguous.
In this field, a new biomarker is emerging: MeMed®BV, a test that combines the quantification of three proteins: PCR, IP-10, and TRAIL. Thus, a MeMed® score ranging from 0 to 100 is obtained, which helps determine the origin of the infection:
0-10: High probability of a non-bacterial infection;
10-35: Moderate probability of a non-bacterial infection;
35-65: Ambiguous;
65-90: Moderate probability of bacterial infection/coinfection;
90-100: High probability of bacterial infection/coinfection.
The aim of the study is to determine whether the number of days of prior clinical symptoms before the patient visits the Emergency Department affects the diagnostic performance of MeMed®BV.

### METHODS

We grouped the MeMed®BV values into two groups, to calculate the Cut-Off, as well as the sensitivity, specificity, specificity, positive predictive value (PPV) and negative predictive value (NPV).
Group 1: ≤48 hours of prior symptoms (N=116; Suspected non-bacterial infection etiology: 22,
Suspected bacterial infection etiology: 94)
Group 2: >48 hours of prior symptoms (N=131; Suspected non-bacterial infection etiology: 37,
Suspected bacterial infection etiology: 94).

### RESULTS

Group 1: CUT-OFF (30.5), Sensitivity (0.798), Specificity (0.864), PPV (0.987), NPV (0.441),
AUC (0.882 [0.839-0.925])
Group 2: CUT-OFF (62), Sensitivity (0.734), Specificity (0.677), PPV (0.932), NPV (0.390), AUC
(0.730 [0.670-0.784])

### CONCLUSIONS

It is observed that the cut-off for Group 2 is similar to the one described in the literature, which uses 65 as the threshold. However, in Group 1, the cut-off differs significantly from the one described. Therefore, it would be worth considering a different cut-off point when the patient presents to the Emergency Department with fewer than 48 hours of symptoms. This conclusion could be groundbreaking, as there is no prior literature to confirm it.
Furthermore, the diagnostic performance of MeMed®BV shows better results as the number of days of prior symptoms decreases.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0684

## AGE-DEPENDENT THROMBOCYTOPENIA INDUCED BY HISTONES IN AN EX-VIVO WHOLE BLOOD MODEL

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### BACKGROUND-AIM

Platelets are key regulators of thrombosis and inflammation. Thrombocytopenia is significantly correlated with the worst outcome in sepsis patients and platelet indices could be potentially useful biomarkers. Platelet count, already included in SOFA score, is influenced by gender, genetic predisposition and age. The aim of this study was to investigate the platelet response to histone treatment, well-known prothrombotic stimulus, in three different age groups: young subjects (<10 years, n=9), adult subjects (>18 years, n= 25) and elderly subjects (>75 years, n=28).

### METHODS

Whole blood was collected in EDTA-K2 tubes, samples were treated with a mixture of histones (200 μg/mL) and Complete Blood Count (CBC) was measured by DxH 690T Beckman Coulter at 0, 30, 60 and 180 min.

### RESULTS

Firstly, our results highlighted significant differences in the control values of platelet counts between adults (215±49 x10^3/μl) and elderly (196±63) compared to the young (312±71) group (p=0.001-0.01). To avoid bias due to different baseline platelet values, we normalized values according to percentage changes. Our findings revealed that histones promoted a rapid platelet depletion, due to aggregation, at 30, 60 and 180 min in adults (p<0.0001), elderly (p<0.0001) and young (p:0.01-0.05) subjects. In elderly subjects the platelet count is reduced by 27% at 30 min, 22% at 60 min and 20% at 180 min; in adults histones induced a platelet decrease by 34% at 30 min, 30% at 60 min and 29% at 180 min. This percentage of depletion at 180 min in adults is significantly higher than in elderly (p:0.01-0.05). The young population showed a platelet count reduction by 16% at 30 min, 12% at 60 and 180 min, whose values were significantly lower at all times compared to adults (p:0.01-0.05).

### CONCLUSIONS

In conclusion our study emphasized that platelet baseline values and histone-induced platelet aggregation are age-related. The adult population showed a more pronounced response in terms of platelet count reduction than the other populations. The youngest group is the least responsive one, followed by the elderly group which is probably protected using pharmacological therapies.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0685

## EVALUATION OF THE CORRELATION BETWEEN EPA LEVELS AND KI-67 EXPRESSION IN HUMAN BREAST CANCER

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**BACKGROUND-AIM**

Breast cancer (BC) is one of the most common types of cancer in women worldwide, with approximately 1.7 million new cases diagnosed each year. Disruption in metabolic processes, including carbohydrate, protein, nucleic acid, and lipid metabolism, is recognized as a hallmark of cancer. Due to the importance of ω-3 polyunsaturated fatty acids, including eicosapentaenoic acid (EPA), in the development and progression of breast cancer, this study aimed to investigate the correlation between EPA levels and Ki-67 (a cellular proliferation marker) in tumor tissue compared to normal tissue.

**METHODS**

Fifty-five pairs of fresh-frozen breast cancer and adjacent normal tissue samples were analyzed to determine EPA composition using gas chromatography. Ki-67 expression was examined using immunohistochemistry (IHC).

**RESULTS**

There was no significant difference in EPA levels between breast cancer tissues and adjacent normal tissues. However, EPA levels were negatively correlated with Ki-67 expression ($P < 0.05$).

**CONCLUSIONS**

The observed association between EPA and Ki-67 supports the reported tumor-suppressive role of EPA in cancer cells. This finding suggests the potential use of EPA in therapeutic strategies; however, further studies are required to validate these results.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0686

## PRELIMINARY COMPARATIVE ANALYSIS OF URINE FLUORESCENCE PROFILE IN PATIENTS WITH PROSTATE CANCER

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### BACKGROUND-AIM

Prostate cancer (PC) is the 3rd most commonly diagnosed cancer in the EU. Standard screening and diagnostic arsenal include digital rectal examination, serum PSA (prostate-specific antigen), transrectal USG, MRI, and biopsy. PET/CT complements these diagnostic possibilities, focusing on recurrent or metastatic disease. Up to 91% of individuals with an elevated PSA may not have PC, raising concerns about overdiagnosis. Additionally, MRI can miss 25% of significant PCs. Recent urinary metabolomic studies have identified metabolite changes that may aid early diagnosis and patient stratification. Urine contains many molecules with native fluorescence. Of these, tryptophan (Trp) and its metabolites are particularly important. Sensitive fluorescence techniques may offer a cost-effective alternative in PC patient management. The aim of presented study is to find and relate fluorescent features of urine profile with a focus on the Trp pathway to clinical measures of PC patients.

### METHODS

Fluorescent urine profiles were analyzed regarding PET/CT findings, Gleason score (GS), and PSA. The study plan involves 474 patients who underwent PET/CT scanning (10/2023-7/2024). Of these, 97 samples were already measured, and 30 were also preliminary analyzed.

### RESULTS

No correlation between GS and PSA was found. The presence of metastases (Ms) in skeleton/parenchymal organs/mediastinum was comparable in patients with GS<7 and GS=7 (38/13/25% vs 20/40/10%) and significantly higher in patients with GS>7 (80/30/40%). Ms were positive in 50% of patients with PSA<20ng/ml and in 93% with PSA≥20ng/mL. Fluorescence analysis shows no correlation with PSA or GS. Patients with Ms in mediastinum have significantly higher (p=0,032) indol-related fluorescence (ex/em 280/370-380 nm), and patients with Ms in parenchymal organs have significantly higher (p=0,033) ratio indol-related/kynurenine-related fluorescence (ex/em 280/370-380 to ex/em 360-370/440-460 nm).

### CONCLUSIONS

Trp metabolism is affected in PC patients with Ms. The preliminary study uncovered fluorescent urine profiles as a valuable data source for perspective machine learning tools in PC patient management.
Work is supported by the project MŠVVaŠ SR: Using artificial intelligence in personalized prostate cancer medicine.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0687

## EVALUATION OF SERUM AMYLASE, LIPASE, TRIGLYCERIDE, TOTAL PRTOTEIN AND ALBUMIN LEVELS IN HIV PATIENTS ON ANTI-RETROVIRAL THERAPY (ART) IN NNAMDI AZIKIWE UNIVERSITY TEACHING HOSPITAL (NAUTH) NNEWI, SOUTH EASTERN NIGERIA

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### BACKGROUND-AIM

On a global scale, HIV has led to an estimated 38 million deaths, with over 75 million people becoming infected since the start of the pandemic.HIV continues to be of public health discuss worldwide especially in Africa, Nigeria inclusive. The aim of this study was to determine the serum triglycerides, total protein, amylase, and lipase level in HIV positive participants on short term and long-term ART in NAUTH, Nnewi, Nigeria.

### METHODS

A total of one hundred (100) HIV positive and control participants, with mean age of 34.35±7.24 years that attended the Voluntary Counseling and Testing Unit (VCT) and Antiretroviral Therapy Unit (ART) of NAUTH, Nnewi were randomly recruited for the study. In line with World Health Organization (WHO) criteria for HIV staging, the participants were grouped into: HIV positive symptomatic subjects on long term ART for a period of more than five (> 5) years (n=29); HIV positive symptomatic subjects on short term ART for a period of 1-4 years (n=30) and the HIV negative group (n=30). Six milliliters of blood sample were collected from each of the participants, centrifuged, the supernatants used for analyses. Whole blood used for CD4 counts analysis.HIV antibody presence was determined using the Enzyme-Linked Immunosorbent Assay (ELISA) technique, CD4+ cell counts was determined using Flow cytometric technique. Serum triglycerides, albumin, amylase, lipase and total protein were analyzed by laboratory routine methods with the serum stored at -20°C until analyzed.

### RESULTS

Results showed that the serum amylase and lipase activity levels; serum triglyceride (TG), albumin, total protein and CD4 counts were observed to be significantly higher in symptomatic HIV subjects on long term and short term ART than in control group while serum amylase, lipase activity levels, total protein and CD4 counts were all on long term and short term ART

### CONCLUSIONS

. In conclusion, the study revealed that the serum amylase and lipase activity levels, TG, albumin, total protein and CD4 counts were observed to be significantly higher in symptomatic HIV subjects on long term and short term ART than in HIV negative group.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0688

**PATIENT SUSPECTED OF STRESS CARDIOMYOPATHY. A CASE REPORT**

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**BACKGROUND-AIM**

Takotsubo or stress cardiomyopathy is characterized by an acute reduction in left ventricular ejection fraction in the absence of obstructive coronary artery disease. The clinical picture includes chest pain, ST-segment elevation and/or T-wave inversions on ECG, or increased troponins.
In this case, we describe a case of Takotsubo syndrome and the importance of the laboratory as part of the diagnostic approach.

**METHODS**

A 64-year-old woman attended the emergency department with hypertensive crisis. The patient begins with non-radiating central chest pain in the morning upon waking up, without previous exertion, without vegetative symptoms. She says that she has suffered a recent episode of work-related stress. Her blood pressure has been around 200/100 mm Hg for a few days.

**RESULTS**

In the Emergency Service, an electrocardiogram (ECG) was performed, showing slight ST elevation, reduced left ventricular ejection fraction and the analytical results showed normal blood count and coagulation, biochemistry with creatinine and ions within normal range, creatinine kinase at 45 U/L, troponins (TnT) at 3.5 ng/L on admission. Subsequently, serial measurements of TnT were performed, the results of which were: 161 ng/L at 3 hours, 180.8 ng/L at 4 hours and 161.9 ng/L at 6 hours.
The patient was admitted. During her stay she presented normal laboratory results, except for pro-BNP (value 2673 ng/mL, normal range >900 pg/mL between 55 and 75 years) and urine with the presence of leukocytes in a scarce form. The evolution was favorable and the EKG at discharge showed negative T waves. The final diagnosis was Takosubo syndrome.

**CONCLUSIONS**

This cardiomyopathy continues to challenge physicians with its diverse clinical manifestations, which often mimic acute coronary syndrome. Its diagnostic criteria include moderate troponin elevation with marked elevation of natriuretic peptides. Several studies have reported that cardiac biomarkers generally peak at the time of initial acute presentation. However, they do not appear to follow the slow rise and fall kinetics observed with conventional acute coronary syndromes or myocardial infarction.
The prognosis of Takotsubo cardiomyopathy is generally favorable, with most patients recovering left ventricular function within weeks.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0689

**A CASE REPORT. LABORATORY DIAGNOSIS OF ADENOCARCINOMA OF THE LUNG.**

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**BACKGROUND-AIM**

Adenonocarcinoma of the lung is a type of non-small-cell lung cancer that originates in the mucus-secreting glands. It is the most common type of lung cancer, accounting for about 30 % of cases, and is the most common malignancy of the lung among non-smokers and adults under 45 years of age.

**METHODS**

A 35-year-old man attended a primary care clinic for a week of dyspnoea, which began with cough associated with haemoptotic sputum. He also reported significant weight loss in recent days. His personal history includes toxic habits, smoking 5 cigarettes a day for 16 years.

**RESULTS**

Laboratory tests showed the following parameters: calcium 13 mg/dL, lactate dehydrogenase (LDH) 265 U/L, c-reactive protein (CRP) 131.7 mg/L. Blood count: 23,000 leukocytes, haemoglobin: 10.7 g/dL and 800,000 platelets. The laboratory requested the following tumour markers: carcinoembryonic antigen (CEA): 32.31 ng/mL, SCC antigen: 4.40 ng/mL, Ca 125: 74.7 U/mL, Ca 15.3: 230.1 U/mL, Cyfra 21.1: 8.5 ng/mL, Neuronal Specific Enolase (NSE): 18.9 ng/mL. In view of these results, a personalised report is drawn up commenting on the significant increase in these markers, compatible with epithelial neoplasia. The combination of these, together with the clinical history, suggested a pulmonary origin, with a high probability of NCICP (probable adenocarcinoma, pending PET/CT study). The latter showed findings suggestive of a left suprahilar pulmonary neoformative process, with probable involvement of the lingula of the atelectasis area, and probable right frontal metastasis, to be correlated with MRI. Cranial MRI showed the presence of a large right frontal mass with lobulated edges, solid content and a central necrotic appearance, highly suggestive of probable metastasis of the patient's primary process. The pathological anatomy study confirmed that it was a non-small cell carcinoma, compatible with adenocarcinoma.

**CONCLUSIONS**

This case underlines the importance of the clinical laboratory in the identification and characterisation of malignant neoplasms, given that the results of tumour markers are available earlier than those of imaging tests. The determination of these tumour markers has been key in guiding the diagnosis towards an epithelial neoplasm, with a high probability of pulmonary origin.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0690

**IGD MULTIPLE MYELOMA. A CASE REPORT.**

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**BACKGROUND-AIM**

Multiple Myeloma (MM) is a type of malignant monoclonal gammopathy, characterized by the clonal proliferation of plasma cells. It is considered the second most common type of hematologic cancer.
IgD MM is a rare and complex entity within monoclonal gammopathies. It is more common in men and tends to present at younger ages (53-57 years). It is characterized by an aggressive course and difficult diagnosis representing less than 2% of all MM cases.

**METHODS**

We describe the clinical case of a 64-year-old male with a one-month history of lumbar pain, lower limb muscle weakness and weight loss. To diagnose his condition the following test were performed:
Blood test to asses hematologic and biochemical parameters, protein electrophoresis to identificate any monoclonal proteins in the serum, inmunofixation to confirmed the presence of a band and urine analyses.

**RESULTS**

Blood tests showed moderate anemia (hemoglobin: 9.5 g/dL), altered renal function (creatinine: 6.5 mg/dL), and hypercalcemia (calcium: 11 mg/dL) raising suspicion of MM.
Protein electrophoresis was performed, revealing a slight gamma peak. Following immunofixation, a monoclonal Lambda band was confirmed.
Considering the presence of a monoclonal band in the serum that did not correspond to IgG, IgA, or IgM antisera, and with normal serum values for these, immunofixation for IgD and IgE confirming the presence of an IgD peak (monoclonal component: 1.15 g/dL). Free light chain values for lambda and Kappa were also measured, with a free lambda value of 2350.3 mg/L.
Urine analysis confirmed the presence of free lambda light chains.
To complete the patient's study, a bone marrow aspirate showed 10% plasma cells and the presence of bone lesions.
The final diagnosis was IgD Lambda secretory MM at stage III, according to the International Staging System(ISS).

**CONCLUSIONS**

The patient presented typical CRAB symptoms (Calcium increase, Renal impairment, Anemia, and Bone lesions), along with elevated β2-microglobulin levels.
Also, the presence of bone lesions in three different areas further worsened the patient’s prognosis.
The diagnosis of IgD MM is a challenge for the laboratory because in approximately 40% of cases, a monoclonal peak is not observed in serum electrophoresis and it may be confused with a light chain secretory myeloma.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0691

**DIFFERENTIAL REACTIVITY OF PSA IN EXTRACELULAR VESICLES TO COMERCIAL ASSAYS: A SOURCE OF DISCREPANCIES IN SERUM TOTAL PSA QUANTIFICATION BETWEEN METHODS.**

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**BACKGROUND-AIM**

Prostate-specific antigen (PSA) associated with extracellular vesicles (ev-PSA) holds diagnostic potential for prostate cancer. Althought not designed with that purpose, comercial assays for total PSA can react with ev-PSA. We aimed how ev-PSA reacts to different assay kits, and wether ev-PSA can cause a bias in total PSA quantification.

**METHODS**

EVs were isolated from serum samples of 83 prostate cancer patients using size exclusion chromatography with Exo-spin™ midi kit (Cell Guidance System, Cambridge, UK) or ultracentrifugation (100,000xg, 90 minutes) in a Hitachi CS150NX micro ultracentrifuge (Hitachi Koki Co., Tokyo, Japan).
PSA concentrations were measured in serum, EVs, and serum devoid of EVs (supernatant) using Elecsys, Atellica, Immulite, Liaison, and Kryptor immunoassays. Linearity was assessed with LNCaP cell line exosomes, and inter-assay differences were analyzed using Bland-Altman test.
Nanoparticle tracking analysis (NTA) quantified EV content in WHO IS 17/100 and a serum sample used as control in a NanoSight LM20.

**RESULTS**

Assays showed varying sensitivities to ev-PSA: Elecsys ≈ Atellica > Immulite > Liaison > Kryptor. Only Elecsys and Atellica detected ev-PSA in all samples. Regression analysis revealed strong correlations between ev-PSA measurements ($r > 0.900$) except for Kryptor ($r = 0.718$). Proportional bias was observed, with Elecsys reporting higher ev-PSA concentrations than other methods at low concentrations (<3 µg/L) and lower than Atellica at ev-PSA < 1 µg/L. The ev-PSA proportion of total PSA varied by method, correlating with discrepancies in total PSA.
NTA showed significantly fewer EVs in WHO IS 17/100 than in serum control (4.7 × 10^7 vs. 6.6 × 10^8 particles/mL), with ev-PSA comprising 0.2% and 0.7% of total PSA, respectively.

**CONCLUSIONS**

Commercial kits designed for serum PSA quantification can also detect ev-PSA in serum, but the reactivity between methods is significally differrent. This variability in ev-PSA detection can contribute to discrepancies in total serum PSA results across different commercial assays.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0692

## ESTIMATION OF THE REFERENCE CHANGE VALUE FOR TUMOR MARKERS IN OUR LABORATORY

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### BACKGROUND-AIM

Detecting a significant change in the concentration of a specific tumor marker (TM) between two consecutive measurements can provide valuable information about the progression of antitumor treatment and is crucial for the early detection of a possible recurrence. The reference change value (RCV) expresses this significant change, which occurs when the variation between two results exceeds both the analytical variability and the biological variability, and it is generally calculated as a percentage change. Analytical variability is different for each laboratory, so it is advisable for each laboratory to determine its own RCVs.

### METHODS

The RCV was calculated using the formula $RCV = 2^{1/2} \times Z \times (CV_A^2 + CV_I^2)1/2$, where $Z = 1.96$ for $p<0.05$; $CV_A$ represents the analytical variability expressed as a coefficient of variation, and $CV_I$ represents the intra-individual biological variability expressed as a coefficient of variation.
The $CV_A$ values were calculated from the internal controls of our laboratory (Roche Diagnostics, Switzerland). The $CV_I$ values were obtained from the database of the European Federation of Clinical Chemistry and Laboratory Medicine (EFLM). Statistical analysis was performed using SPSS v.26 software (SPSS, Inc., USA).

### RESULTS

Our RCVs are as follows: CA 15.3 = 20.1%; CA 19.9 = 63.5%; CA 72.4 = 140.9%; CA 125 = 37.9%; CEA = 50.7%; AFP = 75.5%; CYFRA 21.1 = 67.8%; ß-hCG = 48.6%; NSE = 37.7%; proGRP = 17.8%; HE4 = 30.9%; PSA = 19.9%; free PSA = 20.5%.

### CONCLUSIONS

Some of our RCVs differ slightly from those described in the literature. The variety of measurement techniques and differences in quality management influence analytical variability, while biological variability can vary depending on the sources consulted and the study subpopulations. These $RCV_S$ estimates will serve as a starting point for assessing their real-world application in patient monitoring and for providing comments in reports to ensure the correct interpretation of serial results.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0693

**EPIDEMIOLOGICAL, ANATOMOPATHOLOGICAL AND BIOLOGICAL PROFILE OF METASTATIC BREAST CANCER**

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**BACKGROUND-AIM**

Breast cancer is the most frequent female cancer, while the discovery at a metastatic stage requires an emergency in the management. Our aim is to evaluate the epidemiological, anatomopathological and interest of CA15-3 and ACE MT profile of metastatic breast cancer.

**METHODS**

This is a retrospective follow-up study of 100 female patients. Data were collected from the patients' medical records from January 2000 to April 2021.

**RESULTS**

The median age of patients is 49 years, stage IV represents 35.80% of the population and ICC represents 83 .95% of patients, 66.66% are ICC grade II SBR, with 68.49% of tumors are Rh positive, 60.5% of tumors are HER2 negative. The most frequent metastases in our population are bone metastasis with 44% and lung metastasis with 25%. We found that 48% of the patients developed metastasis after 1 to 5 years from the primary cancer. Wilcoxon comparison tests found a significant difference between baseline CA15-3 and CEA values and values at the time of bone, liver and lung metastasis and values after treatment. In contrast, there was no significant difference between the values during brain metastasis. A positive correlation was found between baseline CA15-3 and CEA values and values at the time of bone and liver metastasis. A positive correlation was found between the values at the time of metastasis and after treatment for CA 15-3 and CEA respectively.

**CONCLUSIONS**

TMs have great value in metastatic breast cancer, with the presence of a positive correlation between TMs and bone, liver and lung metastases. CA 15-3 is of great value in the follow-up and/or monitoring of patients undergoing treatment.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0694

## RETROSPECTIVE STUDY OF OVARIAN CANCER IN AN ALGERIAN POPULATION

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### BACKGROUND-AIM

The incidence of ovarian cancer:9th in total cancers in the world and 8th most common cancer in women Objective: to evaluate epidemiological, anatomopathological and biological profile of ovarian cancer in an algerian population

### METHODS

This is a retrospective study from 2016-2022 carried out in collaboration with the Medical Oncology Department of the EHS Pierre and Marie Curie on 181 patients who developed ovarian cancer. The data is collected, entered and analysed on Epi info.

### RESULTS

The mean age of the Algerian patients was 56 years. Serous epithelial tumors were the most common histological type (54.14%) with advanced IIIC and IV stage 41.54% and 10.77% respectively. 85.83% were married, 83.33% of patients were multiparous, 75.76% had breastfed their children, and 55.56% did not take contraceptives
The average age of menarche was 13 years, the menstrual cycle was irregular in 3 patients. In our series, 73.08% of patients were menopausal, 75 patients had a family history of cancer.
Concerning the histological type, we found 76.22% of tumors were epithelial, of which 54.14% had serous adenocarcinoma, 7.73% mucinous adenocarcinoma.
According to FIGO, 41.54% of patients were stage IIIC. 88.89% of patients developed multiple metastases, including 75.69% to the peritoneum.
According to immunohistochemistry, 50% of tumors were positive for CK7, CA 125, RO, WT, P53, RP, Ki67. And more than 90% of tumors did not express CK20 CDX2.

### CONCLUSIONS

Ovarian tumors are a public health problem in Algeria. High-grade serous adenocarcinoma is the most common histological subtype. Ovarian cancers are often diagnosed late. Knowledge of the histological type makes it possible to better conduct a therapeutic strategy and assess the prognosis

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0695

**RELIABILITY OF CAPILLARY BLOOD SUGAR MEASUREMENT COMPARED TO VENOUS BLOOD SUGAR**

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**BACKGROUND-AIM**

Diabetes is a major concern due to its serious and debilitating complications stemming from the difficulties in achieving a satisfactory glycemic balance. This underscores the necessity for rigorous glycemic self-monitoring.
Several self-monitoring devices are marketed, which frequently raises questions about the reliability of their measurements.
The aim of our study is to attempt to classify four glucometers available on the Algerian market, based on an analytical accuracy study and an analysis of their clinical relevance.

**METHODS**

This is an analytical performance study compared to a reference system, with a clinical relevance analysis of the glucometers BIONIME, CHECK-3, DIAGNO CHECK sens, and VITAL CHECK involving 100 participants.

**RESULTS**

Our results show that the average venous glucose levels are lower than those of capillary glucose obtained by the glucometers: CHECK-3 (0.9789 g/l), DIAGNO-CHECK sens (1.0098 g/l), and VITAL CHECK (1.15 g/l), while it was higher than the average capillary glucose levels obtained with the BIONIME (0.9003 g/l). The analysis of variance of the average capillary measurements compared to the reference blood glucose showed a statistically significant difference for the BIONIME and VITAL CHECK, while this difference was not statistically significant for CHECK-3 and DIAGNO-CHECK sens.
A difference in performance among the four glucometers was observed after comparing the measurement results to the ISO 15197:2013 standard, with compliant results of 75% for the BIONIME, 73.33% for DIAGNO-CHECK sens, 66.66% for CHECK-3, and 33.33% for VITAL CHECK for venous glucose levels below 1 g/l, while for venous glucose levels equal to or above 1 g/l, the compliant results were 72.50% for DIAGNO-CHECK sens, 62.50% for BIONIME, 55% for VITAL CHECK, and 52.50% for CHECK-3.

**CONCLUSIONS**

According to our study, the ranking of the four tested glucometers based on their performance places DIAGNO-CHECK sens in first position, CHECK-3 in second, followed by BIONIME, leaving VITAL CHECK in last place.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0696

## PROSTATE-SPECIFIC ANTIGEN (PSA). MODELLING OF INTRA- AND INTERINDIVIDUAL VARIATION IN HEALTHY POPULATIONS

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### BACKGROUND-AIM

There are few large studies on changes in PSA. Having access to a large data base, we wanted to assess:
What does the distribution of PSA for men at a given age look like?
What is the rate of increase of PSA at a given age?
How large is the variation within (intra-individual) and between (inter-individual) individuals?

### METHODS

PSA results were collected from all Norwegian laboratories and collected in a large database comprising over 8 million PSA test results. Prostate cancer records from The Norwegian Cancer Registry to exclude individuals with prostate cancer. Changes in PSA over time were then modelled for men using either Frequentist Fixed Effects modelling ( R lm package), Frequentist Mixed Effects modelling (R lme package) or Bayesian modelling (R brms package).

### RESULTS

PSA behaves log-normally, e.g. increases with a certain percentage per year. Here, the increase is approx. 39% per 10 year, corresponding to a PSA doubling time of 21.3 years.
When modelling with a more complex (cubic) model, PSA growth flattens after 80 years.
PSA is clearly heteroscedastic, upon increasing age, the standard deviation increases.
The inter-individual standard deviation for log PSA is much larger (0.838) than the intra-individual standard deviation (0.460).

### CONCLUSIONS

The main findings were:
PSA increases with a constant percentage per year, and flattens somewhat past eigthy years
With increasing age, the standard deviation increases. Upper percentiles increase more than lower percentiles.
The inter-individual variation is much larger than the intra-individual variation.
We believe that these findings can be useful when designing clinical studies. In clinical studies, patients covering a large age span are often aggregated into a single group. Our findings make age standardizing of PSA possible, with a greater comparability between studies.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0697

**PAP TEST A PREFERABLE CERVICAL CANCER SCREENING TEST IN POST-MENOPAUSAL WOMEN: A PHYSIOLOGICAL AND ANATOMICAL CHANGES ANALYSIS IN POST-MENOPAUSAL WOMEN.**

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**BACKGROUND-AIM**

Cervical cancer is the fourth most common cancer in women, and the seventh overall (Globocan data, 2012). Cervical cancer is one of the world's deadliest but most easily preventable forms of cancer for women (Reena et al.2017). Cervical cancer is the highest burden of cancer in Zambia. In 2018, Zambia had the third-highest incidence rate of cervical cancer in the world with 66.4 new cases per 100,000 women (age-standardized for the world population). The Zambia's prevalence rate is 36.6% in post-menopausal women and 13.3% in pre-menopausal women (WHO Zambia, 2024).The study was aimed at compare physiological and anatomical changes that occur in post-menopausal women that justify the Pap test as the preferable cervical cancer screening test in postmenopausal women and other traditional screening tests.

**METHODS**

Cross-sectional study conducted in selected facilities (Laboratories) that offer Cervical Cancer screening and testing in Lusaka Province of Zambia. A literature review for the past 10 years compared the data in the laboratories. And SPSS version 14 and Excel were used to analyze collected data.

**RESULTS**

We discovered that some literature showed that 52.5% of the biopsy tests in post-menopausal were classified as false positive (FP), with respect to the biopsy and Visual Acetic Acid Test (VIA) (2017 to 2023).. Another study done in 2021 to compare the presence of Transformation Zone in pre- and post-menopausal women 76.6% compared cases had no transformation zone (TZ) in the biopsies. For data analysed, of 286 patients' mortality and prevalence rate for post-menopausal and pre-menopausal women was 15.4 %: 7.5% and 20.6%:14.5%, respectively, with p##0.05. Data was analysed using SPSS version 23.

**CONCLUSIONS**

Our data suggests enough evidence that a cytological pap test is the preferable screening test for post-menopausal women. This is because of the physiologic and anatomical changes that occur in menopausal and post-menopausal women due to a hypo-estrogenic state (Munro et al., 2021).This ultimately indicates a potential missing of HPV, perhaps due to an inability to visualize the involved area in older women due to an upward migration of the Transformation Zone (Jaime et al.2021).

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0698

## THE IMPORTANCE OF THE MEASUREMENT OF SERUM PROPSA - 11 YEARS OF MOVEMBER IN THE UNIVERSITY HOSPITAL PILSEN

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### BACKGROUND-AIM

Movember is an annual event which aims to raise awareness of Men's Health issues, such as prostate cancer. The University Hospital in Pilsen (Czech Republic) has been participating in this event already for 11 years via offering to the men of 50+ years of age the assassement of serum cancer biomarker prostate specific antigen (PSA) and its derivatives in order to estimate the risk of prostate cancer. The aim was to evaluate the benefits of this effort.

### METHODS

The interested men have to undergo a blood collection and their serum PSA is measured. If the PSA level is above 2 µg/L, free PSA and proPSA are subsequently measured and prostate health index (PHI) calculated. Serum PSA, and free PSA and proPSA are measured via chemiluminisce immunoassay (CLIA) UniCell DXi 600 Access Immunoassay Systém) Beckman Coulter, USA). If the proPSA level is above 25 ng/L, the person gets the recommendation to see a clinician and undergo an annoying examination, very often a biopsy.

### RESULTS

The number of participants has been continuously increasing from 50 (2014) to 1554 (2024). Around 30% of participants have the indication for freePSA and proPSA assessment. Between 3-8% of participants were recommended to the clinic, and approximately 80% of those were diagnosed of prostate cancer.

### CONCLUSIONS

The assessment of PSA derivatives, namely proPSA, and PHI calculation, has a great importance in prostate cancer screening as it allows the avoidance of an important unnecessary biopsies without compromising the prostate cancer detection. The growing interest of men to this screening is also beneficial.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0699

## EXPLORING THE IMPACT OF BIOMARKERS AND LEUKOCYTE POPULATIONS ON SEPTIC SHOCK DIAGNOSIS AND PROGNOSIS

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### BACKGROUND-AIM

Septic shock is one of the leading causes of mortality in intensive care units, characterized by a systemic inflammatory response and multiorgan dysfunction. Timely diagnosis and accurate severity assessment are crucial for improving clinical outcomes. Recent studies have highlighted the importance of specific biomarkers, such as interleukin-6 (IL-6), proadrenomedullin (proADM), and procalcitonin (PCT), in the monitoring and prognosis of patients with septic shock. Additionally, septic shock involves the activation of different leukocyte populations, each playing a specific role in the immune response.
The primary aim of this study is to evaluate the ability of hematochemical parameters to predict the clinical deterioration of patients, anticipating potential changes in organ function. A secondary aim is to enhance knowledge about biochemical markers in comparison to hematological parameters and to formulate hypotheses about the mechanisms underlying the clinical progression of patients.

### METHODS

This research analyzes daily serum concentrations of these analytes and hematological data from patients admitted to the intensive care unit of the neuromotor division of AOU-Careggi over a 4-week period, until discharge (recovery, death, or transfer to a lower-intensity care setting).

### RESULTS

Preliminary analyses have shown that proADM predicts the onset of septic shock 24 hours earlier than PCT, likely related to an earlier detection of organ damage deterioration. Further analyses to elucidate the role of IL-6 are ongoing.
Notably, interesting correlations have emerged between proADM and monocyte counts, proADM and the number of immature granulocytes, PCT and the neutrophil/monocyte ratio, as well as IL-6 and the monocyte fluorescence parameter (and its dispersion).

### CONCLUSIONS

Additional analyses are required to better characterize the interaction between these biomarkers and the different leukocyte populations activated during septic shock, as well as to evaluate the utility of hematochemical parameters in the management of critically ill patients.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0700

## ALKBH5-MEDIATED M6A REGULATES THE ALTERNATIVE SPLICING EVENTS OF SRSF10 IN OVARIAN CANCER

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### BACKGROUND-AIM

N6-methyladenosine (m6A) methylation was found to be involved in the tumorigenesis and development of ovarian cancer. Until now, it is not clear to identify the mechanism by m6A demethylase ALKBH5 affects RNA splicing in ovarian cancer.

### METHODS

We examined ALKBH5 protein expression and m6A levels by immunohistochemistry and analyzed their correlation with clinical features and prognosis in patients with ovarian cancer. Cell proliferation, cell cycle, plate cloning and cell migration assays were used to detect the phenotypic changes of ovarian cancer cells with ALKBH5 depletion using the siRNA strategy or the CRISPR/Cas9 knockout (KO) method. The ALKBH5 knockdown ovarian cancer cells were subjected to m6A RNA methylation sequencing and transcriptome sequencing to analyze the key target genes and pathways of m6A modification mediated by ALKBH5, and the interaction between ALKBH5 and m6A modification target genes was verified by fluorescence quantitative PCR and RNA immunoprecipitation.

### RESULTS

We identified the elevated expression of ALKBH5 and a general reduction in the level of m6A in ovarian cancer patients. ALKBH5 depletion inhibit ovarian cancer cell proliferation, cell cycle and migration. In addition, ALKBH5-regulated m6A RNA modification mainly affects RNA splicing function in ovarian cancer cells. SRSF10 is a key target gene involved in alternative splicing regulation through ALKBH5-m6A. ALKBH5 knockdown resulted in increased retention of SRSF10 exon 5 and decreased expression of transcript SRSF10-211.

### CONCLUSIONS

The alternative splicing regulation effect by ALKBH5-mediated m6A suggests a novel promising approach for m6A modification in OC and provides novel insights into the mechanisms involved in ovarian cancer therapy.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0701

**TOXICITY PRODUCED BY VITAMIN D IN OUR HEALTHCARE AREA**

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**BACKGROUND-AIM**

Vitamin D poisoning occurs from excessive intake of supplements, never from diet or sun exposure. The consequences of poisoning cause increased bone resorption and intestinal absorption of calcium, leading to hypercalcemia that can cause nausea, vomiting, weakness, bone pain, and kidney problems due to the formation of calcium stones. The objetives are to study how the determinations of this hormone have evolved, the cases of intoxication by vitamin D and to identify patterns.

**METHODS**

Vitamin D levels were determined using the 25-hydroxy-Vitamin D analyte (main circulating form) using the paramagnetic particle chemiluminescent immunoassay technique in a DxI unit (Beckman Coulter). High values are considered from 80 ng/mL and the upper safety limit, from which it can cause toxicity, above 100 ng/mL. The data for the years 2018-2021 were obtained retrospectively through the SIL laboratory Modulab (Werfen).

**RESULTS**

In 2018, 1099 determinations and 3 cases of poisoning (>100) were made; in 2019, 2110 and 5; in 2020, 2580 and 5, and in 2021, 4470 and 10, respectively. From 2018 to 2021, the determinations made of vitamin D have increased remarkably, reaching 4,470 in 2021 (4 times more than in 2018). The cases of poisoning have also increased, going from 3 in 2018 to 10 cases in 2021. 78.2% of the cases of poisoning occurred in women, and according to the age range, 91% of the cases were older than 43 years.

**CONCLUSIONS**

The treatment of intoxication consists of the suspension of vitamin D intake, dietary calcium restriction, restoration of the intravascular volume deficit and, if severe, administration of corticosteroids or bisphosphonates. This increase in the number of determinations could be due to the administration of vitamin supplements. Almost 80% of the poisonings occurred in women and in adult patients (one case in adolescents and none in minors).

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0702

## A BETTER BIOMARKER TO EVALUATE ENDOTHELIAL DYSFUNCTION IN ASYMPTOMATIC PATIENTS WITH DIABETES MELLITUS

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**BACKGROUND-AIM**

The prevalence of diabetes mellitus is increasing worldwide, and although this is primarily due to an increase in the incidence of type 2 diabetes mellitus.

**METHODS**

A screening selection among 350 subjects was performed and their results were compared to the same age and sex matched control group. Carotid atherosclerosis was evaluated by IMT with ultrasound investigation. Endothelial function was assessed with ADMA. Lipide profile and hs-CRP were evaluated in addition.

**RESULTS**

We found a highly correspondent endothelial atherosclerotic process in patients with diabetes. Increased parameters (LDL, hs-CRP, total cholesterol) correlated to serum ADMA levels ($r=0.909$; $P<0.05$). We found no correlation between glycated hemoglobin and ADMA levels ($r=0.221$; $P<0.005$). Diabetes duration in the first group shows no connection to ADMA and FMD, while a relation was established in the second one.

**CONCLUSIONS**

Changes in endothelial dysfunction patients with diabetes begin before IMT changes and sharply varied. It is probably caused by combination between impaired endothelial function and expressed atherosclerosis changes in vessels. Quantification of new biomarkers for endothelial function in patients with diabetes might provide an opportunity for diagnosis of atherosclerotic disease.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0703

## WHEN HEMOGLOBIN A1C IS UNRELIABLE: A CASE REPORT OF HEMOLYTIC ANEMIA

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### BACKGROUND-AIM

Hemoglobin A1c (HbA1c) is a key biological parameter widely used in the management of diabetic patients. Despite the high utility of HbA1c, it has some limitations.

### METHODS

We present a case of a Type 2 diabetes (T2D) patient in whom the HbA1c measurement became uninterpretable when compared to blood glucose levels.
The patient was diagnosed as DT2 in 2018 at age of 55 years. He was addressed to our hospital for Hepatitis C in 2021.

### RESULTS

In January 2021, HbA1c level was measured at 9.1 %, hepatic parameters were within normal ranges and the complete blood count shows isolated thrombocytosis at 571 G/L. Face to a persistent thrombocytosis in November 2021, he was referred to the hematology unit and the final diagnosis of essential thrombocythemia V617F JAK2 mutation was made in February 2022. At this time, HbA1c was 7.3% consistent with self-monitoring blood glucose. The patient was later hospitalised for anemia in July 2023. Biological results are those of hemolytic anemia (HA) with negative Coombs test: Hb 7.9 g/dL, reticulocytes 19.9%, haptoglobin <0.1 g/L, total bilirubin 45 µmol/L and direct bilirubin 14 µmol/L. HbA1c level was at 3.1 %.
Past results in march 2023 showed an HbA1c at 3.4% and fasting plasma glucose at 11.7 mmol/L highlighting a discrepancy between HbA1c and blood glucose levels. This should have alerted the clinician and prompted further prescription of an alternative test for monitoring diabetes, such as fructosamine.

### CONCLUSIONS

Physiological conditions that affect the lifespan of red blood cells can falsely elevate or decrease HbA1c results. In our laboratory, all HbA1c results were accompanied with a long comment with possible interferences on HbA1c results but this case highlights that the limitations are not always well taken into account. So, we decided to add fructosamine for all HbA1c values below 4%.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0704

**LEMMEL SYNDROME: A CASE REPORT**

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**BACKGROUND-AIM**

Introduction:
Periampullary diverticula are very common and generally asymptomatic. However, in some cases, they can cause biliopancreatic obstruction, duodenal obstruction, perforation, and bleeding. Lemmel syndrome is a very rare condition characterized by obstructive jaundice secondary to the presence of a duodenal diverticulum.

**METHODS**

Clinical Case:
A 70-year-old woman presented to the emergency department with colicky abdominal pain localized to the epigastrium, radiating to the back, associated with early satiety lasting 5 months. One month prior to admission, she developed jaundice that sporadically resolved.
Her initial lab results showed a normal complete blood count, glucose, urea, and creatinine. The hepatic profile showed elevated alkaline phosphatase, GGT, and mild direct hyperbilirubinemia, with slight increases in transaminases. An abdominal ultrasound and magnetic resonance cholangiography revealed dilatation of the common bile duct up to 12 mm, without other abnormalities.

**RESULTS**

Due to the persistence of abdominal pain and altered liver function tests, an endoscopic retrograde cholangiopancreatography (CPRE) was performed, which showed dilatation of the common bile duct and an image of a juxtapapillary duodenal diverticulum causing compression. An endoscopic sphincterotomy was performed with abundant bile drainage but no stone extraction. Four weeks after the procedure, her hepatic profile had normalized, and the abdominal pain had resolved.

**CONCLUSIONS**

Discussion:
The diagnosis of Lemmel syndrome is challenging, as complementary tests often fail to detect these anomalies, as seen in our patient, where a magnetic resonance cholangiography was performed without detecting the diverticular formation.
Therefore, in conclusion, in patients with obstructive jaundice without evidence of choledocholithiasis or periampullary tumors, a juxtapapillary duodenal diverticulum should be considered in the suspicion of Lemmel syndrome. In addition to jaundice and a cholestatic pattern, abdominal pain is commonly associated, though it can be quite nonspecific. Endoscopic and/or surgical treatment should be considered based on the symptoms and clinical presentation of each patient.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0705

## NEW METHOD TO IDENTIFY PLEURO-PERITONEAL COMMUNICATION IN ICODEXTRIN DIALYZED PATIENT

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### BACKGROUND-AIM

Pleural effusion secondary to pleuro-peritoneal communication occurs in approximately 2% of patients undergoing peritoneal dialysis (PD), with an increased risk of recurrence if PD continues. Although it was first named as "sweet hydrothorax" due to the leakage of dextrose from PD fluid into the pleural cavity, nowadays it has been replaced with icodextrin, a glucose polymer which also acts as osmotic agent but is dextrose free.
Thus, it is imperative to develop new biochemical methods to identify these cases, as traditional direct glucose measurements may no longer be sufficient.
In this work, we present a novel detection method to assess the presence of icodextrin in pleural effusion in a patient with suspected pleuro-peritoneal communication.

### METHODS

An in-house acid-heat procedure was used to disrupt glucose bonds in icodextrin. The analyzed samples included pleural fluid from the patient (PPF), icodextrin solution (IF), and a random pleural fluid as negative control (NPF). In brief, 1.5 mL of each fluid were mixed with 0.5 mL of Hydrochloric acid 1N and heated for 10 minutes. Glucose concentrations were measured before and after the procedure using Atellica CH system (Siemens Healthineers). An increase in glucose concentration following the treatment would be indicative of glucose liberation from icodextrin.
Additionally, five drops of Lugol's solution were added to aliquots of PPF, IF, and NPF to detect potential color changes, indicating icodextrin presence.

### RESULTS

Lugol's staining did not yield a clear distinction in the color of PPF when compared to the other samples. However, glucose concentrations before and after the intervention were as follows (mg/dL):
• IF: Before: <4, After: 285
• PPF: Before: 108, After: 166
• NPF: Before: 81, After: 76

### CONCLUSIONS

The marked glucose increase in IF confirms the disruption method's effectiveness. The rise in glucose in PPF suggests the presence of icodextrin, supporting the pleuro-peritoneal communication diagnosis. The lack of change in NPF strengthens this conclusion.
Imaging techniques could not confirm the leakage between peritoneal and pleural cavities; anyway, the patient was switched to hemodialysis to prevent further complications.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0706

## RHABDOMYOLYSIS AND MULTIORGAN DAMAGE ASSOCIATED WITH COCAINE USE

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### BACKGROUND-AIM

Rhabdomyolysis is a condition affecting skeletal muscle, where muscle fibers break down and release their contents into the bloodstream, such as creatinine kinase, myoglobin and potassium, among others.
The main risk factors are extreme exercise, trauma, dehydration, metabolic disorders, infections, medications and drugs.

### METHODS

A 34-year-old man presented to the emergency room with an emetic condition for 2 days after cocaine use. He also reports weakness in both upper and lower limbs over the past 24 hours, causing several falls, as well as decreased diuresis with dark-colored urine.
His personal history includes regular cocaine use by inhalation and follow-up by Mental Health for depression. He had two previous episodes of angor after cocaine abuse. He had no history of kidney disease.
The first laboratory analysis showed deterioration of renal function and serum electrolyte alterations, such as hyperkalemia and hypocalcemia. Urinalysis revealed leukocyturia, hematuria and marked proteinuria. Creatinine kinase (CK) had a value of 873 U/L, so at first it was not oriented rhabdomyolysis.

### RESULTS

After 12 hours of fluid therapy, the patient remained oliguric, with worsening kidney function (creatinine: 9.14 mg/dl), increased hyperkalemia (K: 6.0 mEq/L), a marked rise in CK: 246898 U/L and transaminases (AST: 2294 U/L, ALT: 702 U/L). This was accompanied by pitting edema in the lower limbs.
Following 17 days of hospitalization and four sessions of hemodialysis, the patient showed progressive improvement. He was discharged from the hospital with a final diagnosis of oliguric acute renal failure, probably related to toxic acute tubular necrosis caused by rhabdomyolysis, and acute hepatitis also of toxic origin.

### CONCLUSIONS

The CK peak observed in the second analysis allowed the diagnosis of rhabdomyolysis, defined as a CK over 1000 U/L or 5 times the normal value.
Although the association between cocaine use and rhabdomyolysis is known, this diagnosis was not initially considered in this case. Thanks to the laboratory's intervention, nephrology was alerted to the worsening renal and hepatic function observed in the second analysis, as well as the significant CK increase. This facilitated timely medical intervention and prevented further deterioration of the patient's condition.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0707

## THE VALUE OF TUMOR MARKERS CA 72-4, CA19-9 AND CEA IN THE DETECTION AND MONITORING OF GASTRIC CANCER

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### BACKGROUND-AIM

Gastric cancer is a malignant disease that results from the uncontrolled growth of cells in the gastric mucosa, leading to the formation of malignant tumors that can invade nearby tissues and metastasize to other organs. To improve the diagnosis and monitoring of gastric cancer, it is essential to use advanced diagnostic methods, including biological markers. The aim of this study is to show the diagnostic and monitoring value of the markers CA 72-4, CA 19-9 and CEA in a population group with gastric cancer.

### METHODS

The study was conducted at the “Intermedica” medical clinic. For each of the patients, a form was filled out with personal data and peripheral blood was taken which was used to measure the level of markers CA 72-4, CA 19-9 and CEA in the cobas 6000 instrument with the ECL technique. The collected data were analyzed using advanced statistical software.

### RESULTS

This study included a total of 100 individuals, with 39% of the sample being male and 61% female. Of these participants, 13.9% represented the 27-45 age group, while the majority (86.1%) represented the 46-89 age group. Analysis of the percentage of normal and abnormal values by age group showed that younger individuals (27-45 years old) tended to have a higher percentage of normal values for all three biomarkers compared to the 46-89 age group: Chi-Square ($X^2$) test analysis showed that gender did not have any statistically significant effect on the results for the biomarkers CA 72-4, CA 19-9 and CEA. Logistic regression analysis showed that age had a significant effect on the presence of abnormal values for CA 19-9 and CEA, while gender had a significant effect only for CA 19-9. For the CA 72-4 marker, neither age nor gender had a statistically significant effect.

### CONCLUSIONS

In accordance with the data of the study conducted by Yu, a trend of increasing positivity rates of these biomarkers with the progression of the tumor stage was observed, especially for CA 19-9 and CA 72-4. The best marker, although not ideal, is CA 72-4, which has a higher specificity for the diagnosis of gastric cancer. The CEA marker serves as the second auxiliary marker in this study, followed by CA 19-9. If these indicators are used together, they bring an increase in effectiveness in the diagnosis and monitoring of gastric cancer.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0708

## IDENTIFICATION OF PREDICTIVE BIOMARKERS FOR COMPLICATIONS AND CARDIOVASCULAR RISK IN SAUDI WOMEN WITH TYPE 2 DIABETES

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### BACKGROUND-AIM

The rising prevalence of T2DM in Saudi Arabia, driven by urbanization and lifestyle changes, necessitates improved management. This study explores the relationship between specific biomarkers and cardiovascular risk in Saudi females with T2DM, aiming to predict complications and provide insights for early detection and better disease management.

### METHODS

A cross-sectional study of 500 Saudi females (≥35 years) in Al Madinah (2018–2023) analyzed fasting serum biomarkers, including homocysteine, osteocalcin, ferritin, melatonin, adiponectin, ANGPTL8, leptin, uric acid, glucose, HbA1c, and lipid profiles, to assess their role in predicting cardiovascular risk and diabetes-related complications.

### RESULTS

This study found that elevated homocysteine levels were associated with increased glucose and triglyceride-to-HDL ratios, indicating higher cardiovascular disease (CVD) risk in Saudi females with T2DM. Reduced osteocalcin levels correlated with poor glycemic control, while elevated ferritin contributed to insulin resistance. Increased uric acid levels were linked to dyslipidemia and CVD risk. Lower melatonin levels were associated with insulin resistance and diabetic complications. Elevated betatrophin and leptin levels correlated with obesity and metabolic dysfunction, while lower adiponectin levels were linked to reduced insulin sensitivity. Biomarker screening can support early detection and improved diabetes management.

### CONCLUSIONS

Biomarker profiling is crucial for predicting complications and cardiovascular risk in Saudi females with T2DM. Elevated homocysteine and ferritin levels increase CVD risk, while reduced osteocalcin affects glycemic control. Higher uric acid and leptin levels link to obesity and metabolic dysfunction, underscoring the need for routine screening and early intervention.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0709

**COBALT(III)-BASED BIOREDUCTIVE PRODRUGS REPRESENT AN INNOVATIVE APPROACH FOR TARGETING HYPOXIC TUMOR MICROENVIRONMENTS IN BREAST CANCER THROUGH SELECTIVE DRUG ACTIVATION.**

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**BACKGROUND-AIM**

Breast cancer is one of the most aggressive and heterogeneous malignancies, remaining a leading cause of mortality among women globally. Tumor hypoxia, characterized by low oxygen levels, plays a pivotal role in promoting cancer progression, metastasis, and resistance to therapy. Hypoxia-inducible factor 1-alpha (HIF-1$\alpha$) is a key regulator of the hypoxic response, driving the expression of genes such as VEGF and GLUT1 that support tumor survival. This study explores the potential of Cobalt (III)-based nanoconjugates, functionalized with doxorubicin (Cobalt-Dox), as a novel therapeutic strategy to selectively target the hypoxic tumor microenvironment.

**METHODS**

Cobalt-Dox nanoconjugates were synthesized and characterized for their physicochemical properties and hypoxia-specific drug release. In vitro studies using the MDA-MB-231 triple-negative breast cancer cell line assessed cytotoxicity, migration, invasion, and colony formation. Gene and protein expression levels of HIF-1$\alpha$, VEGF, and GLUT1 were analyzed via qRT-PCR and Western blotting. Biodistribution studies in rats evaluated systemic distribution and tumor-targeting efficiency. Tumor growth inhibition was further assessed in xenograft models.

**RESULTS**

Cobalt-Dox demonstrated significant cytotoxicity under hypoxic conditions and effectively inhibited migration, invasion, and colony formation in vitro. qRT-PCR and Western blot analyses showed downregulation of HIF-1$\alpha$, VEGF, and GLUT1. In vivo studies revealed selective accumulation in hypoxic tumor regions with enhanced tumor growth inhibition compared to conventional chemotherapy.

**CONCLUSIONS**

Cobalt-Dox nanoconjugates represent a promising therapeutic strategy for targeting hypoxic breast tumors by inhibiting HIF-1$\alpha$ signaling pathways. These findings provide a foundation for future clinical translation in breast cancer treatment.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0710

## ASSESSMENT OF SERUM OSTEOPONTIN, OSTEOPROTEGERIN AND BONE-SPECIFIC ALP AS MARKERS OF BONE TURNOVER IN PATIENTS WITH DISORDERS OF THYROID FUNCTION IN NIGERIA, SUB-SAHARAN AFRICA

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### BACKGROUND-AIM

Disorders of thyroid function, the 2nd commonest endocrine disorder globally is a cause of metabolic bone diseases. These metabolic bone complications are often subtle, but manifest as bone pains and increased fracture risks. The gold standard for diagnosis, Dual Energy X-ray Absorptiometry, is unavailable in this environment due to its cumbersomeness and cost. However, bone biomarkers have shown prospects in assessing alterations in bone remodeling. The study, being novel in this environment, is aimed at evaluating serum levels of bone-specific ALP (BALP), osteopontin (OPN) and osteoprotegerin (OPG) markers of bone turnover, alongside the traditional markers of total calcium (Tc), ionized calcium (Ic) and inorganic phosphate (Ip) in patients with these disorders.

### METHODS

This cross-sectional study, carried out over a period of 1 and 1/2 years included 40 patients with thyroid dysfunctions, aged 20 to 51 years, and 38 age and sex matched euthyroid controls. Patients were further stratified into hyperthyroid (hyp>) and hypothyroid (hyp<) groups. BALP, OPN and OPG, alongside Tc, Ic and Ip were assayed for all patients and controls. 5 mls of blood was collected in a plain bottle and serum harvested following clotting and centrifugation. Serum samples were assayed for BALP, OPN and OPG using ELISA technique, and Tc with Ic, using a direct ISE. Ip was assayed using automated photometry.

### RESULTS

The hyp> and hyp< groups had significantly increased median BALP (30.40 and 26.50) ng/ml and significantly lower median OPG (0.80 and 0.80) ng/ml than the controls (10.81 and 1.30) ng/ml respectively, $p < 0.05$. However, serum OPN was significantly higher and lower in the hyp> and hyp< groups respectively, when compared with the controls (11.00 and 2.10 vs 3.70) ng/ml, $p < 0.05$. The hyp> and hyp< groups had significantly higher mean serum Tc, Ic and Ip than the controls (2.49 ± 0.28, 1.27 ± 0.14 and 1.33 ± 0.33) mmol/l and (2.41 ± 0.04, 1.20 ± 0.04 and 1.15 ± 0.16) mmol/l vs (2.27 ± 0.11, 1.17 ± 0.06 and 1.08 ± 0.16) mmol/l respectively, $p < 0.05$.

### CONCLUSIONS

The patients had metabolic imbalance of all the studied markers, suggesting a higher bone turnover. The traditional bone markers will be an invaluable tool for monitoring bone health in them, while the less available ones can be introduced as supplementary tools.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0711

**ADVANTAGES OF USING CAPILLARY ELECTROPHORESIS FOR GLYCATED HAEMOGLOBIN ANALYSIS**

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**BACKGROUND-AIM**

Glycated hemoglobin (HbA1c) is a well-known biomarker for screening and diagnosis of diabetes mellitus and prediabetes. Therefore, its accurate measurement is extremely important. The aim of this study is to demonstrate the advantages of using capillary electrophoresis for HbA1c determination.

**METHODS**

For the determination of HbA1c was used the Capillarys 3 Octa analyzer (Sebia, France) operating on the principle of capillary electrophoresis. This technique separates fractions of haemoglobin based on size-to-charge ratio through capillary zone electrophoresis in an alkaline medium.

**RESULTS**

Over the course of 1 year, we captured 10 samples with variant hemoglobin during routine HbA1c testing, representing a several-fold increase in capture compared to the previous HPLC-based Arkray Adams 8180V analyzer.

**CONCLUSIONS**

The slower migration of the sample in the capillaries, leading to more efficient separation of individual fractions, is an undeniable advantage of this technique and can help reveal the presence of atypical fractions of variant hemoglobin. The HbA1c result in a patient with variant hemoglobin may be distorted not only due to analytical interference but also by possible effects on red blood cell lifespan or the degree of glycation. The laboratory's role is to detect these variants and inform the clinical department, which will initiate further steps in the diagnostic process.
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Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0712

## IMPORTANCE OF HIGH-FLUORESCENCE CELL ANALYSIS IN CSF: LABORATORY APPROACH TO THE DIAGNOSIS OF TUMORAL PATHOLOGY

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### BACKGROUND-AIM

High-fluorescence cells (HF-BF) are cells with a high nucleus-to-cytoplasm ratio and elevated nucleic acid content. Their presence and count in biological fluids are correlated with the presence of malignant cells originating from solid tumors, among other conditions.

### METHODS

A 75-year-old male presented to the Emergency Department with vomiting, diarrhea, and general deterioration. He was under oncology follow-up for stage IV lung adenocarcinoma (cT4N3M1). During hospitalization, he experienced progressive neurological decline, with episodes of disorientation, drowsiness and incoherent speech, prompting a lumbar puncture.

### RESULTS

Clear cerebrospinal fluid (CSF) was received at the Emergency Laboratory. Biochemical analysis showed hyperproteinorrachia (total protein: 685.8 mg/dL) and glucose: 82 mg/dL. A cell count was performed using the Sysmex XN-1000 analyzer, revealing 10 leukocytes/μL, of which 75% were mononuclear and 25% polymorphonuclear, and 77 HF-BF/μL.
Given the high number of HF-BF and the presence of hyperproteinorrachia, cytocentrifugation was performed, followed by staining to examine cellular cytology. Predominantly, large atypical cells were observed, highly basophilic, with irregular borders, multinucleation, polar vacuoles, and arranged in cellular nests. Additionally, signet-ring cells and abnormal mitotic figures were identified.
These findings suggested that the nature of the fluid was related to the patient's solid tumor. Cranial MRI showed findings compatible with leptomeningeal carcinomatosis, confirming our suspicion.

### CONCLUSIONS

Leptomeningeal carcinomatosis is a rare condition characterized by diffuse dissemination of tumor cells within the CSF and/or leptomeninges. It is more common in hematologic malignancies than in solid tumors, with lung cancer being the most frequent among the latter. The presence of this condition is associated with a poor prognosis.
The laboratory can expedite diagnosis by performing differential leukocyte counts, basic biochemical analysis, and cytological examination. The HF-BF parameter aids in early detection, as its presence in CSF is sufficient to prompt microscopic review of cellularity due to its correlation with neoplastic cells.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0713

## HBA1C MEASUREMENT: COMPARISON OF BIORAD D10 (HPLC) AND SEBIA CAPILLARYS 2 METHODS

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### BACKGROUND-AIM

HbA1c test provides information on metabolic control in diabetes and could also be used for its Diagnosis, it is essential to have accurate and precise HbA1c methods covering a range of measurement principles. We report an evaluation of the Biorad D10 kit (Hplc) versus Sebia capillarys 2 Kit (capillary electrophoresis) .

### METHODS

Measurements of HbA1c were carried out in whole blood samples (K3edta tubes ) from 111 patiens from different departments in Ziv medical Center- Israel using both Sebia Capillarys 2 Flex piercing (Capillary Electrophoresis) and analyzers Biorad D 10 (HPLC method) .

### RESULTS

There was a good concordance between the results of capillary electrophoresis and HPLC ($R2 = 0.97$, $P < 0.0001$) There is no significant difference between the results obtained from both technique.

### CONCLUSIONS

both technique suitable for the clinical application in the analysis of HbA1c. it is concluded that the results obtained after testing samples in Sebia capillarys Flex Piercing II and Biorad D10 are in a good concordance and there is no significant difference in the results obtained. The advantage of of using Biorad D10 has benefit of shorter testing time Whereas Sebia capillarys can detecte underlying hemoglobinopathies and high throughput.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0714

## POTENTIAL ROLE OF PROCALCITONIN IN THE DIAGNOSIS OF BACTERIAL MENINGITIS: AN INSIGHT FROM EASTERN PART OF NEPAL

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**BACKGROUND-AIM**

Meningitis is a fatal condition with high mortality and morbidity requiring prompt diagnosis and management. Differentiating between bacterial and non-bacterial meningitis is crucial in reducing antibiotic overuse and shortening hospital stays to diminish nosocomial infections. Lumbar puncture is invasive and cerebrospinal fluid (CSF) culture is time consuming. In contrast, procalcitonin (PCT) is an acute phase reactant that can be quickly measured in medical laboratories and offers a cost-effective alternative to CSF analysis. Many studies suggest elevated serum PCT level in infectious conditions such as meningitis. However, precise cut-off values for PCT in meningitis remain undefined. This study aimed to evaluate the potential of serum PCT as a reliable biomarker for diagnosing bacterial meningitis in children.

**METHODS**

The cross-sectional study was conducted over one year at B.P. Koirala Institute of Health Sciences, Dharan, Nepal. Thirty children aged 1 month to 15 years with suspected meningitis were included. Complete blood counts, CSF analysis and serum PCT were analyzed. Based on clinical features and CSF findings, patients were categorized into bacterial and non-bacterial meningitis groups. Data were analysed using SPSS software.

**RESULTS**

Among 30 children diagnosed with meningitis, 11 (36.66%) cases were classified as bacterial meningitis while 19 (63.34%) as non-bacterial meningitis. At the serum PCT cut-off value of >0.354 ng/mL, the sensitivity and specificity in predicting bacterial meningitis were 90.9% and 84.2%, respectively. The diagnostic accuracy of serum PCT in differentiation between bacterial and non-bacterial meningitis was 86.66%. The area under the ROC curve (AUC) was 0.933 (0.827-1.039; $p < 0.01$). In addition, the positive and negative predictive values of serum PCT at this cut-off for detecting bacterial meningitis were 76.9% and 94.1%, respectively.

**CONCLUSIONS**

Serum PCT analysis serves as a valuable biomarker for differentiating bacterial from non-bacterial meningitis in children. Thus, it can be considered as a propitious marker, enabling the swift distinction of meningitis cases and ensuring timely and appropriate management.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0715

## HEMOGLOBIN A1C METHOD COMPARISON OF SEBIA CAPILLARY AND TRINITY BORONATE AFFINITY SYSTEMS

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### BACKGROUND-AIM

Hemoglobin A1c (HbA1c) measurement devices are widely used to evaluate glycemic control in diabetic patients. Several analytical methods have been developed for HbA1c analysis. The most frequently used are ion-exchange chromatography and affinity chromatography for total glycated hemoglobin. Our aim in this study was to investigate the comparability of two HbA1c instruments.

### METHODS

154 fresh whole blood samples from diabetic patients and controls, with different HbA1c levels (4.5%-15.8%) were analyzed simultaneously with boronate affinity and capillary electrophoresis. Two systems were compared according to The CLSI document (EP9-A2) - Method comparison and Bias estimation using patient samples, approved guideline. %Mean difference was calculated via Bland Altman graphics. Regression equation was expressed with Passing-Bablok.

### RESULTS

Mean difference was found to be 0.5562% (-0,1317 to 1,2440%). The Regression equation was Sebia = 0.150756 + 0.971008 Trinity. Intercept [0.1508 (0.0000 to 0.4154)] and slope [0.9710 (0.9231 to 1.0000)] values were including 0 and 1, respectively. Correlation coefficient was 0.9858.

### CONCLUSIONS

Our result indicates that HbA1c on Sebia electrophoresis showed values comparable to chromatographic method. HbA1c assay on Sebia electrophoresis is a viable alternative to HPLC for measuring HbA1c in clinical laboratories.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0716

## PROGRAMMED CELL DEATH FACTOR 4 AGGRAVATES SEPSIS-INDUCED LIVER DAMAGE THROUGH DISTURBED MITOCHONDRIAL QUALITY CONTROL SYSTEM

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### BACKGROUND-AIM

Sepsis is the most common cause of death in intensive care units, caused by deregulated immune response to infection. Sepsis-induced acute liver dysfunction occurs in the early stage of sepsis and can aggravates the progression of sepsis. However, there is a lack of specific diagnostic markers for sepsis-induced liver injury (SLI). Therefore, our study would screen potential biomarkers and elucidate their roles in pathogenesis of liver damge during sepsis, which is of great significance for clinical diagnosis and provides therapeutic targets for disease management.

### METHODS

Lipopolysaccharide (LPS) built the SLI mouse model. H&E staining observed liver pathology, ELISA analyzed liver function, and Western Blot assessed inflammatory/pro-apoptotic proteins. LC-MS/MS screened, validated by Western Blot and RT-PCR. CCK8 and TUNEL assay evaluated cell proliferation and apoptosis. MitoSOX and JC1 stained for mitochondrial stress and potential. Mito/lyso-tracker and Western Blot detected mitochondrial quality control (MQC) changes.

### RESULTS

Increased inflammatory and apoptotic responses were observed in the SLI mouse models, with liver dysfunction. PDCD4 was screened and identified to be significantly upregulated during sepsis-induced liver damage ($p < 0.05$), LPS-induced by genetic ablation reduced it. Molecular investigations confirmed that loss of PDCD4 protected liver against sepsis though inhibiting mitochondrial oxidative stress and membrane potential dysregulation. Furthermore, upon LPS stress PDCD4 disrupted MQC, induced pathological mitochondrial fission and mitophagy, and inhibited mitochondrial fusion and biogenesis. Co-IP assays indicated that the accumulation of PDCD4 regulated mitochondrial fusion through the combination with mitochondrial inner membrane protein YME1L1, contributing to the imbalance in MQC.

### CONCLUSIONS

Our data show that LPS-induced liver damage is associated with PDCD4 upregulation, which is followed by disrupted mitochondrial quality control through the combination with YME1L1, causing hepatocyte inflammation and apoptosis. Based on this, new potential therapeutic strategies for reducing PDCD4 and enhancing mitochondrial quality control could be expected to treat spesis-induced liver damage.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0717

## THE PLASMA LEVELS AND DIAGNOSTIC UTILITY OF METALLOPROTEINASE 26 (MMP-26) IN ENDOMETRIAL CANCER PATIENTS

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### BACKGROUND-AIM

Matrix metalloproteinases (MMPs) can be divided into 7 groups: collagenases, gelatinases, metalloelastases, stromelysins, matrilysins, membrane-type MMPs (MT-MMPs), and other MMPs. MMPs play an important role in cancer cell invasion and metastasis by degrading the extracellular matrix. In this study, we investigated the plasma levels of matrylysin 26 (MMP-26) in comparison to tumor marker CA125 in endometrial cancer patients and in relation to the healthy subjects.

### METHODS

Tested group included 30 endometrial cancer patients (stage I-III in FIGO, type adenocarcinoma endometrioides). The control groups consisted of 30 healthy volunteers. Plasma level of MMP-26 was determined using immunoenzyme assay (ELISA), CA125 concentrations - by chemiluminescent microparticle immunoassay (CMIA).

### RESULTS

Plasma levels of MMP-26 (median 13,17ng/ml), CA125 (19,85 U/ml) were significantly higher in endometrial cancer patients as compared to the healthy control (3,281ng/ml, 14,67 U/ml; respectively). MMP-26 received higher diagnostic sensitivity (76%), specificity (66,47%), the positive and negative predictive values (PPV - 90 %, NPV – 72,56%) than CA 125 values (69,93%, 62,46%, 83% and 55,52%; respectively). The combined use of tested parameters resulted in the increase of the sensitivity and NPV range (84% and 82%). The highest area under the ROC curve (AUC) were observed for MMP-26 (0,8567) than CA 125 (0,7156).

### CONCLUSIONS

These results suggest a potential usefulness of MMP-26 in diagnostic of endometrial cancer patients, especially in combined use with CA125 as a new diagnostic panel.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0718

**BIOMARKERS IN ALZHEIMER'S DISEASE: IMPACT OF BIOLOGICAL DIAGNOSIS STANDARDIZATION.**

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**BACKGROUND-AIM**

The diagnosis of Alzheimer's disease (AD) relies on identifying cognitive complaints, brain imaging, and analysis of biomarkers in cerebrospinal fluid. Recently, the harmonization of biochemical marker's interpretation has been proposed. This multicentred study engaged all age groups experiencing neurocognitive disorders. These recommendations are implemented in our laboratory through a harmonized biological report, enabling the identification of a β-amyloidopathy (Aß) (increased Aß 1-40/1-42, N <14.7) and a (phospho)taupathy (increased PTau, N <59 pg/ml and Tau, N <410 pg/ml).
The aim of our study was to analyze the harmonized biological report compared to the final diagnosis adopted.

**METHODS**

In this monocentric study, we retrospectively analyzed 104 harmonized biological reports intended for specialized geriatric during one year (2024). These were associated with a provisional diagnosis, an hippocampal atrophy observed on magnetic resonance imaging (MRI) using the Scheltens score and a final diagnosis clearly documented in patient's digital medical record. Biomarkers were assayed using immunochemiluminescence (Lumipulse G600, Fujirebio, ZA Courteboeuf, France).

**RESULTS**

88 harmonized biological reports were retained (14 excluded due to missing imaging data, 2 due to lack of final diagnostic).
Among the 48 reports with AD as final diagnosis, harmonized biological report was concordant in 47/48 and Scheltens score was ≥2 in 35/48 cases.
For the 40 reports whose final diagnosis ruled out AD, 37/40 had a biological profile incompatible with AD, while 3 reports had a biological profile compatible with AD. 21 of these had a Scheltens score ≥2. The concordance between the biological report and the final diagnosis was 97.78% for reports with AD and 92.5% for those for whom AD was ruled out.
Scheltens score differed between AD and non-AD groups ($p = 0.0034$). However, concerning reports with final diagnosis other than AD, we found no difference was found between scores $< 2$ and $\geq 2$ ($p = 0.65$).

**CONCLUSIONS**

Our study emphasizes the impact of standardized biological reports and biological practices for geriatric population. A limitation is potential bias from centers with larger populations. Scheltens score showed expected limitation to differentiate physiological aging and pathological changes.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0719

## FIRST INSIGHTS INTO THE ANALYTICAL PERFORMANCE AND STABILITY ASSESSMENT OF THE QUANTUM BLUE FPELA ASSAY

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### BACKGROUND-AIM

Fecal pancreatic elastase (FPE) is an established biomarker for the assessment of pancreatic function in patients suffering from pancreatic exocrine insufficiency. It is very stable during intestinal transit. The present work assesses the stability and evaluates the analytical performance of a new FPE lateral flow assay to determine elastase levels in extracts of human stool samples.

### METHODS

Potentially interfering substances such as oral pharmaceuticals, nutritional supplements as well as hemoglobin were assessed in the Quantum Blue fPELA assay (CLSI EP07-Ed3). Two samples were spiked with the recommended test concentration of presumable interfering substances and compared to unspiked samples. Bias in results exceeding 30% was considering interference. Test cassette stabilities, i.e., accelerated, transport and in-use stability were established with an allowable deviation from baseline of ±30% (CLSI EP 25 2nd ed.).

### RESULTS

Following substances tested up to the listed concentrations in µg/mL did not interfere with the detection of the analyte: acetylcysteine (Fluimucil®) (120), elexacaftor (14), tezacaftor (7) ivacaftor (10.5), metformin (120), glimepiride (0.08), prednisolone (60), prednisone (60), ciprofloxacin (19.5), lansoprazolum (4.6), pantoprazole (1.9), esomeprazole (2.2), omeprazole (2.9), ibuprofen (96), multivitamin (Berocca®) (0.6) and hemoglobine (10). In addition, human CELA 2A, trypsin (porcine), chymotrypsin (bovine) and elastase (porcine) did not show any antibody cross reactivity at a concentration of 1 µg/mL, The accelerated stability was conducted at three elevated temperatures (35, 40 and 45°C), a preliminary initial shelf life of at least 12 months at 2-8°C was confirmed (Arrhenius analysis). The test cassettes are stable under extreme transport condition of 5 days at -29°C + 3 days at 38°C and 85% RH + 2 days at 50°C. The in-use stability results show that opened test cassette stored at room temperature can be used up to 4 hours.

### CONCLUSIONS

The Quantum Blue® fPELA showed no interferences for the substances of interest. The test cassettes are stable for at least 12 months at 2-8°C, they can endure extreme transport conditions (even 2 days at 50°C) and are stable after been opened for up to 4 hours at room temperature.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0720

**THE ASSOCIATION OF MALIGNANCY AND TUBERCULOSIS WITH ELEVATED SERUM COBALAMIN (VITAMIN B12) CONCENTRATIONS IN A SOUTH AFRICAN POPULATION.**

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**BACKGROUND-AIM**

Associations between elevated serum cobalamin (vitamin B12) levels and various pathologies have been observed, with a paucity of data in African populations. These have presented cobalamin as a potential marker for malignancy, tuberculosis (TB), renal (RD) and liver disorders (LD). This study aimed to explore this relationship within a South African (SA) cohort at Tygerberg Academic Hospital (TAH).

**METHODS**

A retrospective audit of serum cobalamin laboratory requests was performed over a five-year period (2017-2021) to obtain descriptive data on request frequency and the distribution of the population's age, sex, and cobalamin levels. To investigate the association of malignancy, TB, LD and RD with serum cobalamin levels, a retrospective cohort study was conducted using laboratory requests from within TAH between 2017 and 2019. After excluding requests based on pre-defined criteria, cobalamin data was divided into two groups: a control (normal levels of 145-569 pmol/L; n = 3,068) and exposed group (elevated levels >569 pmol/L; n = 1 220). Using statistical power calculations, 773 requests were randomly selected from each group for further analysis. Laboratory records were reviewed for each patient to assess the number of laboratory-confirmed malignancies diagnosed within a three-year period following serum cobalamin measurement. The frequency of TB infection, LD and RD was also assessed.

**RESULTS**

A total of 55 169 requests were received from 2017 to 2021, with approximately 33% originating from within TAH and 67% from external facilities. Females accounted for 62% of all requests, and 76% of all analyses showed serum cobalamin concentrations within the normal reference interval. Among the 5 416 requests received from patients admitted at TAH from 2017 to 2019, the largest proportion (±50%) was received from emergency departments (medical, trauma, paediatrics, and maternity). Following exclusion, preliminary data analysis shows a relative risk of 2.86 for TB, 1.79 for LD, 1.63 for RD, and 0.95 for malignancy among the exposed group.

**CONCLUSIONS**

With the exception of malignancy, preliminary findings suggest a higher prevalence of TB, LD and RD among individuals with elevated serum cobalamin concentrations in an SA population.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0721

**ROLE OF THE CLINICAL LABORATORY FOR THE CORRECT DIAGNOSIS OF WILSON'S DISEASE**

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**BACKGROUND-AIM**

Wilson's disease (WD) is a hereditary autosomal recessive disorder of copper metabolism characterised by copper accumulation in the liver, brain, cornea and kidneys. Alterations in copper transport also interfere with its incorporation into ceruloplasmin, the main copper transport protein in the blood. WD presents decreased copper and ceruloplasmin levels in serum, along with increased urinary copper excretion. WD should be considered in the differential diagnosis of any acute or chronic liver disease of unknown origin. Diagnosis may be easily overlooked and often involves a combination of blood and urine tests, as well as a liver biopsy and genetic tests to identify mutations in the ATP7B gene on chromosome 13.

**METHODS**

A 22-year-old woman with a prior diagnosis of chronic liver disease presented to the Emergency Department with decompensated cirrhosis, right pleural effusion and ascites. Laboratory results showed decreased serum copper (15 μg/dL [80-155 μg/dL]) and ceruloplasmin levels (<6 mg/dL [20-60 mg/dL]) and high levels of 24-hour urinary copper excretion (123 μg/24h [0-60 μg/24h]), aspartate aminotransferase (220 U/L [10-50 U/L]), alanine aminotransferase (269 U/L [13-37 U/L]) and total bilirubin (22,8 mg/dL [0,3-1,2 mg/dL]).

**RESULTS**

Patient’s examination revealed a golden-green ring around the cornea in her right eye; a Kayser-Fleischer ring as a result of copper accumulation. Given the suspicion of WD, a genetic test was performed using DNA Next-Generation Sequencing (NGS) techniques. This study revealed a homozygous variant in the ATP7B gene: c.3694A>C (Thr1232Pro). This, together with the liver symptoms, the presence of the Kayser-Fleischer ring and the laboratory findings confirmed the diagnosis of WD.

**CONCLUSIONS**

WD should be suspected in any patient with hepatic biochemical alteration of unclear cause, especially in young patients. The only confirmatory test of WD is genetic screening. This case highlights the laboratory’s crucial role in the determination of key analytical values, as well as the genetic study which allows the final diagnosis.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0722

## URINARY STEROID PROFILING BY GC-MS AS A DIAGNOSTIC TOOL FOR EVALUATING MALIGNANCY OF ADRENOCORTICAL TUMORS – SHOULD THIS BE ROUTINE FOR ALL PATIENTS?

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### BACKGROUND-AIM

Adrenocortical carcinomas (ACC) are rare but aggressive cancers, and the ability to differentiate between these and benign adrenocortical adenomas (ACA) is essential. Current diagnostic workup in Denmark relies on clinical assessment, functional tests, and imaging, with urinary steroid profiling as a supplementary analysis. However, no consensus exists in terms of which steroids are relevant to include in such a profile.
Thus, the first aim of this study was to systematically evaluate the literature to decide on an evidently ideal steroid profile for discriminating between benign and malignant adrenocortical tumors. Secondly, our aim was to implement and evaluate the diagnostic value of the ideal profile.

### METHODS

Our systematic review was performed according to the Cochrane Collaboration guidelines. The retrospective study was done according to local hospital guidelines including relevant ethical approvals.

### RESULTS

Based on our selection criteria, our systematic review identified twelve relevant original studies. Since not all studies evaluated the same steroids or employed comparable experimental approaches, we developed a scoring system to score the apparent significance of individual steroids for inclusion in an ideal profile. With this approach, we identified seven steroids with reported high diagnostic value.
Five of the identified steroids were already part of our routine GC/MS-generated steroid profile based on 24h urine sampling. To evaluate the diagnostic value of the proposedly ideal profile, we added the two remaining steroids to our current profile and did a retrospective study (Dec 2022 until Oct 2024) employing data from patient medical records combined with historical GC/MS data. Due to recent implementation of GC/MS, the amount of data was limited to two ACC and 41 ACA patients. Thus, we are currently planning a prospective study. However, both ACA cases would have been identified employing the ideal profile.

### CONCLUSIONS

Our preliminary findings indicate that urine steroid profiles could be considered to play a more significant role in the diagnostic workup of these patients and should be implemented at an earlier step in the diagnostic algorithm.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0723

## GFAP AND UCH-L1 AS PREDICTORS OF INJURY IN BRAIN TRAUMA

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### BACKGROUND-AIM

Brain trauma (TBI) is a very common health problem in Uruguay requiring a computed tomography scan (CT) to be diagnosed. Of all TBIs 90% are mild according to the Glasgow Coma Scale, and relevant brain injuries are 10%. Two brain proteins have been identified: Carboxy-terminal ubiquitinL1 hydrolase (UCHL1) and Glial fibrillary acidic protein (GFAP) that could predict brain injury in plasma/blood facilitating the management of patients with mild TBI.
Our aim is to assess the association of brain injury (GFAP and UCH-L1) in the identification of patients with mild traumatic brain injury with head CT as the Gold standard.

### METHODS

Inclusion criteria: patients over 18 years with clinical suspicion of Mild TBI whitin 12 hours, and score on the Glasgow Coma Scale of 13-15.Plasma determinations were performed using the i-Alinity Abbott through a chemiluminescent microparticle immunoassay, whose results were compared with the patient's CT evaluating the correlation between presence or absence of intracranial lesions with the test values. Chi square test and ROC curves with Microsoft-Excel and Medcalc.Sensitivity and specificity were determined

### RESULTS

72 blood samples were obtained, GFAP and UCH-L1 tests correctly identified 22 patients with brain injury according CT (true positive) and 20 without injury (true negative). The remaining 30 patients had a positive test, of which 4 presented CT with injury 48 hours after the event.

### CONCLUSIONS

The statistical analysis showed that the test has a high sensitivity (100%) and a high negative predictive value (100%), which indicates that it is reliable in excluding the presence of lesions in patients with negative results, and as a great possible predictor of injury, before that evidenced by CT

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0724

## INTERACTION BETWEEN CHEMOKINES, OXIDATIVE STRESS AND ANTIOXIDANT STATUS - POSSIBLE PATHOGENIC ROLE AND DIAGNOSTIC USEFULNESS IN PRIMARY BILIARY CHOLANGITIS

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### BACKGROUND-AIM

Primary biliary cholangitis (PBC) is a slowly progressing cholestatic, autoimmune liver disease, leading to fibrosis, cirrhosis and liver failure, characterized by the presence of specific serum antimitochondrial (AMA) and antinuclear antibodies (ANA). In the present study we determined markers of oxidative injury, antioxidant components like glutathione (GSH), and chemokines: CXCL8 and MCP-1 concentration, which may be associated with oxidative stress. Our aim was to evaluate whether the degree of lipid peroxidation, measured by the serum level of 8-isoprostane influences the PBC progression and study the correlation between level 8-isoprostane, chemokines and specific autoantibodies and its possible usefulness in laboratory diagnostics.

### METHODS

Material - sera from 40 patients with PBC and 20 healthy subjects. Chemokines levels, 8-isoprostane, glutathione, aldehydes concentration and superoxide dismutase (SOD) activity were evaluated using commercial ELISA assays.

### RESULTS

PBC patients had significantly higher levels of aldehydes (MDA and 4-HNE) and SOD activity compared to healthy controls, $p = 0.03$ and $p = 0.15$, respectively. GSH was significantly reduced ($p \leq 0.001$). Elevated levels of studied chemokines were measured in 55% patients with PBC, but in AMA and/or ANA -positive PBC group we found 68% of patients with higher levels of CXCL8 or MCP-1. Serum 8-isoprostane was also elevated in PBC patients - 238.9 [3.8–500.0] pg/mL as compared to healthy controls - 12.3 [1.6–22.1] pg/mL, $p < 0.001$, and positively correlated with CXCL8 and MCP-1 higher concentration, bilirubin concentration and severe liver fibrosis, as graded by liver biopsy. The mean concentration of MCP-1 in the group of PBC was 410.2 pg /mL vs healthy control 176.0 pg /mL, $p < 0.0001$. 8-isoprostane, CXCL8 and MCP-1 levels increased and glutathione levels decreased gradually with progression from mild fibrosis to cirrhosis.

### CONCLUSIONS

A major contribution of oxidant/antioxidant imbalance can provide to the progression of liver injury in PBC, which suggests the involvement of oxidative damage. Our findings confirmed an interaction between MCP-1, CXCL8 and oxidative stress in PBC. Interesting results indicate that serum 8-isoprostane might be a candidate marker for the prediction of the degree of liver fibrosis.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0725

## THE ASSOCIATION BETWEEN TYPE 2 DIABETES AND CANCER PROGNOSIS

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### BACKGROUND-AIM

Type 2 diabetes is a chronic metabolic disease. Several studies have shown that the hyperglycemia and chronic inflammation that characterize this disease could promote tumor progression and the development of metastases. In this context, our study aimed to evaluate the association between type 2 diabetes and the presence of metastases in cancer patients

### METHODS

A retrospective study included 89 cancer patients followed at the Salah Azaiez Institute from January 1 to December 31, 2022. Patients were divided into two groups: one with type 2 diabetes and the other without diabetes. The definition of diabetes was based on a fasting glucose level ≥ 126 mg/dl on two occasions or a glucose level > 2 g/l at any time of the day .Data collected included demographics, cancer type, and metastasis status. Data analysis was performed using SPSS version 22.0

### RESULTS

The mean age was 60.36 ± 11.95 years, with female predominance (gender ratio: 0.35). 55.1% were diabetic and 44.9% were non-diabetic. Median glucose was significantly higher in diabetics (9.910 mmol/L) than non-diabetics (5.365 mmol/L). Metastasis frequency was significantly higher in diabetics (42.9%) compared to non-diabetics (12.5%) ($p = 0.002$). Certain tumor locations, including breast cancer (32.7%) and endometrial cancer (8.2%), were overrepresented in the diabetic group, while for non-diabetics, it was breast cancer (45%) and cavum cancer (12.5%).

### CONCLUSIONS

Our preliminary results showed that uncontrolled type 2 diabetes is associated with an increased frequency of metastases, indicating a poor prognosis. These observations reveal that diabetic balance could play a crucial role in disease progression and underscore the importance of closely monitoring diabetic cancer patients and optimizing their glycemic control to limit tumor progression. It would be more interesting to confirm our results on a larger sample

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0726

## CORRELATION OF CA125 WITH LYMPHOCYTE-TO-MONOCYTE RATIO IN OVARIAN CANCER

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### BACKGROUND-AIM

CA 125 is the most widely used tumor marker in the management of ovarian cancer (OC). It helps assess surgical resection, chemotherapy sensitivity, and diagnose recurrences. Studies have shown that lymphocytes contribute to the elimination of tumor cells and improve chemotherapy response, while monocytes promote tumor progression. The lymphocyte/monocyte ratio (LMR) has thus been proposed as a prognostic factor in various cancers. The aim of our study was to explore the association of CA 125 with lymphocytes, monocytes, and LMR in patients with OC

### METHODS

The study involved 59 patients followed for OC at the Salah Azaiez Institute in Tunis between January 2021 and June 2024. All patients underwent a biological assessment, including a complete blood count (CBC) performed on a Sysmex XN100 automated analyzer and CA 125 measurement on a Cobas 6000 (threshold value < 30 U/ml). Statistical analysis was conducted using SPSS version 23.0, and the correlation between hematological parameters and CA 125 was assessed using the Spearman correlation coefficient.

### RESULTS

The mean age of the patients was 59.29 ± 11 years. The serum CA125 level ranged from 102.22 to 896.30 U/ml. CA125 was significantly and positively correlated with monocytes ($r = 1$, $p = 0.003$) and negatively correlated with LMR ($r = -0.370$, $p = 0.004$). CA125 was not significantly correlated with lymphocytes.

### CONCLUSIONS

Our preliminary results are in agreement with the literature, which indicates that a low LMR is strongly correlated with high histological grades of tumor and advanced FIGO stages, as well as high serum levels of CA-125, which is associated with a poor prognosis for OC. This suggests that LMR could serve as a prognostic biomarker in the follow-up of OC. It would be more interesting to complete our study on a larger sample to confirm our results.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0727

## SCREENING AND DIAGNOSIS OF BLADDER CANCER USING URINE SUPERNATANT AND SEDIMENT BASED ON THE SERS TECHNIQUE

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### BACKGROUND-AIM

Bladder cancer is a common urological malignancy that poses a serious threat to human health. Screening and diagnosis of bladder cancer is crucial to stop the deterioration of bladder function, but conventional diagnostic methods often require complicated diagnostic procedures or cause pain to patients. Therefore, label-free surface-enhanced Raman spectroscopy for the analysis of urinary biomarkers is a potential alternative method to rapidly obtain fingerprint vibrational profiles of biomolecules from urine for early screening and definitive diagnosis of bladder cancer patients.

### METHODS

Here, for urine supernatant, we designed a novel SERS substrate based on filter paper to rapidly acquire SERS spectral data from urine supernatant by stepwise assembly of Au-Ag alloy nanoshuttles and Ag nanoparticles on the surface of the filter paper for early screening of bladder cancer patients. For urine sediment, we designed a novel bowl-shaped SERS substrate to obtain the SERS signals of exfoliated cells in urine sediment, thus providing further definitive diagnosis of bladder cancer patients. Finally, the SERS signal features are automatically extracted by advanced deep learning techniques for classification.

### RESULTS

The accuracy of the analysis based on urine supernatant reached more than 98%, and based on urine sediment, bladder tumor cells can be accurately classified from other cells.

### CONCLUSIONS

Therefore, the analysis method based on urine metabolites is expected to provide early screening and definitive diagnosis of bladder cancer patients.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0728

## NEUROFILAMENT LIGHT CHAIN AS A BIOMARKER FOR NEUROLOGICAL DAMAGE IN NITROUS OXIDE ABUSE

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### BACKGROUND-AIM

In recent years, the recreational misuse of nitrous oxide has significantly increased, becoming a public health concern in many countries. Diagnosis currently relies on clinical evaluation and patient-reported consumption. The biological assessment of $N_2O$ misuse is based on biochemical markers of vitamin B12 metabolism, total homocysteine and plasma methylmalonic acid. Unfortunately, these are neither specific nor sensitive. However, plasma neurofilament light chain (NfL), a well-established biomarker for assessing axonal damage, has never been studied in this context. Our study aims to determine the utility of NfL, particularly with the recent improvements in its measurement in plasma, in the diagnosis and monitoring of neurological damage caused by nitrous oxide misuse.

### METHODS

Between September 2023 and July 2024, we collected plasma samples from 15 patients suspected of nitrous oxide intoxication, confirmed by elevated plasma total homocysteine levels > 50 µmol/L (normal values < 15 µmol/L). In parallel, plasma samples from age- and sex-matched control patients were collected. Plasma neurofilament light chain (NfL) levels were measured using electrochemiluminescence (Lumipulse G NfL Blood, Fujirebio®).

### RESULTS

We observed a significant increase in plasma NfL concentrations among $N_2O$ users (p-value = 0.001). Control patients showed mean NfL concentrations of 9.89 pg/mL (normal values < 10 pg/mL) with a 95% confidence interval (CI) of 6.28–13.49, compared to a mean of 33 pg/mL (CI 20.0–46.0) in nitrous oxide abusers. Among the 13 nitrous oxide abusers, all reported excessive consumption, reaching up to six canisters per day over extended periods (from several months to years). Most clinical presentations revealed progressive paresthesia affecting all four limbs, resulting in difficulties with walking. The patient with the most severe impairment (requiring a walker for mobility) had a plasma NfL concentration of 29.33 pg/mL.

### CONCLUSIONS

Our findings demonstrate that plasma NfL concentrations are significantly elevated in patients with nitrous oxide abuse compared to controls. These results suggest that NfL could serve as a reliable biomarker to aid in the diagnosis and monitoring of neurological damage caused by $N_2O$ intoxication.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0729

## THE ROLE OF THE LABORATORY IN DIAGNOSIS OF A YOUNG ADULT PATIENT WITH MYOPERICARDITIS AND INTERSTICIAL PNEUMONIA

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### BACKGROUND-AIM

Myopericarditis refers to the concurrent inflammation of the myocardium (heart muscle) and pericardium (the sac surrounding the heart). It represents a spectrum of inflammatory cardiac diseases where pericardial involvement is predominant.Myopericarditis occurs in individuals of all ages but is more common in young adults, with a slight male predominance. It is often associated with viral infections, systemic inflammatory processes or autoimmune conditions

### METHODS

A 17-year-old male patient presents to the emergency room with dyspnea, chest pain and flu-like symptoms for several days, fatigue, fever cough, headache, muscle pain. Laboratory tests are performed at Laboratory Networks, University Hospital Center "Mother Teresa", Tirana, Albania .For biochemical tests, the sample was collected with a gel tube and measurements were made with Alinity (troponin with the CMIA method, CRP immunoturbometry, CK and AST with the enzymatic method. Leukocytes were measured with Sysmex XN-1000 Hematology, with K3EDTA tubes.

### RESULTS

Laboratory tests showed a troponin of 3.872 ng/ml (reference <0.034 ng/mL ) in the first measurement. After 2 hours repeated and additional tests: Troponin-I 8.824ng/mL(reference <0.034 ng/mL) , WBC 23,1 K/Ul (reference 4-10.5 K/Ul), CK 497 U/L (reference 30-200 U/L) AST 42 U/L (reference 14-35 U/L )was found.The tests performed after 4 hours showed the following results.Troponin-I 9.432 ng/mL, CK 1160U/L CK-MB 27.1 ng/mL CRP 15.48 mg/dL, AST 93 U/L.After completing the chest scan, electrocardiograme changes ,echocardiography, clinical symptoms and clinical biochemical tests, the patient is diagnosed with myopericarditis and interstitial pneumonia and treatment is started. Laboratory tests performed 3 days after starting treatment refer to : Troponin-I 3.582 ng/mL CRP 6.99 mg/dL ,CK 320U/L , AST 41 U/L ,WBC 10.0K/uL In the last recheck after 7 days :Troponin-I 0.02 ng/mL , CRP 0.38 mg/dL ,CK 87U/L AST 14 U/L , WBC 9.0K/uL

### CONCLUSIONS

This case demonstrates the importance of early diagnosis in myopericarditis and interstitial pneumonia and the importance of laboratory parameters such as troponin, crp, and leukocytes in the course of the disease and its prognosis.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0730

**DIFFERENTIAL BIOMARKER PROFILES OF EARLY STAGE INTESTINAL AND DIFFUSE GASTRIC CANCER**

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**BACKGROUND-AIM**

Gastric cancer (GC) is a leading cause of cancer-related morbidity and mortality globally, with distinct subtypes —intestinal gastric cancer (IGC) and diffuse gastric cancer (DGC)—exhibiting unique pathogenic and clinical characteristics. Early detection of GC significantly improves prognosis, underscoring the importance of effective screening strategies.This study aimed to compare serum biomarker profiles between early-stage IGC and DGC patients to explore potential diagnostic distinctions.

**METHODS**

Plasma samples from 452 patients (236 IGC, 216 DGC) at initial GC diagnosis were analyzed using the GastroPanel® test to measure H. pylori IgG, Pepsinogen I (PG I), Pepsinogen II (PG II), and Gastrin-17 levels. Statistical analyses assessed differences in biomarker levels, demographic factors, and clinicopathological characteristics between the two groups.

**RESULTS**

Patients with DGC were significantly younger (mean age 55.2 vs. 64.9 years, $p < 0.001$) and exhibited an equal sex distribution, unlike the male predominance in IGC (4:1 ratio). While the prevalence of H. pylori infection and atrophic gastritis were similar across groups, intestinal metaplasia was more common in IGC patients. Biomarker analysis revealed that PG I and PG II levels were significantly elevated in IGC patients compared to DGC patients, with notable distinctions in PG II levels.

**CONCLUSIONS**

This study identifies differential biomarker profiles and demographic characteristics between early-stage IGC and DGC patients, highlighting the potential for biomarker-based strategies to enhance early detection and subtype differentiation of gastric cancer. Further research is warranted to validate these findings and optimize screening protocols.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0731

## PRESENTATION OF THE RESULTS OF RHEUMATOID FACTOR TESTING FOR THE PERIOD OF 2021 TO MID 2024 IN PUBLIC HEALTH ORGANIZATION CLINICAL HOSPITAL DR TRIFUN PANOVSKI - BITOLA, NORTH MACEDONIA

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### BACKGROUND-AIM

Rheumatoid factors (RFs) are autoantibodies targeting diverse antigenic determinants on the Fc portion of immunoglobulin G (IgG). While immunoglobulin M (IgM) is the predominant RF isotype, IgG and IgA-RF are less common. Initially identified in rheumatoid arthritis (RA) patients over 70 years ago, RFs are also found in various autoimmune and nonautoimmune conditions, including infections like hepatitis C, cryoglobulinemia, cancer and in an insignificant number of healthy individuals. RFs can appear early in the disease process, sometimes years before RA onset.

### METHODS

From 2021 to mid-2024, the Department of Medical Biochemistry at Public Health Organization Clinical Hospital Dr. Trifun Panovski in Bitola conducted 4,485 RF tests using Abbot Alinity CI. Of these, 209 tested positive (RF <30 IU/ml, reference value).

### RESULTS

Among the positives, 154 were females with a median age of 67 and 55 were males with a median age of 65. Age in females varied from 15-87 years old while in males from 28 to 86 years old. RF concentrations in females ranged from 30 to 3,250 IU/ml with a median value of 87.1 IU/ml, while in males, concentrations ranged from 30.1 to 1,790 IU/ml with a median value of 69.6 IU/ml. The overall median RF value for both genders was 82.3 IU/ml.

### CONCLUSIONS

We can conclude that there was no statistically significant age difference between males and females, however, females had higher RF concentrations.
Elevated RF levels may indicate a more severe disease course in RA, often correlating with greater joint erosions and more frequent extra-articular manifestations compared to seronegative RA.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0732

## PREVALENCE AND CO-EXPRESSION OF ANTI-NUCLEAR ANTIBODIES AND HLA-B27 GENE IN PATIENTS AT GENIUSLAB

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**BACKGROUND-AIM**

This study aimed to assess the prevalence and co-expression of Anti-Nuclear Antibodies (ANA) and the HLA-B27 gene in patients tested at GeniusLab, exploring their potential association and diagnostic relevance in autoimmune conditions.

**METHODS**

A total of 72 patients were jointly tested for ANA and HLA-B27. ANA was assessed using immunofluorescence microscopy, while HLA-B27 gene amplification was performed using the QuantStudio 7Flex Real-Time PCR system. Data were analyzed to identify prevalence and co-expression patterns.

**RESULTS**

Among the 72 patients tested, 3.1% were found to be positive for both Anti-Nuclear Antibodies (ANA) and the HLA-B27 gene, indicating a co-expression of these markers. Additionally, 15.4% of the patients tested positive for ANA but were negative for HLA-B27, while 4.4% showed positivity for HLA-B27 but tested negative for ANA.

**CONCLUSIONS**

This study demonstrated a low co-expression rate of ANA and HLA-B27, with a higher prevalence of isolated ANA positivity. The limited overlap between these markers suggests potentially independent roles in autoimmune diagnostics. Further research with larger sample sizes is recommended to better understand their combined diagnostic value.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0733

## SERUM FERRITIN AS A PROGNOSTIC MARKER OF MORTALITY IN COVID-19: ASSOCIATION WITH INFLAMMATORY RESPONSE AND DISEASE SEVERITY

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### BACKGROUND-AIM

Ferritin is an iron storing protein, but also an acute phase reactant, and a marker of inflammation. Moreover, it's a mediator of immune dysregulation in severe COVID-19 and an active player in the cytokine storm, that characterizes severe disease. During the cytokine storm in COVID-19, many inflammatory cytokines are rapidly produced, including IL-6, TNF-$\alpha$, IL-1$\beta$, IL-12, and IFN-$\gamma$, which stimulate hepatocytes, Kupffer cells, and macrophages to secrete ferritin. This study aimed to investigate the association between serum ferritin levels on admission and during hospitalization, representing the inflammatory state and hospital mortality in COVID-19 patients.

### METHODS

A total of 100 hospitalized patients with PCR proven symptomatic COVID-19 were included in the study, divided into two groups (50 with lethal outcome and 50 recovered patients). A panel of biochemical and immunological parameters were measured on admission and on the day of death/discharge: ferritin (chemiluminescence enzyme immunoassay, Access2, Beckman Coulter); C-reactive protein (CRP), lactate dehydrogenase (LDH) and procalcitonin (PCT) (AU480, Beckman Coulter). Collected data was analyzed using SPSS software, version 19.0. Continuous variables were expressed as means and standard deviations (mean ± SD).

### RESULTS

The mean age of the group with lethal outcome was significantly higher than the recovered group (65.81±12.52 years vs. 55.90±12.94 years, $p<0.05$). On admission patients with lethal outcome exhibited significantly higher serum CRP (228.34±101.19 mg/l vs 94.16±55.98 mg/l, $p<0.0001$), LDH (2237.09±1622.86 U/L vs 731.24±335.79 U/L, $p<0.05$), PCT (8.55±3.89 ng/ml vs 0.19±0.11 ng/ml, $p<0.05$) and ferritin (1595.21±1148.30 ng/ml vs 631.78±484.59 ng/ml, $p<0.05$) than those in the recovered group. Ferritin tended to increase during hospitalization in both groups (2010.85±1786.20 vs 872.74±777.49, $p<0.05$). A decrease in CRP (176.22 ± 86.66 mg/l vs 50.83 ± 28.80 mg/l, $p<0.0001$), LDH (2006.16 ± 1327.27U/L vs 695.58 ± 329.67 U/L, $p<0.0001$) and PCT (8.55±3.89 ng/ml vs 0.19±0.11 ng/ml, $p<0.05$) on the day of death/discharge was observed.

### CONCLUSIONS

Our results show that elevated serum ferritin is associated with a poor outcome in COVID-19 and can forecast the severity of the disease.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0734

## ANALYSIS OF TUMOR MARKERS IN PLEURAL EFFUSION: CONTRIBUTION TO THE EARLY DIAGNOSIS OF NEOPLASMS IN 2024

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### BACKGROUND-AIM

Pleural effusion is the abnormal accumulation of fluid in the pleural space, which can hinder lung expansion and cause respiratory symptoms. Depending on its nature, it can be classified as transudate or exudate. Pleural exudate, rich in protein and inflammatory cells, is often associated with various types of neoplasms at their onset. The aim of this study is to determine how many pleural effusions analyzed in our hospital were malignant and to identify the type of neoplasms associated with them.

### METHODS

We counted the total number of pleural fluid samples analyzed in our laboratory during the year 2024. We then filtered for cases where tumor marker tests were performed (CEA, CA 15-3, CA 19-9, and CA 125). To classify an effusion as malignant, we applied an algorithm based on the ratio of tumor marker levels in pleural fluid to the corresponding levels in the patient's serum: if the ratio > 1.2, the effusion was considered malignant. These samples were analyzed using the Alinity CI-series analyzer for biochemical parameters.

### RESULTS

A total of 175 pleural fluid samples were analyzed in our laboratory, of which 78 underwent tumor marker analysis to determine their etiology. Among these, 15 cases were classified as malignant based on our algorithm, representing 19.2% of the total cases where tumor markers were tested. Notably, only one of these 15 cases had a prior diagnosis of neoplasia, while the remaining 14 cases were diagnosed as a result of malignant pleural effusion. Among the 14 newly diagnosed cases: 64.3% (9 cases) were identified as pulmonary neoplasms, 21.4% (3 cases) were identified as ovarian neoplasms, and 14.3% (2 cases) were identified as gastrointestinal neoplasms.

### CONCLUSIONS

In 2024, we contributed to the diagnosis of 14 new neoplasms through the analysis of tumor markers in pleural effusion. Among the pleural fluid samples tested for tumor markers, 19.2% were positive according to our algorithm, underscoring the significance of analyzing this type of effusion for the early detection of neoplasms. This percentage also demonstrates the effectiveness of our algorithm, which utilizes the pleural fluid-to-serum ratio, as a reliable screening tool. Pulmonary neoplasms were the most prevalent malignancy associated with pleural effusions (64.3%), followed by ovarian neoplasm (21.4%).

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0735

## ANALYSIS OF B12 HYPERVITAMINOSIS IN HEMATOLOGY AND ONCOLOGY PATIENTS: ASSOCIATED CONDITIONS AND CLINICAL PROFILES

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### BACKGROUND-AIM

Hypervitaminosis B12 is not a direct cause of cancer, but can serve as an indirect marker for certain malignancies because of the metabolic alterations associated with these diseases. This study aimed to analyze the clinical data of patients with B12 hypervitaminosis in hematology and oncology departments, identifying associated conditions and the prevalence of various diseases within these fields.

### METHODS

Serum sample results were obtained from key medical specialties associated with neoplastic pathologies, and the clinical histories of the 92 patients with vitamin B12 levels exceeding the instrument's measurement range (>2000 pg/mL) in 2024 were reviewed. Patients were categorized based on their clinical conditions and prescribed medications.

### RESULTS

Among the 92 patients analyzed, hematological conditions were predominant, with 27 cases identified. Of these, 40.7% (11 cases) had high-grade B-cell lymphoma,18.5% (5 cases) had chronic myeloid leukemia, and 11.1% (3 cases) had monoclonal gammopathy. Regarding solid tumors, the most frequent were breast cancer in 35.7% (10 cases) of patients, and pancreatic cancer in 17.9% (5 cases). Additionally, 22.8% (21 patients) with B12 hypervitaminosis were receiving vitamin supplementation, while 17.4% (16 patients) had no clear associated diagnosis and were excluded from classification.

### CONCLUSIONS

The results suggest a potential association between B12 hypervitaminosis and various hematological conditions, especially lymphoma and chronic myeloid leukemia. A relationship was also observed with certain types of solid cancers, such as breast cancer and pancreatic cancer. These findings highlight the need for further research to better understand the underlying causes of B12 hypervitaminosis in patients without associated pathologies, which could facilitate early screening and detection of certain types of neoplasms.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0736

## NEURODEGENERATION BIOMARKERS IN CSF OF PATIENTS WITH ADULT CHRONIC HYDROCEPHALUS

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### BACKGROUND-AIM

Adult chronic hydrocephalus (ACH) is characterized by ventricular system dilation, accompanied by the clinical triad of gait disturbance, cognitive decline, and urinary incontinence, among other symptoms.
In these patients, the production and turnover of cerebrospinal fluid (CSF) are reduced, impairing the elimination of neurotoxins. This phenomenon has been proposed in recent years as a possible cause of dementia.
Decreased clearance promotes the accumulation and deposition of beta-amyloid 1-42 peptide (Aß42), among others, facilitating the formation of amyloid plaques.
This study aims to assess neurodegeneration biomarker concentrations in CSF of patients with ACH treated at our center.

### METHODS

This retrospective study analyzed the levels of Aß42, Aß42/Aß40 ratio, Tau, and pTau in patients with ACH. Measurements were performed using a chemiluminescent enzyme immunoassay (Lumipulse, Fujirebio) during 2024.
The normal cutoff values applied were:
•Aß42: >599 pg/mL
•Aß42/Aß40 ratio: >0.069
•Tau: <404 pg/mL
•pTau: <56.5 pg/mL

### RESULTS

67 patients were evaluated for dementia, of whom 14 were diagnosed with ACH.
• Pathological Aß42 concentrations were observed in 85.7%, although the Aß42/Aß40 ratio was altered in only 35.7%.
• Only 14.28% of patients also had pathological levels of Tau and pTau, leading to a concurrent diagnosis of Alzheimer's disease.

### CONCLUSIONS

A decrease in Aß42 levels is evident in most of our patients diagnosed with ACH, even when the Aß42/Aß40 ratio remains within normal values. This finding underscores the importance of reporting both absolute concentrations and ratios of amyloid biomarkers to improve the identification of patients with impaired amyloid clearance.
In patients with low Aß42 concentrations who demonstrate clinical improvement following CSF drainage, further studies are essential to confirm the diagnosis of ACH. This is particularly important as ACH represents a reversible cause of dementia, where timely identification and treatment can prevent cognitive decline and restore function.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0737

## EFFICACY OF CA125 AS A BIOMARKER IN OVARIAN CANCER

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### BACKGROUND-AIM

Ovarian cancer represents a significant health concern, ranking as the eighth most common cause of cancer-related mortality among women globally. This study aimed to evaluate the efficacy of Ca125 in the diagnosis, post-treatment follow-up, and early detection of ovarian cancer recurrence, as well as to examine the clinicoepidemiological characteristics of the affected population.

### METHODS

A retrospective study was conducted on 50 patients with ovarian cancer registered at two medical centres between September 2012 and April 2021. Clinicoepidemiological characteristics were analysed using a detailed information sheet. Ca125 levels were evaluated in relation to FIGO stage, histological type, metastases, and treatment. Data analysis was performed using IBM SPSS version 23 software.

### RESULTS

The mean age of patients was 60.88 ± 12.208 years, with 74% being postmenopausal. Epithelial ovarian cancer was the predominant histological type (94%), with serous adenocarcinoma being most prevalent (76%). The majority of cases (74.3%) were diagnosed at advanced stages (III and IV). The initial Ca125 level was ≥ 35 IU/ml in 87.24% of patients, with a mean of 1160.62 ± 2085.99 IU/ml. Ca125 levels were significantly higher in epithelial type cancers compared to stromal and sex cord tumours (p=0.001). Patients with metastases exhibited higher mean Ca125 levels than those without (p=0.033). The ROC curve analysis demonstrated that at a Ca125 threshold of 95.35 IU/ml, the sensitivity was 93% and specificity was 71% for detecting ovarian cancer metastases (AUC=0.69, p=0.033). Post-surgical Ca125 levels decreased in 78.5% of patients.

### CONCLUSIONS

This study elucidates the value of Ca125 as a biomarker in ovarian cancer management. The findings demonstrate its utility in diagnosis, particularly in differentiating between cancer types and detecting metastases. The significant decrease in Ca125 levels post-surgery further corroborates its role in monitoring treatment response.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0738

**CARCINOEMBRYONIC ANTIGEN, TRANSCELOMIC PATHWAY.**

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**BACKGROUND-AIM**

The most common etiologies of pericardial effusion are idiopathic, uremic or neoplastic. The last one, has the highest incidence, associated with lung and breast tumors, followed by hematological malignancies. In this case, we present a 61-year-old male, smoker of 1 pack of cigarettes a day since the age of 15. He was admitted at the internal medicine unit due to 1 month's duration constitutional syndrome associated with dyspnea on minimal effort, increased edema in the lower limbs, and persistent dry cough. During the examination, the patient had skin pallor, he remained eupneic at rest, with hypoventilation in the left hemithorax and no audible murmurs.

**METHODS**

During the second day of admission, he developed moderate-to-severe pericardial effusion, as well as moderate bilateral pleural effusion. Given the situation of cardiac tamponade, a pericardiocentesis was performed, extracting 900cc of serohematic fluid. The sample was sent to the laboratory urgently

**RESULTS**

The following results were obtained: 953000 Erythrocytes/µL, 1748 Leukocytes/µL, 32% Mononuclear cells, 68% Polymorphonuclear cells, 150% Other cells (per 100 leukocytes), 150 mg/dL Glucose and 4.37 mg/dL Total proteins.
After obtaining the results and due to the large number of highly fluorescent cells, a microscope observation is carried out, presenting a high number of atypical cells with a large nucleo/clitoplasm ratio. Based on this finding, the CEA tumor marker was expanded from the laboratory in pericardial fluid and plasma, obtaining a value of 531 and 80.7 ng/mL respectively.

**CONCLUSIONS**

Pericardial fluid is an important source of information that allows determining its etiology and treatment. After determining the mentioned parameters and seeing that he also had a pleural effusion secondary to a possible pulmonary neoplasia, the evaluation of the pericardial fluid/plasma CEA ratio was possible due to the proximity of the pleura to the pericardium, which allows a movement of pleural fluid and CEA marker via transcoelomic pathway towards the heart. In this case, due to the lack of pleural fluid to calculate the ratio, the determination of CEA in pericardial fluid allowed us to reinforce the suspicion of the tumor mass in the lung. Finally, pathological anatomy confirmed the presence of non-small cell lung carcinoma.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0739

## EVALUATING THE ROLE OF KYNURENINE/TRYPTOPHAN RATIO IN INDIAN INFLAMMATORY BOWEL DISEASE PATIENTS- A CASE CONTROL STUDY

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### BACKGROUND-AIM

Inflammatory bowel disease (IBD) encompasses Crohn's Disease (CD) & Ulcerative Colitis (UC) & is characterized by dysbiosis. Routinely used disease monitoring biomarkers like C-reactive protein (CRP) & fecal calprotectin (FC) have inherent limitations posing a need to assess surrogate markers. Tryptophan (T), an essential amino acid metabolizes primarily to kynurenine (K) (~90%) by the enzyme indolamine 2, 3-dioxygenase 1 (IDO1). IDO1 is expressed in macrophages, dendritic cells & intestinal epithelial cells. In IBD, IDO1 activity increases favoring kynurenine formation with a corresponding increase in the K/T ratio. Thus, we hypothesize that alteration in K/T ratio may be a surrogate marker for inflammation in IBD.
We aim to assess K/T in IBD patients & correlate the same with disease activity & fecal calprotectin.

### METHODS

We recruited 55 healthy controls, 55 with active IBD (20 CD & 35 UC) & 55 IBD patients in remission (20 CD & 35 UC) from November 2020 – March 2023. Ultra-high pressure liquid chromatography (UPLC) was used to simultaneously estimate plasma kynurenine & tryptophan levels using Ultraviolet & Fluorescence detectors respectively. In 25 patients (10 CD & 15 UC) follow-up samples were also collected with change in disease activity.

### RESULTS

Median plasma K/T ratio was significantly elevated in patients with active disease. The K/T cut-off of ≤41 with a sensitivity of 92.73% and specificity of 76.36% with an AUC of 0.9 (95% CI, 0.83-0.95, p <0.001) was used to distinguish patients in remission/healthy controls. Twenty-five patients when followed from active disease to remission showed a decrease in K/T ratio with a median (IQR) fold change of 1.5 (1.2-1.9) in 20 patients while, in the remaining 5 the ratio remained the same. K/T ratio moderately correlated (r= 0.53, p<0.001) with FC levels at a diagnostic cutoff of 250ug/g.

### CONCLUSIONS

K/T ratio with a cutoff of 41 correlated with disease activity in 82% of patients. In 80% of follow-up patients the ratio correlated remarkably, while FC correlated in 76% of patients. These findings suggest the K/T ratio alters with disease activity in IBD patients. These findings can be further assessed in a larger study cohort of IBD patients.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0740

## EFFECT OF ALPHA LIPOIC ACID ON CERTAIN PARAMETERS OF OXIDATIVE STRESS IN PATIENTS WITH PRECANCEROUS LESION OF THE CERVIX

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### BACKGROUND-AIM

Alpha lipoic acid has recently generated considerable clinical interest as biologically active agent that can be effective in relieving symptoms related to numerous diseases. ALA functions as the cofactor of oxidative decarboxylation reactions in glucose metabolism; the function that requires the disulfide group of the lipoic acid to be reduced to its dithiol form, dihydrolipoic acid. It has been proven that the same process contributes to its efficiency as antioxidant in biological systems. Limited scientific evidence shows that ALA can induce regression rates of low-grade squamous intraepithelial lesions. The main goal of this research was to investigate if 3-month supplementation with 600 mg ALA can significantly affect antioxidant status and on oxidative stress parameters of patients with LSILs contributing in such manner to significant efficiency in promoting LSIL regression.

### METHODS

The study was designed as a double-blind, randomized, placebo-controlled trial that recruited 100 participants with confirmed diagnosis of LSIL. Spectrofluorometric and spectrophotometric measurements were conducted in 96-well plates using Victor X3 plate reader. Oxidative status indicators (ORAC, TEAC, FC, FRAP, SOD, GSH, MDA) were determined in collected blood samples

### RESULTS

Obtained results showed that oxidative status biomarkers were not significantly affected by ALA supplementation. However, SOD activity was positively affected in the subgroup of patients with higher dietary antioxidant intake

### CONCLUSIONS

Larger studies are necessary to gain additional insights on the clinical significance of ALA as an antioxidant and to optimize its potential application in LSIL treatment.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0741

**TARGETING SKP2 BY TANSHINONE IIA AS A KEY LIQUID BIOPSY BIOMARKER IN OF CHEMORESISTANCE IN COLORECTAL CANCER**

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**BACKGROUND-AIM**

Fluorouracil (5-Fu)-based chemotherapy is a first-line treatment option for advanced colorectal cancer (CRC), the expressive status of Skp2 can be used as potential markers of liquid biopsy to predict the sensitivity and prognosis of CRC to combined chemotherapy. This study clarifies targeting Skp2 by Tanshinone IIA (Tan IIA) as a new key biomarker in liquid biopsy of chemotherapy sensitization.

**METHODS**

The expression of Skp2 was examined in 50 primary and 50 recurrent colorectal cancer tissues and by IHC, and Skp2 expression levels were analyzed in serum from 30 same colorectal cancer patients before and after chemotherapy resistance by qRT-PCR. Tan IIA inhibits glycolysis in CRC cells via downregulation of HK2. Targeting Skp2 is required for Tan IIA-mediated glycolysis inhibition by ubiquitination analysis and Western Blot, the stability of Skp2 protein changes in HCT116R in combination chemotherapy-resistant cells by CHX assay.

**RESULTS**

The protein expression and mRNA of Skp2 was markedly up-regulated in the tumor tissues and serum of colorectal cancer to combined chemotherapy resistance. The expression level of Skp2 in serum after chemotherapy resistance was significantly higher than before. The cell viability, soft agar and immunofluorescence results all indicate that Tan IIA can selectively reduce the tumorigenic properties of CRC cells. Tan IIA has been identified as a proposed 5-Fu sensitizer. We found that Tan IIA inhibits aerobic glycolysis in CRC cells via suppressing Skp2/Akt/HK2 signaling. Tan IIA induces ubiquitination-mediated Skp2 degradation by attenuating the interaction between USP2 and Skp2.

**CONCLUSIONS**

The shRNA library screening targeting deubiquitinating enzymes found that the stability of the Skp2 protein and thus enhance the resistance of colorectal cancer cells to 5-Fu combined with irinotecan, the results illustrated that interfering with glycolysis via promoting Skp2 ubiquitination and degradation to inhibit Akt/HK2 signaling pathway is one of the potential mechanisms of the antitumor effect of Tan IIA. This study elucidates a novel mechanism of 5-Fu resistance and offers a promising combination treatment option and a key biomarker in liquid biopsy for overcoming chemoresistance.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0742

## QUANTIFICATION OF PLACENTAL GROWTH FACTOR (PLGF) AND SOLUBLE FMS-LIKE TYROSINE KINASE-1 (SFLT-1) AS BIOMARKERS OF PREECLAMPSIA: A COMPARISON STUDY OF TWO AUTOMATED IMMUNOANALYZERS

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### BACKGROUND-AIM

Preeclampsia is a serious complication of pregnancy. Placental growth factor (PlGF) and soluble fms-like tyrosine kinase (sFlt-1) are angiogenic factors that can contribute to the prediction and diagnosis of preeclampsia. This study aimed to compare the quantification of both preeclampsia biomarkers (including the sFlt-1:PlGF ratio (PE-ratio)) with two different analytical platforms, Cobas 8000 e801 (Roche) and Atellica Solution (Siemens Healthineers) at University Hospital Antwerp.

### METHODS

44 serum samples were analyzed by Cobas and Atellica both using sandwich immunoassays with respectively electro- and chemiluminescence. These samples were also sent to an external laboratory for analysis (Cobas). Analytical performance was evaluated using CLSI-EP15 protocol, Passing-Bablok regression and Bland-Altman plots.

### RESULTS

For Atellica, the results for precision and bias of PlGF were within the desirable specification. The results for precision and bias of sFlt-1 were also mostly within desirable specification, except the precision of level 1 and the bias of level 2 of sFlt-1. For Cobas the results for precision of PlGF were within the minimal specification, but not for bias. Cobas exceeded systematically the allowed bias. The results for sFlt-1 on Cobas were similar to PlGF. Together, the ratio of Cobas was correctly preserved, meeting the optimal criteria.
For both Cobas and Atellica, the Passing Bablok regression (PE-ratio) showed a very good correlation (compared to the external laboratory). However, the results of sFLT-1 obtained by the Atellica were strongly elevated in comparison to the values obtained with the Cobas analyzer. This is not an obstacle to exclude preeclampsia (rule out). The diagnosis and prediction of preeclampsia (rule in) with Atellica, on the other hand, needs further investigation regarding a recommended rule in cut-off.

### CONCLUSIONS

Cobas 8000 e801 and Atellica Solution have similar performance. However, the precision and bias of Atellica is generally better. Both Cobas and Atellica showed a very good correlation for PE-ratio. Further research regarding a (recommended) rule in cut-off for Atellica is needed. The (recommended) cut-offs used for Cobas in practice have already been described in the literature.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0743

## ASSOCIATION BETWEEN SERUM GAMMA GLUTAMYL TRANSFERASE, DYSLIPIDEMIA AND GLYCAEMIC CONTROL IN SAUDI ADULTS

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### BACKGROUND-AIM

Hyperlipidemia, hyperglycemia and hypertension are risk factors for cardiovascular diseases. Studies have shown a strong association, of serum γ-glutamyl transferase (GGT) activity, with incident cardiovascular events independently of traditional risk factor. We aimed to investigate the association of GGT level with measures of dyslipidaemia, and dysglycemia in Saudi adults not previously diagnosed with diabetes.

### METHODS

Volunteers were recruited randomly from public healthcare centres in Jeddah. Demographic information, blood pressure (BP), and anthropometric measurements were taken. Fasting blood samples were drawn, then again following 1-hour oral glucose tolerance test. Glycated hemoglobin (HbA1C), fasting (FPG) and 1-hour plasma glucose (1-hPG), lipid profile, and GGT were measured.

### RESULTS

Complete data was found for 775 men and 603 women. Prediabetes and diabetes were detected in 14.5% and 2.6% of the population, respectively. Dyslipidaemia was detected in 656 (47%) people, with a significantly higher percentage of dysglycemia compared to those with normal lipid profiles (22.6% and 12.1%, respectively, $P < 0.001$). The mean GGT level was significantly higher in people with dyslipidaemia and/or dysglycemia compared to those with normal values ($P < 0.001$ in both cases). The prevalence of hypertriglyceridemia and high LDL-C increased with the gradual increase in GGT, even in the normal range ($p < 0.001$ in both cases).

### CONCLUSIONS

Controlling GGT in people with normoglycemia and impaired glucose tolerance can reduce the risk of hyperlipidaemia.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0744

## FIRST EVIDENCE OF TGF-BETA 1 SIGNATURE IN NEURONALLY DERIVED EXTRACELLULAR VESICLES: POTENTIAL DIAGNOSTIC AND THERAPEUTIC APPLICATIONS FOR PARKINSON'S DISEASE AND PROGRESSIVE SUPRANUCLEAR PALSY

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### BACKGROUND-AIM

Progressive supranuclear palsy (PSP) is a neurodegenerative tauopathy characterized by vertical gaze palsy, postural instability, and cognitive dysfunction, which complicates its differentiation from other parkinsonian syndromes like Parkinson's disease (PD) and Multiple System Atrophy (MSA). Accurate diagnosis is crucial as these conditions have distinct prognoses and treatment responses. This study investigates the diagnostic potential of TGFβ1 and LAP levels within neuronal-derived extracellular vesicles (NDEVs) as biomarkers for PSP.

### METHODS

We analyzed serum samples from a cohort of 33 PSP patients, 39 PD patients, 8 MSA patients, and 50 healthy controls (HC), quantifying TGFβ1 and LAP levels using Simple Plex™ and ELISA. NDEVs were isolated through an L1CAM-based immunoaffinity approach followed by protein analysis for TGFβ1 and LAP expression. The isolated EVs were characterized using tunable resistive pulse sensing (tRPS) and transmission electron microscopy (TEM), and findings were validated using a 3D model of sporadic PSP.

### RESULTS

Initial analyses of serum demonstrated no significant differences in TGFβ1/LAP levels among the groups. In contrast, NDEVs showed strong expression of active TGFβ1 and LAP, with statistically significant differences that effectively distinguished PSP from HC, PD, and MSA. Validation through 3D organoid models corroborated these trends, suggesting the utility of NDEVs enriched with TGFβ1/LAP as biomarkers for PSP.

### CONCLUSIONS

The detection of TGFβ1/LAP within NDEVs offers a promising non-invasive biomarker for differentiating PSP from PD and MSA, enhancing early diagnostic accuracy and emphasizing TGFβ1 as a potential therapeutic target. Further studies are essential to validate these findings and explore their implications for personalized treatment strategies in neurodegenerative diseases. Integrating NDEV-derived biomarker data with clinical assessments and neuroimaging could significantly improve patient management and outcomes in individuals with PSP and related disorders.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0745

## POSITIVE ANTI-CASPR2 AUTOANTIBODIES AND THEIR ROLE IN AUTOIMMUNE ENCEPHALITIS

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### BACKGROUND-AIM

Autoimmune encephalitis is a rare condition caused by autoantibodies targeting neuronal proteins, leading to nervous system dysfunction. Anti-CASPR2 antibodies, associated with voltage-gated potassium channel complexes, are linked to encephalitis, nerve hyperexcitability, or Morvan syndrome. This condition predominantly affects men around 60 years old and is associated with neoplasms, such as thymoma, in 20-40% of cases. This study presents a case of rapidly progressive autoimmune encephalitis with anti-CASPR2 antibodies, emphasizing diagnostic and therapeutic strategies.

### METHODS

A 61-year-old male exhibited a three-month history of cognitive decline, including memory loss, spatial disorientation, and difficulty recognizing acquaintances. He experienced episodes of brief disconnection, hyperventilation, tremors, and incoherent speech with subsequent amnesia. Neurological examination revealed temporal disorientation, fine tremors, stereotypic hand movements, tremulous speech, and impaired social recognition. Cognitive assessments indicated deficits, with MiniCOG 3/5 and partial impairments in praxis tasks.

### RESULTS

CSF analysis confirmed anti-CASPR2 antibodies at a titer of 1:40, with normal cell count and biochemistry. Beta-amyloid levels were preserved (944 ng/L), and Tau levels (total: 273 ng/L; phosphorylated: 54 ng/L) excluded Alzheimer's disease. Cranial CT showed punctate hypodensities in the parietal lobe white matter, indicative of inflammation, while EEG revealed diffuse low-voltage activity with mild theta slowing. Based on these findings, autoimmune encephalitis was diagnosed, and treatment with intravenous corticosteroids was initiated.

### CONCLUSIONS

Anti-CASPR2 autoimmune encephalitis presents with diverse cognitive and neurological symptoms, often mimicking conditions like viral encephalitis, Hashimoto's encephalitis, or paraneoplastic syndromes. Preserved beta-amyloid and normal Tau levels are crucial in excluding Alzheimer's disease. Diagnosis relies on identifying anti-CASPR2 antibodies alongside imaging and clinical evaluation, with potential links to tumors. Prompt diagnosis and treatment are essential for positive outcomes.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0746

## INCREASED OCULAR PLASMA CELLS INDUCE DAMAGING α-SYNUCLEIN+ MICROGLIA IN AUTOIMMUNE UVEITIS

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### BACKGROUND-AIM

Autoimmune uveitis (AIU) is an immune-inflammatory disease that can lead to blindness. However, incomplete understanding of the involved immune cell subsets and their contributions to retinal injury has hindered the development of effective AIU therapies. This study will elucidate potential mechanisms underlying the neuroimmune inflammatory response and highlights the previously unrecognized role of infiltrating PCs in AIU, offering novel therapeutic targets for this disease.

### METHODS

We mainly used scRNA-seq and flow cytometry, to collect peripheral blood mononuclear cells from the eyes of 15 normal mice and 15 EAU mice. Further validation of mouse and human samples was conducted using immunofluorescence, flow cytometry, and gene knockout mice to explore how ocular inflammatory cells affect the development of EAU and related autoimmune responses.

### RESULTS

We identified α-synuclein+ microglia as the primary subset of damaged ocular cells in the eyes of the experimental autoimmune uveitis (EAU) mouse model. Ocular-infiltrating plasma cells (PCs) were shown to express multiple inflammatory factors, particularly, TNF-α, which promoted the production of α-synuclein+ microglia. Studies of heterogeneous PC subtypes revealed that MUC1+ PCs represent the primary pathogenic subset, secreting multiple proinflammatory cytokines. Finally, the small G protein Rab1A, also expressed in the PCs of Vogt-Koyanagi-Harada (VKH) patients, was found to mediate autophagy and NF-κB expression, influencing PCs survival and inflammatory responses. Silencing or knocking down Rab1A in PCs inhibited their survival.

### CONCLUSIONS

Overall, this study identifies key inflammatory signaling pathways between ocular and immune cells, including the TNF/IL-15/IL-1α receptor axis, IL-33/ST2 axis, and IFN-γ/ISG15 axis. It demonstrates that infiltrating PCs, as a major source of inflammatory factors, exacerbate retinal damage in EAU mice by promoting the production of α-SYN+ microglial subsets and activating DCs and T cells via TNF-α, IL-1α, and IL-15 (and their receptor-ligand interactions). Furthermore, Rab1A, a small G protein, was shown to regulate PC survival and inflammatory factor secretion, offering new insights into the pathogenesis of autoimmune uveitis and potential therapeutic targets.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0747

## INTERPRETATION OF SERIAL MEASUREMENTS OF MULTIPLE TUMOR MARKERS IN THE POSTOPERATIVE PERIOD OF RADICAL CYTOREDUCTIVE SURGERY

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### BACKGROUND-AIM

Radical cytoreductive surgery (RCS) is a procedure involving the removal of peritoneal surfaces in the abdomen affected by the tumor, often accompanied by hyperthermic intraperitoneal chemotherapy (HIPEC). The laboratory can assess significant analytical changes in the concentration of tumor markers (TMs) using the reference change value (RCV). The aim of this strategy is to detect early disease activity changes, since persistent postoperative elevation or evidence of long time to normalization of MTs is associated with worse prognosis.

### METHODS

The aim of the study was to assess the RCV of CEA, CA125, CA19.9, CA72.4, and LDH in the immediate postoperative period in a group of patients with peritoneal carcinomatosis and sarcomas.

### RESULTS

All patients who underwent CRS-HIPEC were women. This group showed no significant differences in age (p=0.364), hospital stay duration (p=0.438), or presence of carcinomatosis (p=0.091) compared to the group that did not require this intervention. The behavior of TMs was not significantly different between the two groups.
The reference change values (RCV) estimated were: CA125=37.9%, CEA=50.7%, CA19.9=63.5%, CA72.4=140.9%, and LDH=16.5%.
During the first two weeks, an increase in CA125 exceeding the RCV was observed, followed by a decrease in the third week. Levels exceeding the reference threshold were only found in the presence of postoperative complications. Levels of CEA, CA72.4, and CA19.9 remained stable. The increase in LDH on the first postoperative day was not observed in subsequent days.

### CONCLUSIONS

The RCV of CA125 is the most informative for follow-up. The optimal time for its monitoring is between the second and third week postoperatively. CEA, CA72.4, and CA19.9 did not show significant variations. LDH behavior was irregular. The initial decrease in all TMs is likely due to postoperative hemodilution.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0748

**THE ROLE OF HUMAN CARTILAGE GLYCOPROTEIN IN METABOLIC BONE DISEASES.**

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**BACKGROUND-AIM**

Osteoporosis is one of the metabolic diseases of bone. According to the WHO it is most important health problems in the world and occupies the 4th place after cardiovascular pathology, oncological diseases and diabetes mellitus. Due to the complexity of the recovery process, the treatment of osteoporotic fractures is one of the important problems of modern traumatology. Diagnostic markers are needed to monitor the recovery period.
Human cartilage glycoprotein -39, which has been studied so far in inflammatory processes in the bones, may allow the development of the correct treatment regimen, reflecting the level of metabolic processes in the bone tissue.

**METHODS**

The study was performed to examine the dynamics of human cartilage glycoprotein-39 (HCgp39) in the blood serum during osteoporosis and fracture healing. The material of the study is formed by the examination results of 68 people aged 38-83. Group I - control group consisted of 14 practically healthy people, group II - 14 patients with osteoporosis, group III - 15 patients with non-osteoporotic fractures, group IV - 25 patients with osteoporotic fractures. The level of this indicator was observed in dynamics 3 times during the first month. Statistical analysis of the obtained indicator was carried out using the SPSS 22.0 package.

**RESULTS**

As a result, in the first month of the recovery period, the concentration of HCgp39 decreased in the blood serum of osteoporotic patients by 2.0 times compared to the control, but increased by 13.9% and 30.3% in patients with osteoporotic fractures and non-osteoporotic patients, respectively. This proves its role in the pathogenesis of fractures. The treatment period for patients with osteoporosis anad osteoporotic fractures did not change significantly for HCgp39 concentration, while in non-osteoporotic subjects it decreased significantly by 30.0%.

**CONCLUSIONS**

HCgp39, a regulator of bone and cartilage metabolism, is significantly increased in osteoporotic fractures. However, the decrease in HCGP39 suggests that it is an important and informative factor in the fracture healing process after treatment.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0749

## UNUSUALLY LOW RECOVERY OF THYROGLOBULIN AFTER PEG PRECIPITATION USING THE ABBOTT HIGHLY SENSITIVE THYROGLOBULIN ASSAY

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### BACKGROUND-AIM

Thyroglobulin (Tg) is a thyroid-specific biomarker marker used to monitor and manage patients with differentiated thyroid cancer (DTC) after total thyroidectomy and radioactive iodine ablation. Persistence of Tg after ablative management generally portends residual or recurrent disease, however the specificity and clinical value of Tg can be compromised by interfering antibodies, including anti-thyroglobulin antibodies (ATA) and heterophile antibodies (HA). For the former, concurrent measurement of ATA is recommended to mitigate risk associated with typically falsely undetectable Tg. For the latter, recent European clinical and laboratory expert consensus guidance recommends polyethylene glycol (PEG) precipitation as a method to identify interference. A case of suspected Tg interference causing an apparently falsely elevated Tg prompted our laboratory to investigate the utility of PEG for detecting Tg interference in a small pilot study.

### METHODS

Tg and ATA were measured on the Abbott Alinity immunoassay platform using the Abbott highly sensitive Tg (Alinity i Thyroglobulin) and ATA (Alinity i Anti-Tg) assays, respectively. PEG precipitation was performed on residual samples from patients undergoing routine Tg and ATA measurement, using 25% PEG 6000 (w/v) in PBS.

### RESULTS

Unexpectedly, in 75% of routine samples (with Tg concentrations ranging from 0.91 to 8405 ug/L), PEG precipitation led to undetectable Tg and PEG recovery of 0%. Measurable Tg recovery ranging from 8-63% was observed in 25% of samples. ATA concentrations in samples with undetectable Tg on PEG precipitation ranged from 4 – 12 IU/L and 5 – 198 IU/L in samples with measurable Tg after PEG.

### CONCLUSIONS

The mechanism underlying the abolition of Tg immunoreactivity on PEG precipitation remains to be determined. However, the extremely high proportion of samples with undetectable Tg on PEG precipitation is out of keeping with published literature on the prevalence of HA interference, which is estimated at approximately 1%. Our data suggest that PEG precipitation may not be suitable to investigate Tg interference, at least for the Abbott Alinity method.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0750

## HK3: A POTENTIAL PROGNOSTIC BIOMARKER WITH METASTASIS INHIBITION CAPABILITIES IN HEPATOCELLULAR CARCINOMA

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### BACKGROUND-AIM

Hepatocellular carcinoma (HCC) stands as one of the prevalent malignant tumors worldwide. The effectiveness of immunotherapy frequentlydepends on the intricate dynamics of immunomodulation within the tumor microenvironment (TME). The current study aims to identify prognostically relevant genes and their functional roles in HCC. This is achieved by utilizing immune scores and mutations as the basis, through the application of bioinformatics and molecular biological analysis.

### METHODS

Differentially expressed genes (DEGs) analysiswas conducted using the "clusterProfiler" package for functional enrichment. Cox regression analysis and LASSO regression analysis were performed for prognostic gene screening. Kaplan-Meier curve were further utilized to verify the prognostic value of these genes. The relationshipbetween selected genes and immune cells was analyzed using ssGSEA algorithm and TIMER. The HK3 expression in HCC cells was tested by Western blot. Additionally, wound healing and transwell assays were utilized to detect the impact of HK3 on HCCmetastasis.

### RESULTS

Patients who had higher ESTIMATE, stromal, and immune scores exhibited more favorable overall survival rates. There are 17 genes that overlap among the DEGs related to the immune-stromal-ESTIMATE scores, mutated genes, and DEGs in HCC tissues compared to normal tissues. Among the DEGs, three genes (STAB1, COL15A1 and HK3) emerged with the most profound association concerning survival outcomes. Notably, the HK3 genes displayed a pronounced correlation with immune infiltration. Concurrently, diminished expression levels of HK3 were observed in HCC tissues and upregulation of HK3 resulted in a significant reduction in HCC cell metastasis in vitro and in vivo.

### CONCLUSIONS

HK3 emerges as a novel prognostic biomarker for HCC, exerting regulatory influence over cellular proliferation, metastasis, and invasiveness. These findings indicate that HK3 holds promise as a potential candidate for treatment and prognosis of HCC.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0751

**HSA_CIRC_0008135 INHIBITS CELL FERROPTOSIS VIA SLC7A11 ACTIVATION IN NPM1-MUTATED LEUKEMIA**

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**BACKGROUND-AIM**

Acute myeloid leukemia (AML) with mutated nucleophosmin (NPM1), which displays a distinct circRNA expression profile, has been defined as a unique subgroup in the new classification of myeloid neoplasms. However, the biological roles of key circRNAs in the development of NPM1-mutated AML are currently unclear. Here, we aimed to investigate the functional and mechanistic roles of the circRNA hsa_circ_0008135 in NPM1-mutated AML.

**METHODS**

The expression of hsa_circ_0008135 was analyzed with a public database and further determined by qRT-PCR in NPM1-mutated AML samples and cell lines. The cause of upregulated hsa_circ_0008135 expression was investigated by MeRIP-seq assays. The functional role of hsa_circ_0008135 in ferroptosis and proliferation was evaluated using western blot analysis, glutathione (GSH) assay and malondialdehyde (MDA) assay, a Cell Counting Kit-8 (CCK-8) assay, a 5-ethynyl-2′-deoxyuridine (EdU) incorporation assay, flow cytometric analyses and animal studies. The action mechanism of hsa_circ_0008135 was explored through RNA fluorescence in situ hybridization, RNA pulldown and RNA immunoprecipitation assays.

**RESULTS**

hsa_circ_0008135 was highly expressed in NPM1-mutated AML. High hsa_circ_0008135 expression was induced in part by mutant NPM1 via FTO-dependent m6A modification. Importantly, hsa_circ_0008135 inhibited ferroptosis and promoted proliferation both in vitro and in vivo. Mechanistic investigations demonstrated that nuclear hsa_circ_0008135 upregulated SLC7A11 level in part via FOXS1-dependent transcriptional regulation, while cytoplasmic hsa_circ_0008135 acted as a sponge for miR-145-5p to increase SLC7A11 expression.

**CONCLUSIONS**

Taken together, our findings identify two oncogenic regulatory axes in NPM1-mutated AML centered on hsa_circ_0008135: one involving FOXS1 and SLC7A11 in the nucleus and the other involving the miR-145-5p/SLC7A11 axis in the cytoplasm. Our study indicates that hsa_circ_0008135 may be a promising therapeutic target for this distinct leukemia subtype.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0752

**INTERFERENCE OF HEMOLYSIS AND LIPEMIA ON PENTRAXIN 3 CONCENTRATION IN SERUM**

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**BACKGROUND-AIM**

Hemolysis and lipemia, the most prevalent interferences in a clinical laboratory setting, represent a significant source of laboratory errors leading to inaccurate interpretation of results. Pentraxin 3 (PTX3) is a novel promising inflammation marker linked to many different clinical conditions such as infectious diseases and sepsis, autoimmune diseases, female fertility and cancer. The aim of this study was to assess the influence of hemolysis and lipemia on PTX3 measurement in serum since there is no data available in the published literature nor within the manufacturer declarations.

**METHODS**

A total of 20 leftover patients' sera were included in the study, ten samples for lipemia and ten for hemolysis testing. To examine the effect of lipemia, SMOFlipid 200 mg/mL (Fresenius Kabi Austria GmbH, Graz, Austria) was added to serum aliquots to achieve final concentrations of 0, 100, 300, 500 and 1000 mg/dL of SMOFlipid. Furthermore, for hemolysis testing, hemolysate prepared from concentrated erythrocytes was diluted with serum samples in the following ratios 1:10, 1:25, 1:50 and 1:100. Afterwards, the concentration of free hemoglobin was measured in all of the samples using the UV-1900i spectrophotometer (Shimadzu, Kyoto, Japan). The concentration of PTX3 was analysed using the Human pentraxin 3 ELISA kit (BioVendor Group, Brno, Checz Republic) in duplicate. Mean values for each measurement pairs were used to calculate the biases from native samples. Total error (33%) was used as acceptance criterion according to the published literature.

**RESULTS**

For the different concentration of free hemoglobin (0.58, 1.08, 2.02, 4.77 g/L), the obtained biases from the native sample were 6.1, 5.9, 11.8 and 1.3%, respectively. Additionally, for different SMOFlipid concentrations (100, 300, 500, 1000 mg/dl) the obtained biases were -1.8, 0.8, -1.3 and 2.9%, respectively. All obtained biases from hemolysis and lipemia interference testing were within the acceptance criteria.

**CONCLUSIONS**

The results of this study show that hemolysis up to 5 g/L of free hemoglobin and lipemia up to 1000 mg/dL of SMOFlipid have no significant influence on PTX3 measurement in serum samples.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0753

**SERUM TGF-β1 LEVELS AND EXPRESSION IN PERIPHERAL BLOOD MONONUCLEAR CELLS (PBMCS) IN PATIENTS WITH BRAIN ANEURYSMS.**

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**BACKGROUND-AIM**

Rupture of the aneurysmal wall causes subarachnoid hemorrhage, with a mortality rate of 35-50%. The rupture of an brain aneurysm is associated with pathological changes in the arterial wall, including endothelial cell (EC) damage, fragmentation of the internal elastic lamina, degeneration of smooth muscle cells, and inflammatory responses. Transforming growth factor-beta (TGF-β), produced by ECs, leukocytes, platelets, and astrocytes, plays a crucial role in maintaining vascular integrity and regulating vascular remodeling. Studies have demonstrated increased TGF-β expression in aneurysm walls, highlighting its role in the development of brain aneurysms. Furthermore, elevated expression of TβR-I and TβR-II receptors has been associated with a higher risk of aneurysm rupture. The study aimed to evaluate serum TGF-β1 levels and its expression in peripheral blood mononuclear cells (PBMCs) in patients with intracranial aneurysms (IA) compared to healthy individuals.

**METHODS**

The study included 31 patients with intracranial aneurysms (IA), of whom 24 had unruptured aneurysms (UIA) and 7 presented with aneurysmal subarachnoid hemorrhage (ASAH). The results were compared to a control group (N=20). Serum TGF-β1 concentrations were measured using the ELISA method. Total RNA was extracted from PBMC samples from both the study and control groups. TGF-β1 expression was quantified using the QuantStudio™ 5 Real-Time PCR System with GAPDH, as the reference gene.

**RESULTS**

Serum TGF-β1 concentrations and expression in PBMCs were not significantly different between patients with IA and healthy controls. However, serum TGF-β1 levels were significantly higher in the ASAH group compared to the UIA group. No significant difference in TGF-β1 expression was observed between the two groups. The AUC of serum TGF-β1 concentration was 0.726, indicating its diagnostic utility in differentiating patients with UIA from those with ASAH.

**CONCLUSIONS**

Serum TGF-β1 concentration may serve as a diagnostically useful biomarker for the risk of brain aneurysm rupture. Further studies are needed to confirm these findings in larger patient groups, particularly in the context of clinical applicability and pharmacotherapy.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0754

## THE SIGNIFICANCE OF FECAL α1-ANTITRYPSIN DETERMINATION IN THE DIAGNOSIS OF INTESTINAL DISEASES

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### BACKGROUND-AIM

α1-antitrypsin (A1AT) is a serine protease whose presence in the stool indicates fecal protein loss, suggesting increased mucosal permeability.
To determine the most common clinical conditions where the fecal A1AT (fA1AT) were measured in our Clinical Center, the fA1AT level in them, and the correlation between fA1AT and fecal calprotectin (FC).

### METHODS

We examined 65 patients treated at the University Clinical Center of Vojvodina (Novi Sad, Serbia), from January to December 2024, who had fA1AT measurement. They were 30 (46.2%) women and 35 (53.8%) men aged 18 to 70 years. fA1AT and FC were measured by ELISA method (Alegria ELISA analyzer, ORGENTEC Diagnostika GmbH, Germany). Statistical analysis of the results was performed by calculating of mean value, standard deviation, and percentage differences, and significance was tested by Student's t-test.

### RESULTS

All requests for fA1AT determination (71.4%) came from the Clinic for Gastroenterology and Hepatology and the Clinic for Infectious Diseases (8.6%), as well as outpatient check-ups (20.0%). Elevated fA1AT were measured in 51.4% of patients, (1011.9±716.8 μg/g; diagnoses: inflammatory bowel diseases (IBD), gastrointestinal malignancies (GIM), gastroenteritis, colitis), while 48.6% had normal values (206.9±120.7 μg/g; diagnoses: irritable bowel syndrome (IBS), cholelithiasis, dyspepsia, gastroesophageal reflux). The highest fA1AT were measured in patients with IBD ($p<0.001$) and GIM ($p<0.05$), while in other diagnoses, elevation was not significant. A positive correlation between fA1AT and FC was most significant in patients with IBD ($p<0.001$) and GIM ($p<0.05$), while in patients with IBS, cholelithiasis, and dyspepsia, the correlation wasn't statistically significant.

### CONCLUSIONS

The most requests for fA1AT measurement came from the Clinic for Gastroenterology and Hepatology because that's where the diagnosis and treatment of patients with diarrhea usually takes place. Elevated values in these patients indicate that fA1AT is a reliable endogenous marker of increased mucosal permeability and protein exudation. Because of normal values in IBS patients, fA1AT could be a significant biochemical marker for the differential diagnosis of IBS and IBD.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0755

## LIPOPROTEIN - ASSOCIATED PHOSPHOLIPASE A2 (LP-PLA2) LEVELS IN PATIENTS WITH DIABETIC NEPHROPATHY

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### BACKGROUND-AIM

The prevalence of type 2 diabetes mellitus (T2DM), has rapidly risen over a decade. T2DM leads to abnormalities in protein, lipid, and glucose metabolism. One of diabetic patients' most frequent microvascular complications and a significant cause of mortality is diabetic nephropathy (DN). The most common biomarker for diagnosing DN is still microalbuminuria. By regulating blood lipid metabolism, lipoprotein-associated phospholipase A2 (Lp-PLA2) leads to vascular inflammation. It is generally accepted that Lp-PLA2 is a crucial marker of primary vessel disease. Still, its association with microvascular disease, such as DN, has not been thoroughly investigated. The study aimed to determine the levels of lipoprotein-associated phospholipase A2 (Lp-PLA2) in patients with DN and Lp-PLA2's predictive value for ESRD in patients with DN.

### METHODS

94 patients included in this cross-sectional study with DN were divided into five stages of chronic kidney disease (CKD) according to CKD-EPI: Stage II (n=20), Stage IIIa (n=29), Stage IIIb (n=38), and Stage IV (n=7). Forty-four healthy subjects were used as a control group. In addition to anamnestic data (age, gender, body weight, height, glycemic control), in the blood serum, we measured the concentration of glucose, total cholesterol, triacylglycerols, blood urea, and creatinine using standard photometric methods. Lp-PLA2 concentration/activity was measured by chemiluminescence immunoassay - CLIA. Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) serum creatinine was used to determine the GFR and CKD stages. The Ethics Committee of the Faculty of Medicine in Skopje, Republic of North Macedonia, approved this study, (No: 03-5602/11 from 16.12.2022).

### RESULTS

We found significant differences among subgroups of patients with DN divided according to CKD stage and healthy subjects regarding age, body mass index, duration of disease, blood glucose, glycated hemoglobin, total cholesterol, triacylglycerols, blood urea, serum creatinine, GFR, and Lp-PLA2. A significant negative correlation was found between Lp-PLA2 and GFR. ROC analysis showed that Lp-PLA2 has a positive predictive value of 98.3% in patients with DN. Lp-PLA2 gradually increased in stages of DN.

### CONCLUSIONS

Lp-PLA2 should be considered a potential predictive biomarker for the progression of DN to ESRD.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0756

**INFLUENCE COMBINED ANTIVIRAL THERAPY ON ACTIVITY ALANINE AMINOTRANSFERASE IN PATIENTS WITH CHRONIC HEPATITIS C (CHC)**

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**BACKGROUND-AIM**

The primary goal of antiviral treatment is virologic cure implying eradication of viral infection and consequently prevention of disease progression with possible liver-related complications.
Until recently, "standard" antiviral therapy of CHC consisted of a combination of Pegilated Interferon Alpha (IFN$\alpha$) plus Ribavirin (RBV).
The beneficial impact of the therapy is evident in the decrease of Alanine Aminotransferases (ALT) levels to normal values (Biochemical Response-BR), and reduction of histological liver activity with lessening of liver fibrosis (histological response).
Measurement of serum aminotranseferases activity before, during and after therapy is of particular interest with regard to antiviral treatment, because these enzymes are associated with the damage to liver parenchyma characterized by the amount of hepatocyte necrosis.
The aim of this study was to evaluate the incidence and predictive factors of normalization of serum ALT after antiviral treatment in CHC patients.

**METHODS**

This retrospective study included clinical and laboratory data of 310 patients with CHC treated in the Clinic for Infectious and Tropical Diseases, Clinical Centre of Serbia, Belgrade, from January 1, 2008 to December 31, 2012.

**RESULTS**

The binary logistic regression revealed several significant variables for normalization of ALT: age older than 40, viral genotype 1, liver cirrhosis and high viral RNA as negative variables, and genotype 3 as the positive variable. Age over 40 was the most significant negative variable ($P < 0.0005$; OR - 0.331; 0.122 - 0.454) in multivariate regression analyses.

**CONCLUSIONS**

This study confirms that successful antiviral treatment leads to normalizing of ALT activity in the majority of patients, which can be used as a positive marker for prediction of viral elimination. It also reflects diminishing liver necrosis as the most essential benefit of treatment for CHC. Among other characteristics of patients for this opportunity, younger age is the most important predictive factor.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0757

## FUBP3 AS A POSSIBLE CANDIDATE BIOMARKER FOR DIAGNOSIS OF OSTEOPOROSIS

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### BACKGROUND-AIM

Osteoporosis (OP) is a complex disease marked by low bone mineral density (BMD), which increases the risk of fractures. Despite advances, current diagnostic and treatment strategies are often insufficient to address early detection and individualized care. Genome-wide association studies (GWAS) have provided valuable insights, identifying numerous genetic loci associated with BMD. However, many of these candidate genes, including Far Upstream Element Binding Protein 3 (FUBP3), remain poorly characterized in the context of bone health.

### METHODS

This study focused on determining the role of FUBP3, a transcriptional regulator, in bone metabolism and its potential as a diagnostic biomarker for OP. We analyzed bone samples from 43 individuals divided into osteoporotic, osteoarthritic, and healthy control groups. Using RT-qPCR, we observed a significant downregulation of FUBP3 expression in osteoporotic bone tissue compared to controls.

### RESULTS

Diagnostic performance was evaluated using receiver operating characteristic (ROC) curve analysis, performed with the pROC package in R. FUBP3 in combination with BMD exhibited a high diagnostic accuracy with an AUC of 0.843, outperforming BMD alone (AUC = 0.829), which remains the clinical standard for OP diagnosis.

### CONCLUSIONS

Our findings suggest that FUBP3 is not only implicated in bone physiology but could also serve as an innovative biomarker for early-stage OP detection and risk assessment. If future studies confirm that its expression in bone correlates with circulating levels, FUBP3 may offer a non-invasive means of improving OP diagnostics and patient stratification. These results underline the importance of further functional studies on FUBP3 and its role in bone health.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0758

**CLINICAL VALUE OF CREATINE KINASE IN THE CONTEXT OF COMPARTMENT SYNDROME AND RHABDOMYOLYSIS.**

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**BACKGROUND-AIM**

Compartment syndrome occurs when pressure within a muscle compartment increases to dangerous levels, compromising blood circulation and causing ischemia in the affected tissues due to the inability of the fascia, the membrane surrounding the muscle compartments, to expand to compensate for this pressure. This condition can trigger rhabdomyolysis, a pathological process in which damage to muscle fibers causes the release of intracellular substances, such as creatine kinase (CK), into the bloodstream.

**METHODS**

An 82-year-old woman came to the emergency room with pain, coldness and edema in the left lower extremity. She underwent thrombectomy during which a prophylactic fasciotomy was performed due to suspicion of compartment syndrome in the extremity. After the first 24 hours after the operation, the patient presented dark urine, which led to suspicion of muscle damage and CK was measured, obtaining a value of 53,000 U/L. In this context of rhabdomyolysis, the patient presented acute renal failure (ARF) as a consequence of the high concentration of CK in addition to the finding of calcification in the left renal artery, which worsened the ARF.

**RESULTS**

The patient was admitted to hospital for 10 days. During admission, CK, lactate dehydrogenase, creatinine and ion levels were altered, the first two due to rhabdomyolysis and the second two due to renal failure. Fluid therapy and diuretic drugs were administered to increase renal flow until CK and creatinine levels returned to normal.

**CONCLUSIONS**

The CK parameter is the most specific in the monitoring of rhabdomyolysis since its elevation in blood is mainly derived from damage to skeletal muscle. In this case, it is the triggering finding for an adequate diagnosis and subsequent treatment of the patient.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0759

## CHOSEN ENDOCANNABINOIDS AND NEUROPEPTIDES ON BLOOD PRESSURE REGULATORY IN CHILDREN AND ADOLESCENTS

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### BACKGROUND-AIM

Many systems are involved in the regulation of blood pressure (BP). The most important and known is the renin-angiotensin-aldosterone system (RAAS). RAAS can be divided into two opposite pathways. The classical pathway (CP) represented by angiotensin II (ang II) has a strong hypertensive effect. The alternative pathway (AP) is represented by angiotensin 1-7 (ang 1-7) have a hypotensive effect. It is supposed, that also the endocannabinoid system (ECS) represented by 2-arachidonylloglicerol (2-AG) and some neuropeptides (NP) like nesfatin-1 (nes-1) and galanin (gal) affect the BP. Therefore a relation of chosen ECS and NP with BP in populations of obese and normal weight children and adolescents with primary arterial hypertension (PAH) was analyzed.

### METHODS

We have studied 28 lean PAH patients (15.05 ± 2.98 y/o), 17 obese PAH patients (13.95 ± 3.79 y/o), and 29 obese patients (13,50 ± 3.39 y/o). 52 healthy age-matched children were control group (12.95 ± 3.69 y/o). PAH was diagnosed based on the Pediatric Hypertension Guidelines 2016 developed by the European Society of Hypertension (ESH). Obesity was defined as body mass over 97. Centile. All compounds were measured by ELISA in fasting EDTA plasma.

### RESULTS

Ang II, ang 1-7 and 2-AG didn't show differences. Nes-1 concentrations were significantly lower in obese PAH patients ($p=0.005$) and obese patients ($p=0.022$) than in the control. Nes-1 concentration correlated ($p<0.001$) with ang II ($r=0.638$) and ang 1-7 ($r=0.477$). Linear regression analysis shows Nes-1 and ang II have $r^2=0.584$ in PAH group and $r^2=0.545$ in obese PAH patients. Nes-1 and ang 1-7 have $r^2=0.523$ in PAH group. Gal concentration were significantly lower in obese PAH patients ($p=0.045$) and obese patients ($p=0.035$) as compared to control. Nes-1 concentration correlated ($p<0.001$) with ang II ($r=0.833$) and ang 1-7 ($r=0.558$). Linear regression analysis shows gal and ang II have $r^2=0.711$ in PAH group and $r^2=0.762$ in obese PAH patients. Gal and ang 1-7 have $r^2=0.584$ in PAH group and $r^2=0.622$ in obese PAH.

### CONCLUSIONS

Lower concentrations of NPs in patients with obesity and PAH may indicate the impact NPs on the development a PAH in obese patients. High correlation NPs with ang II indicate a interaction between NPs and CP of RAAS.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0760

## GLYCOSYLATED HEMOGLOBIN AS A MARKER OF DIABETES CONTROL: MODERN APPROACHES TO ANALYSIS

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### BACKGROUND-AIM

The purpose of this study is to assess the level of glycosylated hemoglobin (HbA1c) as a predictor of the risk of diabetes complications for different age categories and sex to determine the patterns and evaluate risk factors for prevention of serious complications of diabetes.

### METHODS

According to the Ministry of Health of the Kyrgyz Republic, as part of the Results-Oriented Project (ROP), laboratory equipment has been purchased since 2020 - Mindray analyzers for the determination of glycosylated hemoglobin for 52 healthcare organizations. The Endocrinological Center of the Kyrgyz Republic installed Mindray analyzers (BS-240 and BS-430), where an enzymatic-chemical analysis method is used to determine glycosylated hemoglobin.
The NGSP method was used to calculate the HbA1c level.
The study included all patients who have been registered at our center with a confirmed diagnosis of diabetes mellitus since 2000. The study did not include children, pregnant and lactating women.

### RESULTS

During the period from 2022 to 2024, 11655 patients were examined for HbA1c at the Endocrinology Center. Of all the examined patients, 2116 patients (18.1%) had a glycosylated hemoglobin level of <7.0%, which indicates that there is no risk of developing macrovascular complications. In 9556 patients (81.9%), the glycosylated hemoglobin level was >7.0%, which indicates a high risk of developing macrovascular diseases and may lead to a deterioration in the quality of life of these patients. Among all patients, females' group (65.5%) was significantly larger than males (34.5%).

### CONCLUSIONS

Based on the results of the analysis, the following conclusions can be drawn:
Most of the patients with diabetes still have high levels of HbA1c despite of being treated during long period of time.
Among all the examined people, middle-aged patients were found to be predominant among all age groups who have high levels of glycated hemoglobin. Interestingly, that the senile-aged category has shown the lowest levels of HbA1c, lower than 9%.
Males are at higher risk of having diabetes complications than females, considering that males' group was relatively smaller.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0761

## THE DETECTIVE VALUE OF XPERT BLADDER CANCER IN NON-MUSCLE-INVASIVE BLADDER CANCER

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### BACKGROUND-AIM

Bladder cancer ranks as the fourth most common cancer among men. Most cases are non-muscle-invasive, either low-grade superficial or high-grade tumors. Recurrence is common, and neglected superficial tumors may progress to invasive cancers. Surveillance methods include ultrasonography, cystoscopy, and cytology. Ultrasonography is non-invasive but may miss small lesions. Cystoscopy, the gold standard, is invasive. Cytology is minimally invasive but ineffective for low-grade tumors. The Bladder Xpert kit (Cepheid Inc.) is an mRNA-based assay detecting five oncogenes (ABL1, CRH, IGF2, UPK1B, ANXA10) via RT-PCR, analyzed using linear discriminant analysis (LDA).

### METHODS

Twenty-nine patients diagnosed with urothelial cancer undergoing TURBT provided a 50 mL fresh urine sample one day before surgery. Samples were treated with the Xpert Urine Transport Reagent Kit and analyzed using the GeneXpert System. LDA >0.5 indicated a positive result. TURBT specimens were examined by a single uro-pathologist.

### RESULTS

The Bladder Xpert kit showed a positive predictive value of 91.66%, sensitivity of 61%, and specificity of 80%. False negatives occurred in Ta low-grade superficial TCC cases. In five low-grade tumor cases, Bladder Xpert was positive while cytology was negative. Only one case showed suspicious cytology with a negative Bladder Xpert result.

### CONCLUSIONS

The Bladder Xpert test is a simple, RNA-based, non-invasive tool for detecting urothelial malignancies, especially high-grade tumors, though it missed small, superficial low-grade tumors. Incorporating it into bladder cancer surveillance could reduce cystoscopy frequency and enhance patient care. Larger cohort studies are needed to validate its utility.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0762

## ANGIOGENIC MARKERS FOR THE SCREENING AND PREVENTION OF PREECLAMPSIA

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### BACKGROUND-AIM

Preeclampsia is one of the leading causes of maternal and fetal morbidity and mortality. Early screening of patients at risk for developing preeclampsia enables the initiation of aspirin treatment in women at risk, thereby reducing its incidence and the associated complications.
Retrospectively evaluate the predictive capacity and prevention of a sequential screening for preeclampsia using the angiogenic marker (PLGF).

### METHODS

A retrospective cohort analytical study was carried out focused on the screening of first trimester for the detection of preeclampsia. Pregnant women who were seen in prenatal screening consultation between January 2023 and June 2024 were included. 2,525 pregnant patients were included after an initial evaluation of the risk of preeclampsia based on maternal history, blood pressure, mean uterine artery pulsatility index (UtAPI) and Pregnancy associated plasma protein-A (PAPP-A). 335 patients were specifically screened for preeclampsia by determining PlGF with the Elecsys PlGF reagent by cobas 601 autoanalyzer. For the statistical analysis of preeclampsia screening, the Chi Square test was used to evaluate the relationship between qualitative variables, establishing a level of statistical significance of $p<0.05$.

### RESULTS

Patients were analyzed (335) classifying them into two groups: 127 patients (38%) are not at risk, while 208 patients (62%) present some type of risk of developing preeclampsia (42% were at risk for late-onset preeclampsia, 31% for early-onset, and 27% both combined risk). Stadistic data analysis revealed a significant association between preeclampsia, elevated BMI, and diabetes. We also have observed that lower levels of PAPP-A, higher UtAPI, and elevated mean arterial pressure are associated with an increased risk of preeclampsia.

### CONCLUSIONS

Early preeclampsia screening allows for the identification of a greater number of patients at high risk of developing preeclampsia, who otherwise might not have been detected using other criteria. This facilitates the possibility of offering preventive treatment with aspirin (ASA), which has demonstrated significant benefits for pregnant women. Its administration during the early weeks of gestation in high-risk patients has been shown to reduce perinatal incidences to levels similar to those of women without this risk.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0763

**PREDICTING RISK OF TYPE 2 DIABETES – NEW UNCONVENTIONAL LIPID RATIOS**

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**BACKGROUND-AIM**

The aim of the study was to determine new lipid ratios: CholIndex, Castelli risk index I (CRI) and Castelli risk index II (CRII) and implication of these indices in predicting risk of type 2 diabetes mellitus (DM).

**METHODS**

Observational cross-sectional study was on 419 patients, of which 238 DM and 181 control patients. CholIndex was calculated as LDL-HDL (TG<400 mg/dL); LDL-HDL + 1/5 of TG (TG ≥ 400 mg/dL); CRI as TC/HDL and CRII as LDL/HDL. Cut-off limits: CholIndex <2.07; CRI <3; CRII <3.3.

**RESULTS**

Our study observed an increase of CholIndex ($p<0.05$), CRI and CRII ($p<0.0001$) at DM patients vs. control. Linear regression equations showed a positive correlation of CholIndex with CRI and CRII ($p<0.0001$) at DM patients. Diagnostic evaluation for CRI: 62.77% assay accuracy; 82.77% sensitivity; 36.46% specificity; 56.80% disease prevalence and relative risk = 1.3. For CRII: 50.6% assay accuracy; 25.63% sensitivity; 83.43% specificity; 56.80% disease prevalence and relative risk = 2.06. Multivariate logistic regression analysis showed that patients with high CRI are 2.75 times more likely to have DM [OR 2.75, 95% CI: 1.75-4.33; $p<0.0001$]. Also, patients with high risk CRII have 1.73 times to develop DM [OR 1.73, 95% CI: 1.06-2.82; $p<0.005$]. At DM patients, even if cholesterol and LDL-cholesterol were in reference range, risk indices were high.

**CONCLUSIONS**

There is a certain correlation between CholIndex, CRI, CRII and DM, the higher the risk the more likely it is to develop DM. So, studied indices could be useful markers for DM assessment.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0764

## THE IMPORTANT ROLE OF PHOSPHATIDYLSERINE, ADAM17, TNF-α, AND SOLUBLE MER ON EFFEROCYTOSIS ACTIVITY IN CENTRAL OBESITY

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**BACKGROUND-AIM**

Obesity is expected to hinder efferocytosis due to ADAM17-mediated cleavage of the MER tyrosine kinase receptor, producing soluble MER (sMER) that disrupts MERTK binding to cell death markers. However, the intracellular efferocytosis pathway in central obesity remains elusive, particularly the role of low-grade chronic inflammation in its initiation and identification of binding signals that disrupt efferocytosis. We investigate the efferocytosis signaling pathway in men with central obesity and its relationship with inflammation, cell death, and related processes.

**METHODS**

A cross-sectional study was conducted, and clinical data and blood samples were collected from 56 men with central obesity (obese group) and 29 nonobese individuals (control group). Clinical evaluations and predefined biochemical screening tests were performed. The efferocytosis signaling pathway was investigated by measuring phosphatidylserine (PS), ADAM17, TNF-α, and sMER.

**RESULTS**

Metabolic syndrome was detected in more than half of the participants in the obese group according to the predefined tests. Mean levels of PS, TNF-α, and sMER were higher in the obese group but not significantly different from those of the control group. Further analysis based on waist circumference (WC) ranges in the obese group revealed a significant increase in PS and sMER levels between the control group and the obese group with WC greater than 120 cm. ADAM17 levels were significantly higher in the obese group than in the control group. PS was positively correlated with WC and ADAM17. ADAM17 was positively correlated with TNF-α and sMER, indicating impaired efferocytosis.

**CONCLUSIONS**

Central obesity appeared to cause a disturbance in efferocytosis that began with cell damage and death, along with an enlargement of the WC and an ongoing inflammatory response. Efferocytosis was disrupted by proinflammatory cytokine regulators, which induced the production of sMER and interfered with the efferocytosis process.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0765

**THE ROLE OF UCH-L1 AND GFAP IN EMERGENCY CLINICAL PRACTICE**

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**BACKGROUND-AIM**

Traumatic brain injury (TBI) is the most common neurological disorder worldwide, contributing to more death and disability than any other traumatic injury. Advancements in biomarker research have the potential to transform the assessment and care of TBI patients, as opposed to current diagnostic tools for TBI which have several limitations, most notably unnecessary exposure to radiation.

**METHODS**

The study involved patients admitted to the Emergency Department of University Clinical Hospital Mostar from December 2023 to October 2024 with suspicion of brain injury. All patients underwent Glasgow Coma Scale (GSC) and head CT scan. The concentrations of glial fibrillary acidic protein (GFAP) and ubiquitin carboxyl-terminal hydrolase L1 (UCH-L1) in the serum samples were determined by the chemiluminescent microparticle immunoassays (CMIA) method on Alinity ci analyzer. The measured results of GFAP ≥ 35.0 ng/L and/or UCH-L1 ≥ 400.0 ng/L indicate a positive result due to value being higher than cut-off. Data analysis was performed using MedCalc® Statistical Software version 22.006 (MedCalc Software Ltd, Ostend, Belgium).

**RESULTS**

The study included 77 participants, of whom 19 were female and 58 were male. The respective median age was 51 (18 - 89) years of total number participant. All study participants had a GCS of 14 or 15. The median concentration of GFAP was 102.7 (24.9 – 294.2) ng/L, and for UCH-L1 was 364.8 (158.8 – 669.7) ng/L. Furthermore, the median concentration of UCH-L1 in patients with GSC 15 (n=61) was 384.7 (144.8 - 677.5) ng/L, and the concentration of GFAP in them was 84.3 (24.9 - 199.3) ng/L, while the concentration of UCH -L1 in patients with GSC 14 (n=16) was 366.3 (222.8 - 674.3) ng/L and for GFAP 260.3 (26.8 - 864.3) ng/L. Of the total number of participants, 70% had a positive TBI and only 33% had a positive head CT scan. All patients with negative TBI had a negative head CT scan.

**CONCLUSIONS**

This study confirmed a good negative predictive value of TBI in clinical practice, but future research and improvement of existing laboratory tests are needed for the use of UCH-L1 and GFAP in clinical practice for rational head CT diagnostic.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0766

## EVALUATION OF THE SNIBE PIVKA-II ABEI ASSAY

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### BACKGROUND-AIM

PIVKA-II (Protein Induced by Vitamin K Absence or Antagonist-II) is a biomarker used for diagnosing hepatocellular carcinoma (HCC), offering superior performance to AFP in detecting recurrent HCC with negative preoperative PIVKA-II values. This study evaluated the analytical performance of the SNIBE PIVKA-II ABEI assay and its comparability with established methods.

### METHODS

Verification was performed in Brussels using the Maglumi X6 analyzer, following CLSI EP15-A3 guidelines. Snibe-provided QC materials (L1 and L2) were analyzed in duplicate twice daily for five consecutive days. Coefficients of variation (CV) for within-run, between-run, and within-laboratory precision (imprecision) and bias were calculated and compared to manufacturer criteria (L1: within-run < 4.20%, between-run < 1.17%, within-laboratory < 6.57%; L2: within-run < 2.79%, between-run < 1.57%, within-laboratory < 4.55%).
Method comparisons were conducted in both Brussels and Belgrade. In Brussels, 31 patient samples were analyzed on the Maglumi X6 and compared with the Fujirebio Lumipulse assay. In Belgrade, 55 patient samples were tested on the Maglumi 4000 and compared with the Roche Cobas assay. Bland-Altman and Passing-Bablok regression analyses were used to assess comparability. Statistical analysis was performed using MedCalc.

### RESULTS

Within-run CVs for L1 and L2 were 17.19% and 3.65%, between-run CVs 1.47% and 2.14%, and within-laboratory CVs 15.45% and 3.90%. Biases were 13.51% for L1 and 0.53% for L2.
In Brussels, Maglumi X6 and Fujirebio Lumipulse results showed excellent agreement (r = 0.975). Passing-Bablok regression indicated a constant difference, and Bland-Altman analysis revealed an absolute bias of -22.35 and relative bias of -33.67%.
In Belgrade, Maglumi 4000 and Roche Cobas results showed good agreement (r = 0.794). Passing-Bablok regression showed no significant differences, and Bland-Altman analysis showed an absolute bias of -1060.78 and relative bias of -21.79%.

### CONCLUSIONS

The SNIBE PIVKA-II assay demonstrated acceptable analytical performance and strong comparability with established platforms, supporting its clinical utility in HCC diagnosis and monitoring.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0767

## GLUCOSE TRANSPORTER TYPE 1 (GLUT1) DEFICIENCY SYNDROME: CASE REPORT AND DIAGNOSTIC INSIGHTS

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### BACKGROUND-AIM

GLUT1 Deficiency Syndrome is a neurological disorder caused by mutations in the SLC2A1 gene, which follows an autosomal dominant inheritance pattern. The condition leads to impaired glucose transport in the brain, with a highly variable clinical presentation that may include early-onset epilepsy, psychomotor delay, secondary microcephaly, intellectual disability of varying severity, movement abnormalities, and, in rare cases, asymptomatic adults.

### METHODS

Diagnosis is primarily based on a blood glucose concentration below 2.5 mmol/L and a CSF-to-blood glucose ratio of less than 0.50, confirmed by identifying a pathogenic variant in the SLC2A1 gene. MetaGLUT1 test has become a first-line, non-invasive diagnostic tool.: it quantifies the expression of the GLUT1 transporter on erythrocyte membranes via a flow cytometry-based assay. A Receptor Binding Domain (RBD) biomarker, conjugated with Green Fluorescent Protein (GFP), is used to detect GLUT1 levels, with results analyzed using the METAFORA v3.0 software algorithm. The test demonstrates a sensitivity of 80% and a specificity of 99%.Patients under 3 months of age and those with sickle cell disease (which can cause false negatives) are excluded from the test.

### RESULTS

We present a case of a child of Ivorian and Franco-Senegalese descent who presented with seizure-free epilepsy under dual therapy. The patient tested positive for GLUT1 deficiency using the MetaGLUT1 test on two occasions, with a reduction in GLUT1 transporter expression on erythrocytes quantified at -28% and -33%, both exceeding the threshold of -25% for a positive result. However, the blood glucose-to-glycemia ratio was normal at 0.65 when lumbar puncture and genetic testing did not reveal any pathogenic variant in the SLC2A1 gene. These factors raised suspicion of a false-positive result.
The patient did not have sickle cell disease or evidence of G6PD or PK deficiency. Further investigation revealed a collapsed haptoglobin concentration, suggesting significant hemolysis. A potential red blood cell membrane pathology, such as elliptocytosis, is currently under investigation, which may explain the false-positive MetaGLUT1 results.

### CONCLUSIONS

Any abnormality in red blood cell physiology—interfere with the MetaGLUT1 test, leading to false positives.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0768

## SEROLOGICAL EVALUATION OF WT1 FOR DIAGNOSIS OF OVARIAN CANCER

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### BACKGROUND-AIM

WT1 gene expression has prognostic importance in ovarian cancer and it is detected by immunohistochemistry or qPCR. Here, we evaluated the serum level of WT1 in ovarian cancer (OC) patients.

### METHODS

We collected pre-therapy serum samples from 30 ovarian cancer patients and 11 benign ovarian cyst patients, the mean age being 49.5 years (21–70). The serum levels of CA 125 and WT1 were measured (ELISA). A cutoff of 3.35 ng/mL was set using ROC curve analysis at 64% sensitivity and 63% specificity with an AUC of 0.61.

### RESULTS

High and low WT1 were seen in 19/30 (63.3%) and 11 (36.6%) cancer cases, respectively. Known staging is available in 27 out of 30 cases. Metastases were seen in 2 cases, one from breast and the other from cecum. One case of borderline sero-mucinous tumor was seen. It was found that WT1 increases with stage in ovary cancer patients (Table 1). Stages I & II of ovarian cancer cases showed low WT1 values, while stages III and IV cases showed positive values. WT1 was higher in the higher age group (p = 0.55) (table 2).
WT1 was more specific in detecting OC than CA125, p-0.0098. CA 125 has sensitivity and specificity of 70% and 50%, respectively, whereas the same with WT1 is 62% and 95% (Table 3).

### CONCLUSIONS

Serum WT1 level may be a better biomarker in the diagnosis of OC. This is the first pilot study on ovarian cancer that studies the serum level of WT1 as a diagnostic biomarker.
Key words: WT1, CA 125, ovarian cancer

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0769

## SEROLOGICAL EVALUATION OF WT1 FOR DIAGNOSIS & PROGNOSIS OF OVARIAN CANCER

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[2]*Serological evaluation of WT1 for diagnosis & prognosis of ovarian cancer*

### BACKGROUND-AIM

WT1 gene expression has prognostic importance in ovarian cancer and it is detected by immunohistochemistry or qPCR. Here, we evaluated the serum level of WT1 in ovarian cancer (OC) patients.

### METHODS

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### RESULTS

High and low WT1 were seen in 19/30 (63.3%) and 11 (36.6%) cancer cases, respectively. Known staging is available in 27 out of 30 cases. Metastases were seen in 2 cases, one from breast and the other from cecum. One case of borderline sero-mucinous tumor was seen. It was found that WT1 increases with stage in ovary cancer patients (Table 1). Stages I & II of ovarian cancer cases showed low WT1 values, while stages III and IV cases showed positive values. WT1 was higher in the higher age group ($p = 0.55$) (table 2).
WT1 was more specific in detecting OC than CA125, p-0.0098. CA 125 has sensitivity and specificity of 70% and 50%, respectively, whereas the same with WT1 is 62% and 95% (Table 3).

### CONCLUSIONS

Serum WT1 level may be a better biomarker in the diagnosis of OC. This is the first pilot study on ovarian cancer that studies the serum level of WT1 as a diagnostic biomarker.
Key words: WT1, CA 125, ovarian cancer

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0770

**ASSESSMENT OF IMAGING AND COGNITIVE IMPAIRMENT TESTS IN PATIENTS WITH SUSPECTED ALZHEIMER'S DISEASE: A RETROSPECTIVE STUDY.**

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**BACKGROUND-AIM**

Alzheimer's disease(AD) is a neurodegenerative disorder characterized by the deposition of amyloid-β42(Aβ)and neurofibrillary TAU tangles. AD patients present lower concentrations of Aβ and higher concentrations of total TAU(TAUt) and phosphorylated TAU(pTAU)proteins compared to healthy controls. Diagnosis is based on the quantification of these biomarkers in cerebrospinal fluid(CSF),imaging tests and cognitive impairment evaluation.
The aim of this study is to evaluate the differences in magnetic resonance imaging(RMI),Minimental Test(MT) and Reisberg Global Deterioration Scale(GDS)between AD, prodromal AD(pAD) and discarded AD(dAD) patients.

**METHODS**

A retrospective study of patients with suspected AD in 2023 in our health area was carried out by the quantification of TAUt,pTAU and Aβ in CSFsamples.
Diagnosis was carried out using the National Institute on Aging and Alzheimer's Association(NIA-AA)criteria and patients were classified as AD,pAD and dAD patients.They were further evaluated using GDS,MT and MRI(presence/absence of hippocampal atrophy).
The determination of light chain neurofilaments(NfL) was requested to assess neurodegeneration in patients whose biomarker levels were close to the limits of normality.

**RESULTS**

66 patients with a mean age of 65.3±6.5years old were studied;52.5%male and 48.5%female. The values obtained were TAUt=223.51±105.37pg/mL, pTAU=21.64±12.90pg/mL and Aβ=995.59±619.84pg/mL. In 31 patients determination of NfL was requested and 9 presented values indicative of neurodegeneration.
Using the NIA-AA criteria,22(33.3%) of the patients were diagnosed with AD,16(24.2%) pAD,27(40.9%)were ruled out for AD, and one was indeterminated.
Comparison of MRI,MT and GDS results between the above-described groups showed that ADpatients presented significantly lower values of MT when compared with dAD patients($p=0.042$).GDS levels were, moreover, significantly increased in AD patients in comparison with both pAD($p<0.001$) and dAD($p=0.001$)patients. In reference to MRI no statistically significant differences were found.

**CONCLUSIONS**

GDS levels were increased in AD compared with both pAD and dAD patients,MT presented lower values in AD compared with dAD patients. MRI didn't show differences between groups.
NfL determination allowed us to assess whether neurodegeneration was present.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0771

## SERUM CALPROTECTIN LEVELS MEASURED BY CHEMILUMINESCENCE: COMPARISON WITH ELISA VALUES AND ROLE AS AN INFLAMMATION BIOMARKER IN RHEUMATOID AND PSORIATIC ARTHRITIS

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### BACKGROUND-AIM

Calprotectin (CLP) is a heterodimeric protein, secreted mainly by neutrophils, traditionally used as a fecal marker of inflammation (fCLP) in the gastrointestinal tract. Similarly, circulating calprotectin (cCLP) levels, mainly determined by ELISA methods, was found elevated in rheumatoid (RA) and psoriatic (PsA) arthritis patients correlating with disease activity. Recently, a chemiluminescence immunoassay (CLIA) for fCLP was successfully adapted to measure cCLP in serum samples. Our objective was to compare cCLP levels measured by CLIA and ELISA methods and to assess CLIA cCLP levels as an inflammatory and activity marker in RA and PsA patients.

### METHODS

Eighty-eight subjects were studied: 1) RA patients treated with disease modifying drugs (DMARD) with low or no activity by common clinical indexes (rRA=11), 2) RA patients candidate to start treatment with biological DMARD (aRA=23), 3) PsA patients treated with DMARD with low or no activity by common clinical indexes (rPsA=11), 4) PsA patients candidate to start treatment with biological DMARD (aPsA=10) and 5) non-disease controls (n=33). Serum calprotectin levels were measured by CLIA (Liaison, Diasorin), in comparison with ELISA (Bülhmann, Palex). Activity scores were DAS28 (RA) and DAPSA (PsA). Different serum and plasma inflammatory markers were analyzed. GraphPadv7.0S, SPSSv26 and MedCalc (v20.218) statistics were used.

### RESULTS

cCLP values were comparable by ELISA and CLIA, with a strong correlation between results ($r=0.97$, $p<0.0001$). ELISA and CLIA cCLP values were also statistically similar in every studied group (RA, PsA and controls; $p<0.05$). Moreover, Bland-Altman plot showed a mean bias of 1.09 and 95% limits of agreement of -2,84 and 5,03. Kappa agreement index was 0.84. cCLP concentrations were significantly increased in aRA and aPsA vs controls, as well as, in aRA vs rRA. cCLP levels were directly correlated with other biochemical inflammatory parameters (ESR, CRP, SAA), and with DAS28 and DAPSA activity indexes.

### CONCLUSIONS

Therefore, CLIA resulted to be a fast and reliable alternative method to determine cCLP serum levels both in RA and PsA patients. In addition, cCLP is a suitable inflammation biomarker, well correlated with other biochemical inflammatory parameters and with the degree of disease activity.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0772

## DIAGNOSTIC VALUE OF KAPPA FREE LIGHT CHAIN INDEX IN PEDIATRIC PATIENTS WITH POSTINFECTIOUS CNS INFLAMMATORY DISEASE: A DESCRIPTIVE STUDY

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### BACKGROUND-AIM

Kappa free light chain (κFLC) index has emerged as a promising biomarker for diagnosing multiple sclerosis (MS), showing diagnostic performance equal to or even better than visual detection of oligoclonal bands (OCB) in cerebrospinal fluid (CSF), the gold standard for detecting intrathecal immunoglobulin synthesis. However, MS is rare in children, limiting OCB analysis in pediatric cases, as a positive result can also occur in other autoimmune, demyelinating, and infection-related disorders. Thus far, few studies have evaluated the use of the κFLC index in diagnosing such conditions.
Here, we measured κFLC concentration in CSF from patients under 18 years with neurological symptoms seen at our hospital in 2023-2024 and correlated it to their clinical diagnosis.

### METHODS

CSF and serum samples were collected using sterile and gel separator tubes, respectively. κFLC and albumin quantification in CSF needed to calculate κFLC index was performed by turbidimetry on the Optilite analyzer (The Binding Site), while quantification of albumin in serum was obtained using the Alinity c analyzer (Abbott Laboratories). OCB were assessed using agarose gel isoelectrofocusing followed by immunofixation (Sebia).

### RESULTS

Of 9 samples analyzed, all presented moderate/severe neurological symptomatology and 5 had a κFLC index above the reference limit (6.6). Of these, 2 were diagnosed with postviral acute encephalitis, while the other 2 corresponded with patients diagnosed with postinfectious acute cerebellitis. Of the 4 samples, 2 exhibited intrathecal OCB, while the other 2 showed no OCB in either CSF or serum. Lastly, one patient showed a κFLC index of 330.8 and positive OCB, who was later diagnosed with MS. On the other hand, samples with a κFLC index < 6.6 corresponded with patients who had neurological symptoms of different non-inflammatory etiologies.

### CONCLUSIONS

We suggest that κFLC index could be used as a biomarker independent of OCB to support an earlier diagnosis of an inflammatory/infectious disease in children with neurological symptoms, which is important for timely treatment and preventing further disease progression. However, we believe other studies including a larger cohort of pediatric patients are needed to validate our results.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0773

## CONTRIBUTION OF TUMOR MARKERS DOSING OF PUNCTURE FLUID IN THE DIAGNOSIS OF CYSTIC PANCREATIC CANCER: ABOUT A CASE

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### BACKGROUND-AIM

Cystic pancreatic cancer accounts for 5% of pancreatic cancers. It is a public health problem that is constantly increasing. Its diagnosis is based on clinical, pathological, radiological and biological aspects. Tumor markers are tools to aid in diagnosis, therapeutic monitoring and prognosis.
Objective
The aim of our work is to determine the value of measuring ACE and CA19.9 in puncture fluid for the diagnosis of pancreatic cancer.

### METHODS

This is patient D.Ch, aged 35, admitted to the oncological surgery department of the EHS Pierre et Marie Curie, with no particular medical history, whose diagnosis of corporeo-caudal mucinous cystadenoma of the pancreas was established by computed tomography and anatomopathology.
Tumor markers ACE and CA 19.9 were measured by the ECLIA method according to the following protocol: - preoperatively, only on blood.
- per-operatively on both blood and puncture fluid.

### RESULTS

Preoperatively , the results of tumor markers (ACE and CA 19.9) were 0.85 ng/ml and 17.6 IU/ml, respectively. These values are normal, whereas high values were expected. The radiological examination showed a corporeo-caudal cystic formation in favor of a large corporeo-caudal mucinous cystadenoma of the pancreas with mural thickening . The anatomopathological examination carried out on a fine needle aspiration cytology in turn showed a morphological aspect in favor of a mucinous cystadenoma with low-grade dysplasia lesions of the corporeo-caudal site of the pancreas with no signs of degeneration.
Intraoperatively, it was a cystic tumor of malignant appearance. large, approximately 150 mm in size, with no possibility of resection. The values of ACE and CA 19.9 in the puncture fluid are 9528 ng/ml and >1000000 IU/ml respectively , whereas the values in the blood are 0.69 ng/ml and 24.15 IU/ml respectively . The anatomopathological examination carried out on a tumor biopsy is in favor of a mucinous cystadenoma with low-grade dysplasia of the corporeo-caudal location of the pancreas, a result identical to that carried out on fine-needle aspiration cytology.

### CONCLUSIONS

The appearance of the tumor during surgery guided the dosage of tumor markers in the puncture fluid, made it possible to diagnose cystadenocarcinoma and refer the patient to oncology for neoadjuvant chemotherapy.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0774

**OTHER RATIOS AS NOVEL BIOMARKERS IN ALZHEIMER'S DISEASE**

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**BACKGROUND-AIM**

The use of cerebrospinal fluid (CSF) biomarkers for the diagnosis of Alzheimer's disease is a standard in clinical practice, as they show high concordance with PET-CT results and patient clinical assessments. The most commonly used biomarkers are total Tau, phosphorylated Tau 181 (p-Tau), and the Aß1-42/Aß1-40 ratio. Additionally, the p-tau/ Aß42 ratio can be used, yielding results similar to those of the aforementioned ratio Aß1-42/ Aß1-40. In this study, we evaluated a new parameter named BetaPtau, which has not been studied before. This parameter calculates the difference between the two previously mentioned ratios, tau/(Aß1-42)-(Aß1-42)/(Aß1-40).

**METHODS**

A retrospective observational study was conducted with data from 96 patients. These patients, evaluated by the neurology department due to dementia symptoms, underwent CSF testing for total Tau (146-410 pg/mL), p-Tau 181 (21,50-59,00 pg/mL), beta-amyloid 1-40 (Aß1-40) (7755-16715 pg/mL), beta-amyloid 1-42 (Aß1-42) (725-1777 pg/mL), and calculation of the Aß1-42/Aß1-40 ratio (<0.069 indicative of Alzheimer's disease) using a Lumipulse Fujirebio® immunoassay.
Diagnosis was based on Aß1-42/Aß1-40 ratio thresholds, with further evaluation for definitive classification depending on parameter alterations and literature-supported cutoffs.
The BetaPtau parameter was calculated, and we defined a negative value (suggestive of no Alzheimer's disease) as less than 0, and a positive value (suggestive of Alzheimer's disease) as greater than 0.

**RESULTS**

Ratio Aß1-42/ Aß1-40:
Sensitivity:100%
Specificity:82,76%
Positive Predictive Values:93,05%
Negative Predictive Values:100%
AUC:0,91
BetaPtau:
Sensitivity:100%
Specificity:89,66%
Positive Predictive Values:95,71%
Negative Predictive Values:100%
AUC:0,95

**CONCLUSIONS**

The results suggest the potential use of the BetaPtau parameter for the diagnosis of Alzheimer's disease. Notably, this parameter involves a simple calculation that is easy to obtain and incurs no additional costs. It could also serve as a support tool, particularly in cases where not all biomarkers are concordant. Based on the findings of this study, this new parameter should be further validated in a larger patient cohort to ensure its reliability.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0775

**USE OF PROCALCITONIN, C-REACTIVE PROTEIN, AND LEUKOCYTE COUNT IN NEONATAL SEPSIS**

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**BACKGROUND-AIM**

Neonatal sepsis is a systemic infection that occurs within the first 4 weeks of life. It has a significant incidence and the diagnosis is sometimes complicated mainly due to its nonspecific symptoms. Among markers of sepsis, procalcitonin (PCT) is considered the most sensitive and specific marker of bacterial infection.

**METHODS**

A descriptive and retrospective study was carried out over 10 months that included neonates with a suspected bacterial infection. In the serum of each patient, PCT was determined by immunoassay and PCR by turbidimetry. Besides, a hemogram was performed to study the leukocyte count and blood culture, according to traditional techniques. The comparison of the two groups was carried out using the Mann-Whitney U test.

**RESULTS**

117 neonates aged between 1 and 29 days (median: 11 days) were studied, 66 boys and 51 girls. Of them, 23 (19.7%) were diagnosed with bacterial infection, with a median age of 7 days. The infection was confirmed by blood culture, which was positive for Escherichia coli (9), Streptococcus agalactiae (6), Streptococcus pneumoniae (4), Streptococcus mitis (2), Enterobacter cloacae (1), and Staphylococcus warneri (1). The final diagnosis in neonates evaluated with a negative or possibly contaminated blood culture was prematurity (83/94), risk of perinatal infection due to maternal fever (6/94), febrile syndrome secondary to filariasis (4/94), or reflux suffocation crisis gastroesophageal (1/94). The median PCT was 1.63 ng/mL in positive blood culture while in negative blood culture was 0.35 ng/mL ($p < 0.001$). The median CRP was 18.90 mg/L in positive blood culture while in negative blood culture was 4.15 mg/L ($p = 0.006$). The median leukocyte count was 10.02 x 109/L in positive blood culture and 11.86 x 109/L in negative blood culture ($p > 0.05$). The AUC of the studied markers concerning the blood culture result was 0.800 for PCT, 0.683 for CRP, and 0.446 for leukocyte count.

**CONCLUSIONS**

There are significant differences in PCT and CRP between the two groups studied, the concentrations being higher when blood cultures are positive. In contrast, the leukocyte count shows a similar distribution in the two groups studied. Because of this, PCT and CRP quantification is recommended in neonates with suspected bacterial infections to guide the diagnosis of sepsis.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0776

## EVALUATING THE RISK OF BREAST CANCER IN NORTH INDIAN WOMEN: THE IMPACT OF SERUM FERRITIN, VITAMIN D, AND PATHOLOGICAL FACTORS – A CASE-CONTROL STUDY

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**BACKGROUND-AIM**

Breast cancer is one of the most common cancers worldwide, and early detection remains a significant challenge. Researchers are exploring safer, more accessible methods to identify the disease at its earliest stages. Serum biomarkers like ferritin and vitamin D show potential for aiding early detection and risk assessment.Aim: This study investigates the role of these biomarkers in assessing breast cancer risk, with the goal of improving early diagnosis and creating more effective screening methods.

**METHODS**

A case-control study included 50 breast cancer women (cases), diagnosed before treatment, and 50 healthy controls. Serum ferritin levels were assessed using a Sandwich ELISA with Ferritin SA Elisa Kit, while vitamin D levels were measured using an autoanalyzer (Avantor CL-1000i). Pathological data, including estrogen receptor (ER), progesterone receptor (PR), Her2neu, Ki67, lymphovascular invasion, and disease stage, were also collected. Statistical analysis was conducted using IBM SPSS Statistics version 26.0, with significance at $p \leq 0.05$.

**RESULTS**

Mean serum ferritin levels in breast cancer patients (281.83 ± 39.43 ng/mL) were significantly higher than those in healthy women (85.21 ± 42.22 ng/mL, $p = 0.340$). Vitamin D levels were notably lower in cases (10.06 ± 2.68 ng/mL) compared to the controls (15.66 ± 2.78 ng/mL, $p < 0.001$). Area under the curve (AUC) for ferritin and vitamin D levels was similar (AUC = 0.419 for ferritin, AUC = 0.476 for vitamin D), indicating weak discriminatory power in distinguishing cases from healthy controls. However, the Mann-Whitney U test showed a strong and statistically significant difference (Z score = 8.31383, $p < 0.0001$) between these biomarkers in the studied population.

**CONCLUSIONS**

This study shows a significant link between breast cancer, vitamin D deficiency, and elevated ferritin levels. However, these biomarkers lack sufficient diagnostic power for clinical use in breast cancer detection. Further research with larger, more diverse populations is needed to explore their potential role in predicting prognosis and refining breast cancer screening strategies.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0777

## INTERFERENCE ON HBA1C MEASUREMENT: A CASE REPORT

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### BACKGROUND-AIM

Glycated hemoglobin (HbA1c) is considered as the gold standard for long-term glycemic monitoring and the diagnosis of diabetes mellitus. This report describes the case of a 65-year-old female patient admitted to the Department of Nephrology at University Hospital Dubrava following a diagnosis of jaundice and liver cirrhosis in the Department of Emergency Medicine, attributed to chronic alcohol abuse. As part of her clinical evaluation, HbA1c measurement was requested.

### METHODS

The Clinical Department of Laboratory Diagnostics performed HbA1c analysis on whole blood K3EDTA samples (BD, Plymouth, UK) using the BioRad D10 ion-exchange HPLC analyzer (Bio-Rad, Hercules, CA, USA) with the Hemoglobin A1c Program. In collaboration with the treating physician, whole blood K3EDTA and lithium heparin samples were sent to external laboratories for alternative HbA1c testing methods. These included enzymatic analysis (Abbott Architect c, Abbott Laboratories, Chicago, IL, USA) and immunoassay (Roche Cobas c513, Roche Diagnostics, Basel, Switzerland).

### RESULTS

The initial chromatogram revealed an A1c peak of 59.8% and an A0 peak of 44.2%, accompanied by a flag indicating that the result exceeded the measuring range. This result was repeated, and a new sample was requested due to suspected preanalytical interference. However, the A1c peak remained consistent at 60%. During hospitalization, the patient's glucose and total hemoglobin values remained within the reference interval. The alternative methods yielded HbA1c values of 3.8% and 4.0%, respectively, with no additional analytical flags.

### CONCLUSIONS

The discrepancy between the HbA1c results suggested the presence of a hemoglobin variant with unknown glycation characteristics. This variant, while clinically silent and without significant hematological abnormalities other than macrocytosis, interfered with the HPLC chromatogram by migrating with the A1c peak. The abnormally low results from the alternative methods likely underestimated the patient's true HbA1c level. For this patient, fructosamine measurement or fasting plasma glucose evaluation remains the only reliable approach for assesing long-term glycemic control and diagnosing diabetes mellitus.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0778

## MEASUREMENT OF HEMOGLOBIN A1C LEVEL IN THE BLOOD OF DIABETIC PATIENTS WITH SICKLE CELL DISEASE AND SICKLE CELL TRAIT

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### BACKGROUND-AIM

Sickle cell trait (SCT) and sickle cell disease (SCD) are both inherited conditions that affect hemoglobin. The prevalence of SCD in Saudi Arabia varies significantly in different parts of the country, with the highest prevalence is in the Eastern province, followed by the southwestern provinces. The reported prevalence for SCT ranges from 2% to 27%, and up to 2.6% will have SCD in some areas. Some of these patients were also affected by diabetes meletus and need to be monitored by a glycemic marker such as hemoglobin A1c (HgbA1c). In this study we aimed to measure and compare HgbA1c in both sickle cell conditions in Saudi population.

### METHODS

A total of 21 diabetic patients with either SCD or SCT were included in this study. Whole blood in EDTA was collected from each patient and sent to the lab for measurement of HgbA1c and hemoglobin fractionations and complete blood count (CBC). HgbA1c, hemoglobin type and CBC were measured by HPLC D100 (Bio-Rad), Capillary electrophoresis (Sebia), and Alinity HQ (Abbott) respectively.

### RESULTS

The age mean and standard deviation of the studied group was 21±13 year and female were 13 (62%). There were 6 (29%) patients with SCD with HgbA1c mean and standard deviation of (8.49%±0.47) compared to those for SCT (5.99%±1.03) (p=0.0004). The averages of red blood cells (RBC), total hemoglobin (Hgb), hematocrit (Hct) and platelets (Plat) were found to be 3.0±0.7 1012/L, 92±13 g/L, 0.27±0.05 L/L, 473±153 109/L respectively for SCD. And for those with SCT were found to be 4.4±1.1 1012/L, 113±21 g/L, 0.34±0.07 L/L, 280±141 109/L respectively. There were a significant differences CBC results in patients with SCT and SCD for RBC (p=0.0068), Hgb (p=0.0230), Hct (p=0.0254), Plat (p=0.0084).

### CONCLUSIONS

The HPLC method has quantified the level of HgbA1c in the blood of patients with either SCT and/or SCD. However, the reliability of HgbA1c in patients with SCD was not confirmed as possibility of interference was concluded due to the absence of hemoglobin A in these homozygote patients with two sickle cell genes. It was recommended to measure other glycated proteins such as fructoseamine in those patients with SCD.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0779

**ELEVATION OF PROCALCITONIN IN THE ABSENCE OF INFECTION**

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**BACKGROUND-AIM**

Procalcitonin (PCT) is widely used as a marker for bacterial infection and sepsis risk. It is produced in the C cells of the thyroid and is a precursor of calcitonin. Despite being a highly specific marker, it is known to increase in other conditions such as surgery, trauma, burns, multiorgan failure, and cardiogenic shock. In this case we present a 66-year-old woman with paresthesias, constitutional syndrome, asthenia and hyporexia. Present with a procaltonin of 44.40 ng/mL (0.00-0.1 ng/mL) in the absence of infection. The laboratory ruled out the main causes described in the literature.

**METHODS**

To rule out the main interferences that can cause procalcitonin elevation. The determinations are performed on the cobas C702 and e801 equipment.
Biotin, rheumatoid factor (9.9 IU/mL), acetaminophen (<0.4 g/mL). Additionally, serial dilutions were performed, with no loss of linearity observed.

**RESULTS**

After ruling out the above interferences, the patient's marked constitutional syndrome prompted further evaluation of the following markers:
CEA: 998 ng/mL (0.0-5.0), neuron-specific enolase (NSE): 95.30 ng/mL (0.0-16.30), calcitonin: 4053 pg/mL (0.0-5.0), chromogranin: 245.5 ng/mL (<101.9), while other analyzed markers (CA 19.9, CA 125, CA 15.3, AFP) were within normal ranges, raising suspicion of small cell lung cancer or medullary thyroid carcinoma.
Radiological studies revealed a nodule in the right thyroid lobe, two spiculated pulmonary nodules suspected to be malignant, central nervous system involvement, and liver metastases.
Histopathological analysis showed neoplastic cells, scant eosinophilic cytoplasm, and hyperchromatic nuclei, with nuclear TTF1, as well as patchy calcitonin and chromogranin staining. This led to the final diagnosis of a neuroendocrine neoplasm, compatible with a grade 2 neuroendocrine tumor/atypical carcinoid.
A biopsy of the thyroid nodule was not performed due to its small size, and genetic studies were not conducted at the patient's request.

**CONCLUSIONS**

An unexplained elevation of procalcitonin, inconsistent with the patient's history and clinical findings, should prompt the exclusion of potential interferences and consideration of other etiologies. In the case of our patient, the synthesis of procalcitonin appears to originate from a neuroendocrine tumor.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0780

## MARGINAL ZONE LYMPHOMA PRESENTING WITH ELEVATED CA-125 AND CA-19-9 LEVELS

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### BACKGROUND-AIM

Marginal zone lymphomas (MZL) are a heterogeneous group of B Non-Hodgkin's lymphomas (NHL) with variable clinical characteristics. Elevated CA-125 and CA-19-9 levels have been reported in NHL patients and are possibly associated with prognosis. We report a case of MZL presenting with ascites, abdominal lymphadenopathy and elevated CA-125 and CA-19-9.

### METHODS

A 90 year old male presented with new, progressive dyspnoea. His medical history included type two diabetes, atrial fibrillation and he also reported gas poisoning from a wood burning stove 20 years ago. Upon physical examination, abdominal distension and thoracic lympadenopathy were apparent with subsequent computer tomography detecting pleural effusion, ascites and extensive abdominal lymphadenopathy without evidence of a primary tumor. Laboratory workup revealed peripheral lymphocytosis with atypical, vacuolated lymphocytes upon blood smear microscopy and elevated Ca 19-9 and Ca 125 (127,90 U/mL and 952 U/mL respectively) levels.

### RESULTS

Based on the aforementioned findings the diagnosis of lymphoma was suspected and further investigation, including a subclavian lymph node biopsy, was conducted. Based on lymph node morphologic and immunohistochemical characteristics a diagnosis of B-NHL MZL lymphoma was confirmed.

### CONCLUSIONS

Within relevant clinical context, elevated CA-125 and/ or CA-19-9 levels should raise the suspicion of NHL, particularly in the absence of an identifiable primary tumor.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0782

**THE DIAGNOSTIC UTILITY OF METALLOPROTEINASE 3 (MMP-3) IN ENDOMETRIAL CANCER PATIENTS**

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**BACKGROUND-AIM**

Endometrial cancer is one of the most lethal malignancies affecting women, ranking as the fourth leading cause of cancer-related deaths. Tumor markers such as CA125 have been widely used in clinical practice to monitoring of endometrial cancer, but they are not fully reliable for early detection or diagnosis due to their limited sensitivity and specificity. There is a critical need for novel biomarkers that could complement or even outperform existing diagnostic tools.

Matrix metalloproteinases (MMPs), a family of enzymes involved in the degradation of the extracellular matrix, have been implicated in cancer cell invasion and metastasis. Among them, stromelysin 3 (MMP-3) plays a key role in tissue remodeling and tumor progression. In this study, we investigated the plasma levels of MMP-3 in endometrial cancer patients and compared them with the classical tumor marker CA125, in an effort to evaluate the diagnostics of MMP-3 in endometrial cancer

**METHODS**

Tested group included 30 endometrial cancer patients (stage II-IV in FIGO, type adenocarcinoma endometrioides). The control groups consisted of 30 healthy volunteers. Plasma levels of MMP-3 were determined using immunoenzyme assay (ELISA), CA125 concentrations by chemiluminescent microparticle immunoassay (CMIA).

**RESULTS**

Plasma levels of MMP-3 (median 9,635 ng/ml), CA125 (19,85 U/ml) were significantly higher in endometrial cancer patients as compared to the healthy control (4,361 ng/ml, 14,67 U/ml, respectively). MMP-3 diagnostic sensitivity received higher values (89,99%) than the tumor marker CA 125 (69,63%). Furthermore diagnostic specificities (91,15%), the negative predictive values (NPV 83,93%) and positive predictive value (PPV 93,37%) were also higher for MMP-3 than compared marker (91,15%, 83,93%, 93,37%, respectively). The combined use of tested parameters resulted in the increase of the sensitivity and NPV range (92%, 88%). The higher area under the ROC curve (AUC) was observed for MMP-3 (0,9100) than the value of AUC of CA125 (0,7156).

**CONCLUSIONS**

These results suggest a potential usefulness of MMP-3 in diagnostic of endometrial cancer patients, especially in combined use with tumor marker CA125.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0783

## NETWORK PHARMACOLOGY AND MOLECULAR DOCKING ANALYSIS OF KANGTAI DECOCTION'S THERAPEUTIC MECHANISM AGAINST LUNG CANCER

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**BACKGROUND-AIM**

To use the LCBP risk assessment model to evaluate tumor markers combined with imaging diagnosis, stratify the risk of pulmonary nodules, and predict the probability of disease malignancy in patients.

**METHODS**

A total of 80 patients with pulmonary nodules on lung CT examination in the Affiliated Hospital of Shaanxi University of Traditional Chinese Medicine from January 2020 to April 2021 were enrolled as the experimental group, and 60 patients with pulmonary nodules were selected as the control group. Blood samples were collected from patients without treatment, and ProGRP, CEA, SCC-AG and CYFRA21-1 serum biomarkers were determined by chemiluminescence immunoassay.

**RESULTS**

There were statistically significant differences in serological markers between the two groups ($P < 0.05$), and the evaluation of the malignant probability of pulmonary nodules by imaging indicators and the presence or absence of burr signs were statistically significant ($P < 0.05$). The AUC of the low-risk group was 0.761, the AUC of the intermediate-risk group was 0.749, and the AUC of the high-risk group was 0.804.

**CONCLUSIONS**

The LCBP risk assessment model based on serological markers, imaging findings and clinical data has a good ability to distinguish the risk stratification of pulmonary nodules

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0784

## TOLL-LIKE RECEPTOR 2 EXPRESSION AND ITS ASSOCIATION WITH SCHIZOPHRENIA: A POTENTIAL LINK BETWEEN IMMUNE DYSFUNCTION AND PSYCHOSIS

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**BACKGROUND-AIM**

Schizophrenia is a complex and debilitating psychiatric disorder characterized by hallucinations, delusions, and cognitive impairments. Recent studies have implicated immune dysfunction in the pathogenesis of schizophrenia, with Toll-like receptors (TLRs) emerging as key players in the immune system's response to pathogens and stress.

**METHODS**

This study aimed to investigate the association between Toll-like receptor 2 (TLR2) and schizophrenia and to explore the potential mechanisms underlying this relationship. This case-control study involved 60 schizophrenia patients and 60 healthy controls. Flow Cytometry was used to quantify TLR2 receptor expression by evaluating the proportion of cells exhibiting the receptor on the surface of lymphocytes.

**RESULTS**

The results showed that TLR2 receptor expression was significantly elevated in schizophrenia patients compared to healthy controls. The mean and standard deviation for the proportion of cells exhibiting TLR2 receptors on the surface of lymphocytes was 6.14 ± 0.11 for cases and 1.10 ± 0.003 for controls ($p < 0.001$). Furthermore, a positive correlation was observed between TLR2 expression and the severity of psychotic symptoms, as measured by the Positive and Negative Syndrome Scale (PANSS).

**CONCLUSIONS**

This study highlights a strong association between TLR2 and schizophrenia, suggesting immune dysregulation contributes to the disorder's development and progression. Elevated TLR2 expression may amplify immune responses, triggering increased production of pro-inflammatory cytokines and exacerbating psychotic symptoms. These findings have important implications for developing novel therapeutic strategies targeting the immune system in schizophrenia. Further research is needed to elucidate the mechanisms underlying the TLR2-schizophrenia association and to explore the potential of TLR2 as a biomarker for schizophrenia diagnosis and treatment.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0785

**ABSTRACT. BACKGROUND: LIHC (LIVER HEPATOCELLULAR CARCINOMA) IS THE MOST COMMON MALIGNANT CANCER AROUND WORLD. RECENT STUDIES REPORTED THAT MIRNA PLAYS VITAL ROLES IN TUMOR DEVELOPMENT AND PROGRESSION, SUGGESTING THE MIRNA IN LIHC COULD BEEN REGARDED**

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**BACKGROUND-AIM**

LIHC (Liver Hepatocellular Carcinoma) is the most common malignant cancer around world. Recent studies reported that miRNA plays vital roles in tumor development and progression, suggesting the miRNA in LIHC could been regarded as potential prognostic biomarkers.
Assessment of the up-regulated miRNA and its target protein as novel cancer biomarkers in LIHC cancer cells.

**METHODS**

First, we assessed the up-regulated and down-regulated miRNA in LIHC and normal tissue from The Cancer Genome Atlas (TCGA) database. Next, we performed the survival plot and time ROC plot to select the LIHC related miRNA. Then,by introduction of TargetScan Human software and TCGA database, we got the miRNA related proteins. Lastly,by series of cell biology and biochemistry assays, we illustrated miRNA targeted proteins could affect cancer cell physiological function.

**RESULTS**

Identification of miR-10b-5p,miR-224-5-p,miR-183-5p,miR-182-5p,miR-217,miR-196b-5p,miR-452-5p and miR-9-5p are overexpressed in LIHC than in normal tissue. The elevated expression of miR-452-5p and miR-9-5p are associated with significantly poorer over survival of LIHC patients,miR-9-5p and miR-452-5p could restrict the expression of PDK4 and COLEC10 respectively, down-regulated level of PDK4 and COLEC10 are correlated with poorer over survival in LIHC patients. Moreover, overexpression of PDK4 and COLEC10 in LIHC cancer cells generated cell apoptosis and growth retardation, cell derived xenograft assay found the PDK4 and COLEC10 brought the development and progression retardation of LIHC. GO and KEGG analysis showed that PDK4 and COLEC10 positive correlation genes are involved in PPAR signaling pathway and PI3K−Akt signaling pathway.

**CONCLUSIONS**

We found two new diagnostic markers in LIHC, miR-9-5p and miR-452-5p, which may facilitate the early diagnosis and treatment, we also uncovered that PDK4 and COLEC10 could been identified as tumor suppressors by misregulation of cell psychological function. In LIHC cancer cell, miR-9-5p and miR-452-5p acted as oncogene factors by directly suppress the expression of PDK4 and COLEC10.Activation of PPAR signaling pathway and PI3K-Akt signaling pathway may be viewed as potential therapeutic approach in LIHC.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0786

**ELEVATED NUCLEOBINDIN-1 PLASMA CONCENTRATIONS IS A POSSIBLE MARKER IN HIV-RELATED ANXIETY**

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**BACKGROUND-AIM**

To investigate the prevalence for anxious and depressive disorder among HIV-infected population and preliminarily explore the underlying mechanisms.

**METHODS**

Individuals who were newly HIV diagnosed were assessed on the Hospital Anxiety and Depression scale (HAD-A and HAD-D). Then SHIV-infected rhesus monkey model presented syndromes related psychiatric illness that mimic those observed in human neuroAIDS was used to investigate the possible involvement of nucleobindin-1 (NUCB1) and cannabinoid type 1 receptor (CNR1) protein in psychiatry-like behavior.

**RESULTS**

The prevalence rate of depression disorder among newly confirmed HIV cases was 27.33% (41/150). The mechanism research results showed elevated NUCB1 levels in cerebrospinal fluid (CSF) from HIV-infected patients suffering from depression were confirmed by western blotting compared to those of HIV-infected patients. Also, immunohistochemical analysis indicated expression of NUCB1 in the cerebral cortex neurons of SHIV-infected monkey was higher than that of healthy control. Conversely, CNR1 expression were down-regulated at protein level.

**CONCLUSIONS**

Anxiety are common in HIV infection and associate with NUCB1 expression increase; and NUCB1 may be a potential target for anxiety among HIV-infected subjects

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0787

## CONSTRUCTING A PAN-CANCER UBIQUITINATION REGULATORY NETWORK TO DETERMINE TUMOR HISTOLOGY FATE AND PATIENT PROGNOSIS

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### BACKGROUND-AIM

Ubiquitination is a significant post-translational modification that governs cellular processes and has an influence on tumor progression. Pan-cancer investigations, capitalizing on the comprehensive data from The Cancer Genome Atlas (TCGA), can identify ubiquitination signatures that are closely related to cancer and their potential associations with tumor classification.

### METHODS

We integrated gene expression and prognosis data of 4040 cases of lung cancer, esophageal cancer, cervical cancer, melanoma, bladder cancer, and urothelial cancer from 15 data sets. By constructing ubiquitination regulatory networks, we mapped out the complex interactions of ubiquitination-related molecules. Prognostic analysis was executed using Cox regression and Kaplan-Meier survival analysis. Functional enrichment and protein-protein interaction were also carried out to uncover key downstream pathways. Combining cellular and molecular biology experiments with patient cohort validation ensured the reliability of our findings.

### RESULTS

The major accomplishment of this study was the identification of the key nodes and prognostic pathways within the ubiquitination modification network. Based on these findings, a ubiquitination-related prognostic signature (URPS) was established and validated in different cancer patients. Moreover, in cancer types where immunotherapy has been extensively applied, the URPS has the potential to identify patients who are likely to derive benefits from immunotherapy. By conducting a comprehensive analysis of the protein relationships associated with the URPS, novel interaction partners involved in cancer-related processes can be identified, which may serve as promising drug targets for the development of innovative cancer therapeutics. At the single-cell resolution level, the URPS enables more precise classification of distinct cell types and has been found to be associated with macrophage infiltration within the tumor microenvironment. In cell lines and patient cohorts, it was verified that OTUB1-TRIM28 ubiquitination is crucial for affecting the MYC pathway and patient prognosis.

### CONCLUSIONS

In conclusion, we constructed a pan-cancer ubiquitination regulatory network and prognostic model, and provided value for predicting patient prognosis and understanding the biological mechanism.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0788

## THE INTRICATE NETWORK OF COLORECTAL CANCER LUNG METASTASIS: SMYD3-DRIVEN MACROPHAGE REPROGRAMMING

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**BACKGROUND-AIM**

Tumors originating from the left-sided colon and rectum, distinguished by their embryonic germ layer origins from those of the right-sided colon, frequently metastasize preferentially to the lungs instead of the liver. Nevertheless, the underlying factors propelling this metastatic pattern remain elusive.

**METHODS**

We conducted an exhaustive analysis of the tumor microenvironment in 17 patients with colorectal cancer (CRC) lung metastasis via single-cell sequencing (scRNA-seq). Integrating spatial transcriptomics, we delved into the key elements that induce the colonization of CRC within the pulmonary parenchyma. Validation was executed using bulk public datasets and 62 paraffin-fixed specimens sourced from our center. Subsequently, a lung metastasis model of the MC38 and CT26 cell lines was established through tail vein injection to validate our findings in vivo.

**RESULTS**

We retrieved and integrated scRNA-seq data encompassing a total of 370,000 cells from three public datasets. Our analysis revealed that the transcription factor SMYD3 was markedly up-regulated in metastatic CRC cells, and then SMYD3 activated the downstream MYC signaling pathway, thereby facilitating the metastatic process of CRC. In comparison to normal lung tissues, metastatic tumors exhibited a significant reduction in the proportion of myeloid cells. Specifically, alveolar macrophages within these metastatic lesions underwent a phenotypic shift towards a mesenchymal-like state, characterized by the secretion of inhibitory cytokines and a concomitant loss of antigen presenting capabilities. The interaction between SEMA3C, whose secretion is regulated by SMYD3, and NPR1/2 on the surface of macrophages was posited to be the underlying mechanism accounting for this phenotypic metamorphosis. Moreover, targeting NPR1 has been shown to be beneficial for enhancing the efficacy of immunotherapy against CRC and reducing tumor metastasis. By generating SMYD3-knockout and over-expressing MC38 cell lines, we confirmed the SMYD3 mediated the process of alveolar macrophage domestication by metastatic tumor cells.

**CONCLUSIONS**

In summary, through the integration of scRNA-seq sequencing techniques, we have elucidated the pivotal role played by alveolar macrophages in the process of CRC lung metastasis.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0789

## TUMOR NECROSIS FACTOR-α AND INTERLEUKIN-10 IN PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS

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### BACKGROUND-AIM

Systemic lupus erythematosus (SLE) is a prototype of systemic autoimmune diseases. Numerous factors can influence the onset of SLE and development of some clinical disease manifestations with various organ involvements and occurrence of characteristic symptoms and disease signs. This paper studies the values of tumor necrosis factor- α (TNF-α) and interleukin-10 in the serum of patients with SLE.

### METHODS

Complete laboratory processing of the biomaterial, enabled classification of SLE patients (n=55), into the following groups: patients with predominant cutaneous disease manifestation, S-SLE; patients with neurolupus, N-SLE, patients with joint changes, J-SLE; patients with blood vessel changes–vasculitis,V-SLE. Twenty blood donors, comprised the control group. Concentration of TNF-α and IL-10 was determined by commercial ELISA tests.

### RESULTS

The increase of the TNF-α was highest in patients with neurolupus (P<0,001) and joint dise-ase(P<0,01), while cutaneous and vascular forms were of lesser significance (P<0,¬05). Comparing the groups, we noticed significant TNF-α increase in joint and neurolupus related to vascular SLE (P<0,05). The increase of the IL-10 concentration is of statistical significance in neurolupus patients (16,25±4,31pg/ml) and in vascular disease (15,23±2,18pg/ml) compared to controls 5,13±1,51, for P<0,01 and skin disease (12,87±2,28 pg/ml), with somewhat lower significance of P<0,05.

### CONCLUSIONS

The results of this paper indicate that TNF-α can be of special importance in the N-SLE pathology. TNF-α released from inflammatory cells act synergistically in the circulation, inducing peripheral vasodilatation, increase of vascular permeability and alteration of endothelial function favoring thrombosis. Increased IL-10 can be attributed to its increased production in monocytes and associated with neuropsychiatric menifestations of the disease. Inhibitors of cytokine production are being extensively studied as potential therapeutics in various immunologic diseases.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0790

## INVESTIGATION OF MRNA BIOMARKERS IN URINE FOR EARLY DETECTION OF NON-MUSCLE INVASIVE BLADDER CANCER

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**BACKGROUND-AIM**

Recent research on non-invasive diagnostic tools for bladder cancer has shown promise in developing methods that offer better sensitivity and specificity compared to traditional approaches such as cystoscopy and cytology. This study assessed a diagnostic panel of mRNAs related to tumor progression in urine samples from patients with non-muscle invasive bladder cancer (NMIBC) and control subjects.

**METHODS**

A total of 129 participants were carefully selected for this study, consisting of 67 NMIBC patients, 31 patients with hematuria due to non-malignant urological disorders, and 31 healthy individuals. The reverse transcription-quantitative polymerase chain reaction (RT-qPCR) technique, known for its sensitivity and specificity in quantifying gene expression, was used to identify ten mRNAs (CA9, CDK1, CD24, TERT, CEP55, TOP2A, IQGAP3, UBE2C, BIRC5, and CRH) in the urine samples collected from the participants.

**RESULTS**

The mRNA levels of CA9, CDK1, CD24, TERT, CEP55, TOP2A, IQGAP3, UBE2C, and CRH were higher in the urine of patients with NMIBC compared to healthy individuals. Additionally, the mRNA levels of CD24, TOP2A, IQGAP3, UBE2C, and CRH were significantly elevated in NMIBC patients when compared to those experiencing hematuria. The analysis of the five-gene profile showed a sensitivity of 98% and a specificity of 100% for distinguishing low-grade tumors from healthy individuals. It also demonstrated a sensitivity of 98% and a specificity of 90% when differentiating low-grade tumors from patients with hematuria. For diagnosing high-grade tumors, the sensitivity was 96% with a specificity of 100% compared to healthy subjects, and a sensitivity of 100% with a specificity of 83% when compared to the hematuria group.

**CONCLUSIONS**

These results highlight the potential of urine mRNA profiling for the early diagnosis of NMIBC.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0791

## SERUM SUBFATIN AND CHROMOGRANIN-A LEVELS IN PATIENTS WITH PROLIFERATIVE DIABETIC RETINOPATHY: A CROSS-SECTIONAL STUDY

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**BACKGROUND-AIM**

Proliferative Diabetic retinopathy (PDR) is a disease that occurs due to damage to blood vessels in the retina due to diabetes. In this study, we aimed to determine the levels of Subfatin and Chromogranin A (CgA) proteins in PDR patients.

**METHODS**

A total of 96 volunteers, including individuals from the PDR, Diabetes Mellitus (DM), and control (CT) groups, were included in the study. Serum samples were collected from blood drawn from both the patient and control groups. Subfatin and CgA protein levels in the serum samples were measured using the ELISA method.

**RESULTS**

A comparison of the glucose and HbA1c values of the PDR, DM, and CT revealed that the glucose levels of men and women in the PDR group were significantly higher than those of the other groups ($p < 0.05$). The subfatin level in the PDR group was found to be 3.57±0.97 ng/mL, which was the lowest compared to the other groups, and this difference was found to be statistically significant ($p<0.05$). In the study, a significant correlation was determined between CgA protein levels and weight and BMI only in the CT group.

**CONCLUSIONS**

Consequently, the level of subfatin was found to be diminished in patients within the PDR group. Additionally, the levels of glucose and HbA1c were observed to be elevated. Based on these findings, it can be postulated that this may be a significant factor in the pathogenesis of PDR disease.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0792

**PROGNOSTIC SIGNIFICANCE OF PLATELET-TO-LYMPHOCYTE RATIO IN PATIENTS WITH TRIPLE-NEGATIVE BREAST CANCER: SYSTEMATIC REVIEW AND META-ANALYSIS**

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**BACKGROUND-AIM**

Platelet-to-lymphocyte ratio (PLR), a key systemic inflammatory parameter, has been associated with response to neoadjuvant therapy in breast cancer (BC). However, this relation is not established for triple-negative BC (TNBC) patients. This meta-analysis aims to evaluate the association of PLR with survival outcomes in patients with TNBC.

**METHODS**

This systematic review and meta-analysis followed Cochrane Collaboration guidelines and was registered on PROSPERO. Eligible studies included TNBC patients and reported on overall survival (OS), disease-free survival (DFS), or progression-free survival (PFS). Data were extracted by two independent authors. The risk of bias was assessed using the Quality in Prognosis Studies (QUIPS) tool. Hazard ratios (HR) were used to calculate associations, with statistical heterogeneity assessed using Cochran's Q test and $I^2$ statistics.

**RESULTS**

Six studies comprising 819 patients with TNBC were included. Cut-off values for PLR were provided in 5 studies, 2 of which were derived from previous studies, and another 3 were obtained from receiver operating characteristic curve (ROC) curves.
High PLR level was not significantly associated with the OS rate (HR 1.35; 95% CI 0.99-1.84; p=0.06; $I^2$=43%). When eliminating the only study with a high risk of bias we found a decrease in the OS rate in the high PRL group (HR 1.55; 95% CI 1.21-2.00; p=0.006 and $I^2$=0%).
A high PLR level was not significantly associated with low PFS rate (HR 1.73; 95% CI 0.69-4.33, p=0.24; $I^2$=79%).
Conversely, a high PLR level was significantly associated with low DFS rate (HR 1.69; 95% CI 1.25- 2.28; p=0.0006; $I^2$=0%).

**CONCLUSIONS**

This meta-analysis suggests that PLR is a promising prognostic marker for DFS in TNBC patients treated with NACT. While PLR was not significantly associated with OS or PFS, it may serve as a predictor of chemotherapy outcomes in TNBC. Further studies with larger sample sizes and standardized PLR cut-off values are needed to validate its role as a biomarker and elucidate its mechanistic involvement in treatment response.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0793

## POPULATION-SPECIFIC CUT-OFF POINTS FOR UCHL-1 AND GFAP IN THE EVALUATION OF MILD TRAUMATIC BRAIN INJURY

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### BACKGROUND-AIM

Mild traumatic brain injury (mTBI), defined by a Glasgow Coma Scale (GCS) score of 13-15, accounts for 70-90% of all TBIs. Cranial computed tomography (CT) is the standard tool for assessing intracranial injuries. Its use in mTBI lacks consensus, leading to overuse. Serum/plasma biomarkers GFAP (Glial Fibrillary Acidic Protein) and UCH-L1 (Ubiquitin C-terminal Hydrolase L1) can aid in deciding whether a CT is necessary. Negative results for these biomarkers within 12 hours post-trauma can rule out the need for a CT, with a high negative predictive value (NPV).
This study aims to evaluate the correlation between UCH-L1 and GFAP biomarkers and CT findings, and to establish specific cut-off points for our population.

### METHODS

Prospective study was performed. Samples were collected from 144 patients meeting criteria for mTBI (GCS 13-15), within 12 hours post-trauma, and who underwent CT. Blood samples were collected in lithium heparin Vacutainer tubes, and UCH-L1 and GFAP were analyzed using Abbott's Alinity i system. ROC curves were generated with MedCalc to establish population-specific cutoff points using the Youden Index.

### RESULTS

The diagnostic performance of GFAP and UCH-L1 was assessed using ROC curve analysis, with AUCs of 0.86 (95% CI 0.79-0.91) and 0.79 (95% CI 0.71-0.85), respectively. At optimal cut-offs, GFAP (85.6 pg/mL) showed 90.0% sensitivity (IC95% 73.5-97.9), 70.0%, specificity (IC95% 60.5-78.4) and 96.2% NPV (IC95% 89.4-99.2), while UCH-L1 (799.6 pg/mL) showed 68.8% sensitivity (IC95% 50.0-83.9), 80.2% specificity (IC95% 71.5-87.1) and 89.9% NPV (IC95% 82.2-95.0).
Using the manufacturer's cut-offs (35 pg/mL for GFAP and 400 pg/mL for UCH-L1), CT could have been avoided in 9.7% of the patients, while population-specific cut-offs could have avoided CT in 45.1% of the patients with 97.0% NPV (IC95% 90.0-100.0), 93.8% sensitivity (IC95% 79.0-99.0%), 58.0% specificity (IC95% 48.0-67.0).

### CONCLUSIONS

UCH-L1 and GFAP demonstrated high diagnostic utility for ruling out intracraneal injuries in mTBI. Using population-specific cut-off points, 45.1% of CT could be avoided, maintaining a 97.0% NPV. This highlights their potential to reduce unnecesary radiation exposure, optimize resources and improve early clinical management.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0794

## EVALUATION OF A NEW AUTOMATED CHEMILUMINESCENT ANTI-NUCLEAR ANTIBODY ASSAY

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### BACKGROUND-AIM

Antinuclear antibody (ANA) testing is used to screen for autoimmune disorders such as SLE. The most frequently used ANA assay is indirect immunofluorescence (IMF) (90% of CAP EQA participants). Non-IMF assays are being introduced. We provide the performance evaluation of a new automated chemiluminescent ANA test (SNIBE, China) compared to IMF (Euroimmun, Germany) in 152 samples.

### METHODS

In the SNIBE assay (Maglumi2000) patient sample, buffer and magnetic microbeads coated with nuclear antigens are mixed and incubated at 37oC to form immune-complexes. Following incubation, sample materials are bound to the microbeads and held in a magnetic field. Unbound materials are washed away followed by addition of a labelled antibody (ABEI-mouse monoclonal antihuman IgG) to form a sandwich complex. After precipitation in a magnetic field, the supernatant is decanted followed by another wash. Addition of a starter buffer generates a chemiluminescent reaction and the light signal is measured. The relative light unit is proportional to the sample ANA concentration; results >50AU/mL are positive. Assay time is 25-30 min. The Euroimmun IMF test is performed using Hep2 cells; titers<1:80 are considered negative. Concordance between positive and negative IMF and SNIBE samples were assessed.

### RESULTS

Inter-assay precision (CV) for the kit level 1 & 2 controls are 4.2 & 3.0% respectively. We verified the functional sensitivity (@20%CV) of the assay as 1.3 AU/mL (claimed 1.0) with a linearity up to 393AU/mL (claimed 400AU/mL). For IMF negative samples, SNIBE was 86.3% concordant (101/117); for IMF positive samples, SNIBE results were 85.7% concordant (30/35). Notably only 30/46 (65.%) SNIBE positive samples were concordant with IMF.

### CONCLUSIONS

The concordance between the two ANA tests is acceptable. The SNIBE chemiluminescent assay seems attractive given the automation, throughput, availability of rapid results and possibly greater sensitivity. Larger studies are awaited.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0795

## PERFORMANCE EVALUATION OF A NEW AUTOMATED CHEMILUMINESCENT DOUBLE-STRANDED DNA ANTIBODY ASSAY

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### BACKGROUND-AIM

Antibodies to double-stranded DNA (ds-DNA Ab) testing is used to aid in the diagnosis and monitoring of systemic lupus erythematosus (SLE) . The most frequently used ds-DNA Ab assay is non-chemiluminescent immunoassay (CAP EQA participants). We provide the performance evaluation of a new automated chemiluminescent ANA test (SNIBE, China) compared to enzyme immunoassay (Bio-Rad) in 111 samples.

### METHODS

In the SNIBE assay (Maglumi2000) patient sample, buffer and magnetic microbeads coated with ds-DNA antigens are mixed and incubated to form immune-complexes. Following incubation, sample materials bound to the microbeads are held in a magnetic field; unbound materials are washed away. Thereafter, a labelled antibody (ABEI-mouse monoclonal antihuman IgG) is added to form a sandwich complex. After precipitation in a magnetic field, the supernatant is decanted followed by another wash. Subsequent addition of a starter buffer generates a chemiluminescent reaction and the resulting light signal is measured. The relative light unit is proportional to the sample anti-ds-DNA concentration; results >30 IU/mL are positive. Assay time is 25-30 min. The Bio-Rad enzyme immunoassay (EIA) considers titers<30 IU/mL negative. Concordance between positive and negative EIA and SNIBE samples were assessed.

### RESULTS

Inter-assay precision (CV) for the kit level 1 & 2 controls are 2.3 & 2.6.0% respectively. We verified the functional sensitivity (@20%CV) of the assay as 7.0 IU/mL (claimed 1.0) with a linearity up to 768 IU/mL (claimed 800 IU/mL). For EIA negative samples, SNIBE was 86.1% concordant (62/72); for EIA positive samples, SNIBE results were 92.3% concordant (36/39). Notably 36/46 (78.3%) SNIBE positive samples were concordant with EIA.

### CONCLUSIONS

The concordance between the two ds-DNA tests is acceptable. The SNIBE chemiluminescent assay seems attractive given the automation, throughput, availability of rapid results and possibly greater sensitivity. Larger studies are awaited.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0796

## COMPARISON OF INFLAMMATORY MARKERS IN HOSPITALIZED AND NON-HOSPITALIZED PATIENTS WITH COVID-19

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### BACKGROUND-AIM

The COVID-19 pandemic caused by the SARS CoV-2 has presented an unprecedented challenge, with various factors such as viral invasion, host immune response, and lifestyle habits. This study aims to investigate the correlation between inflammatory markers including CRP, procalcitonin (PCT) and interleukin 6 (IL-6), in hospitalized and non - hospitalized infected with SARS CoV-2. IL-6 is pro-inflammatory cytokine that plays significant role in the host's immune response, whereas PCT severs as biomarker of bacterial infection and iron metabolism disturbances. IL-6 plays a crucial role in COVID-19 patients by promoting inflammation and contributing to the cytokine storm, which can exacerbate disease severity and lead to complications such as respiratory failure.

### METHODS

This is a cohort study. A total of 30 patients infected with SARS-CoV-2, are included in the study. CRP, PCT, and IL-6 levels were measured in 15 hospitalized COVID-19 patients and 15 non-hospitalized COVID-19 patients.
The inclusion criteria are patients over the age of 18, while excluding pregnant and breastfeeding women, individuals with malignancy, and those under the influence of immunosuppressive therapy

### RESULTS

Significant differences were observed in the levels of CRP, PCT, and IL-6 between hospitalized and non-hospitalized COVID-19 patients. Hospitalized patients had higher mean levels of CRP (184.83 ± 89.37 vs. 13.72 ± 11.38, $p < 0.01$), PCT (9.59 ± 9.33 vs. 0.0484 ± 0.0278, $p < 0.001$), and IL-6 (67.18 ± 96.39 vs. 3.13 ± 0.98, $p < 0.01$). Strong correlations were found for CRP ($r = 0.933$), moderate for PCT ($r = 0.634$), and moderate for IL-6 ($r = 0.576$), indicating significant associations between these biomarkers and hospitalization status in COVID-19 patients.

### CONCLUSIONS

CRP, PCT, and IL-6 are significantly elevated in hospitalized COVID-19 patients, suggesting their potential as markers for inflammation and infection severity. CRP showed the strongest correlation with hospitalization, while PCT and IL-6 also reflected substantial differences, though with weaker correlations. These findings support the use of these biomarkers in monitoring inflammation and guiding clinical decisions in hospitalized COVID-19 patients.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0797

## PIVKAII IN CLINICAL PRACTICE IN PATIENTS WITH HEPATOCELLULAR CARCINOMA: EXPERIENCE FROM A TERTIARY CENTER

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### BACKGROUND-AIM

Hepatocellular carcinoma (HCC) is the 6th most common cancer worldwide and represents more than 90% of primary liver cancer.
Prothrombin induced by vitamin K absence-II (PIVKA-II) is primarily used in Asia as a non-invasive diagnostic and prognostic biomarker of hepatocellular carcinoma. (HCC). PIVKA II is an abnormal form of prothrombin secreted into the blood when the carboxylase activity in the liver, dependent on vitamin K, is inhibited due to the absence of vitamin K or the presence of vitamin K antagonists.

### METHODS

In a monocentric study in a tertiary center, we compared two immunological methods for PIVKAII measurement in current clinical practice on Lumipulse (Fujirebio) and Maglumi x6 (Snibe).
For 55 patients, we obtained the final diagnosis and compared it with alfa foeto protein results when available.

### RESULTS

We compared the results obtained for 55 patients within the linearity range of the two methods.
Patients were suffering from different diseases: most of them (37 patients/55%) had an HCC, 10/ 18 % had another digestive cancer, and 8/14.5% of patients presented with cirrhosis or metabolic diseases.
Mean +/-SD were respectively 701.3.5 +/-194.9 mAu/mL with Maglumi x6 and 787.7 +/-234.4 mAu/mL with Fujirebio.
The correlation between the two techniques was high (R2: 0.9799). The mean bias of difference versus average (Blant Altmann analysis) was -101.4.
When comparing patients with and without HCC, both assays showed a significant difference between patient groups, evidencing their ability to discriminate between the two groups.
In our cohort, many patients displayed low AFP values (46 patients); indeed, many patients for whom PIVKAII is measured in our clinical practice are patients presenting low AFP concentrations, for whom PIVKAII represents a good alternative.

### CONCLUSIONS

PIVKA-II is an effective adjunct to AFP in monitoring HCC. Multiple methods are available for measuring this biomarker, and the present study introduces a new assay that can be effectively used in clinical practice.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0798

**DETERMINATION OF SERUM CEA CUT OFF IN END-STAGE CHRONIC RENAL FAILURE HAEMODIALYSIS PATIENTS**

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**BACKGROUND-AIM**

Increased concentrations of serum tumor biomarker may be found in non-malignant diseases and their specificity can be affected in end-stage chronic renal failure patients undergoing haemodialysis.
The aim of our study was to assess the impact of haemodialysis on Carcinoembryonic Antigen (CEA) results in patients at end stage of chronic renal failure and to determine serum CEA cut off in haemodialysis patients.

**METHODS**

The study included 80 patients at end-stage of chronic renal failure undergoing haemodialysis for at least one month and 55 healthy subjects which constituted a control group. Smokers and benign or malignant causes of increased CEA were excluded, no neoplasia was detected for a period of 06 months. Serum CEA assay was performed on Beckman Coulter Access 2 before the first dialysis session of the week. Manufacturer CEA threshold was 3ng/ml for no smoker.

**RESULTS**

Statistical tests have shown that the serum CEA level was significantly higher in the haemodialysis group compared to the control group ($p < 0.05$), we found 36% of false positive results. The mean value of CEA was 3.54±2.43 ng/ml in haemodialysis group and 1.45±0.76ng/ml in control group. The serum CEA 95th percentile on Beckman coulter access 2 determined in our study was 8.5 ng / ml. There was no correlation between serum CAE and BMI, dialysis lenght, uremia, creatininemia and GFR.

**CONCLUSIONS**

The increase of serum CEA concentration in haemodialysis patient remains within the limits observed for benign diseases. Therefore, CEA way be used as indicator in malignant diseases with the precaution to set a cut off in haemodialysis patients. The 95th percentile on Beckman coulter access 2 determined in our study is 8.5 ng / ml. Through this study, we underline the need to use an haemodialysis specific cut-off for CEA to improve the interpretation of results and their clinical application .

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0799

## KAPPA-INDEX TEST PROTOCOL TO DETECT INTRATHECAL IMMUNOGLOBULIN SYNTHESIS IN MULTIPLE SCLEROSIS

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### BACKGROUND-AIM

Traditionally intrathecal immunoglobulin synthesis in Multiple sclerosis (MS) is detected by oligoclonal band (OCB) testing. Kappa free light chain (KFLC) based K-index is proposed as an efficient substitute providing rapid turnaround times. Literature is inconsistent regarding cut-offs and handling of undetectable Cerebrospinal fluid (CSF) KFLC values. Our objective was to develop a streamlined and accurate testing protocol with K-index and reflex OCB for laboratory diagnostics of MS.

### METHODS

K-index and OCB was analyzed in 432 paired CSF and serum samples. K-index was also analyzed in a clinical cohort of 77 OCB positive samples from MS and non-MS patients. All K-index subtests (KFLC and albumin) were measured on Optilite platform (The Binding Site) and OCB with isoelectric focusing on Hydrasys platform (Sebia). The performance of K-index was compared to negative or positive OCB result by receiver operating characteristic (ROC) analysis. Undetectable CSF KFLC results were assigned e.g. the assay limit of detection (LOD) or zero.

### RESULTS

K-index distinguished OCB negative and positive cases with area under curve (AUC) of 0.93. Different handling of the undetectable CSF KFLC levels to calculate K-index had a significant effect on the obtained cut-offs, in part explaining variation in the literature. When we used the LOD value for undetectable CSF KFLC and fixed sensitivity and specificity against OCB negativity/positivity to 95%, the negative/positive cut-offs were <4.45 and >12.92, respectively. Reflexing only results in between to OCB leads to a 69% reduction in OCB testing. When undetectable CSF KFLC was considered as a negative result (n=269), specificity was 99.7% and sensitivity 92.7%. With this approach only 6% would be reflexed to OCB. In our clinical cohort 65/77 cases (84%) had K-index above the positive cut-off (12.92) and K-index above 38.6 indicated MS diagnosis.

### CONCLUSIONS

Faster turnaround times and reduction in OCB testing can be obtained by K-index testing. In the most efficient protocol samples with CSF KFLC <LOD are interpreted as negative, and samples with K-index 4.45-12.92 are reflexed to OCB testing. Our results support the substitution of OCB with K-index in the clinical laboratory setting.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0800

## PLEURAL FLUID TO SERUM ALBUMIN RATIO IMPROVES DIAGNOSTIC ACCURACY OF LIGHT'S CRITERIA IN DISCRIMINATING BETWEEN TRANSUDATIVE AND EXUDATIVE EFFUSIONS

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### BACKGROUND-AIM

Laboratory analysis of pleural fluid (PF) is a key component in the diagnosis and management of pleural effusions. The use of the albumin PF/serum ratio (ALB PF/S) could hold promise as an alternative or complementary diagnostic tool. The aim of our research was to evaluate ALB PF/S, either as a stand-alone diagnostic marker or in combination with the lactate dehydrogenase (LDH) ratio to potentially replace the total protein ratio currently measured in the setting of classical Light's criteria.

### METHODS

We collected a comprehensive consecutive set of 102 PF samples over a one-year period. We carried out biochemical and cellular tests. We performed statistical analysis focusing on ROC curves, with the objective to identify the most effective cut-off value for the ALB PF/S to discriminate between transudative and exudative effusions. Albumin was measured in both PF and serum by immunoturbidimetric assay (DiAgam on Abbott Alinity system) that offers higher specificity compared to dye-binding assays.

### RESULTS

The ROC curve analysis for the ALB PF/S showed an Area Under the Curve (AUC) of 0.849, with a 95% confidence interval (CI) ranging from 0.764 to 0.912 and provided a clear optimal cutoff of 0.6. Analysis of the total protein PF-to-serum ratio yielded an AUC of 0.890, with a 95% CI ranging from 0.813 to 0.944. Combining parameters, the abbreviated Light's criteria (total proteins and LDH ratios) achieved a sensitivity of 85% (95% CI: 75-92%) and specificity of 79% (95% CI: 58-93%). The diagnostic performance of modified Light's criteria (albumin and LDH ratios) showed slightly lower sensitivity, i.e. 81% (95% CI: 70%–89%) and slightly higher specificity, i.e. 83% (95% CI: 63%–95%), suggesting an improved accuracy to exclude exudative effusions.

### CONCLUSIONS

Our research highlights that ALB PF/S is a reliable and effective biomarker for diagnosing pleural effusions by providing a clear optimal cutoff of 0.6. Clinicians can confidently rely on ALB PF/S to guide their diagnostic decision-making improving the efficiency of pleural effusion management.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0801

## AN APPARENT HIGH DOSE HOOK EFFECT FOR CHROMOGRANIN A USING TRACE TECHNOLOGY

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### BACKGROUND-AIM

Chromogranin A (CgA) is a critical 48-60KDa hydrophilic protein found in the secretory granules of neuroendocrine, endocrine, and nerve tissues. As a significant biomarker for diagnosing and assessing prognosis in neuroendocrine tumors-such as carcinoid tumors, pheochromocytoma, and neuroblastoma-CgA plays an essential role in clinical evaluation.

### METHODS

In this study, we report a striking divergence in CgA concentrations in a patient suspected of harboring a neuroendocrine tumor, measured both with and without dilution using automated CgA immunoassays on the ThermoFisher Brahms Kryptor compac. This discrepancy was corroborated by an RIA assay from Cis bio, revealing a consistent hook effect across both methodologies.

### RESULTS

Documented instances of the hook effect in CgA measurements are limited, with previous studies indicating its occurrence in high doses through ELISA assays in about 15% of patients. However, TRACE technology was proposed to be resistant to such hook effects. We investigated this analytical challenge in 25 patients and did not evidence of any similar effect in CgA measurements.

### CONCLUSIONS

By recognizing this issue, we aim to enhance the accuracy of CgA assessments and ensure the reliability of neuroendocrine tumor diagnostics.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0802

## SEX-DIMORPHIC PATTERN OF URINARY FETUIN-A-DERIVED PEPTIDE EXCRETION IN PATIENTS WITH TYPE 2 DIABETES AND NORMOALBUMINURIA

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### BACKGROUND-AIM

Recent evidence of an elevated level of urinary posttranslationally modified peptide fragments of fetuin-A (uPTM3-FetA) in type 2 diabetic (T2D) patients with deteriorating kidney function suggests its potential use as a biomarker of diabetic nephropathy (DN).
In this study, we investigated the association of u-PTM3-FetA excretion with metabolic and renal variables in T2D patients with normal albuminuria and estimated glomerular filtration rate (eGFR)>60 ml/min/1.73m$^2$.

### METHODS

120 adult T2D patients [F/M=80/40] were included in this study. U-PTM3-FetA was measured by a dedicated kit (DnLITE uPTM3-DKD-ELISA) in aliquots of 24h urine specimens, while renal and metabolic parameters (albuminuria, eGFR, $HbA_{1c}$, lipid status, metabolites, liver enzymes) were determined by routine laboratory methods.

### RESULTS

The median/IQR u-PTM3-FetA level was 11,73/6,4 µg/24h, with no difference between female and male T2D patients (P=0,6634).
Multiple regression analysis found an independent positive association between u-PTM3-FetA levels and bilirubin in both men (P<0,001) and women (P=0,004) and a negative association with LDL-cholesterol in male T2D patients only (P=0,036).
The patients were classified according to the median of albuminuria in the low-normal- (LNA; N=60) and high-normal-albuminuria (HNA; N=60) groups. Significantly higher BMI (median/IQR: 32,6/7,4 vs 29,9/7,2 kg/m$^2$; P=0,019) and eGFR (median/IQR: 92/20 vs 89/19 ml/min/1.73m$^2$, P=0,034) was observed in the HNA when compared to LNA group in the entire cohort. However, the sex-specific analysis revealed significantly higher levels of u-PTM3-FetA in male patients with HNA when compared to the LNA group (median/IQR: 14,3/7,8 vs 9,9/7,2 µg/24h; P=0,028), whereas no such difference was observed in female T2D patients (median/IQR: 11,8/7,9 vs 11,7/5,0 µg/24h; P=0,843). In logistic regression analysis, log-transformed u-PTM3-FetA level was independently associated with albuminuria in males (odds ratio: 565,396; 95% CI: 3,872 to 82570,757; P= 0,013), but not female T2DM patients.

### CONCLUSIONS

Our findings suggest a possible role of u-PTM3-FetA in early renal changes among male T2D patients, highlighting the importance of a sex-specific approach in diabetes research.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0803

## THE CORRELATION OF C-REACTIVE PROTEIN, PROCALCITONIN AND PRESEPSIN IN PATIENTS WITH SEPSIS

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### BACKGROUND-AIM

Early diagnosis and management of infections, particularly sepsis and septic shock, are critical in intensive care units, where patients often present with nonspecific symptoms due to their severe clinical condition. This study aims to find the correlation between three key infection biomarkers: C-Reactive Protein (CRP), Procalcitonin (PCT) and Presepsin (PSEP) with sepsis.

### METHODS

The study involved 50 patients, with an average age of 59.58. Samples were collected from two intensive care UNITS (Central Intensive Care Unit and Intensive Unit of the Infectious Diseases Clinic) over a six-month period (June 2024 to November 2024). Levels of CRP, PCT and PSEP were measured to evaluate their correlation with infections in general and sepsis in particular. CRP was measured with immunoturbidimetry method, PCT was measured by an electrochemiluminescence immunoassay (ECLIA) and PSEP with chemiluminescence immunoassay (CLIA).

### RESULTS

Sepsis showed pronounced changes in all three biomarkers, due to its systemic and severe nature. PCT and PSEP levels were strongly associated with the severity of sepsis and septic shock, while CRP, although useful, was less specific. CRP mean levels were 113.68 mg/L, PCT 13.00 ng/mL and Presepsin 1181.01 pg/mL. PSEP had a strong correlation with sepsis ($r = 0.88$), PCT ($r = 0.80$) and CRP ($r = 0.85$). Reductions in CRP, PCT, and PSEP levels indicated an improved response to treatment and reduced inflammation and infection.

### CONCLUSIONS

This study highlights the potential of the combined use of CRP, PCT and PSEP as a diagnostic tool to improve the management and prognosis of critically ill patients, improving timely intervention and treatment of sepsis-related complications. PCT and PSEP, in particular, offer greater specificity for bacterial infections than CRP, making them useful for distinguishing sepsis from other causes of inflammation. The combined use of these biomarkers improves diagnostic accuracy, early detection and provides important prognostic information.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0804

**PROCALCITONIN: IMPROVING EARLY DETECTION OF SEPSIS**

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**BACKGROUND-AIM**

Sepsis is a life-threatening condition caused by a dysregulated response to infection. Procalcitonin (PCT) is a specific biomarker that rises rapidly in bacterial infections, allowing differentiation between Gram-positive, Gram-negative, and viral etiologies. This makes it a crucial tool for early diagnosis and the management of severe infections.
In contrast, bacterial cultures, though the gold standard for identifying the infectious agent, take 24–72 hours to yield results. The rapid processing time of PCT provides a significant advantage for timely and targeted treatment.

**METHODS**

Assess the utility of PCT in differentiating Gram-positive and Gram-negative infections.
Highlight its value in early management before bacterial culture results are available.
A unicentric, observational, and retrospective study based on 150 laboratory analyses from adult patients hospitalized with suspected sepsis, according to clinical records. Inclusion criteria required PCT measurement (Atelica Siemens) in the first laboratory test upon admission. Patients with immunodeficiencies were excluded.
Reference range:
≤ 0.1 ng/mL: No risk.
10.0 ng/mL: High probability of severe sepsis.
Statistical analysis:
SPSS® was used for ROC curve analysis and comparison of median biomarker levels.

**RESULTS**

A total of 150 patients with suspected sepsis were included, of which 142 (94.7%) were confirmed by bacterial culture, and 8 (5.3%) did not meet the criteria.
PCT levels:
Gram-negative: Median 13.2 ng/mL.
Gram-positive: Median 8.7 ng/mL.
Viral infections: Median 0.4 ng/mL.

**CONCLUSIONS**

PCT allows early differentiation between Gram-positive and Gram-negative infections, offering a critical advantage over the longer processing time required for bacterial cultures.
Its rapid availability enables timely and targeted treatment, improving outcomes for patients with severe infections.
Routine use of PCT as a diagnostic tool in clinical laboratories is recommended for optimizing the management of patients with suspected sepsis.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0805

## CLINICAL SIGNIFICANCE OF MONOCLONAL SERUM FREE LIGHT CHAIN QUANTIFICATION ON ASSISTING IN DIAGNOSING MULTIPLE MYELOMA AND SYSTEMIC LIGHT CHAIN AMYLOIDOSIS

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### BACKGROUND-AIM

The aim of this study was to investigate the clinical significance and establish a preliminary cut-off for monoclonal serum free light chain(FLC) for the differential diagnosis of multiple myeloma (MM) and systemic light chain (AL) amyloidosis.

### METHODS

A total of 562 inpatients were included,which were classified into 128 cases of malignant plasma cell diseases (43 first-onset cases), including 94 cases of MM, 15 cases of AL amyloidosis, and 19 cases of MM and AL amyloidosis; 194 cases of chronic kidney injury; 107 cases of cardiovascular function impairment; and 133 cases of other diseases.

### RESULTS

(1)Monoclonal serum FLC levels increased with increasing renal impairment. Both of serum free κ light chain and serum free λ light chain had good positive correlations with serum creatinine in non-M-protein-related disease, with rs of 0.792 and 0.805, respectively (both P values <0.001). (2)ROC analysis showed that considering patients with chronic kidney injury or cardiovascular injury as controls, the cut-off for the ratio of involved to non-involved free light chain(rFLC) was 2.15 in diagnosing MM and AL amyloidosis, and the area under the curve (AUC) was 0.831(95%CI: 0.782-0.881), the sensitivity(SEN) and specificity(SPE) were 0.656 and 0.981, respectively. And the cut-off for the difference between involved and non-involved free light chain(dFLC) levels was 48.06mg/L, the AUC was 0.699 (95% CI: 0.634-0.764). The cut-off for the level of involved free light(iFLC) chains was 268.50 mg/L, with an AUC of 0.569 (95% CI: 0.499-0.640). (3) In diagnosing first-onset MM and AL amyloidosis, both rFLC and dFLC showed higher clinical diagnostic efficacy, with diagnostic AUCs of 0.9 or more. When the cut-off of rFLC and dFLC were 2.5 and 43.00 mg/L, respectively, their diagnostic SEN and SPE could be more than 0.95 and 0.82. However, the diagnostic AUC for iFLC levels was only 0.776.

### CONCLUSIONS

The quantitative monoclonal serum FLC assay has good significance in clinical auxiliary diagnosis of AL amyloidosis and MM, especially for the first-onset diagnosis. It is worth noting that its auxiliary diagnostic cut-off is different from that of the polyclonal FLC. And the conclusion still needs to be further validated in different medical centers.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0806

**COMPARISON OF FOUR ASSAY METHODS FOR MEASURING ANTI-CARDIOLIPIN ANTIBODIES**

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**BACKGROUND-AIM**

Anti-cardiolipin antibodies (aCL), IgG and IgM, are critical biomarkers for diagnosing antiphospholipid syndrome (APS), associated with thrombosis and pregnancy complications. This study compares the performance of four diagnostic platforms: BIO-FLASH, Phadia™ 250, Alegria® 2, and BioPlex® 2200.

**METHODS**

A total of 72 serum samples (40 IgG, 32 IgM) were analyzed using: BIO-FLASH: QUANTA Flash® aCL IgG/IgM (Werfen, San Diego, CA, USA), Phadia™ 250: EliA® Cardiolipin IgG/IgM (Thermo Fisher Scientific, Uppsala, Sweden), Alegria® 2: REAADS® Anti-Cardiolipin IgG/IgM (ORGENTEC Diagnostika GmbH, Mainz, Germany), BioPlex® 2200: Antiphospholipid Panel IgG/IgM (Bio-Rad Laboratories, Hercules, CA, USA)Measurement values were reported in CU (BIO-FLASH) and GPL-U/mL or MPL-U/mL (Phadia, Alegria, BioPlex). Descriptive statistics compared inter-platform agreement and detection thresholds. Sensitivity and diagnostic accuracy were not assessed.

**RESULTS**

For IgG, BIO-FLASH had higher mean values (12.5 CU) than Phadia (8.3 GPL-U/mL) and Alegria (6.7 GPL-U/mL), while BioPlex often reported values <1.6 GPL-U/mL. For IgM, BIO-FLASH also had the highest mean (10.2 CU), followed by Phadia (4.1 MPL-U/mL) and Alegria (2.8 MPL-U/mL), with BioPlex frequently below 1.6 MPL-U/mL. Significant discrepancies were observed among platforms.

**CONCLUSIONS**

Differences in assay performance highlight the need for standardized calibration to improve consistency. BIO-FLASH demonstrated higher sensitivity for low-level detection. Further studies with larger sample sizes are recommended to validate these findings and harmonize methodologies.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0807

**TOTAL GASTRIN VS. GASTRIN-17: DIAGNOSTIC IMPACT**

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**BACKGROUND-AIM**

Gastrin is a major gastrointestinal hormone that stimulate gastric acid secretion. In serum, it appears as a mixture of different length peptides, being gastrin-17 (G17) and gastrin-34 (G34) the main circulating forms. Measurement of serum gastrin is used in the diagnosis of gastrinomas and other neuroendocrine tumors (NETs).
This work aims to verify if the measure of only G17 could lead to false negatives resulting in missed tumor diagnoses.

**METHODS**

136 patient's samples with a gastrin result (Siemens Immulite 2000) were re-tested using Snibe Maglumi 800 analyzer, to measure G17. Both procedures are chemiluminescent sandwich immunoassays.
Results were categorized as normal, high or low based on the reference values for each technique: gastrin [13-115 pg/ml] and G17 [1.7-7.6 pg/ml].
Patients with discordant classifications were selected and their clinical diagnoses were reviewed.

**RESULTS**

G17 results ranged from 1.55 to 340.4 pg/ml and gastrin from 5.1 to 1801 pg/ml.
Among the 136 samples, 115 (84.6%) showed concordance with both techniques: 56 normal, 54 pathological (elevated), 1 low, and 4 low according to gastrin but normal according to G17; considering them concordant since the difference between a low and a normal result has no clinical relevance. The remaining 21 samples (15.4%) were non-concordant: normal gastrin but pathological G17.
The latter were classified into four diagnostic groups:
1. Gastritis/digestive symptoms: 8 (38.1%)
2. Suspected NET: 5 (23.8%)
3. Active NET / recurrence: 2 (9.5%)
4. NET in remission: 5 (23.8%)
5. Other tumors: 1 (4.8%)
Furthermore, it was found an elevated chromogranin A in 14 of 17 cases (82.3%) where it had also been tested.

**CONCLUSIONS**

Gastrin and G17 results are not interchangeable due to differences in measured peptides. Interpretation must rely on each assay's reference values.
In our patient classification both methods agreed in 84.6% of cases, while 15.4% showed discordance, with G17 indicating pathology but not total gastrin. In 66.6% of these discordant samples (14 out of 21), Chromogranin A was elevated. These discrepancies were found in patients with moderate elevations of G17, up to 23.81 pg/ml.
Therefore, measuring only gastrin-17 does not pose a risk of false negatives and its results are consistent with other tumor markers.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0808

## INTRATHECAL SYNTHESIS OF ANTI-TREPONEMA IGA, IGG AND IGM: A NEW APPROACH IN THE DIAGNOSIS OF NEUROSYPHILIS

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### BACKGROUND-AIM

Neurosyphilis (NS) is a spirochetal disease with diverse clinical manifestations, which can spread to the Central Nervous System (CNS) within hours to days after inoculation with the bacterium Treponema pallidum. The diagnosis of NS can be difficult due to the lack of specificity of the findings or because it presents clinical manifestations similar to other pathologies.

### METHODS

This study aims to report the case of a 69-year-old male patient, treated at a clinic in the Central-West region of Brazil, presenting with amnesia, headache, progressing to dysarthria, dizziness and motor impairment, tremors in the extremities and bradykinesia.

### RESULTS

Upon examination of the anamnesis, the patient reported being immunocompetent and diagnosed with syphilis years ago. Eligible for CSF analysis, a lumbar puncture was performed and revealed clear and colorless cerebrospinal fluid (CSF). The patient presented increased cellularity, 9 nucleated cells/mm3 (93% lymphocytes, 4% monocytes and 3% segmented neutrophils), slightly elevated protein levels (47.6 mg/dL), decreased glucose/glycemia ratio (0.51) and non-reactive VDRL. Given the persistence of symptoms and still under suspicion of NS, the Reiber normogram was proposed. This technique is based on the principle of the CSF/serum ratio for immunoglobulins IgA, IgG and IgM with hyperbolic graphs, which maintains a reliable statistical relationship for studies of intrathecal synthesis and barrier breakdown. The result indicated intrathecal synthesis of IgA, IgG and IgM, without dysfunction of the blood-brain barrier (BBB), confirming the biobehavior of NS. Additionally, FTA-ABS IgG and IgM were performed on the CSF, and FTA-ABS IgG was reactive. Based on clinical and laboratory evidence, the patient was diagnosed with NS. Drug treatment was initiated, the symptoms disappeared after treatment, and a new CSF collection was requested to elucidate the therapeutic efficacy. When repeating the laboratory analyses, the CSF was within normal values in all parameters analyzed.

### CONCLUSIONS

In conclusion, Reibergrams proved to be a technique of choice in NS, being possible to characterize the function of the BBB and the intrathecal synthesis of immunoglobulins in this pathology.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0809

**SEARCH FOR NEW DIAGNOSTIC BIOMARKERS FOR ENDOMETRIOSIS**

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**BACKGROUND-AIM**

Endometriosis is a chronic inflammatory disease characterized by the presence of endometrium-like tissue on the outside of the uterus. Endometriosis affects 10% of women worldwide and is associated with menstrual pain, can affect fertility and lead to inflammation and cancer. Diagnosis is usually made by laparoscopy and can take up to 7 years. The work presented here aims to describe a panel of possible biomarkers for the early diagnosis of endometriosis.

**METHODS**

In our search, instead of comparing the concentrations of biomarkers with reference values in healthy individuals, we selected multiple metabolite ratios. This approach has the advantage of being insensitive to variability caused by possible confounders. For this project, 287 human plasma samples were used in the discovery study and a further 235 in the replication study. Samples were collected from patients at different stages of the disease and analyzed with HPLC system coupled with mass spectrometer. Analyte concentrations were measured with the Biocrates p180 kit. Metabolite selection was performed by machine learning with randomForest on all metabolites and all possible metabolite ratios. The possible candidates were further narrowed using a generalized linear model. Model performance was based on the value obtained for reporter-operator curves with area under the curve (AUC).

**RESULTS**

The model was applied to any form of endometriosis and to specific types such as: peritoneal, ovarian and mixed. Our study found that the combination of three pairs of metabolites provided the best diagnostic performance and that different classes of metabolites (e.g. lipids and amino acids) must be included in the model. Of all types of endometriosis studied, the best result was obtained for peritoneal where, AUC=0.80, specificity=0.74 and sensitivity=0.75 were found. These values were obtained with the following metabolite combination: lysoPC aa C16:0/SM(OH) C16:1 + PC aa C32:0/SM C18:0 + PC aa C32:0/PC aa C38:3 (where LysoPC= lysophosphatidylcholine, SM(OH)= hydroxysphingomyelin, SM= sphingomyelin, PC= phosphatidylcholine).

**CONCLUSIONS**

The development of an effective analytical methodology for the quantification of these metabolites is currently underway. This could lead to a useful non-invasive test for endometriosis.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0810

## ANTI-NEURONAL-YO ANTIBODY POSITIVITY IN A MALE WITH LUNG CANCER: A CASE REPORT

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### BACKGROUND-AIM

A 73-year-old male patient presented to the emergency department with progressive generalized weakness, evolving over several months, associated with strength loss, parkinsonism, and cognitive decline. Relevant medical history includes type 2 diabetes, hyperlipidemia, smoking 20 cigarettes/day since age 14, and moderate alcohol consumption. A CT scan revealed probable adult hydrocephalus, a 9mm left temporal focal lesion (possibly a cavernoma), and chronic lacunar infarcts in the bilateral basal ganglia. Upon admission to the neurology department, an MRI confirmed a left parieto-temporal cavernoma. Due to the patient's progressive decline over subsequent weeks, a more extensive workup was conducted, including an autoimmune panel and tumor marker assessment.

### METHODS

The neuronal antibody study was performed using immunoblotting with the EUROLINE neuronal antigen profile on the EUROBlotOne analyzer (EUROIMMUN). Tumor marker levels were determined using the “i” module of the Alinity analyzer (Abbott).

### RESULTS

The autoimmune panel was positive for anti-neuronal-Yo antibodies, suggesting the possibility of a malignancy, potentially causing at least part of the observed neurological manifestations (paraneoplastic neurological syndrome). An expanded tumor marker panel revealed: carcinoembryonic antigen (CEA): 28.1 ng/ml, CA 15.3: 38.1 U/ml, CA 19.9: 155.9 U/ml, and Cyfra 21.1: 7.91 ng/ml, indicating a high risk of epithelial malignancy, likely lung adenocarcinoma, which was confirmed by imaging studies.

### CONCLUSIONS

This case is striking because anti-neuronal-Yo antibodies are typically found in women (99% of cases), with only isolated reports in men. Additionally, lung cancer is rarely associated with this antibody. Neuronal antibodies are valuable as diagnostic markers for brain diseases and, in some cases, can reveal an underlying malignancy, facilitating faster diagnosis, early treatment, and improved prognosis. In this context, the laboratory plays a crucial role in detecting anti-neuronal antibodies and tumor markers (which may be altered in a potential associated malignancy).

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0811

## RELATIONSHIP BETWEEN ANTI-JO1 DETERMINATIONS AND THE DIAGNOSIS OF ANTI-SYNTHETASE SYNDROME: A CLINICAL AND IMMUNOLOGICAL ANALYSIS

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### BACKGROUND-AIM

Antisynthetase syndrome (AS) is a rare autoimmune disease characterized by the presence of specific autoantibodies, most frequently Anti-Jo1. The syndrome manifests with a range of clinical features, including myositis, interstitial lung disease, arthritis, Raynaud's phenomenon, and skin manifestations. This study aims to investigate the relationship between Anti-Jo1 determinations performed in our hospital and the clinical diagnosis of antisynthetase syndrome, as well as the associated immunofluorescence patterns.

### METHODS

In 2024, a total of 196 Anti-Jo1 quantifications were performed in our hospital in patients with suspected autoimmune disease. Positive results were obtained by enzyme-linked immunosorbent assay (ELISA) and subsequently evaluated for clinical significance. Autoantibody patterns in Anti-Jo1 positive cases were analyzed by indirect immunofluorescence in Hep-2 cells.

### RESULTS

Of the 196 Anti-Jo1 determinations, 6 (3.1%) were positive. Among these, 5 patients (83.3%) were clinically diagnosed with antisynthetase syndrome, while 1 patient (16.7%) was classified as having an undifferentiated connective tissue disease. Notably, 4 of the 6 Anti-Jo1-positive cases (66.7%) exhibited a positive cytoplasmic pattern on indirect IF, further supporting their clinical diagnosis of antisynthetase syndrome.

### CONCLUSIONS

The presence of Anti-Jo1 is strongly associated with antisynthetase syndrome, with 83.3% of positive cases in our hospital meeting the diagnostic criteria for the disease. Furthermore, the identification of cytoplasmic patterns on indirect IF in Anti-Jo1-positive cases serves as an additional diagnostic tool. These results highlight the diagnostic value of Anti-Jo1 testing and indirect IF patterns in the identification of antisynthetase syndrome.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0812

## PROADM AS A PREDICTOR OF HOSPITAL ADMISSION IN PATIENTS PRESENTING TO THE EMERGENCY DEPARTMENT WITH SUSPECTED INFECTION

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### BACKGROUND-AIM

The high workload in Emergency Department (ED) makes it crucial to have biomarkers that support decisions on discharging or keeping a patient under observation when clinical presentation is ambiguous, as often occurs in infections.
Pro-adrenomedullin (MR-proADM) has been proposed for use in emergency labs as a prognostic marker for risk stratification during triage, improving resource management:
• MR-proADM<0.87 nmol/L: Discharge
• MR-proADM<1.5 nmol/L: Observation
• MR-proADM>1.5 nmol/L: Admission
The aim is to study proADM levels in patients treated in ED for suspected infection, comparing its usefulness as a prognostic marker for admission with other widely used biomarkers, such as procalcitonin, C-reactive protein(CRP) and lactate.

### METHODS

From October to December 2023, MR-proADM (LiaisonXL®), lactate (Gem5000®), CRP (Cobas-c702®), and procalcitonin (Cobas-e801®) were measured in 144 adult patients with suspected infection.
Patients were classified based on whether they required admission, and the cut-off point (Youden's index (Y)), area under the curve (AUC), sensitivity (Se) and specificity (Sp) of each biomarker were calculated using the pROC (v.1.18.5) in R.

### RESULTS

109 patients (75.7%) required admission. Biomarker's results were:
MR-proADM: Y=1.515nmol/L; Sp=0.857; Se=0.624; AUC=0.782(0.701-0.864)
Lactate: Y=14.5mg/dL; Sp=0.697, Se=0.549; AUC=0.642(0.530-0.754)
Procalcitonin: Y=0.335ng/mL; Sp=0.970; Se=0.565; AUC=0.816(0.745-0.888)
CRP: Y=42.45mg/L; Sp=0.715; Se=0.752; AUC=0.795(0.716-0.875)

### CONCLUSIONS

The MR-proADM cut-off point for patient admission was 1.51nmol/L, consistent with published data.
While MR-proADM showed good discriminatory ability (AUC), procalcitonin and CRP performed slightly better.
Since patients presented with infection symptoms, this may explain the high specificity of procalcitonin and improved AUC.
To fully support including MR-proADM in emergency protocols, more studies should include diverse consultation reasons. However, in patients with suspected infection, MR-proADM is a valuable indicator for assessing severity in triage, especially combined with other markers like procalcitonin, CRP, or lactate. This is especially relevant when clinical presentation is unclear, aiding in discharge or admission decisions, and reducing pressure in ED.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0813

**IMPACT OF IRON DEFICIENCY ANAEMIA ON THE RELIABILITY OF HBA1C LEVELS.**

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**BACKGROUND-AIM**

Glycated haemoglobin (HbA1c) is a widely used clinical marker for assessing glycaemic control in patients with diabetes. However, certain conditions can affect the reliability of this marker, with anaemia, particularly iron deficiency anaemia, being a common factor influencing HbA1c variability.
This study aimed to determine the upper limit of total haemoglobin concentration above which HbA1c measurements become unreliable for interpretation.

**METHODS**

The study included 100 patients with iron deficiency anaemia, with three main parameters measured: HbA1c, total haemoglobin, and fructosamine. The population was stratified into three groups according to the severity of anaemia, and a correlation study was performed between HbA1c and fructosamine, a glycaemic marker independent of anaemia.

**RESULTS**

The results were as follows. In the total sample, a significant positive correlation ($r = 0.508$, $p < 0.001$) was observed. A statistically significant correlation was also noted in the moderate ($r=0.39$, $p=0.007$) and mild anaemia subgroups ($r=0.647$, $p<0.001$), but not in the severe anaemia group ($p=0.257$).

**CONCLUSIONS**

These findings suggest that in cases of severe anaemia, HbA1c is an unreliable marker for assessing glycaemic control, and the use of alternative markers such as fructosamine is an alternative solution until iron deficiency is corrected.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0814

## EFFECT OF DIFFERENT BLOOD COLLECTION ANTICOAGULANTS ON THE VARIATION OF COMPLETE BLOOD COUNT UNDER PHYSIO-PATHOLOGICAL CONDITIONS

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### BACKGROUND-AIM

The Complete Blood Count (CBC) is a clinical analysis, performed on anticoagulated whole blood, that quantifies and characterizes all blood cells to assess the general state of health of individuals. Anticoagulants play a critical role in blood collection, and they are commercially available in different formulations: acid ethylenediaminetetraacetic (EDTA-K2 and EDTA-K3), Sodium Heparin (NH), Sodium Citrate (9NC), Citrate Dextrose (ACD). EDTA-K2 is defined by ICSH as the gold standard anticoagulant for CBC. The aim of our study was to compare the CBC obtained with the five different anticoagulants up to six hours at RT, and to investigate the cellular response to two proinflammatory and prothrombotic triggers, depending on the anticoagulant used.

### METHODS

Whole blood from healthy volunteer donors (n=12) was collected in EDTA-K2, EDTA-K3, NH, 9NC and ACD and treated with LPS (1μg/mL) and a mixture of histones (200μg/mL). Readings were obtained at 0, 1, 2, 3, 4, 5 and 6 hours in controls and at 30 min, 1 and 3 hours in treated samples through Beckman Coulter DxH 690T.

### RESULTS

Results confirmed that EDTA-K2 is the most appropriate anticoagulant for CBC determination. Values obtained with EDTA-K3 were not significantly different from EDTA-K2. Liquid anticoagulants, 9NC and ACD, induced significantly lower CBC values than EDTA-K2 because of hemodilution; this difference is adjusted using conversion factors. NH was not eligible for platelet index analysis due to heparin-induced pseudo-thrombocytopenia. CBC is stable for up to 6 hours with all the anticoagulants. Histones induced rapid and significant platelet depletion (due to aggregation), mean platelet volume increase and Monocyte Distribution Width (MDW) enhancement in blood collected with EDTA-K2 and EDTA-K3, whereas significantly different results were observed with 9NC and ACD. LPS promoted a significant time-dependent increase in MDW in all tubes, except for 9NC and ACD, where MDW decreases after 3 hours due to the possible anti-inflammatory effect of citrate.

### CONCLUSIONS

In conclusion, EDTA is the most suitable anticoagulants for CBC, also recommended by Beckman Coulter for the reliability of MDW. The potential use of selected liquid anticoagulants would require appropriate correction factors but needs further investigation.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0815

## VARIATIONS OF MONOCYTE AND NEUTROPHIL CELL POPULATION DATA BY GRAM-NEGATIVE AND GRAM-POSITIVE BACTERIA: DO THEY REPRESENT EMERGING EARLY SEPSIS BIOMARKERS?

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### BACKGROUND-AIM

Sepsis is a life-threatening organ dysfunction caused by a dysregulated host response to the infectious agent. Early diagnosis is a major challenge for patients in emergency departments. Monocyte Distribution Width (MDW), obtainable from hematological analyzer Beckman Coulter, is an early sepsis biomarker with high negative predictive value. MDW is included in Complete Blood Count (CBC) along with Cell Population Data (CPD) which are potential time and cost saving biomarkers obtained through Volume Conductivity Scatter technology. This study is focused on the investigation of Neutrophil (NE) and Monocyte (MO) activation during infection as reflected by Volume (V), Conductivity (C) and Axial Light Loss (AL2) alterations.

### METHODS

Whole blood (n=24) was treated with live E. coli and S. aureus (10^6 and 10^8 CFU/ml), lipopolysaccharide (LPS) 1μg/ml, and lipoteichoic acid (LTA) 200μg/ml. CBC and CPDs were obtained at 0, 30, 60, and 180 min using DxH 690T (Beckman Coulter).

### RESULTS

Firstly, our results proved that E.coli, S.aureus and their PAMPs induced an early and significant time- and dose-dependent increase in Mean Monocyte Volume (MN_V_MO) ($p<0.0001$). E.coli, LPS, S.aureus 10^8 CFU/ml and LTA also induced at each time a significant enhancement of Volume Standard Deviation (SD_V_MO) (p:0.001-0.01) and a significant decrease in MN_C_MO. MN_AL2_MO significantly decreased with E.coli 10^6 and E.coli 10^8 CFU/ml (p:0.0001-0.001) while SD_AL2_MO was significantly increased by both live bacteria and LPS (p:0.001-0.01). The mean volume of neutrophils (MN_V_NE) is differently affected from that of monocytes, decreasing significantly after treatment with E.coli, LPS, S.aureus 10^8 CFU/ml, but accompanied by a significant increased anisocytosis reflected by SD_V_NE. Moreover, E.coli and LPS significantly increased MN_AL2_NE and decreased MN_C_NE values. SD of AL2 and C in neutrophils were significantly enhanced by both bacteria and PAMPs.

### CONCLUSIONS

In conclusion, since monocytes and neutrophils are the main actors during infectious diseases, CPDs characterising their morpho-functional changes could be potential biomarkers to discriminate sepsis patients according to the pathogen. Our findings highlighted CPDs' emerging role as part of an integrated sepsis screening approach.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0816

## AGE-RELATED VARIATIONS IN MONOCYTE DISTRIBUTION WIDTH TO LIPOPOLYSACCHARIDE AND HISTONES IN AN EX-VIVO WHOLE BLOOD MODEL

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### BACKGROUND-AIM

Monocyte Distribution Width (MDW) is an FDA-approved early diagnostic biomarker of sepsis, a clinical condition defined as a life-threatening organ dysfunction caused by a dysregulated host response to infection. Monocytes are crucially involved in the immune response against pathogens and MDW reflects monocyte anisocytosis. MDW is measured with the Beckman Coulter hematology analyzer as part of Complete Blood Count (CBC) with differential leucocyte formula. The focus of this study is to investigate the monocyte response to Lipopolysaccharide (LPS), a Pathogen-Associated-Molecular Pattern (PAMP) and to histone, a Damage-Associated Molecular Pattern (DAMP), in three different populations: young subjects (<10 years, n=8), adult subjects (>18 yrs, n= 25) and elderly subjects (>75 yrs, n=28).

### METHODS

Whole blood samples collected in EDTA-K2 tubes were treated with LPS (1 μg/ml) and a mixture of histones (200 μg/mL). CBC was performed at 0, 30, 60 and 180 min through DxH690T Beckman Coulter.

### RESULTS

Firstly, our results showed that MDW control values were not significantly different among the three age groups. LPS induced a rapid and extremely significant increase in MDW in adult and elderly populations at all times considered ($p<0.0001$) whereas in young subjects MDW variation was not significant. In particular, at 180 min LPS promoted MDW enhancement significantly higher in adults (25.4±3.1) compared to young subjects (21.5±1.7) ($p=0.0029$). Histone treatment caused a significant increase in MDW at 30 min in the elderly ($p=0.0209$) and both in adult and elderly populations at 60 min ($p<0.05$) and 180 min (p:0.01-0.001). Young subjects are not affected by significant changes in MDW with histone treatment.

### CONCLUSIONS

In conclusion our findings emphasize that the monocytic response to PAMP and DAMP is age-dependent. The significantly different increase in MDW implies distinct morpho-functional alterations of monocytes according to age, underlying that monocytes in young subjects underwent minor morphological changes in response to stresses compared to adults and elderly.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0817

## MIRNAS DEREGULATED IN HUMAN IPSC-DERIVED FTDP-17 MAPT IVS10+16 MUTATED NEURONS

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### BACKGROUND-AIM

Frontotemporal Dementia (FTD) with parkinsonism linked to chromosome 17 (FTDP-17) is an autosomal dominant neurodegenerative disorder leading to behavioural and personality changes, cognitive impairment, and motor symptoms. There are currently no molecular biomarkers available for its diagnosis. Circulating miRNAs are promising diagnostic biomarkers for neurodegenerative diseases and some of them were described to be differentially regulated in plasma samples of sporadic FTD patients (or other tauopathies). In particular, miR-92a-3p and miR-320b were shown to discriminate between healthy controls and FTD patients, whereas miR-320a could discriminate different tauopathies. We have also identified these miRNAs as MAPT mRNA-interacting and Tau-regulating miRNAs.

### METHODS

We differentiated human induced pluripotent stem cells (hiPSCs)-derived neurons carrying a point mutation found in FTDP-17 patients (IVS 10+16) in comparison with the isogenic wild type (WT) control. Different ages of mutated hiPSCs-derived neurons, compared to the WT, were analysed up to 120 days. The levels of the miRNAs of interest were then tested in both mutated and WT hiPSC-derived neurons (cells and medium), together with the analysis of well-known neurodegenerative protein markers UCHL-1, GFAP, Tau, p-Tau and NEFL.

### RESULTS

miR-320a, miR-320b and miR-92a are deregulated in mutated hiPSCs-derived neurons compared to the WT. In particular, miR-320a and miR-320b levels resulted to be triplicated in mutated neurons compared to WT whereas miR-92a was 1.75-fold more expressed in mutated neurons. To mimic the CSF biofluid, conditionate medium collected from 120 days WT and mutated neurons was examined. The miRNA analyses revealed that all the three miRNAs of interest were significantly overexpressed in mutated samples.

### CONCLUSIONS

Our results suggest a promising potential for the use of miR-92a-3p, miR-320a and miR-320b as biomarkers to distinguish between FTDP-17 patients and healthy individuals. These results not only have strong implications in diagnostics but also in the molecular characterization of similar FTD models for drug screening and validation. Currently, we are also working on the identification of these miRNAs in EVs from the medium of the same hiPSCs-derived neurons.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0818

## RELATED FACTORS OF KIDNEY INJURY IN PRIMARY SJöGREN'S SYNDROME

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### BACKGROUND-AIM

Primary Sjögren's syndrome (pSS) is a common chronic systemic autoimmune disorder which primarily affects the exocrine glands. Patients may have extraglandular disease involving multiple organs, including the kidneys. This study aimed at investigating the clinical data and laboratory markers which were associated with renal function damage or renal involvement.

### METHODS

One thousand two hundred eighty-eight adult pSS patients from the Department of Rheumatology and Clinical Immunology were enrolled in this retrospective cohort study. And there were 334 patients of them followed up for more than two years for analyzing demographic, clinical data and laboratory markers. Statistical analysis was performed by R software (Version 3.6.2).

### RESULTS

Nearly 95% of 1288 pSS patients were women, and the positive rates of anti-SSA (Sjögren's syndrome A) and anti-SSB were 63% and 27% respectively. 12% of the pSS patients presented renal involvement with eGFR < 60 mL/min/1.73 $m^2$, and the mean age of hospital presentation, serum creatinine and urea were the highest ($P < 0.001$), and ANA (antinuclear antibody)-positive, anti-SSB positive and anti-scl-70-positive were more prevalent in this group. Multivariate analyses showed that age, urea, chlorine and anti-SSA indicate a significant association with renal dysfunction. Potassium, sodium and Jo-1 were also confirmed to be related with decreased renal function. The receiver operating characteristic (ROC) analysis including the above factors showed a good performance on the evaluation of renal injury including eGFR < 60 mL/min/1.73 $m^2$ and eGFR 60 -90 mL/min/1.73 $m^2$ in pSS, with area under curve (AUC) values of 0.957 and 0.821, and high sensitivity (77.1% and 84.4%) and specificity (95.5% and 70.5%). After a more than two years follow-up of anti-SSA positive patients, 34.14% of them developed decreased renal function, and 13.58% of them experienced a progression of renal injury with a 23.64% decrease in eGFR.

### CONCLUSIONS

Age, urea, chlorine, and anti-SSA were highly associated with renal injury in pSS. Early screening for autoantibodies would be meaningful for evaluation and prevention of renal injury in pSS.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0819

## BIOMATERIAL PROTOTYPING AS A TOOL FOR SELECTION OF CRITICAL RAW MATERIALS FOR ASSAY DEVELOPMENT

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### BACKGROUND-AIM

Biomaterials used in ELISAs, rapid tests or flow cytometer may not be as good candidates for automated chemiluminescence immunoassays (CLIA) due to different binding kinetics, behavior under automation, interferences, or stabilities among other parameters. Biomaterial prototyping consists in checking functional performance of proteins such as antibodies or antigens using specific CLIA technologies. It has the objective to support internal biomaterial development by giving feedback for identification of the best candidates and for the definition of optimal downstream processes.

### METHODS

Newly developed biomaterials such as pair of antibodies for preeclampsia markers: soluble fms-like tyrosine kinase 1 (s-Flt1) and Placental Growth Factor (PlGF); and recombinant antigens for detection of Toxoplasma (Toxo) IgM and Hepatitis E (HEV) IgG have been evaluated using BIO-FLASH® chemiluminescence autoanalyzer. These biomaterials have been coated to magnetic particles resuspended in reference buffers and tested with appropriate proteins labeled with isoluminol and substrates for the chemiluminescence reaction.

### RESULTS

Thermal stabilities of these protein-coated microparticles have been assessed with satisfactory results (less than 15% bias in performance versus reference). Standard assay definitions have been applied to get appropriate dose curve responses with internal reference materials. Functional performance has been evaluated with at least 40 individual clinical samples comparing to commercial reference assays. For s-Flt-1 and PlGF, a correlation coefficient over 0.9 has been achieved. For HEV and Toxo antigens, sensitivities and specificities over 95% and 90%, respectively, have been obtained. Finally, cross-reactivity studies have been conducted for some of these biomaterials, with no cross-reactant markers detected.

### CONCLUSIONS

Prototyping helps de-risking biomaterials developed for new chemiluminescent immunoassays when comparing to specific reference assay which uses proprietary biomaterials. This characterization may last from three to six months and can accelerate the identification of good raw critical materials before starting the proper assay development phases.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0820

## APOLIPOPROTEINS HAVE A MAJOR ROLE IN CELLULAR TUMOR DORMANCY IN TRIPLE NEGATIVE BREAST CANCER: IN-SILICO STUDY

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### BACKGROUND-AIM

Triple-negative breast cancer (TNBC) lacks targeted therapies due to its hormone receptor negativity. The oocyte's microenvironment could induce dormancy in TNBC cells. This in silico study aimed to identify oocyte extract (OE) proteins capable of inducing dormancy in TNBC cells by analyzing protein-protein interactions.

### METHODS

We employed an in-silico approach to predict and confirm protein design through molecular docking and MD simulations. This study received approval from the Institutional Review Board of the Egypt Center for Research and Regenerative Medicine. Surface markers of the MDA-MB-231 cell line were retrieved from available literature until March 2024. Following proteomic profiling, we filtered OE proteins based on function and sequence similarity. Domain coverage, lack of mutations, and high-resolution structures determined the best selection of proteins. Molecular docking identified potential binding pockets, and MD simulations assessed protein stability and flexibility. RMSD, Rg, RMSF, and SASA analyses provided insights into protein dynamics and intermolecular interactions.

### RESULTS

The proteomic profiling of OE revealed 478 proteins, with 29 shortlisted for molecular docking experiments. Low energy scores were observed for most complexes between OE proteins and MDA-MB-231 surface markers, with APOC3 and APOA1 showing the highest stability. Dynamics simulations confirmed these findings, revealing stability in protein complexes, particularly APOA1-K1C14. Various analyses highlighted the stability and flexibility of APOA1 and APOC3 complexes with key surface markers.

### CONCLUSIONS

Identifying interactions between MDA-MB-231 cell line receptors and human OE proteins provides insights into reprogramming MDA-MB-231 cells. APOs are likely involved in inducing tumor dormancy and are part of key tumor-related pathways. This paves the way for exploring novel therapeutic strategies aimed at inducing dormancy in TNBC.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0821

**STUDY OF IGA DEFICIENCIES IN THE CONTEXT OF CELIAC DISEASE IN A TERTIARY CARE HOSPITAL.**

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**BACKGROUND-AIM**

Celiac disease (CD) is a chronic condition characterized by inflammation and flattening of the intestinal mucosa, leading to malabsorption syndrome. Although the exact etiology is unknown, the toxic agent is well-defined: gliadin.
According to the European Society for Pediatric Gastroenterology, Hepatology, and Nutrition (ESPGHAN), the first diagnostic step for CD is the determination of IgA antibodies against type-2 (tissue) transglutaminase (TGA-IgA), along with total serum IgA levels. In cases of IgA deficiency, IgG class antibodies should be measured. A duodenal biopsy is essential for diagnosing CD in patients with IgA deficiency.
Objective:
• To study IgA deficiencies in patients undergoing TGA-IgA testing.
• To assess the presence of CD in patients with IgA deficiency.

**METHODS**

A review of 12,263 TGA-IgA requests between 13/10/2022 and 31/12/2023 was conducted using the Modulab® Laboratory Information System to evaluate IgA levels. Samples with deficient IgA levels were sent to an external laboratory for IgG antibodies against deamidated gliadin peptide antibodies (DGP-IgG) antibody determination. Patients with positive DGP-IgG (Index ≥1) underwent intestinal biopsy. TGA-IgA was measured on the Bioflash® platform (Werfen®) using chemiluminescence, total IgA on the Immage 800® (Beckman Coulter®) using nephelometry, and DGP-IgG on the DS2® platform (Dynex Technologies®) using ELISA.

**RESULTS**

• Total TGA-IgA -IgA tests: 12,263
• Patients with TGA-IgA testing: 11,129
• Patients with IgA deficiency: 189
• Patients with positive DGP-IgG: 11
• Celiac disease diagnosis: 4

**CONCLUSIONS**

The study of serum IgA levels is crucial for the accurate diagnosis of celiac disease, as it reveals an underdiagnosis in patients with IgA deficiency when only IgA-type antibodies are measured. A total of four patients were diagnosed with CD after undergoing intestinal biopsy, thus preventing misdiagnosis based solely on AATG-IgA results.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0822

## CITRULLINE IN ACUTE MESENTERIC ISCHEMIA: A VIEW FROM CLINICAL PRACTICE

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### BACKGROUND-AIM

Acute mesenteric ischemia (AMI) is a critical and often fatal condition, resulting from inadequate blood flow to the mesenteric circulation. Several biomarkers have been investigated for diagnosis and prognosis, notably including citrulline, D-dimers, procalcitonin, and lactate. The diagnostic performance of these markers varied across studies, but in our experience, citrulline has emerged as the most performant biomarker for AMI.
This study aims to evaluate the longitudinal citrulline results in a monocentric cohort of patients with confirmed AMI and other gastrointestinal diseases at a specialized intestinal stroke center.

### METHODS

We retrospectively analyzed citrulline concentrations obtained for 39 patients with acute mesenteric ischemia and 47 with another diagnosis for whom citrulline was measured in their clinical care course. Briefly, all patients were selected in the stroke center and nutrition assistance unit for one year. Patients without AMI were all suffering from severe intestinal diseases and/or malnutrition. Citrulline concentrations were measured by LC-MS on a Xevo TQS (Waters).

### RESULTS

Among our samples, citrulline ranged between 3 and 95 μmol/L, with a mean of 22 μmol/L (SD /+:- 16.3). We observed a significant difference in the mean values based on sex, with women presenting higher concentrations (mean 27.3 vs 17.57 μmol/L). Citrulline was significantly lower in patients with AMI than other intestinal disorders (Mean 16.9 vs 27 μmol/L; p=0.0006). Performances of citrulline for discriminating patients with or without AMI gave an AUC of 0.712 (95% CI : 0.599-0.825) . We also evidenced that in our cohort, citrulline was significantly correlated to CRP and Albumin. Consequently, inflammation and malnutrition may have an impact on the values in our cohort.

### CONCLUSIONS

AMI is a very rare disease and ameliorating the biological diagnosis is mandatory. Citrulline may be a good additional marker to help in the diagnosis and monitoring of this life-threatening disease. However, as we initially published, the performances for the diagnosis are still too low to be used alone.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0823

**COGNITIVE PROGRESSION AND β-AMYLOID LEVELS IN ALZHEIMER'S DISEASE.**

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**BACKGROUND-AIM**

Alzheimer's disease (AD) is the first cause of neurodegenerative dementia with high socioeconomic burden that poses a global health challenge. AD diagnosis is based on clinical criteria, mainly progressive cognitive impairment, and is confirmed by neuroimaging tests although due to the complexity and cost of these techniques, new diagnostic tools have emerged, such as cerebrospinal fluid (CSF) biomarkers: β-amyloid (βA) peptides (β42 and β40), and Tau proteins. AD has been considered a disease caused by βA brain deposition . New trends suggest that loss of βA normal function in its native soluble state might cause AD´s clinical features. Consequently, subjects with higher levels of βA (high producers) might have a favourable cognitive outcome due to high circulating available βA.
Aim: To evaluate cognitive decline in a cohort of 117 patients, studying if high βA subjects showed slower AD progression.

**METHODS**

215 subjects with suspected cognitive impairment were included. CSF βA40, βA42, total Tau (tTau) and 181-phosphorylated Tau (pTau) were tested by CLIA (Lumipulse, Fujirebio). Reference values: βA40:7755-16751pg/mL; βA42>599pg/mL; tTau<404 pg/mL; pTau<56.5pg/mL. To minimize differences between hβA and nhβA, AD classification was made by Tau proteins and βA42/βA40 ratio (42/40>0.069). AD patients were divided in two groups: high βA (hβA) (βA40>16751) and non-high βA (nhβA) (βA40<16751). Cognitive status was assessed from first to last evaluations by GDS and CDR scales.

**RESULTS**

AD compatible patients (N=117):42/40:0.049±0.01; tTau:621±33.6; pTau:125±5.7; Non-AD (N=76):42/40:0.109±0.013; tTau:280.1±15.8; pTau:36.9±1.9. An inconclusive group (N=32) did not meet classification criteria. Most AD patients were nhβA (βA40:11507±279) but 18% of AD group were hβA (βA40:19114±70.4; p<0.0001 vs nhβA) and showed higher βA42 levels (791±43 vs. 448±13 in nhβA; p<0.001). Patients (N=9) with highest βA42 levels (>800 pg/ml) showed slower progression than other AD patients, 1 point less in CDR scale (mean following time: 4.3 years).

**CONCLUSIONS**

Our results highlight the relationship of phenotypic differences in cognitive progression with AD biomarkers. Characterization of high βA producers patients could lead to a better knowledge of βA role in cognitive function.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0824

## ANALYSIS OF PREANALYTICAL VARIABILITY ON PLASMA MIRNA EXPRESSION PROFILE BY NEXT GENERATION SEQUENCING TO REVEAL SPECIFIC POTENTIAL DIAGNOSTIC BIOMARKERS OF MYELODYSPLASTIC SYNDROME

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### BACKGROUND-AIM

Background: miRNAs represent potential non-invasive circulating biomarkers for oncological diseases as the myelodysplastic syndrome (MDS). Although the effect of biological variability on miRNA expression profile is well documented, limited data are available on the role of preanalytical variability, both relevant in the prospective of an imminent clinical application of these molecules. Indeed, very few data on the combined effects of time and temperature storage on the recommended Platelet-poor plasma (PPP) for miRNAs are available.
Aim: The aim of this study was to: 1) investigate the impact of these preanalytical variables in PPP samples on miRNA expression profile using Next Generation Sequencing (NGS); 2) identify potential circulating miRNAs as diagnostic biomarkers of MDS, using a comparative approach for preanalytical variability in the differential expression analysis.

### METHODS

Methods: EDTA K2 plasma from 12 patients with MDS and 12 healthy donors (HD) were collected, centrifuged to obtain PPP within 3 hours (h). PPP aliquots were stored before miRNA extraction as follows: A= 4°C for 30 minutes; B= 4°C for 24 h; C= RT for 24 h; D= -20°C for 10 days. miRNA libraries were prepared using QIAseq miRNA Library Kit (Qiagen), sequenced in the NGS platform NextSeq550 (Illumina) and analysed using CLC workbench (Qiagen).

### RESULTS

Results: We showed that plasma miRNA expression profile (MEP) is significantly modified by the preanalytical conditions: MEP was affected the most by the C condition (RT for 24 h) followed by B; A and D showed not significant differences. 58 miRNAs were significantly modulated in MDS compared to HD: only 16 miRNAs were constantly differentially expressed in A, B, C and D; in particular, 3 miRNAs upregulated (miR-34a-5p, miR-409-3p, miR-411-5p) and 2 downregulated (miR-16-5p, miR-486-5p) in MDS were strongly significative although influenced by preanalytical conditions.

### CONCLUSIONS

We identify new potential diagnostic biomarkers for myelodysplastic-syndrome through an unbiased comprehensive miRNA-expression profile analysis using NGS, demonstrating how standardization of preanalytical conditions is crucial in research studies for clinical translation.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0825

## EVALUATION OF BIOMARKERS AND HAEMATOLOGICAL PARAMETERS IN THE DIAGNOSIS AND MONITORING OF SEPSIS: A COMPARATIVE APPROACH

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### BACKGROUND-AIM

Sepsis is a syndrome caused by an abnormal response to infection, impairing organ function. It involves inflammatory and immune disorders, leading to immunosuppression and increased mortality risk. Without a diagnostic gold standard, biomarkers aid early diagnosis, prognosis and treatment monitoring.

### METHODS

First we analyzed 40 sepsis patients and 40 subjects with non-infectious diseases from the Emergency Department, assessing haematological parameters with Sysmex XN-9000 and Beckman Coulter DxH 900. Second, we monitored 10 intensive care unit (ICU) patients over five days, focusing on PCR (c-reactive protein), PCT (procalcitonin), presepsin and pro-ADM (pro-adrenomedullin) concentrations, measured with Pathfast, Kryptor Gold, AU5800, and Alinity I. Statistical analysis included Mann-Whitney tests, Pearson correlations and ROC curves to assess diagnostic performance.

### RESULTS

In the first cohort, sepsis patients showed lower basophil (sepsis 0.005±0.009, non-sepsis 0.031±0.022; $p<0.05$) and neutrophil levels (sepsis 5.001±3.804, non-sepsis 2.446±4.697; $p<0.05$) but higher MDW (Monocyte Distribution Width) (sepsis 29.10±11.57, non-sepsis 18.33±2.837; $p<0.0001$) and NEUT-RI (Neutrophil-Reactive Intensity) (sepsis 54.74±10.110, non-sepsis 46.33±3.853; $p=0.0002$). ROC curves indicated high sensitivity (MDW 84.62%, NEUT-RI 89.21%) and specificity (MDW 85%, NEUT-RI 81.25%) for sepsis detection. In the ICU group, PCR significantly decreased from the first day (median 157.90, IQR 80.13-277.50) to fifth day (median 81.41, IQR 16.19-136.50; $p<0.05$). Presepsin, pro-ADM and PCT also declined over time, though not all changes were statistically significant. Correlations showed positive links between MDW and NEUT-RI ($r=0.53$), monocytes and basophils ($r=0.63$), and monocytes and lymphocytes ($r=0.65$), and a strong negative correlation for platelet-lymphocyte ratio (PRL) and platelets ($r=-0.80$).

### CONCLUSIONS

Haematological parameters, presepsin and pro-ADM show promise as diagnostic and prognostic tools for sepsis. However, the limited sample size and preliminary results need further validation. Integrating biomarker panels and their kinetics into therapeutic algorithms could improve diagnosis and treatment and reduce complications.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0826

**CTX/ BAP: UTILITY ON OSTEOLYTIC LESIONS AND PROGRESSION OF MULTIPLE MYELOMA**

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**BACKGROUND-AIM**

Multiple myeloma (MM) is a B-cell malignancy characterized by the production and accumulation of clonal activated plasma cells in bone marrow, which are able to develop bone lytic lesions, often detected at diagnosis by imaging. Bone markers, such as C-terminal telopeptide of collagen type 1 (CTX), a marker for bone destruction, and bone-specific alkaline phosphatase (BAP), a marker for bone formation, offer potential for earlier detection of lesions. An increased CTX/BAP ratio may suggest the presence of bone destruction and may be useful in the diagnosis of MM and providing distinction from diseases such as monoclonal gammopathy of undetermined significance (MGUS) and other hematological pathologies (HP).
The aim of the study was to measure serum CTX and BAP levels, as well as the CTX/BAP ratio, in MM patients with osteolytic lesions and evaluate differences with MGUS, HP, and control (CTL) groups.

**METHODS**

Serum samples from 154 patients (42 MM, 20 MGUS, 43 HP, and 49 CTL) collected between 2019 and 2024 were analyzed. CTX was measured via electrochemiluminescence assay (cobas e601, Roche Diagnostics®; limit of detection: 0.01 µg/L), while BAP was measured using chemiluminescence assay (iSYS, Immunodiagnosticsystems®; limit of detection: 1 µg/L).

**RESULTS**

MM patients exhibited higher CTX levels (mean: 0.61 µg/L) and lower BAP levels (mean: 13.98 µg/L) than other groups, resulting in a significantly elevated CTX/BAP ratio (mean: 0.06). MGUS, HP, and CTL groups showed lower CTX/BAP ratios, averaging 0.02. Kruskal-Wallis test confirmed significant differences between MM and other groups ($p < 0.05$). Receiver-operating characteristic curve (ROC) analysis showed an area under the curve (AUC) of 0.72 for the CTX/BAP ratio, with a cutoff value of 0.029.

**CONCLUSIONS**

CTX levels and CTX/BAP ratio effectively differentiate MM from MGUS and other conditions, reflecting bone destruction associated with osteolytic lesions. The CTX/BAP ratio demonstrates moderate diagnostic ability (AUC: 0.72) and potential for disease staging and monitoring. Longitudinal studies are needed to validate these findings, particularly in populations with age-related bone conditions. This study highlights the utility of CTX and CTX/BAP ratio in improving MM management.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0827

## USEFULNESS OF URINARY GLUTEN IMMUNOGENIC PEPTIDES IN THE MANAGEMENT OF COELIAC DISEASE

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### BACKGROUND-AIM

Coeliac disease (CD) is an autoimmune enteropathy triggered by the ingestion of gluten in genetically predisposed individuals. Strict adherence to a gluten-free diet (GFD) is the cornerstone of treatment. However, some patients experience persistent symptoms and intestinal epithelial damage due to refractory celiac disease (RCD) or unintentional gluten exposure.
Gluten immunogenic peptides (GIP), fragments derived from the incomplete digestion of gluten gliadins and glutenins, are responsible for intestinal damage in CD. The detection of GIP in urine enables the non-invasive identification of recent gluten intake.

### METHODS

We describe the case of a 59-year-old woman diagnosed with CD. Her family history includes a son diagnosed with Crohn's disease. The patient presented with daily diarrhea, intermittent and persistent abdominal pain, asthenia, and significant weight loss despite strict adherence to a GFD. The study for anti-transglutaminase IgA antibodies (anti-TG2 IgA) was negative. Treatment with corticosteroids led to clinical improvement, but symptoms recurred after dose reduction. In this context, a differential diagnosis of inflammatory bowel disease (IBD) was considered, given the clinical presentation and family history. Additional tests were performed to rule out IBD.

### RESULTS

Upper endoscopy revealed duodenal atrophy with villous shortening, confirmed by biopsies (Marsh 3B). Biomarkers, imaging, and pathology ruled out IBD. Given the persistent symptoms and negative tests, GIP were tested in urine using an immunochromatographic method (iVYCHECK GIP Urine from BIOMEDAL). The result was weakly positive, indicating recent gluten exposure.

### CONCLUSIONS

Urine GIP determination is a sensitive and specific tool for monitoring adherence to a GFD. In addition to identifying inadvertent gluten exposures not detected by serology, GIP correlate with intestinal damage, reinforcing their usefulness as biomarkers of risks associated with subclinical inflammation due to continuous exposure. In this case, their detection allowed for adjustments in clinical management, reinforcement of dietary education, and prevention of potential complications, optimizing the comprehensive management of CD.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0828

**CONTRIBUTION OF THE ANA STUDY IN PERICARDIAL FLUID TO THE DIAGNOSIS OF SYSTEMIC LUPUS ERYTHEMATOSUS (SLE).**

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**BACKGROUND-AIM**

Pericardial effusion (PE) is a condition rarely diagnosed in Emergency Department. It is defined as the accumulation of more than 50 mL of fluid in the pericardial space. The etiology is highly diverse, as it can be idiopathic or result from primary pericardial diseases, such as pericarditis of any etiology, or from systemic conditions like acute myocardial infarction and contained cardiac rupture. It can also be caused by cardiac surgery, intrapericardial hemorrhage, metabolic diseases, serous transudation (anasarca), and chylopericardium, among others.

**METHODS**

A 22-year-old woman presents to the Emergency Department with progressive dyspnea over the past 15 days, which has evolved toresting dyspnea, without chest pain. Complementary tests are ordered, with notable results: Troponin:4272 ng/L and D-dimer:9209 ng/mL. Further imaging studies are conducted.

**RESULTS**

CT angiography revealed marked cardiomegaly due to significant pericardial effusion. A pericardial drain was placed with 500 mL of serohematic fluid drained, resulting in improvement of dyspnea. The fluid was sent to the laboratory for analysis.Microbiological tests were expanded to rule out an infectious origin, and pathological studies were conducted to exclude a neoplastic origin. The patient reported a history of polyarthralgia for the past year, frequent conjunctival injection, and intermittent dermal lesions on the upper limbs unrelated to photoexposure. An autoimmune study was expanded both in serum and in the drained pericardial fluid. The study of the pericardial fluid revealed: ANA +1/1280 homogeneous nuclear pattern (AC-1), anti-DNA + 1/160, and positive Extractable Nuclear Antigens (ENA): Ab(IgG) anti-histones, Ab(IgG) anti-SSA/Ro, Ab(IgG) anti-RNP, Ab(IgG) anti-Sm, and Ab(IgG) anti-nucleosomes. Blood tests showed normocytic anemia, hypocomplementemia (C3), positive lupus anticoagulant, and proteinuria. The final diagnosis was myopericarditis with pericardial effusion as the debut of SLE.

**CONCLUSIONS**

SLE is a chronic, multisystemic autoimmune inflammatory disease of unknown etiology, with pericarditis being the most common cardiac manifestation, although it is rare for it to progress to cardiac tamponade. The importance of an autoimmunity study in pericardial fluid is crucial for the diagnosis of such cases.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0829

**DIAGNOSTIC UTILITY OF METALLOPROTEINASE 11 (MMP-11) IN OVARIAN CANCER PATIENTS**

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**BACKGROUND-AIM**

Globally, ovarian cancer is the seventh most common cancer in women and the eighth most common cause of cancer death, with five-year survival rates below 45%. Matrix metalloproteinases (MMPs) belong to a group of zinc-dependent proteins which are thought to play a central role in the breakdown of extracellular matrix. The aim of this study was to investigate the plasma levels of MMP-11 in ovarian cancer patients and healthy subjects, comparing to standard tumor marker (CA 125).

**METHODS**

Tested group consisted of 30 ovarian cancer patients (stage II-IV in FIGO, endometrioid ovarian cancer) and the control group included 30 healthy volunteers. Plasma levels of MMP-11 were determined using immunoenzyme assay (ELISA), CA125 concentrations by chemiluminescent microparticle immunoassay (CMIA).

**RESULTS**

Plasma levels of MMP-11 (median 1420 pg/ml) and CA125 (262,7 U/ml) were significantly higher in ovarian cancer patients as compared to the healthy subjects (530,0 pg/ml; 111,9 U/ml, respectively). MMP-11 diagnostic specificity (74%), diagnostic sensitivity (70.95%), the negative predictive values (NPV 53.15%), and positive predictive value (86.45%) were higher for MMP-11 than to compared marker CA125 (63.15%, 64.14%, 40.15% and 81.47% respectively). The combined use of tested parameters resulted in the increase of the sensitivity to 84% and NPV range to 63,1%. Futhermore higher value of area under the ROC curve (AUC) was also observed for MMP-11 (0,6972), than to the AUC of CA125 (0,5944).

**CONCLUSIONS**

These results suggest a potential usefulness of MMP-11 in diagnostic of ovarian cancer, especially in combined use with CA125

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0830

## FIB-4 AS PROGNOSTIC MARKER FOR LIVER DAMAGE IN BREAST CANCER PATIENTS BEFORE AND AFTER CHEMOTHERAPY

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### BACKGROUND-AIM

Breast cancer is a type of cancer that develops in the breast tissue. It can occur in both men and women, although it is significantly more common in women. The Fibrosis-4 (FIB-4) index is a non-invasive scoring system used to assess liver tissue damage, known as fibrosis, following chemotherapy for breast cancer.

### METHODS

The research was conducted using a tool for collecting laboratory results and other relevant parameters. The Fibrosis-4 (FIB-4) index was calculated using the patients' age, platelet count, and serum levels of alanine and aspartate aminotransferases. In the context of breast cancer patients undergoing chemotherapy, liver damage can arise from the occurrence of hepatic metastases, chemotherapy-induced toxicity, or pre-existing liver conditions. Data analysis was performed using the statistical package IBM SPSS Statistics v17.0, and the results were prepared and presented using Microsoft Word and Excel 2021.

### RESULTS

In this study, we assessed the FIB-4 index in a cohort of breast cancer patients both at baseline and following chemotherapy treatment. The primary aim was to evaluate the relationship between FIB-4 scores and liver function, as well as to explore potential correlations with patient outcomes in response to chemotherapy. At baseline, the mean FIB-4 score among participants was 0.64, indicating a generally normal liver function within this cohort. Following the completion of chemotherapy, we observed that the mean FIB-4 score increased to 0.71. However, this change was not statistically significant, with a p-value greater than 0.05, suggesting that the chemotherapy regimen did not have a notable impact on liver function as measured by the FIB-4 index.

### CONCLUSIONS

Overall, this study found that while the FIB-4 index provides useful insights into liver health and architecture, it did not demonstrate statistically significant changes or associations in our cohort of breast cancer patients. These findings suggest that the FIB-4 index may not serve as a reliable prognostic marker for liver damage in this patient population. Further investigation with larger sample sizes or alternative methodologies is necessary to better elucidate its clinical relevance.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0831

**IDENTIFICATION OF PLATELET INDICES MEDIATED PDGF-B IN PROGRESSION OF MAFLD ASSOCIATED FIBROSIS**

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**BACKGROUND-AIM**

Metabolic (dysfunction) Associated Fatty Liver Disease (MAFLD), is a multifactorial risk in population globally. Platelets are key hematopoietic molecules in development of MAFLD fibrosis. Platelet dysfunction has an important role in activation of hepatic stellate cells along with homeostasis maintenance of Kupffer cells. Platelet-derived growth factor-B (PDGF-B) released from PDGFR-B from activated hepatic stellate cells plays a role in hepatic fibrosis. GATA 4 is specifically expressed in liver sinusoidal endothelial cells, which is linked with liver regeneration. We aimed to assess platelet indices in respect to PDGF-B and GATA-4 in MAFLD and non-MAFLD.

**METHODS**

80 subjects were recruited from Gastroenterology and Medicine OPD at AIIMS,New Delhi. Patients were sub-grouped MAFLD (40) and non-MAFLD (40). Ethics approval was taken. The patient details such as blood investigations, platelet count and platelet indices (MPV, P-LCR, PDW and PCT), non-invasive scores and Transient elastography (TE) findings were illustrated. The GATA-4 and PDGF-B were done by ELISA.

**RESULTS**

Platelet count in MAFLD (234±68.53) and non-MAFLD (173.70± 89.43). Mean platelet volume and Plateletcrit in MAFLD (12.27±1.84 and 0.28±0.06) and Non-MAFLD (11.11±2.03 and 0.26±0.10). Mean platelet volume (MPV) was statistically significant ($p<0.001$). Ratio of MPV/platelet count in MAFLD vs non-MAFLD was 1.75. PDGF-B was significantly increased ($p<0.001$) and GATA-4 was decreased in MAFLD subjects compared to non-MAFLD. PDGF-B ratio in MAFLD vs non-MAFLD was 3.18. PCT vs PDGF-B in MAFLD 0.64 and Non-MAFLD -0.31, MPV vs. PDGF-B -0.45 in MAFLD and Non-MAFLD MPV vs PDGF-B 0.34.

**CONCLUSIONS**

Increased expression of PDGF-B and the ratio of Plateletcrit and Mean platelet volume was actively involved in the progression of MAFLD-associated liver fibrosis. However, the association of GATA-4 in respect to platelet indices was not found with any relations in the activation of platelets. Thus, MPV/PCT ratio could be an non-invasive early-evaluating biomarker for assessment of MAFLD-associated diseases.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0832

## THE VALUE OF NEW BIOMARKERS IN PATIENTS WITH ACUTE DECOMPENSATED HEART FAILURE – PRELIMINARY RESULTS

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### BACKGROUND-AIM

Heart failure (HF) is a severe and progressive clinical syndrome that occurs mainly in the elderly. It is characterized by multiple episodes of acute exacerbations and is associated with a higher risk of re-hospitalization and mortality.
The aim of the study was to compare standard biomarkers (NT-proBNP, hsTnT) with newer biomarkers, namely Growth Differentiation Factor 15 (GDF-15), Galectin-3 (Gal-3) and Soluble Suppression of Tumorigenicity 2 (sST2), in patients with acute decompensated heart failure (ADHF).

### METHODS

The study included 76 ADHF patients (mean age: 77.35±10.91 years, 47.4% women) admitted to the Clinic for Cardiovascular Diseases at the Clinical Hospital Centre Rijeka. Blood samples were taken on the day of hospitalization and serum biomarker concentrations were subsequently analyzed in the Clinical Department of Laboratory Diagnostics. Three months after the initial hospitalization, we used the Integrated Hospital Information System to analyze data on rehospitalizations and in-hospital and out-of-hospital mortality and compared biomarker levels in patients who survived with those who died.

### RESULTS

During the first hospitalization, GDF-15 levels were significantly lower in patients who survived (5952.01±3273.24 pg/ml vs. 8777.53±3849.29 pg/ml, $p<0.05$) than in patients who died (N=6). A significant difference in NT-proBNP levels was observed when comparing surviving patients and patients who died within 3 months (N=15), measured at the time of admission at first hospitalization (6668.28±6303.63 ng/L vs. 17398.80±19264.78 ng/L, $p=0.05$). Gal-3 levels were significantly higher in patients who died during re-hospitalization (N=3) (43.17±8.61 ng/ml vs. 59.27±6.63 ng/ml, $p<0.01$). hsTnT and sST2 levels did not show a significant difference in any patient group.

### CONCLUSIONS

In our study, GDF-15 seems to be a good predictor for an unfavorable outcome during the first hospitalization and Gal-3 levels is potentially good biomarker for predicting mortality during the re-hospitalization.
The determination of newer biomarkers may contribute to a better prognosis for ADHF patients, the combination of several biomarkers could be beneficial and further investigations are desirable.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0833

## COMPARATIVE PERFORMANCE EVALUATION OF THYROGLOBULIN (TG) QUANTITATIVE TESTS: SIEMENS ATELLICA IM THYROGLOBULIN (TG) VS. ROCHE ELECSYS TG II

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### BACKGROUND-AIM

This study evaluated the clinical performance of in vitro diagnostic devices for quantifying thyroglobulin (Tg) in human serum or plasma, a crucial marker for monitoring thyroid function before and after thyroid cancer treatment. Using residual serum samples from routine clinical tests—samples that would otherwise be discarded—this study compared the performance of Siemens' newly released Atellica IM Thyroglobulin (Tg) assay with the established Roche Elecsys Tg II assay.

### METHODS

The study assessed precision, linearity, limit of detection (LoD), limit of quantitation (LoQ), and reference ranges for the Siemens Atellica IM Thyroglobulin (Tg) assay and the Roche Cobas Elecsys Tg II assay. Patient serum samples were analyzed to compare the results of the two assays, and correlation and concordance were evaluated across clinical ranges.

### RESULTS

The precision coefficients of variation (CVs) (%) for both assays were within the manufacturers' specified limits at all tested concentrations. All data points and their confidence intervals fell within the allowable deviation from linearity (ADL) boundaries. A total of 681 patient samples were analyzed to compare the performance of the two assays, and an excellent correlation was observed (Pearson's r = 0.97). Concordance between the assays was evaluated across three clinical ranges. In the low abnormal range, defined as Roche Cobas <3.5 ng/mL versus Siemens Atellica <1.82 ng/mL, concordance was 83%. In the normal range, defined as Roche Cobas 3.5–77 ng/mL versus Siemens Atellica 1.82–111 ng/mL, concordance was 98%. In the high abnormal range, defined as Roche Cobas >77 ng/mL versus Siemens Atellica >111 ng/mL, concordance was 65%. The overall concordance between the two assays was 88%.

### CONCLUSIONS

The Siemens Atellica IM Thyroglobulin (Tg) assay demonstrated performance consistent with the manufacturer's specifications for precision, linearity, LoD, LoQ, and reference ranges. The assay exhibited a strong correlation with the Roche Elecsys Tg II and good overall concordance. However, concordance in the high abnormal range of patient results was comparatively lower, highlighting a potential limitation in this range.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0834

## THE UTILITY OF SERUM MIR-126-3P AND MIR-155-5P EXPRESSION AS EARLY INDICATORS OF DYSGLYCAEMIA IN AN URBAN SOUTH AFRICAN COMMUNITY.

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### BACKGROUND-AIM

Background: The high burden of type diabetes (T2D) worldwide is partly due to the failure of currently adopted diagnostic methods to diagnose individuals early in the disease process before complications or target organ damage. As such, there is a need to explore alternative biomarkers that may facilitate effective screening or early diagnosis. MicroRNAs (miRNAs) regulate glucose metabolism, and their dysregulated expression has been associated with the development of T2D. Therefore, miRNAs have been intensely researched as potential biomarkers for early T2D diagnosis.
Aim: Investigating serum miR-155-5p, miR-146a-5p, and miR-126-3p expression levels in various glycaemic states at baseline and after three years, in an urban South African mixed ancestry population, as potential biomarkers for early T2D diagnosis.

### METHODS

A total of 122 participants aged 20-79 years from the Bellville South community were recruited in the study and they were grouped according to their blood glucose levels as normoglycaemia, prediabetes and T2DM. MiRNA expression was assessed using reverse transcription qPCR, with data normalised using miR-16-5p and the expression patterns of these miRNAs in the three participant groups compared.

### RESULTS

The expression of miR-126-3p and miR-155-5p were significantly lower in normoglycaemia when compared to T2D patients (p=0.041, p=0.009 respectively). Moreover, Spearman correlations revealed a significant negative correlation between miR-126-3p expression and waist to hip ratio (r=-0.244, p=0.012) as well as a positive correlation with body mass index (r=0.259, p=0.007), high-density lipoprotein (r=0.231, p=0.017), serum insulin (r=0.205, p=0.032), glycated haemoglobin (r=0.421, p<0.001), post 2-hour blood glucose (r=0.222, p=0.033) and fasting plasma glucose (r=0.257, p=0.007).

### CONCLUSIONS

Findings from this study revealed dysregulated miRNA expression in T2D relative to normoglycaemia, and hence the potential for miR-126-3p and miR-155-5p to be used for screening and/or early prognosis. Furthermore, these findings suggest miRNAs may have an important role in metabolic/glycaemic regulation. However, these observations require validation in other populations and exploration in animal/cell models to identify biological pathways that are directly regulated by these miRNAs.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0835

## ANALYTICAL AND CLINICAL EVALUATIONS OF SNIBE MAGLUMI S100B ASSAY

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**BACKGROUND-AIM**

To assess the analytical performances of Snibe Maglumi® S100 assay and compare it with the Roche Elecsys® S100B assay in adults with mild traumatic brain injury (mTBI) focusing on reducing unnecessary cranial computed tomography (CT) scans per Scandinavian and French guidelines.

**METHODS**

Analytical performance of the Maglumi® S100 kit was assessed using quality controls from both Snibe and Roche, as well as pooled serums. Clinical performances were assessed using serum from eighty-nine adult mTBI patients presenting to the adult emergency department of Clermont-Ferrand University Hospital with a Glasgow Coma Scale score of 14-15. CT scans were performed according to the Elecsys® S100 measurement, with a decision threshold of 0.10 µg/L.

**RESULTS**

Repeatability and reproducibility coefficients of variation determined using Elecsys® S100B, Maglumi® S100 controls and pooled serums were below 8%. Six (7%) mTBI patients included had clinically relevant intracranial lesions observed on CT scan (CT+), and eighty-three (93%) patients had no lesions (CT-). S100B medians in CT- and CT+ patients were significantly different: 0.125 (0.085-0.219) vs. 0.368 (0.231-0.489) (p= 0.006) for Elecsys®, and 0.073 (0.046 - 0.140) vs. 0.327 (0.230 - 0.353) for Maglumi® (p= 0.004). The areas under the ROC curves for intracranial lesion detection were similar: 0.82 (0.73-0.91; p= 0.0084) and 0.83 (0.75-0.92; p= 0.0063) for Elecsys® and Maglumi®, respectively.

**CONCLUSIONS**

The Maglumi® S100B assay can be used in the management of mTBI patients to exclude unnecessary CT scans. Further studies are needed to validate a clinical decision threshold for CT scan decisions.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0836

## DIAGNOSTIC ACCURACY OF URINARY β2-MICROGLOBULIN FOR PREDICTING EARLY DIABETIC NEPHROPATHY IN PATIENTS WITH TYPE 2 DIABETES MELLITUS: A SYSTEMATIC REVIEW AND META-ANALYSIS.

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**BACKGROUND-AIM**

Predictive indicators for early diabetic nephropathy (DN) in individuals with type 2 diabetes mellitus (T2DM) are currently lacking. The aim of this systematic review and meta-analysis was to evaluate the clinical utility of urinary β2-microglobulin excretion, a measure of renal tubular dysfunction, in the early diagnosis of diabetic nephropathy.

**METHODS**

Two reviewers conducted a thorough search of the PubMed and Google Scholar databases until December 2023. The meta-analysis included studies that reported urine β2-microglobulin in type 2 diabetes patients with normoalbuminuria and microalbuminuria, and that used the urinary albumin/creatinine ratio to evaluate the degree of DN. A 2 × 2 contingency table was created for every investigation. Using a bivariate random effects model, estimates of accuracy such as sensitivity and specificity were computed. The area under the curve (AUC) was calculated and data was pooled using the hierarchical summary ROC approach.

**RESULTS**

The literature search enrolled 95 studies (including reviews) from which 4 studies were finally included in the meta-analysis. The study involved 239 type 2 diabetic patients with normoalbuminuria and 170 type 2 diabetic patients with microalbuminuria. The overall pooled sensitivity and specificity was 0.60 (95% CI 0.38-0.78) and 0.75 (95% CI 0.64-0.83), respectively. The AUC of β2-microglobulin for distinguishing DN patients with normoalbuminuria and microalbuminuria was 0.75 (95%CI 0.71-0.79).

**CONCLUSIONS**

The result of this meta-analysis suggests that urinary β2-microglobulin can be considered a moderate biomarker for early detection of DN in patients with type 2 diabetes.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0837

## DATA INDEPENDENT ACQUISITION (DIA) PROTEOMICS APPLIED TO THE DISCOVERY OF BIOMARKERS: TOWARDS A BETTER DIFFERENTIAL DIAGNOSIS AND PROGNOSIS OF INPH

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### BACKGROUND-AIM

Idiopathic Normal Pressure Hydrocephalus (iNPH) is a subtype of communicative hydrocephalus without identifiable cause, clinically characterised by Hakim's triad. It may be reversible after shunting, though it often coexists with Alzheimer's disease (AD), which impedes shunt response. Given its potential reversibility, discovery of biomarkers towards a more accurate diagnosis and prognosis is crucial.

### METHODS

Cerebrospinal fluid (CSF) samples were collected from 16 patients: 10 had a pure form of iNPH and 6 had concomitant AD, diagnosed in vivo with established CSF biomarkers. All 16 CSF samples were used in data independent acquisition (DIA) for proteomic studies. Generated files were processed with DIA-NN 1.9.2 and statistical analyses were done with Perseus 1.6.15. We normalized with width adjustment, imputed missing values using quantile regression imputation of left-censored data (QRILC), run a two-way Analysis of Variance and removed the batch effect of the sex variable. We run t-tests with s0: 0.1 for proteins, s0: 0.3 for peptides and False Discovery Rate: 5% for both.

### RESULTS

Original matrices included 1.115 proteins and 12.428 peptides. After removal of cRAP proteins, proteins and peptides with -log(P-value) < 1.3 for the disease variable, and proteins/peptides that were absent in more than 70% of the samples, our matrices remained with 29 proteins and 172 peptides. Of those, 9 proteins and 17 peptides were overexpressed in the iNPH+AD group, whereas 6 proteins and 10 peptides were overexpressed in the iNPH group. Five proteins showed statistically significant differential expression on both protein and peptide levels: Autotaxin, Osteonectin and Keratin 5 were overexpressed in the iNPH+AD group, while Pyruvate kinase and protein 14-3-3ζ were overexpressed in the iNPH group.

### CONCLUSIONS

Several molecules showing differential expression between iNPH patients and patients with iNPH and AD are reported, that may present novel biomarkers for a better iNPH differential diagnosis and prognosis. Additional studies in larger cohorts are required to corroborate present findings.

*This project is financially supported by ELKE UniWA (Special Account for Research Funds of University of West Attica).

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0838

## EVALUATION OF NUTRITIONAL RISKS WITH SERUM GHRELIN AND LEPTIN HORMONE LEVELS IN ONCOLOGY PATIENTS

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### BACKGROUND-AIM

The exact cause and treatment of cancer cachexia, which increases mortality in cancer, has not been clarified yet. Our aim in the study was to examine whether serum levels of ghrelin and leptin hormones, which play a central role in hunger-satiety regulation have a diagnostic value and the Nutritional Risk Score-2002 scores and Food Consumption Frequency Questionnaire data, which measure the nutritional support needs of patients in the clinic, have an effect on the risk of malnutrition in gastrointestinal cancer patients.

### METHODS

This study included 85 (47 female and 38 male) non-morbidly obese gastrointestinal cancer patients aged 18-85 years who applied to Tokat Gaziosmanpaşa University, Faculty of Medicine, Chemotherapy Polyclinic. Serum leptin (Jiaxing, Zhejiang, China, Product No: E1559Hu) and ghrelin hormone (Jiaxing, Zhejiang, China, Product No: R3091Hu) levels were analyzed by Enzyme Linked Immunosorbent Assay (ELISA). Nutritional Risk Score-2002 score and Food Consumption Frequency questionnaire were applied. The results were analyzed with appropriate statistical methods using SPSS Statistic 20 (IBM, New York, USA) program. This project was supported by Tokat Gaziosmanpaşa University BAP unit with the code 2022/52.

### RESULTS

The mean age of the patients was 47,5±9,2 years. No statistically significant difference was found between serum ghrelin and leptin hormone levels and age and NRS-2002 scores (p=0.382, p=0.209, respectively). While no difference was found between leptin hormone and gender (p=0.219), ghrelin was detected at higher rates in female patients (p=0.004). No statistically significant difference was found between NRS-2002 score and gender for either gender (p=0.93). When compared with the Turkish Nutrition Guide data, the patients in our sample group consumed meat group, milk group and vegetable group foods at a percentage below the Turkish average (25.4%, 17.9% and 35.8%, respectively), but the percentage of bread group foods was equivalent to Turkey and fruit was above the Turkish average (76.1% and 98.5%, respectively).

### CONCLUSIONS

In gastrointestinal cancer patients, low ghrelin and high NRS-2002 scores are parallel. It can be said that low ghrelin may be a parameter for nutritional risk evaluation.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0839

## THE ROLE OF FECAL CALPROTECTIN IN THE DIAGNOSIS AND MONITORING OF PATIENTS WITH ULCERATIVE COLITIS

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### BACKGROUND-AIM

Determination of fecal calprotectin (FC), a biochemical marker of intestinal mucosal inflammation, reduces the need for frequent endoscopy in patients with inflammatory bowel disease (IBD). In addition to screening, it appears that FC may also be a reliable indicator of the degree of IBD activity.
The study was performed in order to assess the significance of FC determination in the diagnosis and assessment of the activity of ulcerative colitis (UC). We measured, compared and checked interrelations between concentrations of FC, C-reactive protein (CRP) and hemoglobin (Hgb), hematocrit (Hct), number of erythrocytes (RBC), leukocytes (WBC), neutrophil granulocytes (NEU) and platelets (PLT), as well as endoscopic disease activity, in patients with inactive and active UC.

### METHODS

We examined 74 patients with previously pathohistologically diagnosed UC. According to the endoscopic MAYO scoring system, the patients were classified into 4 groups: two with an inactive UC (Group 0 - subscore 0 and Group 1 - subscore 1) and two with an active UC (Group 2 - subscore 2 and Group 3 - subscore 3). The groups are consisted of comparable gender and age subjects, 37 with active and 37 with inactive UC. FC, complete blood count and CRP were measured.

### RESULTS

All examined parameters were significantly higher in patiens with active vs inactive UC. The biggest differences were found for FC (430.07%), followed by CRP (240.15%), WBC (92,16%) and PLT (29.15%). The FC increase was of the highest significance ($p<0.001$), followed by WBC and CRP increase ($p<0.01$), and the decrease in RBC and Hct (<0.05). In patients with active UC, FC significantly correlated with NEU and CRP ($p<0.001$) and WBC ($p<0.05$), while in patients with inactive UC, FC significantly correlated with NEU and PLT ($p<0.05$).
In the entire subjects group, significant correlation with endoscopic findings was established for for all examined parameters, the most significant for FC ($p<0.001$). Also, in all Groups 0-3, FC showed the strongest correlation with endoscopic UC activity.

### CONCLUSIONS

Our results indicate that FC is a useful non-invasive parameter for both diagnosis and monitoring of UC activity, which could be useful in stratifying UC activity without performing endoscopy.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0840

## FECAL CALPROTECTIN IN THE ASSESSMENT OF THE EXTENT OF AN INFLAMMATORY RESPONSE IN IRRITABLE BOWEL DISEASES

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### BACKGROUND-AIM

Background: Chronic inflammatory bowel disease can initially be difficult to distinguish clinically from irritable bowel syndrome (IBS) and inflammatory bowel disease (IBD). Recently, fecal calprotectin (FC) has been proposed as a sensitive biomarker that allows assessment of intestinal inflammation.
Aim: This study investigated the usefulness of FC in assessing the extent of inflammatory response in inflammatory bowel disease.

### METHODS

Fecal calprotectin concentrations were measured in 69 patients using an automated procedure. 40 patients with endoscopic evidence of inflammation in IBD (14 with Crohn's disease and 26 with Ulcerative colitis) and 29 patients with normal endoscopy examination in IBS. The control group (CG) consisted of 20 subjects without inflammatory bowel disease.

### RESULTS

We found statistically significant correlation of FC concentrations with the histologic grade of mucosal inflammation (0.566, P<0.0001). The median FC concentrations were significantly higher (P<0.01) in patients with IBS (74.4μg/g; 95%CI: 38.7 to 92.2) and IBD (601.0 μg/g; 95%: 482.1 to 861.9), than in CG (30.8 μg/g; 95%CI:30.0 to 31.5). We found sensitivity of 73,9% and a specificity of 100% at the cut-off value of 50.0 μg/g, with a positive predictive value (PPV) of 100.0% and a negative predictive value (NPV) of 52.6% for the detection of inflammatory bowel disease. However, we found a lower sensitivity for the detection of separate IBS, but a higher sensitivity for detection of separate IBD and the same specificity (58.6% and 100.0% vs 85.0% and 100.0%) at the same cut-off value 50.0 μg/g. In addition, the PPV of fecal calprotectin was the same, but the NPV was lower for the detection of IBS than for the detection of IBD (100% and 62.5% vs 100% and 76.9%).

### CONCLUSIONS

Our results indicate the significant diagnostic accuracy of FC for inflammatory bowel disease, with a stronger predictive value for IBD than for IBS.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0841

## PREVALENCE OF ABNORMAL PTAU217 IN AGING POPULATION

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### BACKGROUND-AIM

Blood pTau217 is recognized as a good indicator of amyloidosis and may serve as an accurate tool for the diagnosis of Alzheimer's disease. Before implementing this biomarker in clinical practice, data on the general population are required. In this study, we evaluate the prevalence of abnormal pTau217 in an unsuspected Alzheimer population of autonomous aging subjects.

### METHODS

The SarcoPhAge cohort is a Belgian cohort of community-dwelling older adults. pTau217 was measured in 218 plasma samples collected at the second follow-up visit using the Lumipulse pTau217 kit. According to cut-offs previously reported by Arranz et al., negative amyloidosis subjects are <0.130 pg/mL, equivocal amyloidosis subjects are between 0.130 and 0.552 pg/mL and positive amyloidosis subjects are >0.552 pg/mL.

### RESULTS

In our cohort, 64.2 % were negative for pTau217, 33.5 % were in the intermediate zone and 2.3 % were positive for pTau 217. pTau217 was independently associated with age (rho: 0.252, p=0.0002), renal function (rho: 0.295, p<0.0001), MMSE (rho: -0.210, p=0.0019) and body mass index (rho: -0.156; p=0.0210). The percentage of doubtful patients was significantly higher in patients with chronic kidney disease (GFR< 45) (61.5 %) compared to patients with GFR > 60 (30.6 %). Regarding cognitive status, pTau217 was increased in patients with an MMSE score of 28-29 or an MMSE score ≤ 27 compared to subjects with an MMSE score of 30 (p=0.0029).

### CONCLUSIONS

According to our data, one third of the aging population is eligible for neurological evaluation for amyloidosis. Our data support the notion that specific cut-offs or alternative methods should be developed for patients with chronic kidney disease.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0842

## CHARACTERIZATION OF BILE MICROBIOTA IN PATIENTS WITH OBSTRUCTIVE JAUNDICE ASSOCIATED WITH BILIARY TRACT DISEASES

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### BACKGROUND-AIM

Cholangiocarcinoma (CHOL), a malignant tumor of the biliary system, is particularly concerning due to its high malignancy and poor prognosis, often leading to obstructive jaundice. The advent of metagenomic sequencing(mNGS) technology has expanded diagnostic capabilities, including the identification of microbes within tumors and their potential role in cancer progression.

### METHODS

Bile samples from patients with obstructive jaundice admitted to Beijing Friendship Hospital were collected and subjected to 16S rRNA and metagenomic sequencing. The study included patients diagnosed with benign biliary stricture, gallstone, and cholangiocarcinoma. Clinical data and bile chemical components were analyzed. The potential functional roles of the identified microbiota were predicted using bioinformatics tools.

### RESULTS

The study enrolled 13 patients with benign biliary stricture, 19 with gallstones, and 10 with cholangiocarcinoma. Significant differences in bile chemical components and microbial diversity were observed among the groups. The bile microbiota was dominated by distinct phyla and genera across the groups, with Proteobacteria and Fusobacteriota enriched in benign biliary stricture, Firmicutes and Desulfobacterota in cholangiocarcinoma, and Synergistota in gallstone patients. Functional analysis revealed differences in gene functions related to metabolism and other biological processes. A correlation between bile microbiota and biochemical markers was established, and the combination of differential microbiota showed potential as a diagnostic marker for obstructive jaundice of different etiologies.

### CONCLUSIONS

Bile microbiota varies significantly among patients with obstructive jaundice of different etiologies. The identified microbial signatures and their functional roles could serve as novel diagnostic markers and provide insights into the pathogenesis of biliary diseases.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0843

## SERUM PROTEINS, ENZYMES, AND BILIRUBIN AS MARKERS FOR THE DIAGNOSIS, DIFFERENTIAL DIAGNOSIS, AND MONITORING OF INFLAMMATORY BOWEL DISEASE

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### BACKGROUND-AIM

Numerous serum markers have been investigated for non-invasive diagnosis of inflammatory bowel disease (IBD). The aim of this study was to identify differences in common serum biochemical markers between IBD patients and healthy controls (HCs) and for the differential diagnosis of Crohn's disease (CD) and ulcerative colitis (UC).

### METHODS

Serum levels of proteins, enzymes, and bilirubin (BIL) were measured. The two-tailed unpaired t-test and one-way analysis of variance were performed to identify differences among the CD, UC, and HC groups. The area under the receiver operating characteristic curve (AUC) was calculated to determine the accuracy of individual and combinations of markers for the diagnosis of IBD and differential diagnosis of CD and UC.

### RESULTS

Among the analyzed markers, total protein (TP), albumin (ALB), prealbumin (PA), albumin to globulin ratio (AGR), alanine aminotransferase (ALT), aspartate aminotransferase (AST), lactate dehydrogenase (LDH), cholinesterase (ChE), total bilirubin (TBIL), and direct bilirubin (DBIL) were significantly altered in both CD and UC patients ($p < 0.05$). Also, there were significant differences in serum levels of globulin (GLOB), AGR, gamma-glutamyl transpeptidase (GGT), LDH, and DBIL between the CD and UC patients ($p < 0.05$). The combination of PA+LDH was useful to distinguish CD from HCs (AUC = 0.970, 95% confidence interval [CI] = 0.947–0.993, $p < 0.0001$), while the combination of ALB+PA accurately distinguished UC patients from HCs (AUC = 0.941, 95% CI = 0.914–0.968, $p < 0.0001$) and the combination of GLOB+GGT +LDH+DBIL could distinguish CD from UC (AUC = 0.805, 95% CI = 0.738–0.872, $p < 0.0001$). The diagnostic accuracies of the three combinations were validated with an independent validation cohort, which yielded AUC values of 0.979 (95% CI = 0.958–1.000, $p < 0.0001$), 0.931 (95% CI = 0.901–0.962, $p < 0.0001$), and 0.721 (95% CI = 0.635–0.807, $p < 0.0001$), respectively. In addition, serum levels of ALB, PA, AGR, ChE, and TBIL were negatively correlated, while GLOB was positively associated, with C-reactive protein levels in IBD patients and disease severity of UC patients.

### CONCLUSIONS

A series of individual and combinations of biochemical markers were identified for the auxiliary diagnosis, differential diagnosis, and monitoring of IBD.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0844

## AUTOANTIBODY REACTOME ANALYSIS REVEALS DIAGNOSTIC BIOMARKERS AND MOLECULAR CLASSIFICATION FOR RELAPSING POLYCHONDRITIS

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### BACKGROUND-AIM

Lacking effective biomarkers for relapsing polychondritis (RP) poses a significant challenge in the early diagnosis and treatment. This study aimed to identify novel autoantibodies and elucidate the pathogenesis and molecular heterogeneity of RP.

### METHODS

Plasma samples from 467 RP, 186 healthy controls (HCs) and 164 disease controls (DCs) were analyzed using two sequential microarrays and ELISA to discover, validate and verify new autoantibodies, respectively. Machine learning and differential analysis were used to identify diagnostic-specific autoantibodies and their correlation with disease activity, recurrence, and remission.

### RESULTS

The RP group had 1,344 elevated autoantibodies, discriminating RP patients from HCs. These antigenic targets were associated with pathways involving autoimmune responses, infections, and cardiovascular lesion. Two molecular subtypes characterized by different organ involvement and prognosis highlighted RP heterogeneity. Notably, fourteen new autoantibodies were identified, which detected RP in HCs and DCs with a sensitivity of 41% and 49.7% and a specificity of 91.7% and 90.5%, respectively. Among them, six autoantibodies showed a better diagnostic performance and were consistently verified. Specifically, anti-C4B was positively correlated with disease activity; increased anti-KRT16 and anti-C4B predicted RP recurrence within one year; anti-C4B, anti-FNBP4, and anti-KRT10 decreased from acute attack to remission. Furthermore, the deposition of C4B protein in tracheal tissues, coupled with its reduction in plasma of RP patients, indicated that abnormal complement activation might be related to the pathological mechanism of RP.

### CONCLUSIONS

The 14 autoantibodies promoted a non-invasive early detection of RP, predicted disease recurrence and provided new insights into the understanding of RP pathogenesis.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0845

## ELEVATED SERUM LEVELS OF VITAMIN B12 - POOR PROGNOSTIC MARKER IN LUNG CANCER PATIENTS

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### BACKGROUND-AIM

While clinical conditions of vitamin B12 (hereafter referred to as B12 deficiency are widely known, the interpretation of elevated B12 levels is rarely adressed in standard textbooks. Recent studies, however, have linked elevated B12 levels to malignant processes and poorer prognoses in cancer patients. The aim of our study was to compare the examined B12 levels in lung cancer patients who survived to those who died during 17-month follow-up period and at the same time to compare median B12 levels in individual quarters before death.

### METHODS

Between July 2023 and November 2024, a retrospective evaluation of 1262 serum B12 measurements from lung cancer patients was conducted using data from a laboratory information system. Dates of death were continuously recorded, allowing the classification of patients into two groups based on whether they survived the entire follow-up period or they died. The Elecsys B12 II ® diagnostic kits (immunochemical analyzer Cobas e411® Roche) were used for the biochemical analyses. The median reference serum B12 levels reported by the manufacturer are 314 (range 145- 569) pmol/l.

### RESULTS

The median of examined B12 levels in patients who died (n=336) was 827.5 pmol/l (interquartile range - IQR 477.5-1834.5 pmol/L; the median in patients who survived (n=926) was 472 pmol/l (IQR 338.25 – 809.25 pmol/l), significance at $p=3.84 \times 10\#^{23}$ (Mann-Whitney U-test).
At the same time, the median values (and IQRs) of B12 levels (all the following values in pmol/l) were evaluated according to individual quarters (Q) preceding the date of death of the cancer patients; in the 1st Q: 837 (458-1831), in the 2nd Q:1060 (507-2000), in the 3rd Q: 772 (478.25-1297.75) and in the 4th Q before death: 567 (410-567).

### CONCLUSIONS

1. Using this dataset of B12 levels, we observed significantly higher B12 levels in lung cancer patients who died during the study period compared to survivors.
2. The trend of median B12 levels by quarters appear inversely proportional to the time of death, with higher levels noted closer to the date of death.
These findings align with previously published studies suggesting that elevated B12 levels may be associated with a poorer prognosis quoad vitam also in lung cancer patients.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0846

## M2BPGI ASSOCIATED WITH THE RISK OF HEPATOCELLULAR CARCINOMA IN PATIENTS WITH CHRONIC HEPATITIS B

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### BACKGROUND-AIM

The Mac-2 binding protein glycosylation isomer (M2BPGi) in serum is a biomarker for liver fibrosis that has been widely studied in chronic liver diseases. This study examines the role of M2BPGi in predicting hepatocellular carrcinoma (HCC) in patients with chronic hepatitis B (CHB)
Aim: To determine the cut-off threshold, sensitivity (Sp), specificity (Se), positive predictive value (PPV), and negative predictive value (NPV) of the M2BPGi marker between the HCC group and the CHB as control group.

### METHODS

A cross-sectional descriptive study design. The study subjects included patients at University Medical Center HCMC from January 2023 to July 2024. HCC group were diagnosed by CTscan or MRI. CHB served as the control group. M2BPGi quantification was performed using an immunoassay with a commercially available kit (HISCL M2BPGi; Sysmex Co., Kobe, Japan)

### RESULTS

165 HCC (125 males and 40 females) had a median age of 61.0 years (range, 32 to 88). 103 chronic hepatitis patients (64 males and 39 females) had a median age of 44.0 years (range, 22 to 85) have a level of liver fibrosis below stage F2 according to the Metavir classification as control group.
For the whole HCC group (n=165); a cutoff value of M2BPGi level ≥ 1.32 cut off index (COI) yielded an AUROC of 0.762 (p=0.03). The Se of 69.7%; Sp of 75.7%; the PPV of 81.7% was quite high; however, the lower NPV of 61.1%. For HCC non-cirrhotic group (n = 99), a cutoff value of M2BPGi level ≥ 1.22 cut off index (COI) yielded an AUROC of 0.794 (p = 0.03). With a high Se of 79.8%; Sp of 73.8%; PPV of 74.5%; the NPV of 79.2%; the OR of 11.11 (95% confidence interval, 5.75-21.47). These results suggest that M2BPGi is a useful tool in detecting HCC in chronic hepatitis B patients without cirrhosis
M2BPGi Compared to AFP: Using the AUROC of M2BPGi had a significantly higher AUROC value than AFP among patients with HCC (n=165), (0.762 versus 0.612; p = 0.000). In the HCC non-cirrhotic patient group (n=99), M2BPGi also shows a significantly higher AUROC than AFP (0.794 versus 0.695; p = 0.03). In the cirrhotic HCC patient group (n = 66), M2BPGi again demonstrated a significantly higher AUROC compared to AFP (0.715 versus 0.487; p = 0.04)

### CONCLUSIONS

M2BPGi can be used as a useful tool to detect hepatocellular carcinoma in patients with chronic hepatitis B

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0847

## DIAGNOSTIC TRENDS AND OUTCOMES OF CERVICAL BIOPSY SPECIMENS ANALYZED AT CHINSALI GENERAL HOSPITAL: A RETROSPECTIVE CROSS SECTIONAL STUDY IN MUCHINGA PROVINCE ZAMBIA

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**BACKGROUND-AIM**

This study aimed to investigate the diagnostic trends and outcomes of cervical biopsy specimens examined at Chinsali General Hospital in Zambia. The primary objective was to address the knowledge gap on cervical pathology prevalence and diagnostic trends in Muchinga Province, particularly considering the increased efforts in cervical cancer screening. The research seeks to contribute valuable insights into cervical pathology, focusing on demographic and pathological distribution.

**METHODS**

A retrospective cross-sectional study was conducted at Chinsali General Hospital, Muchinga Province, Zambia, from July 2023 to October 2024. During this period, all 290 examined cervical biopsy samples were included in the study. To determine cervical biopsy diagnostic trends and outcomes, data analysis was done, and descriptive statistics were reported

**RESULTS**

Out of 290 results obtained, high-grade squamous intraepithelial lesions (HSIL) were the most prevalent pathology, identified in 78 cases (27%), while adenocarcinoma was the least frequent, with 6 cases (2%). Notable findings included 61 cases of chronic cervicitis (21%), 52 cases of squamous cell carcinoma (SCC) (18%), 39 cases of low-grade squamous intraepithelial lesions (LSIL) (13%), and 54 cases (19%) categorized under other pathologies. Age-specific prevalence analysis revealed a higher incidence among females aged 37–56, with HSIL (53%) exhibiting the greatest diagnostic prevalence in this age group. Monthly trends indicated a consistent increase in biopsy volumes, peaking at 59 specimens (16%) in August 2024.

**CONCLUSIONS**

The study's findings highlight the importance of targeted interventions and surveillance for cervical cancer prevention, particularly in high-prevalence age groups. The high rates of HSIL, SCC, and LSIL emphasize early detection's critical role, while chronic cervicitis and adenocarcinoma cases require continued monitoring. This research provides valuable baseline data for evaluating prevention programs and shaping community interventions, with future efforts focused on refining strategies to reduce cervical cancer burden in affected areas.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0848

**ASYMMETRIC DIMETHYL ARGININE AND ITS ROLE IN ACUTE STROKE**

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**BACKGROUND-AIM**

Ischemic acute stroke is a leading cause for mortality and invalidity in recent years. Clinical trials shows the role of asymmetric dimethyl arginine (ADMA) as endogenous inhibitor of nitric oxide synthase and its connection to acute stroke. The aim of our study was to evaluate serum ADMA concentrations in patients with acute stroke.

**METHODS**

We compared 46 patients with acute stroke to the age and sex matched healthy controls. Also 15 patients with hypertension and 14 with diabetes were included in this study. The average age of all included persons was 44 ± 5; 60.1 % males. Patients were evaluated by NIH Stroke Score (NIHSS), by ultrasound, and laboratory parameters - complete blood count (CBC), lipid profile, high sensitive C-reactive protein (hsCRP), homocysteine, and ADMA. Pearson's and Student's t-test were performed to establish the significance between received parameters. The significance of the dependencies is assumed to be $p<0.05$.

**RESULTS**

Vascular risk factors showed statistical significance in acute stroke patients. Serum hsCRP levels in this study showed no connection to acute stroke. Serum ADMA levels were significantly higher in comparison to healthy controls: $r=0.853$, $p<0.001$. Average serum ADMA concentrations in patients with acute stroke were 1.64 ± 0.16 μmol/L; in control group – 0.37 ± 0.12 μmol/L. Also, we established a statistically significant correlation in patients with acute stroke between ADMA and homocysteine concentrations ($r=0.554$, $p<0.005$). Serum ADMA levels in patients with hypertension were average 1.38 ± 0.07 μmol/L; in those with diabetes – 1.42 ± 0.07 μmol/L. We found a positive significant correlation between patients with hypertension and control group, $r=0.751$, $p<0.001$.

**CONCLUSIONS**

Our results showed that evaluation of serum ADMA concentrations might be used as a predictor of acute stroke (along with other risk factors). This is why it is necessary to introduce this ##p#####p into routine laboratory practice.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0849

## ADMA, ERYTHROFERRONE, AND HS-CRP IN ASYMPTOMATIC PATIENTS WITH ULTRASOUND SIGNS OF CAROTID ATHEROSCLEROTIC CHANGES

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### BACKGROUND-AIM

Stroke is the leading cause for invalidity and mortality in the world, and most often is ishaemic genesis. Iron metabolism is claimed to be involved in function of human vessels. Is it so!? The aim of our study was to evaluate and compare the changes in serum ADMA, erythroferrone, hs-CRP and classic atherogenic factors in asymptomatic patients with ultrasound signs of carotid atherosclerotic changes.

### METHODS

A total of 399 asymptomatic patients (44% males; average age 32 ± 7.5) were included. CBC, lipide profile, hs-CRP, serum iron and erythroferrone were quantified in all volunteers. In addition, IMT was measured. Statistical analyses were used to establish the connection between our findings.

### RESULTS

We found that LDL-cholesterol showed positive correlation to changes of arteries in groups with changed ADMA ($r=0.751$; $P<0.005$) and IMT levels ($r=0.699$; $P<0.01$). ADMA corelated negatively to HDL ($r=-0.845$; $P<0.005$). A positive correlation of IMT index and ADMA to total cholesterol was found ($r=0.751$; $r=891$; $P<0.05$). Serum erythroferrone concentrations were decreased patients with atherosclerotic changes, which was expressed as negative correlation to ADMA and IMT ($r=-0.714$; $r=-0.874$; $P<0.005$).

### CONCLUSIONS

Serum ADMA, erythroferrone and hs-CRP are changed in asymptomatic patients with ultrasound signs of carotid atherosclerotic alterations which is connected to different levels of this process.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0850

## ESTABLISHING REFERENCE INTERVALS FOR ALP ISOENZYME ELECTROPHORESIS IN PEDIATRIC PATIENTS

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### BACKGROUND-AIM

Alkaline phosphatase (ALP) isoenzyme electrophoresis is a crucial diagnostic tool for evaluating liver and bone metabolism in pediatric patients. However, well-defined reference intervals for pediatric populations remain scarce. This study aims to establish reference intervals for ALP isoenzyme fractions in children and adolescents, focusing on a single institution's data.

### METHODS

We retrospectively reviewed ALP isoenzyme electrophoresis results from pediatric patients (<20 years old) at one university hospital over seven years. A total of 4,458 pediatric cases were analyzed, including 2,278 males and 2,180 females. Data included total ALP and fraction distributions (L1, L2, B), categorized by sex and age groups. Statistical analysis was conducted to determine the 2.5th and 97.5th percentiles as reference intervals. Comparisons with established reference ranges were performed.

### RESULTS

A total of 4,458 pediatric cases were analyzed, with 18.2% exceeding the upper limit of conventional total ALP reference values. Male and female distributions showed significant differences in bone fraction ($p < 0.0001$), with females exhibiting higher values. Reference intervals for ALP isoenzyme fractions were determined separately for males and females. For males, the reference intervals (2.5th-97.5th percentile) were L1: 4.1-40.8%, L2: 3.8-10.3%, B: 51.8-89.2%. In females, corresponding values were calculated.
Bone fraction analysis by age groups showed a clear decreasing trend with age. The highest bone fraction values were observed in children under 5 years old, followed by a gradual decline through adolescence. This trend suggests that bone metabolic activity is highest in early childhood and decreases as skeletal maturity progresses.
These results highlight the physiological variations in ALP isoenzymes in pediatric patients and provide a basis for clinical interpretation.

### CONCLUSIONS

This study establishes reference intervals for ALP isoenzyme electrophoresis in pediatric patients, providing a valuable reference for clinical diagnosis. The findings emphasize the necessity of age- and sex-specific considerations in interpreting ALP isoenzyme patterns.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0851

## COMPARISON OF METHODS FOR EARLY DIAGNOSIS OF INFECTIONS BASED ON CD64 AND CD169 MARKER EXPRESSION IN PEDIATRIC POPULATION

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### BACKGROUND-AIM

Infections are among the primary reasons children seek medical attention in hospital emergency departments. The CD64 antigen is a high-affinity receptor for the Fcγ region of the IgG heavy chain and can bind monomeric IgG1 and IgG3 as well as aggregated IgG. Bacterial phagocytosis is mediated by this FcγRI receptor. Conversely, in response to viral infection, host cells immediately produce cytokines, including type I interferons (IFN-I). Among the many effects of IFN-I is the strong induction of CD169 expression on monocytes. Notably, this sialoadhesin is absent on monocytes under non-infectious conditions.
To demonstrate that the expression of CD64 on neutrophil surfaces and CD169 on monocyte surfaces correlates with microbiological diagnosis.

### METHODS

This retrospective observational study was conducted from September 2022 to January 2023 on pediatric patients aged 3 months to 6 years who attended the emergency department.Inclusion Criteria: Pediatric patients with short-duration febrile symptoms and microbiologically confirmed bacterial or viral infections.
Bacterial infections were identified via blood culture using the MALDI-TOF MS technique. Viral infections were diagnosed using PCR (polymerase chain reaction) or routine serological testing by the microbiology department.
For CD64 and CD169 marker determination, the Navios EX flow cytometer (10 colors) was used with a single-step surface staining procedure, followed by analysis with Kaluza Analysis Software. Mean comparisons between the groups were analyzed using Student's t-test with R v4.2.2, considering $p<0.05$ as significant.

### RESULTS

In all microbiologically diagnosed bacterial infections, neutrophils expressed the CD64 marker, whereas monocytes did not express CD169.Among subjects with viral infections, five cases showed cytometric results inconsistent with microbiological diagnoses. This discrepancy may be attributed to co-infections or technical errors.Hypothesis testing demonstrated a clear statistical correlation ($p<0.05$) between cytometric and microbiological results.

### CONCLUSIONS

A strong correlation was observed between CD64 and CD169 marker results and microbiological diagnoses, showing high sensitivity, specificity, and a very high negative predictive value for differentiating viral and bacterial infections.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0852

## PROGNOSTIC VALUE OF RETICULOCYTE (RET), IMMATURE RETICULOCYTE (IRF) AND OSTEOPONTIN (OPN) IN HNSCC PATIENTS TREATED BY RADIATION AND CHEMOTHERAPY

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### BACKGROUND-AIM

Anemia is associated with a poor outcome in patients treated with RT, probably because it leads to low oxygen level in tumors. Plasma OPN and hemoglobin (Hb) may be putative parameters associated with tumor hypoxia in HNSCC patients. The number of reticulocytes (Ret) and immature reticulocyte fraction (IRF) can be used to ensure a more accurate monitoring of changes of the function of erythropoiesis. The aim of this study was to test the clinical utility of parameters of the red blood cell system and the concentration of OPN as a marker of tumor hypoxia.

### METHODS

Between 01/2009 and 08/2013 251 patients with squamous cell carcinoma of oropharynx (39%), hypopharynx (13%), larynx (44%) and oral cavity (4%) were treated with RT alone (48%) or combined with chemotherapy (52%). There were 15 (6%), 112 (45%), 74 (29%), and 50 (20%) patients with T1, T2, T3 and T4 tumor stage, respectively and 99 (40%), 26 (10%), 105 (42%), and 21 (8%) patients with N0, N1, N2 and N3 nodal stage of disease, respectively (no patients with distant metastases were included). OPN and parameters of the red blood cell system were estimated in plasma or blood before treatment and immediately after treatment completion.

### RESULTS

Pretreatment OPN level was generally higher in patients with advanced T stage (T3-4) compared to early (T1-2) stage (p=.024) but was not correlated with N stage (p=.58). Strong negative correlation has been found between patients with anemia (Hb< 11 g/ml) before treatment and OPN (p=.008), IRF (p=.0007) and the hemoglobin content of reticulocytes (p=.05), additionally a negative correlation has been found between patients with anemia after treatment and IRF (p=.002). Significantly longer overall survival (OS) was found for patients with lower OPN (p=.0001) and higher Ret (p=.03) before treatment and lower posttreatment Ret (p=.04). Also in the multivariate analysis, pretreatment OPN and pre- and posttreatment Ret levels were an independent prognostics factors for shorter OS (p=.03; p= .01; p=.02; respectively).

### CONCLUSIONS

Anemia in HNSCC patients before treatment has the nature of chronic disease with stimulated erythropoiesis. Immediately after treatment, ineffective erythropoiesis increases the risk of death. Pre- and posttreatment Ret and pretreatment OPN are independent prognostic determinants of survival.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0853

## IDENTIFICATION AND ANALYSIS OF POTENTIAL OXIDATIVE STRESS-RELATED DIAGNOSTIC MARKERS FOR DIABETIC RETINOPATHY BY WGCNA AND MACHINE LEARNING

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### BACKGROUND-AIM

Diabetic retinopathy (DR) is one of the most serious microvascular complications of diabetes mellitus (DM). Early detection and accurate diagnosis are pivotal for DR, however, the studies at the gene level were limited and biomarkers were still absent. Oxidative stress has a vital part in the etiopathogenesis of DR. This study aimed to screen and identify novel oxidative stress-related genes (OSGs) as potential diagnostic biomarkers for the early diagnosis of DR.

### METHODS

Differentially expressed genes (DEGs) shared between DR, DM, and healthy controls were intersected with oxidative stress-related genes to obtain differential oxidative stress-related genes (DEOSGs). Least Absolute Shrinkage and Selection Operator (LASSO) regression, Weighted Gene Co-expression Network Analysis (WGCNA), and protein-protein interaction (PPI) networks identified hub DEOSGs, which were validated using external datasets and assessed by receiver operating characteristic (ROC) analysis.

### RESULTS

From 713 DEGs and 1399 OSGs, 58 DEOSGs were identified, filtered to 20 based on correlation thresholds, and narrowed to 8 diagnostic candidates via LASSO. WGCNA revealed six modules, with the brown module most strongly associated with clinical characteristics. Two hub genes, LTF and DYSF, were validated, showing significant differential expression and diagnostic value (AUC = 0.76 each). LTF was upregulated, and DYSF was downregulated in DR, with consistent results in 90 plasma samples using RT-qPCR. Additionally, a TF-mRNA-miRNA-lncRNA network was constructed, further underscoring the diagnostic potential of LTF and DYSF.

### CONCLUSIONS

These findings provide new insights into oxidative stress-related mechanisms in DR and highlight LTF and DYSF as promising biomarkers for early diagnosis and intervention.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0854

**METABOLIC AND IMMUNE SIGNATURES IN INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS (IPMN): TOWARDS IMPROVED MALIGNANCY RISK STRATIFICATION**

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**BACKGROUND-AIM**

Pancreatic cystic neoplasms (PCNs), particularly the common IPMN subtype, carry a potential risk of malignant transformation. Identifying biomarkers to differentiate mucinous from non-mucinous lesions remains a critical challenge. While current biomarkers such as carcinoembryonic antigen (CEA), amylase, and glucose show promise, further improvements in sensitivity and specificity are needed. This study investigates the utility of metabolic indices and lymphocyte subsets to distinguish high- from low-risk IPMN and support clinical decision-making.

**METHODS**

Following ethical approval, 26 patients (11 males, mean age 69.5±9 years) undergoing Endoscopic Ultrasound guided Fine Needle Aspiration (EUS-FNA) were enrolled. Peripheral blood, serum, and cystic fluid (CF) samples were analyzed for glucose, CEA, cholesterol fractions and total proteins. Flow cytometry was employed to characterize lymphocyte subsets in blood and CF. A total of 18 CF samples were analyzed by mass spectrometry (MS) for metabolomic profiling.

**RESULTS**

All patients were stratified into low- or high-risk IPMN groups based on imaging features, cystic fluid CEA (>45 μg/L), and serum CA19-9 (>26 KU/L). High-risk patients were significantly older (p=0.003) and 69% exhibited anemia. In high-risk patients, total proteins, LDL cholesterol (p=0.005, 0.031) and lymphocytes (p=0.005) were significantly reduced in CF samples. In blood samples, high-risk patients showed elevated levels of non-MHC-restricted cytotoxic T (p=0.019). ROC analysis showed comparable diagnostic performance of CF-lymphocytes (AUC=0.868), CF-total proteins (AUC=0.859), CF-LDL cholesterol (AUC=0.795), CF-glucose (AUC=0.625), and CF-CEA (AUC=0.878). Metabolomic analysis revealed reduced middle- and long-chain acylcarnitines and altered tryptophan metabolites (kynurenine, methyl indole-3-acetate, and indole-3-lactic acid) in high-risk patients. The reduction of lymphocytes along with the alterations in tryptophan metabolism, in CF of high risk patients, promotes the immune tolerance exploited by tumor cells.

**CONCLUSIONS**

These findings underline the metabolic and immune reprogramming of premalignant IPMN cells, emphasizing the value of combined assessment of glucose, LDL cholesterol, total proteins, and lymphocytes as biomarkers for malignancy risk stratification.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0855

**ROLE OF ANGIOGENIC MARKERS IN MANAGING RECURRENT SEVERE PREECLAMPSIA: A CASE REPORT**

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**BACKGROUND-AIM**

Preeclampsia is a multisystemic disorder driven by endothelial dysfunction, often preceding clinical diagnosis. Affecting 3% of pregnancies globally, it significantly contributes to maternal and neonatal morbidity. The sFlt-1/PlGF ratio, reflecting angiogenic imbalance, is a crucial tool for diagnosing and monitoring preeclampsia.

**METHODS**

A 31-year-old pregnant woman at 29+3 weeks of gestation presented with elevated blood pressure and generalized edema. Her history included chronic hypertension and two prior pregnancies complicated by preeclampsia. The first progressed to incomplete HELLP syndrome, requiring cesarean delivery at 32 weeks, while the second involved fetal growth restriction (FGR) and cesarean at 34 weeks.

**RESULTS**

In her current pregnancy, blood pressure was well-controlled until 20 weeks, requiring escalating antihypertensive therapy. At 24+2 weeks, the sFlt-1/PlGF ratio was 10.89, with no proteinuria or abnormal ultrasound findings. At 29+3 weeks, she presented with a blood pressure of 150/80 mmHg, prompting hospitalization. Laboratory tests were unremarkable, but ultrasound revealed Type I FGR. Considering her history and Spanish Society of Gynecology and Obstetrics (SEGO) guidelines, the laboratory team proactively measured the sFlt-1/PlGF ratio, yielding a value of 249. This result was promptly communicated to clinicians, leading to hospitalization, close monitoring, and fetal lung maturation therapy.
In the following days, the patient developed severe hypertension, epigastric pain, and headaches, necessitating increased antihypertensive therapy. The sFlt-1/PlGF ratio rose further to 368. Subsequently, a non-reassuring cardiotocographic tracing at 30+4 weeks led to an emergency cesarean delivery.

**CONCLUSIONS**

The sFlt-1/PlGF ratio is highly effective in excluding early-onset preeclampsia, with low levels (<38) offering a 99% negative predictive value within one week. Elevated levels indicate placental dysfunction, guiding timely clinical decisions. This case highlights the laboratory's vital role in reassessing angiogenic markers per SEGO recommendations and promptly alerting clinicians. Identifying worsening angiogenic imbalance facilitated early interventions, optimizing maternal and fetal outcomes in this high-risk pregnancy.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0856

## THE COMPARISON BETWEEN DIFFERENT ANALYTICAL ASSAYS FOR THE DETECTION OF ANTI-DOUBLE-STRANDED DNA ANTIBODIES

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### BACKGROUND-AIM

Anti-double-stranded DNA antibodies (anti-dsDNA) are a specific biomarker for the diagnosis of systemic lupus erythematosus. However, different assays for the detection of anti-dsDNA detect anti-dsDNA with different avidities. The aim of this study was to compare two semi-quantitative indirect immunofluorescence assays using Crithidia luciliae (CLIF) kits from different manufacturers and chemiluminescence immunoassay (CLIA) with the in-house Farr-FIA for the detection of anti-dsDNA. We also evaluated two diagnostic algorithms combining these assays.

### METHODS

We analyzed 192 samples from patients from the Department of Rheumatology, UMC Ljubljana, using CLIF kits from Immuno Concepts and Inova Diagnostics, followed by Farr-FIA and the QUANTA Flash dsDNA CLIA on the BIO-FLASH analyzer (Inova Diagnostics). Cohen's kappa was used to evaluate the agreement between the CLIF assays and between CLIA and Farr-FIA. Spearman's correlation coefficient evaluated the correlation between CLIA and Farr-FIA results. The final results (negative or positive) of two diagnostic algorithms were compared (Algorithm 1: CLIF Immuno Concepts and Farr-FIA, Algorithm 2: CLIA and CLIF Inova Diagnostics).

### RESULTS

The kappa value for agreement between the CLIF assays was 0.83, indicating almost perfect agreement. The correlation between Farr-FIA and CLIA was strong, with a Spearman correlation coefficient of 0.71 ($p<0.001$). When comparing results as positive or negative, the kappa value between Farr-FIA and CLIA was 0.76. The diagnostic algorithms identified 62 positive and 109 negative samples, with an agreement of 89.1% (171/192). Discrepancies were found in 10.9% (21/192) of cases. Algorithm 1, which detected only high-avidity anti-dsDNA, found 6 positive samples that were categorized as negative by Algorithm 2, while Algorithm 2, which detected both medium- and high-avidity anti-dsDNA, identified 15 additional positive samples that were categorized as negative by Algorithm 1.

### CONCLUSIONS

Our results show strong agreement between the automated CLIA and the in-house Farr-FIA and between two CLIF assays. The different assays detect anti-dsDNA antibodies with different avidities and the use of algorithms enables the detection of clinically significant anti-dsDNA.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0857

**INVESTIGATING THE COUPLING DYNAMICS BETWEEN ALPHA-1-ANTITRYPSIN AND SINGLE FREE LIGHT CHAINS**

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**BACKGROUND-AIM**

Serum Free Light Chain (FLC) measurements are a routine clinical test for the evaluation of monoclonal gammopathies. While investigating the performance of Optilite® Freelite® assays in the field, we have previously discovered an interaction between kappa FLC and alpha-1 antitrypsin (A1AT) affecting assay calibrator activity. This investigation identifies the interaction mechanism.

**METHODS**

An accelerated stability study was performed on serum-based calibrators and pure FLC proteins. Protein interactions were identified using SDS-PAGE and western blot. Gel excisions were digested with trypsin, acidified, and prepared for liquid chromatography mass spectrometry analysis. Samples were analyzed using a Waters Xevo G2-XS QToF mass spectrometer (MS) with ACQUITY chromatography system. Subsequently, kappa calibrators were depleted of A1AT (and residual A1AT-immunoglobulin complexes) using affinity chromatography, and the accelerated stability study was repeated.

**RESULTS**

The Optilite Freelite kappa calibration activity curve declined in turbidimetric activity by 14.9±0.1% (mean±SEM) over a 4-month accelerated period at 22°C, equivalent to 16 months real time. The Freelite lambda calibration curve was less affected. SDS-PAGE and blotting revealed that FLCs form a 1:1 complex with A1AT, with kappa FLC showing a stronger interaction than lambda. This complex is susceptible to thiol reduction. Proteomic studies identified both cysteinylated and non-cysteinylated forms of A1AT at the C256 position. MS-fragmentation confirmed disulphide-bridge peptides between A1AT and both kappa and lambda FLC. De-cysteinylation of A1AT and FLC increases the formation of the A1AT-FLC complex. Fully A1AT depleted kappa calibrators showed significantly less decline in activity (1.4±1.4%, $p<0.001$) in accelerated stability studies.

**CONCLUSIONS**

A time-dependent kappa/A1AT interaction was observed, which correlated to a reduction in calibrator activity. Although the activity change is within the allowable range of the performance specifications for the kit, it might have contributed to increased kappa FLC values described by recent publications. The interaction was driven by the availability or accessibility of an unpaired cysteine residue on A1AT. Removal of A1AT remediates the issue.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0858

## EVALUATING FUTURE IVD PLASMA P-TAU181 AND APOE4 IMMUNOASSAYS FOR RULE OUT OF AMYLOID PATHOLOGY IN A MULTI-CENTER STUDY REFLECTIVE OF ROUTINE CLINICAL PRACTICE

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### BACKGROUND-AIM

Early detection of amyloid pathology using blood-based biomarkers have emerged as powerful tools in the ADpatient journey. This study investigates the clinical performance of plasma pTau181 in combination with plasmaApoE4 as a potential IVD to detect amyloid pathology from a broad population as seen in routine clinical practice.

### METHODS

In this prospective multicenter study, we enrolled 604 patients aged 55-80 with SCD, MCI, or mild dementia being evaluated for AD or other causes of cognitive decline. Plasma samples from eligible patients were analyzed using Elecsys® pTau181 and ApoE4 plasma assays (Roche Diagnostics International Ltd, Rotkreuz, Switzerland). The discriminative ability of pTau181 alone, or in combination with ApoE4 with respect to amyloid PET visual read status and to CSF ratio of the Elecsys Phospho-Tau (181P) and Elecsys Amyloid (1-42) II CSF was evaluated.

### RESULTS

The study population was heterogeneous regarding sex, race, and comorbidities, reflective of a real-world setting. The AUC of a combination of pTau181 and ApoE4 was 0.896, while for pTau181 alone was 0.873. Based on an amyloid positivity prevalence of 23.0% (based on amyloid PET), the negative predictive value (NPV) was 96.5%,paired with a positive predictive value of 49.8% (sensitivity: 91.3%, specificity: 72.5%). The performance was only minimally impacted by age, sex, body mass index or impaired kidney function. The rule-out performance of pTau181 alone was similar (NPV: 97.3%, PPV: 43.5%). However, the combination with ApoE4 made the clinical performance more robust towards analytical variability.

### CONCLUSIONS

The observed clinical performance in this study highlights the potential of plasma pTau181 with the combination of ApoE4 as robust and accurate tools for ruling out individuals with a low likelihood of amyloid pathology in the early stages of the AD continuum.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0859

## EVALUATION OF CEREBROSPINAL FLUID P-TAU/Aβ42 RATIO COMPARED TO Aβ42/Aβ40 RATIO FOR ALZHEIMER'S DISEASE DIAGNOSIS

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### BACKGROUND-AIM

Alzheimer's disease (AD) is a progressive neurodegenerative disorder associated with cognitive, functional, and behavioural impairments. It is the most common type of dementia.
The current AD diagnosis pathway in our hospital begins with a cognitive screening test, followed by MRI or CT imaging. If the results are indicative of AD, the clinician will conduct cerebrospinal fluid (CSF) biomarker testing, measuring the Total tau (T-tau) and phosphorylated tau at threonine 181 (p-Tau) proteins, along with amyloid peptides (Aβ42/Aβ40 ratio).
The aim of this study was to evaluate the robustness of the p-tau/Aβ42 ratio for AD diagnosis compared to the Aβ42/Aβ40 ratio, and to assess whether it could replace the Aβ42/Aβ40 ratio to reduce costs.

### METHODS

The study population included patients with suspected AD according to our diagnostic pathway.
CSF biomarkers Aβ42/Aβ40 ratio, T-tau, and P-tau181 were measured by CLEIA on the LUMIPULSE G600II platform (Fujirebio Diagnostic).
The diagnostic criteria for AD required the following: Aβ42/Aβ40 ratio < 0.069 and p-Tau > 56.5 pg/mL and t-Tau > 392 pg/mL.
The optimal cut-off point for p-tau/Aβ42 ratio for the diagnosis of AD was calculated using the Youden index in Receiver Operating Characteristic (ROC) analysis.
The status of the new diagnostic criteria (p-tau/Aβ42, p-Tau, and t-Tau) was compared with the status of the existing diagnostic criteria to determine the positive and negative percent agreement (PPA and NPA, respectively) for the calculated optimal cut-off value.

### RESULTS

The study population included 130 patients. Age [median (IQR)]: 74 [68-77] years; 55% female. A diagnosis of AD was made in 41 patients (31%).
The optimal cut-off point for the p-tau/Aβ42 ratio was 0.099 (Area under the curve, AUC: 0.941). The PPA was 0.93 (7% false negatives) and NPA was 1.00 (0% false positives).

### CONCLUSIONS

Using the new criteria for the diagnosis of Alzheimer's disease, a significant portion of patients would not be accurately diagnosed (false negatives). All these patients were classified as high producers of beta-amyloid peptides, with Aβ42 results within the normal range but pathological Aβ42/Aβ40 ratios. Thus, the Aβ42/Aβ40 ratio was necessary for the correct diagnosis of AD in patients who are high producers of beta-amyloid and have Alzheimer's disease.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0860

## DISEASE SPECIFIC BIOMARKERS IN DIABETES MELLITUS PATIENTS

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### BACKGROUND-AIM

Diabetes mellitus(DM) can be assesed by the long term monitoring and control of glucose levels as short term indicator. The measurement of fructosamine (FRU) is useful in monitoring short to medium glycemic control in DM, over the past 2-3 weeks.When blood glucose levels are abnormally elevated the concentration of fructosamine also increases. The aim of this study was to evaluate diagnostic efficiency for monitoring of DM by fructosamine assay.

### METHODS

The studied subjects were the control group(236 healthy students) and the experimental group(288 DM patients). The experimental group divided in four groups: M1 – 154 non-insulin dependent DM patients(NIDDM) on diet; M2- 88 NIDDM patients on oral antidiabetes therapy; M3 –23 NIDDM patients on insulin; M4 –23 insulin dependent patients (IDDM). Patients were both sexes, age matched and monitoring in last 3 weeks. We performed FRU determinations(by NBT colorimetric method). Glucose concentration was measured by GOD-PAP method.

### RESULTS

FRU and glucose values in serum were significantly higher ($p< 0,01$) in all groups of patients compared to the control group of young during whole period of monitoring of DM. FRU was significantly correlated with glycemia over the past 2 weeks. The results of examined parameters in all groups have shown the following values: M1 for glucose 7,36± 1,39 ; and FRU values ranged from 258-320 μmol/l; M2 9,60± 3,77; FRU 346-386μmol/l; M3 12,25±3,62; FRU 447-509μmol/l; M4 15,01 ± 5,95; FRU 497-587μmol/l; control group 5,05 ±0,75; FRU 174-225 μmol/l.

### CONCLUSIONS

Simultaneous determination of both parameters allows us to emphasize the recent metabolic decompensation. The results suggest that fructosamine assay is useful medium-term marker to monitor diabetic patients in regard to their therapy.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0861

## COMPARATIVE ANALYSIS OF TWO METHODS FOR THE DETERMINATION OF ANTI-MPO AND ANTI-PR3

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### BACKGROUND-AIM

Antineutrophil cytoplasmic antibodies (ANCA) are specific antibodies that target white blood cells (neutrophils) and play an important role in autoimmune diseases that cause inflammation of blood vessels and tissues. C-ANCA are antibodies to serine proteinase 3 (anti-PR3) and are an important element in the diagnosis of granulomatosis with polyangiitis. P-ANCA are antibodies to myeloperoxidase (anti-MPO) and are an important element in the diagnosis of microscopic polyangiitis. Anti-MPO are also found in patients with eosinophilic granulomatosis with polyangiitis and polyarteritis nodosa. They can be used to serologically differentiate these diseases from granulomatosis with polyangiitis. In this study, the values of anti-MPO and anti-PR3 were measured using two different methods, chemiluminescent immunoassay (CIA) on the BIO-FLASH® and enzyme-linked immunosorbent assay (ELISA) on the Alegria®, with the aim of conducting a comparative analysis of the selected methods.

### METHODS

The study included patients suspected of having systemic vasculitis. Antibody values were measured in serum. Anti-MPO were measured by CIA QUANTA Flash Anti-MPO on the BIO-FLASH® and Anti-MPO ELISA on the Alegria®, in 43 patients. Anti-PR3 were measured by CIA QUANTA Flash Anti-PR3 on the BIO-FLASH® and Anti-PR3 ELISA on the Alegria®, in 43 patients.

### RESULTS

The agreement between methods was measured by Cohen's kappa.
Anti-MPO: Number of observed agreements: 36 (83.72% of the observations); number of agreements expected by chance: 21.5 (50.08% of the observations); Kappa = 0.674; SE (standard error) of kappa = 0.113; 95% confidence interval: from 0.453 to 0.895
Anti-PR3: Number of observed agreements: 37 (86.05% of the observations); number of agreements expected by chance: 21.5 (49.92% of the observations); Kappa = 0.721
SE (standard error) of kappa = 0.105; 95% confidence interval: from 0.515 to 0.927
Kappa between 0.61 and 0.80: Substantial agreement.

### CONCLUSIONS

The comparison between the two methods, CIA on BIO-FLASH® and ELISA on Alegria®, shows a good level of correlation (Substantial agreement) for both compared tests. Cohen's Kappa does not provide information on the quality of the measurement, but it is very useful for the laboratory to estimate the extent of agreement between two methods.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0862

## SOLUBLE CD10 IN THE SERVICE OF LABORATORY DIAGNOSTICS: NEW OPPORTUNITIES AND ISSUES TO BE SOLVED

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### BACKGROUND-AIM

CD10 is a membrane-bound metallopeptidase found on lung and intestinal epithelial cells, as well as certain myeloid cells, such as neutrophil granulocytes. Its clinical significance remains prominent today, particularly in the diagnosis of acute lymphoblastic leukemia. In addition to its cell surface expression, the soluble form of CD10 is also present in peripheral blood, though its reliable detection has been hindered by technical challenges. In recent years, CD10 has garnered significant attention in cancer research. It has been noted to enhance the metastatic potential of solid tumors, yet the physiological and pathological functions of soluble CD10 remain unclear. Therefore our objective was to develop an analytical method that enables efficient measurement of soluble CD10 activity, paving the way for its potential diagnostic application.

### METHODS

The serum CD10 concentration was determined using a commercially available ELISA kits. Serum CD10 activity was measured with a kinetic chromogenic assay optimized by our team.

### RESULTS

Serum samples from 52 individuals with various medical conditions were analyzed. No direct correlation was observed between CD10 concentrations and activities ($r = 0.01722$), which we attributed to peripheral degradation of CD10. Concentrations determined by the commercial ELISA kit did not show significant differences between patients with tumors and those without tumors (median = 3620 ng/L, [min–max: 1158–33001 ng/L]; $n = 11$ vs. median = 2213 ng/L, [min–max: 149–39633 ng/L]; $n = 41$; $p = 0.0814$). In contrast, the soluble CD10 activity measured with our optimized method was found to be significantly higher in samples from oncology patients (median = 29.77 U/L [min–max: 0.9–65.25 U/L]; $n = 11$) compared to those from individuals without tumors (median = 1.388 U/L [min–max: 0.1–27.06 U/L]; $n = 41$; $p = 0.0005$).

### CONCLUSIONS

Based on our results, soluble CD10 activity may be significantly elevated in individuals with tumors. The soluble CD10 activity assay we optimized could greatly aid clinicians in the early detection of tumor-related changes and in monitoring the effectiveness of drug therapies.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0863

## SERUM HER-2NEU IN DIFFERENT HISTOLOGICAL GRADES OF METASTATIC BREAST CANCER

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### BACKGROUND-AIM

HER2/neu is one of the extensively studied proto-oncogens in breast cancer patients.Accurate and timely assessment of the Human Epidermal Growth Factor Receptor 2 (HER2/neu) over expression is pivotal for the identification of breast cancer patients that could benefit from HER2-targeted therapy. HER 2 neu also serves as a prognostic marker in breast cancer patients.

### METHODS

Serum sample was collected from 60 patients with metastatic breast cancer before start of any anticancer regimen or hormonal therapy. Serum HER2/neuwas estimated using the chemiluminiscent immunoassay in ADVIA Centaur XP and primary histopathology report was used to obtain the histological tumor grade of the patients.

### RESULTS

There was a significant association between tumor grade and serum HER2/neu level. The mean value of serum HER2/neu was 25.53 ng/ml in patients belonging to tumor grade III+IV which is statistically higher ($P<0.001$) compared to the tumor stage (I+II), in which the mean serum HER2/neu was found to be 15.86 ng/ml.

### CONCLUSIONS

Based on the results obtained from our present study, it can be concluded that serum HER2/neu has significant association with the histological tumor grade, which spreads light on the potential use of serum HER2/neu as a tool to assess the tumor burden in the body and it ultimately helps us to track the prognosis.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0864

## STUDY OF HEPATIC STEATOSIS ALGORITHMS AS A POTENTIAL MARKER OF METABOLIC DYSFUNCTION ASSOCIATED STEATOTIC LIVER DISEASE

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**BACKGROUND-AIM**

Metabolic dysfunction associated steatotic liver disease (MASLD) is the most common chronic liver disease worldwide, with increased liver-related morbidity and mortality. Various non-invasive algorithms have been developed for predicting the presence of MASLD using anthropometric and biochemical parameters. Hence, this study aims to determine hepatic steatosis algorithms as a potential marker of MASLD.

**METHODS**

A total of 200 participants were included in the study, of which 100 were MASLD cases, and 100 were healthy control. Serum ALT, AST, TG, and Glucose were estimated, and Hepatic steatosis algorithms (LAP, FSI, TyG, and HSI) were calculated. The ROC curve was estimated to validate algorithms in patients with MASLD.

**RESULTS**

Hepatic steatosis algorithms like FSI, LAP, TyG, and HSI were significantly higher ($p<0.05$) in patients with MASLD compared to healthy control. The AUROC of LAP, FSI, TyG, and HSI was 0.789 (95% CI,0.727-0.851), 0.776 (95% CI, 0.711-0.841), 0.765 (95% CI, 0.697-0.833) and 0.693 (95% CI, 0.620-0.766) respectively. The optimal cut-off value of LAP, FSI, TyG, and HSI for the prediction of MASLD were 31 (71% sensitivity and 70% specificity), 23 (74% sensitivity and 72% specificity), 8.9 (73% sensitivity and 70% specificity) and 34.5 (67% sensitivity and 62% specificity) respectively.

**CONCLUSIONS**

The non-invasive and cost-effective algorithms like LAP, FSI, TyG, and HSI can be potential screening tools for predicting MASLD.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0865

## EVALUATION OF THE COMPETENCE LEVEL OF BRAZILIAN LABORATORIES IN IDENTIFYING ANA PATTERNS FOLLOWING THE BRAZILIAN CONSENSUS ON AUTOANTIBODIES (BCA) AND THE INTERNATIONAL CONSENSUS ON ANA PATTERNS (ICAP)

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**BACKGROUND-AIM**

The indirect immunofluorescence assay on HEp-2 cells (HEp-2 IFA) remains the gold standard for autoantibody screening, offering insights into potential autoantibodies and guiding further testing based on specific clinically relevant patterns. To promote harmonization in testing and reporting, the Brazilian Consensus on Antinuclear Antibodies (BCA HEp-2), established in 2000, and the International Consensus on ANA Patterns (ICAP), initiated in 2014, collaborate to standardize HEp-2 IFA pattern nomenclature and definitions. This study assessed Brazilian laboratories' ability to classify common HEp-2 IFA patterns following BCA and ICAP guidelines.

**METHODS**

In phase one, serum samples exhibiting six competent-level patterns were sent to 64 laboratories, and accuracy rates were calculated based on the correct identification of the expected patterns. Phase two evaluated image recognition accuracy for 22 additional patterns, with accuracy expressed as percentages. All patterns were reported using the alphanumeric code (AC) defined by ICAP (www.anapatterns.org).

**RESULTS**

Negative HEp-2 IFA samples (AC-0) were correctly identified by 95.2% of participants. Positive sample accuracy rates varied: AC-1 (66.4%), AC-2/30 (61.4%), AC-3 (94.1%), AC-4/5/31 (94.6%), and AC-8/9/10 (86.7%). Expert-level image recognition averaged 69.7%, with specific rates of 77.1% (nuclear), 82.4% (nucleolar), 72.2% (cytoplasmic), and 67.3% (mitotic). Accuracy for individual patterns ranged widely: AC-1 (93.5%), quasi-homogeneous (QH) nuclear (50.0%), AC-2 (88.5%), AC-3 (98.1%), AC-4 (94.8%), AC-5 (84.8%), AC-6 (96.6%), AC-7 (78.8%), AC-8 (96.5%), AC-9 (68.3%), AC-12 (58.5%), AC-13 (83.1%), AC-14 (20.0%), AC-19 (72.1%), AC-20 (36.7%), AC-21 (85.2%), AC-23 (95.0%), AC-25 (69.4%), AC-26 (45.5%), AC-27 (86.9%), and AC-29 (62.0%).

**CONCLUSIONS**

Laboratories performed well with AC-0 and achieved high accuracy for most competent-level patterns. However, nuclear patterns with positive metaphase plates (AC-1, AC-2, QH, AC-29) presented significant challenges. Cytoplasmic and mitotic patterns were less consistently recognized than nuclear and nucleolar patterns. These results highlight the need for continued education to enhance pattern recognition, aligning with BCA and ICAP recommendations.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0866

**DETERMINATION OF BRAIN INJURY BIOMARKERS GFAP AND UCH-L1**

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**BACKGROUND-AIM**

A mild traumatic brain injury (mTBI) is a relatively common type of injury seen in emergency department (ED). Due to the severity of the clinical consequences, brain CT scan is a diagnostic procedure that is performed on patients with suspected mTBI. However, the number of patients with proven brain CT lesions is very low. According to literature data, some novel biomarkers have appeared as relatively reliable markers capable to distinguish patients regarding the presence or absence of brain lesions on initial CT scan. The aim of this study was to determine the serum levels of glial fibrillar acidic protein (GFAP) and ubiquitin carboxy-terminal hydrolase L1 (UCH-L1) in ED patients with suspected mTBI.

**METHODS**

The retrospective study included 114 ED patients who undergo brain CT scans based on clinical criteria. Within of 12 hours from initial injury, blood was drown to all patients in order to determine the serum levels of GFAP and UCH-L1. The analysis was performed on Vidas-IVD platform (BioMérieux) using enzyme-linked fluorescence assay (ELFA) metodology. To all patients brain CT scan was performed. The absence of intracranial hemorrhage, brain herniation, or significant pathological alterations in the density of the brain parenchyma is considered a negative CT scan result.

**RESULTS**

The study included 47 female and 67 male patients. The median age was 42 years (18-65). We did not determine statistically significant difference of UCH-L1 level (285.5 (119-2540) pg/ml vs. 333.2 (112-2560) pg/ml; p=0.19= or GFAP level (10 (10-320) pg/ml vs. 14.3(10-167.4) pg/ml; p=0.390) between male and female patients, respectively. A negative predictive value of 100% was obtained for both biomarkers in the examined number of patients.

**CONCLUSIONS**

UCH-L1 and GFAP values did not differ between male and female. These two brain injury related biomarkers have high negative predictive value and therefore with a very high probability, could rule out the need for an unnecessary brain CT scan on patients with suspected mTBI.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0867

**DISCREPANCY BETWEEN TROPONIN T AND TROPONIN I CONCENTRATIONS TWO CASES**

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**BACKGROUND-AIM**

Cardiac troponin is a critical biomarker for the diagnosis of acute myocardial infarction (MI). It consists of three subunits: troponin T (TnT), troponin I (TnI), and troponin C, the first two being measured in routine practice.

**METHODS**

We report two cases of patients with elevated troponin T without signs of cardiac injury. We measured the troponin T and Troponin I level.

**RESULTS**

The first case is a 64-year-old obese woman with a history of hypercholesterolemia, who was admitted to the cardiac intensive care unit upon discovery of an elevated TnT concentration. While her TnT concentration remained elevated during her stay (414-642 ng/l, reference values <14 ng/l), she did not display cardiac symptoms, and a panel of investigations (EKG, coronarography, cardiac echography, transesophageal echocardiography) did not reveal any significant cardiac damage. TnI was measured in another laboratory and was found to be within reference values (12 ng/l, reference values <16 ng/l), pointing to a false-positive TnT elevation.
The second case is an 85-year-old woman with a background of chronic venous insufficiency, hypertension, and metastatic lung adenocarcinoma treated since September 2024 by nivolumab, an immune checkpoint inhibitor (ICI). The day before the first nivolumab administration, her TnT was measured at 11.7 ng/l. Three months later, her TnT was found to be significantly increased at 112 ng/l, and remained stable over a two-week period. Similar to the first case, the patient had no cardiac symptoms, and her EKG was normal. Likewise, TnI was measured in another laboratory and was found to be within reference values (12.4 ng/l, reference values <16 ng/l), again pointing to a false-positive TnT elevation.

**CONCLUSIONS**

Both cases highlight the interest of TnI measurement in case of plateauing TnT concentrations and in the absence of cardiac symptoms, to conclude to false-positivity of TnT elevation. Possible explanations for these discrepancies include heterophilic antibodies and skeletal muscle involvement, as TnT concentrations can increase in certain cases of skeletal muscle injury. Interestingly, non-specific TnT elevation has previously been reported in patients treated with an ICI.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0868

## 25-(OH) D , 24,25-(OH)2D , 1,25-(OH)2 D, 1-84 PTH AND FGF 23 LEVELS IN PATIENTS WITH END STAGE RENAL DISEASE ON DIALYSIS

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### BACKGROUND-AIM

Vitamin D and its metabolites together with bioactive parathormone (1-84 PTH) and Fibroblast Growth Factor 23 (FGF 23) are often abnormal in patients with end stage renal disease on dialysis. These abnormalities include vitamin D deficiency, hyperparathyroidism and extreme elevation of FGF 23 levels. While PTH stimulates 1,25-$(OH)_2$ D production, FGF 23 induce CYP24A1 enzyme activity and may increase production of 24,25-$(OH)_2$D.

### METHODS

66 patients with end stage renal disease on dialysis were analysed for serum levels of 25-(OH) D, 24,25-$(OH)_2$D levels by LC-MS/MS (Agilent, U.S.A). 1,25-$(OH)_2$ D serum levels and 1-84 PTH, intact FGF 23 plasma levels were measured using Diasorin Liaison XL, U.S.A, analyser. We calculated vitamin D metabolic ratio /VMR(24,25/25)/ and correlated the results with each other by Spearman rank correlation test.

### RESULTS

We found 25-(OH) D levels (minimum 5.4, median 26.3, maximum 92.5; μg/L), 24,25-$(OH)_2$D levels (min. 0.42, median 1.68, max. 3.87; μg/L), 1,25-$(OH)_2$ D (min. 20.5, median 61.0, max. 193.0; pmol/L) VMR(24,25/25) ratio (min. 2.13, median 5.75, max. 13.95,%) and 1-84 PTH (min. 0.86, median 7.41, max. 68.90, pmol/L), FGF 23 (min. 99.2, median 4648.0, max. 57 900.0; ng/L plasma levels. We evaluated Spearman rank correlation among analytes. We found significant correlations only between 24,25-$(OH)_2$D and VMR (24,25/25) $r=0.71$ $p<0.0001$ and 24,25-$(OH)_2$D and 25-(OH) D $r=0.48$ $p<0.0001$, 25-(OH) D and 1,25-$(OH)_2$D $r=0.0.27$ $p=0.025$, 1,25-$(OH)_2$D and FGF 23 $r=0.44$, $p=0.0003$.

### CONCLUSIONS

In accordance with few previous reports on 24,25-$(OH)_2$D and VMR (24,25/25) are lower than in healthy population, unexpectedly. Also presumed corelation with FGF23 and 1-84 PTH were not found. We conclude that at least vitamin D metabolism is abnormal in end stage renal disease.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0869

## ASSESSMENT OF LABORATORY HANDLING OF FRUCTOSAMINE REQUESTING IN PATIENTS WITH HAEMOGLOBIN VARIANTS

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### BACKGROUND-AIM

To ascertain the current UK practice concerning requests for HbA1c in patients with variants and to raise awareness of Fructosamine.

### METHODS

We asked 496 participants, in the UK National External Quality Assessment Service (NEQAS) for Glycated Haemoglobins Scheme for their practice in handling HbA1c results with variants and whether they would suggest Fructosamine to provide that service. Fructosamine data from the Scheme was reviewed.

### RESULTS

63% of Participants will report a HbA1c result irrespective of the Haemoglobin variant, 14% will report a HbA1c only with certain variants, while 21% of labs do not report the HbA1c result. 30 Laboratories in the UK return EQA results for Fructosamine. There are method biases between results returned. A comment on variant status would be added by 58% of laboratories, 45% would recommend Fructosamine monitoring.

### CONCLUSIONS

Given that there are method principle differences used for the measurement of Fructosamine, there cannot be a single ‘conversion factor’ between Fructosamine to HbA1c and, by extension, to average blood glucose.
Though the geographical spread of Laboratories offering a Fructosamine service includes London, East and West Midlands conurbations, there are areas of the UK that do not appear to being served. Our survey shows wide variations in how HbA1c variants are managed within laboratories. It is possible that this will disadvantage particular ethnic groups in the provision of diabetic services across the UK.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0870

**CLINICAL UTILITY OF SERUM S100B PROTEIN LEVELS IN THE ASSESSMENT OF MILD TRAUMATIC BRAIN INJURY.**

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**BACKGROUND-AIM**

Cranial computed tomography (CT) is the gold standard for ruling out traumatic brain injury (TBI). Different studies suggest that S-100B (S-100B) protein levels could be useful in the clinical management of TBI, allowing for the avoidance of having to perform a CT in those patients who test negative for S-100B, allowing for less use of CT, which would mean better clinical and economic results.
The objective of our work is to analyze the usefulness of the neuromarker S-100B as a screening test for mild TBI.

**METHODS**

This is a prospective observational study with 91 patients, over a period of 12 months (from October/2023 to October/2024), with mild head trauma of different etiology and a Glasgow score of 13-15, treated in the emergency department. of our hospital center. After the clinical evaluation, determination of S-100B protein and cranial CT were performed. The S-100B protein analysis was performed in cobas pro (ROCHE®) and the value 0.1 μg/L was taken as a positive cut-off point. The relationship between clinical findings, CT results and S-100B levels was evaluated.

**RESULTS**

91 patients were included in the study: Craneal CT was positive in 7 (8%) patients. All patients with positive CT had positive levels of S-100B protein. Overall, S-100B had a specificity of 68.0% and a sensitivity of 100.0%, with a positive predictive value (PPV) of 22.0% and a negative predictive value (NPV) of 100.0%, in relation to imaging tests performed on patients with mild TBI.
In our study, 50 patients had S100B levels < 0.1 μg/L (61.0%).

**CONCLUSIONS**

The high negative predictive value of neuroprotein S-100B (NPV 100.0%) allows CT not to be performed in patients with levels < 0.1 μg/L.
In our study, 61.0% of the CT scans that were performed would not have had to be performed.
The use of S100B could reduce the number of CT scans performed, patient waiting time in the emergency department of our hospital, and associated hospital costs in patients with mild traumatic brain injury.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0871

## USEFULNESS OF PRESEPSIN AS A BIOMARKER FOR SEPSIS: A CLINICAL DIAGNOSIS IN A KOREAN TEACHING HOSPITAL

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### BACKGROUND-AIM

Sepsis remains a significant global health challenge, characterized by high morbidity and mortality rates, necessitating rapid diagnosis and timely management. Presepsin, a soluble subtype of the CD14 receptor, has gained recognition as a potential biomarker for the early detection of sepsis and prognostic evaluation. Emerging evidence underscores the diagnostic utility of presepsin in critically ill patients, highlighting its association with sepsis severity, organ dysfunction, and clinical outcomes. This study evaluates the utility of presepsin over a seven-month period at a teaching hospital in Korea.

### METHODS

The PATHFAST Presepsin (PHC Corporation, Japan) was implemented by the manufacturer's guidelines. The assay's limit of detection (LoD) and precision were validated using serially diluted quality control samples with diluents before implementation. For quantitative reporting, results below 300 pg/mL were categorized as negative, those above 500 pg/mL as positive, and values between 300 and 500 pg/mL as equivocal. From May to December 2024, presepsin test results were collected alongside patient demographic data, including sex, age, clinical department, and clinical diagnosis. Diagnoses related to sepsis were analyzed in correlation with presepsin test outcomes.

### RESULTS

1,719 patients were conducted, comprising 888 males and 831 females, with mean ages of 71.6 and 74.1 years, respectively. The emergency medicine department accounted for most tests (84.3%), followed by general surgery (10.4%). Test results were distributed as follows: 450 (negative), 380 (equivocal), and 889 (positive). The prevalence of sepsis-related diagnoses differed significantly across the presepsin result groups. Among negative and equivocal results, 3.8% and 3.7%, respectively, were clinically diagnosed with sepsis-related conditions. In contrast, 11.1% of patients in the positive group were diagnosed with sepsis. When the positive threshold was increased from 500 pg/mL to 700 pg/mL and 1,000 pg/mL, the proportion of sepsis-related diagnoses rose to 13.7% and 16.5%, respectively.

### CONCLUSIONS

The presepsin assay demonstrated robust performance as a laboratory test for supporting the diagnosis of sepsis and bacterial infections, particularly in emergency department settings for enhancing clinical decision-making in managing sepsis.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0872

## THE RELATIONSHIP BETWEEN SERUM LEVELS OF CARCINOEMBRYONIC ANTIGEN (CEA) IN COLORECTAL CANCER PATIENTS AND TUMOR PATHOLOGICAL CHARACTERISTICS RELATED TO UBE2Q1 GENE EXPRESSION

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**BACKGROUND-AIM**

Despite advancements in diagnosing and treating colorectal cancer, it remains the third most lethal cancer for men and the second for women. Increased UBE2Q1 expression has been noted in colorectal tumors, but its role in cancer progression is still unclear. CEA protein levels also rise in colorectal cancer and serve as an indicator of treatment response. This study aimed to investigate the prognostic relationship between colorectal cancer and elevated UBE2Q1 gene expression by assessing CEA protein levels.

**METHODS**

In this cross-sectional study, 48 tissue and serum samples from patients with colorectal cancer collected in a previous study were included. The patients studied had undergone surgery at Faghihi Hospital of Shiraz University of Medical Sciences. The expression level of UBE2Q1 gene in tumor tissue and adjacent normal tissue of these patients was examined by Western Blot and quantitatively measured by densitometry. Serum CEA levels in these patients' serum samples were measured using ELISA.

**RESULTS**

Data from 48 colorectal cancer patients with a mean age of 57.23 ± 14.58 years, half of whom were female, were analyzed. The mean serum CEA level was 2.35 ± 3.45, and the mean UBE2Q1 gene expression was 5.80 ± 12.39. The mean size of tumors completely removed after surgery was 29.17 ± 46.13 square centimeters. 21.43% of patients had lymph node involvement, and 70% had good pathological differentiation. 35.71% of the tumors were located in the rectum and 33.33% in the colon. The correlation between serum CEA levels and UBE2Q1 gene expression was statistically significant with a correlation coefficient of 0.38; similarly, the correlation between UBE2Q1 gene expression and liver function tests, alkaline phosphatase, and AST, with correlation coefficients of 0.50 and 0.43 respectively, was significant. The correlation between CEA and tumor size, age, and none of the liver function tests was significant.

**CONCLUSIONS**

There is a significant correlation between serum CEA protein levels and UBE2Q1 gene expression, indicating that UBE2Q1 may aid in prognosis and treatment strategies. A significant relationship was also found between UBE2Q1 expression and the alkaline phosphatase and AST tests. However, no significant associations were observed between UBE2Q1 expression and age, gender, or histopathological factors.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0873

## CHITOTRIOSIDASE ACTIVITY IN SARCOIDOSIS AND TUBERCULOSIS

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### BACKGROUND-AIM

Human chitotriosidase (CHIT) is a glycosyl hydrolase secreted by activated macrophages which is considered as important factor of innate immune system. CHIT has shown particularly great importance in the diagnosis and therapy monitoring of patients with Gaucher's disease, sarcoidosis, tuberculosis, amyotrophic lateral sclerosis, multiple sclerosis, beta-thalassemia, acute malaria and many other infectious and parasitic diseases.
The aim of this study was to evaluate the importance of CHIT in predicting the diagnosis of active form of sarcoidosis and tuberculosis.

### METHODS

The CHIT activity was determined by a fluorimetric method using 22 mmol/L 4-methylumbelliferyl b-D-N,N,N – triacetylchitotrioside (Sigma Chemical Co., St. Louis, USA) in citrate-phosphate buffer, pH 5.2. Fluorescence was read on a Cary Eclipse fluorescence spectrometer (Agilent, Santa Clara, CA, USA). CHIT activity was evaluated in a group of 162 patients with active form of sarcoidosis and group of 109 patients with tuberculosis. Range of values for 134 healthy consenting individuals was 6–162 nmol/mL/h.

### RESULTS

Baseline CHIT activity in patients with active form of sarcoidosis was 304.95 nmol/mL/h (range 3.40-1552.01). The initial value of CHIT in patients with tuberculosis was 156.93 nmol/mL/h (range 10.90-468.00). A statistically significant differences in CHIT activity were found between patients with active form of sarcoidosis and a control group of healthy subjects ($p = 0.000$), as well as patients with tuberculosis and a control group of healthy subjects ($p = 0.000$). The results of the ROC analysis have shown that determining the level of CHIT is highly important in predicting the diagnosis of active form of sarcoidosis (AUC=0.888; CI 95% 0.848-0.928, cut-off 142.10 nmol/mL/h), with a sensitivity of 75.3% and a specificity of 97.0%, as well as in predicting the diagnosis of tuberculosis (AUC=0.698; CI 95% 0.655–0.742, cut-off 78.25 nmol/mL/h), with a sensitivity of 78.2% and a specificity of 80.7%).

### CONCLUSIONS

Determining the level of CHIT is important in predicting the diagnosis of active form of sarcoidosis and tuberculosis. Further studies are needed to explore other factors associated with CHIT activity among patients with these pulmonary diseases.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0874

## CARCINOEMBRYONIC ANTIGEN AS A PREDICTIVE INDICATORS FOR THE DEVELOPMENT OF LUNG NODULES INTO LUNG CANCER: A BIG DATA STUDY

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### BACKGROUND-AIM

Pulmonary nodules are the most important clinical manifestation in the early stage of lung cancer. This study aims to obtain indicators for predicting the risk of malignancy in patients with pulmonary nodules.

### METHODS

This real-world study was included patients with lung cancer or pulmonary nodules who visited the outpatient and inpatient departments of the First Affiliated Hospital of Guangzhou Medical University from 2013 to 2022, and collect their clinical information, as well as test results for carcinoembryonic antigen (CEA), carbohydrate antigen 153 (CA-153), carbohydrate antigen 125 (CA-125), neuron specific enolase (NSE), non-small cell lung cancer associated antigen (CYFRA21-1), and squamous cell carcinoma antigen (SCC).

### RESULTS

This study included 3,472 lung cancer patients and 8,987 pulmonary nodule patients. Among lung cancer patients, 13.3% were diagnosed with small cell lung cancer (SCLC) and 8.3% with non-small cell lung cancer (NSCLC). Compared to patients with pulmonary nodules, lung cancer patients have more comorbidities of basic diseases. The positive rate of CEA (42.2% vs. 11.4%, $P = 0.001$), CA153 (22.5% vs. 5.3%, $P = 0.005$), CA125 (28.8% vs. 4.9%, $P < 0.001$) and NSE (60.4% vs. 23.6%, $P = 0.046$) in lung cancer were higher than that in pulmonary nodule. Wayne analysis shows that in lung cancer patients, more patients are only positive for CEA (18.9%) or NSE (22.8%). Meanwhile, there were differences in the levels of different factors between small cell lung cancer and non-small cell lung cancer. In addition, the optimal scale analysis shows that the association between carcinoembryonic antigen and lung cancer was the closest (Cronbach's $\alpha = 0.891$). And the ROC analysis was show that when 2.49 ng/ml was selected as the cut-off for CEA, the sensitivity was 69.8% and the specificity was 66.9%.

### CONCLUSIONS

Overall, compared to patients with pulmonary nodules, the positive rates and concentration levels of CEA, CA153, CA125, and NSE are higher in lung cancer patients. When the concentration of CEA is $\geq$ 2.49 ng/ml, the risk of lung nodule patients developing lung cancer increases, and it is necessary to pay attention and conduct clinical monitoring.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0875

**ROLE OF LCN2, MMP9 AND LCN2/MMP9 COMPLEX AS POTENTIAL BIOMARKERS OF ORAL SQUAMOUS CELL CARCINOMA (OSCC).**

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**BACKGROUND-AIM**

OSCC is a significant health problem in LMICs including India poor outcome due to lack of diagnostic marker. We identified 135 dysregulated candidate proteins in the saliva of OSCC patients using LCMS,of which LCN2 and MMP9 were significantly upregulated.We explored the potential role of these proteins as potential biomarker in OSCC.

**METHODS**

351 OSCC,26 OPMDs and 118 healthy controls were recruited.5ml unstimulated saliva and 3ml blood were collected at baseline and during follow-ups.Protein levels were measured by sandwich ELISA, and analysed using appropriate statistical tests.

**RESULTS**

LCN2 was significantly higher($p \leq 0.0001$)in saliva and serum(median-609.15ng/ml & 186.18ng/ml)of patients compared to OPMD(median-358.47ng/ml & 124.05ng/ml)and controls(median-95.70ng/ml & 85.53ng/ml).Salivary and serum levels of MMP9(median-194.03ng/ml & 3476.755ng/ml)were significantly higher($p \leq 0.0001$)than in OPMD(median-206.50ng/ml & 404.08ng/ml)and controls (median-188.05ng/ml & 540.18ng/ml)respectively.LCN2/MMP9 complex in saliva and serum(median-145.65ng/ml,median-94.37 ng/ml)was also significantly higher($p \leq 0.0001$)than OPMD(median-90.66ng/ml & 55.20ng/ml)and controls(median-70.88ng/ml & 52.76ng/ml)respectively.During follow-ups post-therapy,there was a significant decrease in the level of these proteins.
ROC analysis revealed a significant AUCs for LCN2 in saliva and serum of patients compared to healthy controls(0.7446 & 0.6802)with a sensitivity of(88.64% & 77.25%)and specificity of(60.17% & 60.17%)respectively.For MMP9,the AUC for serum was significant(0.9326),with a sensitivity of 85.01% and specificity of 95.54%.AUC for LCN2/MMP9 complex for saliva and serum were also significant(0.7415 & 0.7266)with a sensitivity of(86.74% & 78.80%)and specificity of(52.54% & 63.56%)respectively.Combining the three proteins using multiple logistic regression a risk prediction model was generated,with a better($p<0.0001$)AUC of(0.8025 & 0.9369).
Survival curve analysis revealed that pretreatment salivary LCN2 and salivary levels of MMP9 can be used as a predictive marker for OS(HR of 1.915 CI 1.173 to 3.127)and DFS(HR of 2.823 CI 0.9813 to 8.122) respectively.

**CONCLUSIONS**

LCN2,MMP9 and LCN2/MMP9 complex can be used as potential biomarkers for the diagnosis and prognostication of patients of OSCC.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0876

## RELATIONSHIP BETWEEN POLYMORPHISMS RS1059703 AND SCLERODERMA DISEASE

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**BACKGROUND-AIM**

Systemic sclerosis (SSc) is a highly heterogeneous disease with multiple clinical manifestations, which may be influenced by single nucleotide polymorphisms (SNPs). This study aimed to investigate the relationship between the rs1059703 polymorphism of the IRAK1 gene and susceptibility to various types of systemic sclerosis.

**METHODS**

The SNP rs1059703 was genotyped using the PCR-RFLP technique. Antibody levels in serum specimens from patients were evaluated using the ELISA method.

**RESULTS**

The results indicated no significant difference in allele or genotype frequency of rs1059703 between the control group and patients. However, the C/T genotype was more frequent in the diffuse group, while the C/C and T/T genotypes were more abundant in the limited group (OR=4.222, p=0.006). In patients of Arabic descent, the C/T genotype was correlated with pulmonary arterial hypertension (OR=9.95, p=0.031). Additionally, the T/T genotype was associated with gastrointestinal symptoms in patients without anti-topoisomerase 1 antibodies (OR=20.63, p=0.013) and in patients with anti-centromere antibodies (OR=22.06, p=0.014).

**CONCLUSIONS**

The findings suggest that the rs1059703 polymorphism of the IRAK1 gene may play a role in the clinical heterogeneity of systemic sclerosis. Specifically, the T/T genotype is linked to an increased risk of visceral symptoms in certain antibody profiles, while the C/T genotype is associated with pulmonary arterial hypertension in patients of Arabic descent. These results highlight the potential of genetic markers in understanding disease variability and guiding personalized approaches to management.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0877

**WHAT CAN THE NUCLEAR DENSE FINE SPECKLED(DFS)PATTERN AUTOANTIBODIES TELL US?**

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**BACKGROUND-AIM**

Antinuclear antibodies(ANAs)are a serological hallmark in the diagnosis of systemic autoimmune rheumatic diseases(SARD).The nuclear dense fine speckled(DFS)pattern ,as detected by indirect immunofluorescence(IIF)on HEp-2 cells, has been a subject of controversy since its definition.
The aim of this study was to explore the clinical value of the DFS pattern by analyzing the clinical diagnoses of patients with this pattern and the presence of anti-DFS70 antibodies.

**METHODS**

A retrospective analysis was conducted on 211 cases of DFS pattern detected between January 2024 and December 2024. All 211 samples were tested for anti-DFS70 antibodies using chemiluminescence, and the results were uniformly positive.The clinical diagnoses of these cases were reviewed to determine the prevalence of various autoimmune and non-autoimmune conditions.

**RESULTS**

Out of the 211 cases,186(88.1%) were diagnosed with non-systemic autoimmune diseases.The remaining 25 cases were diagnosed with various systemic autoimmune diseases:15 withRA,8 with Sjögren's syndrome,1 with systemic sclerosis, and 1 with antisynthetase syndrome. Notably,all patients diagnosed with systemic autoimmune diseases, except for the 7 RA patients, had additional nuclear antibodies such as SSA, Jo-1,and anticentromere B.In contrast, none of the cases diagnosed with non-systemic autoimmune diseases additional nuclear antibodies positivity.

**CONCLUSIONS**

The DFS pattern ,while not specific to SARD, can provide valuable diagnostic information when considered in conjunction with other additional nuclear antibodies.The absence of other antibodies in non-systemic autoimmune disease cases with the DFS pattern suggests that this pattern may represent a benign autoimmune response in some individuals.Further studies are needed to better understand the biological and clinical significance of the DFS pattern and to refine diagnostic algorithms for SARD.The uniform positivity for anti-DFS70 antibodies in all 186 samples suggests that this marker may be useful in exclusion of AARD based on absence of AARD-specific/associated antibodies and clinical presentation, but it should be particularly noted that single positive DFS70 combined with clinical manifestations may still have the possibility of diagnosis of RA.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0878

## THE AGE-ADJUSTED GFAP CUT-OFF VALUE IMPROVES THE TBI TEST SPECIFICITY IN ELDERLY PATIENTS, PRESERVING SENSITIVITY

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**BACKGROUND-AIM**

Patients suffering from concussion can avoid a head computed tomography (CT) scan if the serum Traumatic Brain Injury (TBI) test turns out negative. The result of the Glial fibrillary acid protein (GFAP) and Ubiquitin C-terminal hydrolase L1 (UCH-L1) levels are both significantly elevated in adults over 65 years; however, our previous findings revealed that GFAP is much more responsible than UCH-L1 for the diminished specificity of the TBI test in adults in this range of age. Therefore, the adjustment of the GFAP cut-off value in adults over 65 years is imperative to achieve an improvement in the TBI test specificity, and ultimately, reduce unnecessary head CT scans.
The aim of this study was to establish higher GFAP cut-off values for adults over 65 years and adults over 70 years.

**METHODS**

A retrospective observational study was performed on patients presented to the emergency department of a secondary hospital within 12 hours after suspected mild TBI and Glasgow coma scale of 14-15. 145 patients over 65 years and 138 patients over 70 years were enrolled in the study.
A ROC curve was performed; the best cut-off value was considered the one that improved the most the specificity but maintained the sensitivity (96,43%) of the manufacturer's cut-off value (35pg/mL).

**RESULTS**

By increasing the GFAP cut-off value from 35 to 55,9 pg/mL (without modifying the manufacturer's cut-off value of UCH-L1-400 pg/mL-) the specificity of TBI was doubled (2,43 times increase) (11,97% to 29,06%) in patients over 65 years and tripled (3,86 times increase) (6,36% to 24,55%) in those over 70 years, with unaltered sensitivity (96,43%). The number of CT saved (due to the positivity of either GFAP or UCH-L1) was doubled (8 to 16) in patients over 65 years and almost tripled (2,6 times increase) (5 to 13) in patients over 70 years.

**CONCLUSIONS**

GFAP cut-off values adjusted by age reduce unnecessary CT scans in the elderly population, without increasing the number of false negatives (patients with negative GFAP and positive CT scan), thus improving the cost-effectiveness of the TBI test.
However, the collection of more data in the elderly population is necessary for a finer adjustment of the GFAP discriminant value, as the specificity still remains low compared to that of the younger population.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0879

## GLYCEMIC CONTROL AND HYPOGLYCEMIC OR KETOACIDOSIS COMAS AT EARLY TYPE 1 DIABETES IN A PROSPECTIVE COHORT STUDY IN CHILDREN

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### BACKGROUND-AIM

The objective of our work is to study the relationship between glycemic control and metabolic outcomes (severe hypoglycemia and ketoacidosis).

### METHODS

Among 538 diabetics, we identified 69 patients with hypoglycemic or ketoacid comas. Glycemia was measured by blood glucose meter and glycated heamoglobin (HA1c ) assay was performed on a DCA Vantage® Analyzer.

### RESULTS

The incidence of acidotis coma is 0.93% and the incidence of hypoglycemic coma is 12%. The patients who had an acidotis coma had an HbA1c level between 6.5 and 11.5% with major hyperglycemia (3g/L to >5g/L). 63 diabetics have a hypoglycemic coma with duration of diabetes < 6 years. The number of hypoglycemic comas is inversely proportional to the duration of diabetes. One is more likely to have hypoglycemic comas for HbA1c levels < 7.5%, compared with HbA1c levels 7.5% and 8 or HbA1c levels > 8%. 45% of patients increased their HbA1c levels versus 35% who decreased it in the last quarter compared to the previous quarter.

### CONCLUSIONS

This original work shows that there is an inverse relationship between the incidence of severe hypoglycemia and quarterly HbA1c values. A low HbA1c level exposes the T1DM child to a high risk of hypoglycemic coma. Thus, the fear of severe hypoglycemia would be at the origin of an alteration of the patient's glycemic balance and the high HbA1c values. Thus, multidisciplinary management (adequate treatment and initial therapeutic education) will help avoid metabolic complications in diabetics.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0880

## ROLE OF BIOMARKERS IN THE DIAGNOSIS AND PROGNOSIS OF CENTRAL NERVOUS SYSTEM INFECTIONS: A LITERATURE REVIEW

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**BACKGROUND-AIM**

Infections of the Central Nervous System (CNS) present significant challenges in clinical diagnosis and treatment due to their complexity and high risk of complications. Biomarkers offer new opportunities for diagnosing and prognosing CNS infections by providing detailed insights into inflammation and neural damage, particularly in bacterial and viral infections such as meningitis and encephalitis.

**METHODS**

Literature search was conducted following PRISMA guidelines, targeting primary clinical studies on diagnostic or prognostic biomarkers for CNS infections. Inclusion criteria covered studies with clinical biomarker data in cerebrospinal fluid (CSF) or plasma. Studies lacking clinical data or with sample sizes under 10 patients were excluded. Data extraction was performed by two independent reviewers, capturing details such as study design, sample characteristics, types of CNS infections, and biomarker types. The quality of studies was assessed using the Newcastle-Ottawa Scale (NOS). This study systematically examines the diagnostic and prognostic role of biomarkers in CNS infections, with a focus on new opportunities provided by CSF and plasma biomarkers such as lactate, S100B, and Glial Fibrillary Acidic Protein (GFAP). Analyzing data from studies published between 2009 and 2024, this review identifies biomarkers that aid in distinguishing bacterial from viral infections and assessing the extent of neurological damage.

**RESULTS**

Of the 1,827 articles identified, 25 met the criteria and were systematically analyzed. These studies, covering over 2,000 patients, highlighted the high diagnostic accuracy of CSF and plasma biomarkers. Lactate showed high specificity in distinguishing bacterial from aseptic infections, while S100B and GFAP were associated with reliable assessment of glial damage severity. Notably, Interleukin-6 (IL-6) and heparin-binding protein (HBP) demonstrated strong diagnostic value for bacterial meningitis, with AUC > 0.90 in several studies.

**CONCLUSIONS**

The data underscores the importance of integrating these biomarkers into standardized protocols to optimize diagnostic accuracy and improve patient outcomes through timely and targeted interventions.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0881

## CA19-9 IN NON-CANCEROUS DISEASES

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### BACKGROUND-AIM

Tumor markers can help in the diagnosis of cancer. In this scenario, a differential diagnosis with other diseases with similar symptoms and sometimes with comorbidities that can affect the metabolism of tumor markers should be performed. The presence of a mutation in the FUT2 gene, population does not express the antigen CA 19-9.
The aim of this study is to determine and identify false positives leading to false positives and to identify the population with mutation in the FUT2 gene

### METHODS

We studied 2701 consecutive patients from the rapid cancer diagnostic units of our hospital between January 2017 and December 2018. Of these patients 1425 (52.7%) were men, with a mean age of 69±15 years.
CA19-9 was determined by an electrochemiluminescent method on a COBAS e801 multiparametric analyzer.

### RESULTS

The patients were classified according to their pathology and final diagnosis, with 879 (32.5%) cases of cancer and 1822 (67.5%) cases of benign disease. Among the patients with undetectable CA19-9 values, 11.9% had values below 2 U/mL. Among the 2,383 patients with detectable CA19-9, those with cancer had a significantly higher concentration ($p < 0.001$) of mean±SD 1055±10380 U/mL compared to patients with benign disease (82±1696 U/mL). The percentage of false positive (FP%) CA19-9>37 U/mL was calculated per benign disease group: No associated pathology (N;FP%) (461;9%) pancreatitis (24;37%) liver diseases (89;45%) cholestasis (71;25%). diabetes mellitus type 2 (89;16%),renal failure (216;7%), gynecological diseases (99;15%), digestive diseases (e.g., gastritis, diverticulitis) (73;7%), pneumopathies (177;11%), smokers (184;9%), and pulmonary diseases and smoking (118;10%). It is noteworthy thatvalues exceeding 2000 U/mL were observed in three patients with cholestasis (66418; 11009; 7650 U/mL) and one with a gynecological disease (2870 U/mL).

### CONCLUSIONS

We can conclude that CA19-9 Patients with pancreatitis, hepatopathies, cholestasis, type 2 diabetes and gynecological diseases presented a higher number of false positives. Cholestasis being the pathology with patients above 2000U/mL. The findings of this study indicate that, even at very high values in some pathological conditions, it is necessary to be very restrictive in the interpretation of this marker

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0882

## TOTAL SPECIES IS CORRELATED WITH GLUCOSE AND HBA1C IN UNCONTROLLED TYPE 2 DIABETES, BUT NOT IN CONTROLLED TYPE 2 DIABETES

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**BACKGROUND-AIM**

The gut microbiota composition plays a pivotal role in metabolic health, including type 2 diabetes (T2D). While gut microbiota has been implicated in T2D, the correlation between total gut microbial species and glycemic parameters remains unclear, particularly in controlled and uncontrolled glycemic states. This study investigates the relationship between total gut microbial species and metabolic parameters, such as glucose and HbA1C, in controlled and uncontrolled T2D patients.

**METHODS**

A cross-sectional study was conducted on 90 male T2D patients categorized into controlled (n=29) and uncontrolled (n=61) groups based on HbA1C levels (controlled: HbA1C ≤ 7%; uncontrolled: HbA1C > 7%), aged 30-50 years. Fecal samples were collected from the participants and genomic DNA was extracted. The total species of gut microbiome were investigated in fecal DNA samples using Illumina sequencing of the V3#V4 regions of 16sRNA.

**RESULTS**

The mean total gut microbial species count was 597.14 ± 12.53 in the controlled T2D group and 593.59 ± 10.15 in the uncontrolled group, with no statistically significant difference ($p = 0.945$). In the controlled group, total species count showed a weak, non-significant negative correlation with glucose ($r = -0.235$, $p = 0.22$) and HbA1C ($r = -0.208$, $p = 0.278$). Conversely, in the uncontrolled group, total species count was significantly and positively correlated with glucose ($r = 0.357$, $p = 0.005$) and HbA1C ($r = 0.326$, $p = 0.01$). Taken together, these findings suggest that while the total gut microbial species count is comparable between controlled and uncontrolled T2D, its relationship with metabolic parameters is more pronounced in uncontrolled T2D. This highlights the potential role of gut microbiota dysregulation in worsening glycemic control.

**CONCLUSIONS**

The total gut microbial species count is positively correlated with glucose and HbA1C in uncontrolled T2D patients but not in controlled T2D patients, despite no significant difference in overall species count. These results underscore the importance of glycemic control in mitigating the metabolic impact of gut microbiota in T2D.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0883

## AMYLOID BETA1-42, TAU AND P-TAU CSF MEASUREMENTS IN THE AUTOMATED PLATFORM ROCHE COBAS 8000 AND COMPARISON WITH FUJIREBIO MANUAL ELISA METHODS

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### BACKGROUND-AIM

The establishment of cerebrospinal fluid (CSF) proteins amyloid beta1-42 (Ab42), tau and phosphorylated-tau (p-tau) as reliable neurodegenerative dementia biomarkers according to the AT(N) 2018 classification makes imperative for the clinical labs the transition from tedious manual techniques such as ELISA to automated immunochemical platforms where speed, accuracy and high-throughput can be achieved.

### METHODS

53 CSF samples from patients from the neurodegenerative spectrum (Alzheimer's disease, Frontotemporal Dementia etc.) were collected according to strict pre-analytical conditions and analyzed for all CSF biomarkers with gold-standard Innotest ELISA methods (Fujirebio) and in parallel, with the new CE-IVD Roche reagents that employ the Cobas 8000 automated platform.

### RESULTS

The new Roche reagents are easy to implement, rapid (results within 18 min compared to 20 hours for the ELISA manual procedures) and showed excellent precision results (CV% of internal low and high quality controls ≤5% compared to 8-12% for ELISA). Regression and correlation statistical analysis was performed for the individual measured parameters: a) AbRoche=1.86xAbFujirebio-524, r=0.93, concordance=45% b) tauRoche=0.51xtauFujirebio+47, r=0,97, concordance=83% c) p-tauRoche=0.36xp-tauFujirebio-3, r=0,92, concordance= 66% (n=38) and for the ratios p-tau/ab42 and tau/ab42: i) p-tau/ab42Roche (r=0.93, concordance 95%, n=38), ii) tau/ab42 Roche (r=0.87, concordance 94%). For the concordance analysis of the ratios, we applied literature universal cut-offs for Fujirebio (<0.068 for p-tau/ab42 and <0.44 for tau/ab42) and the FDA-approved values for Roche (<0.023 for p-tau/ab42 and <0.028 for tau/ab42 correspondingly).

### CONCLUSIONS

The Roche and Fujirebio ptau/ab42 and tau/ab42 ratios show excellent concordance and high correlation (however, for the absolute values of the three dementia parameters, they provide statistically correlated results, although not equivalent, as shown in the regression equations). The effort for harmonization and automation of these CSF parameters should continue worldwide. Final and correct adjudication of the cases should be examined during patient monitoring. Replication of results in larger well-ascertained patient cohorts would strengthen our findings.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0884

## ASSESSMENT OF UTILISATION OF CARDIAC BIOMARKERS AT A TERTIARY HOSPITAL IN SOUTH AFRICA

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### BACKGROUND-AIM

Acute coronary syndrome (ACS) is a significant global health challenge, and cardiac biomarkers are pivotal for its diagnosis and management. While serial measurement of high-sensitivity cardiac troponin (hs-cTn) at presentation and again 3 hours later is recommended due to its superior diagnostic accuracy in identifying significant changes indicative of acute myocardial infarction (AMI), adherence to this guideline appears inconsistent in certain settings. At Tygerberg Hospital (TBH), requests for both hs-cTnT and creatine kinase MB (CK-MB) remain common, despite hs-cTnT being the preferred biomarker for suspected myocardial infarction (MI). In this study, the adherence to the use of cardiac biomarkers guidelines at TBH was evaluated.

### METHODS

A retrospective descriptive study was conducted on hs-cTnT and CK-MB test requests at the National Laboratory Service (NHLS) Chemistry Laboratory, TBH from December 2023 to May 2024. The study included patients aged >18years with recorded hs-cTnT and CK-MB results. Patient demographics, test results and hs-cTnT retesting intervals were analysed.

### RESULTS

A total of 2202 results obtained between December 2023 and May 2024 were included in the study, comprising 52.54% males and 47.46% females. Of these, 2130 (96.70%) had only hs- cTnT requested, 19 (0.9%) had only CK-MB requested, and 39 (1.8%) had both hs-cTnT and CK-MB tests requested. The appropriateness of hs-cTnT retesting was low, with only 14.6 % retests deemed appropriate. The annual cost of hs-cTnT only testing was €882.67 compared to €1,434.10 for combined CK-MB and cTnT testing.

### CONCLUSIONS

Despite adherence to guidelines recommending hs-cTn as the preferred biomarker, adherence to retesting guidelines remains unclear. The findings of this study could help optimize cardiac biomarker utilization, thereby enhancing patient management and outcomes.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0885

## LEARNING MORE ABOUT STROKE MANAGEMENT: USEFULNESS OF GFAP AND UCH-L1

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### BACKGROUND-AIM

Serum biomarkers like Glial Fibrillary Acidic Protein (GFAP) and Ubiquitin C-Terminal Hydrolase L1 (UCH-L1) are being studied to improve detection and classification of acute brain injury. GFAP indicates glial activation, while UCH-L1 reflects neuronal damage.
The objetive of this study is to explore the association between GFAP and UCH-L1 levels with stroke type and mortality in adults with acute brain injury due to stroke.

### METHODS

A prospective study was made from June 2022 to April 2024 in a tertiary hospital and included adults with suspected stroke. Blood levels of GFAP, UCH-L1, and creatinine were measured at admission using the Alinity ci analytical platform (Abbott, US) in heparin plasma samples. Results were expressed as percentages and medians with interquartile ranges [p25-p75]. Patients were classified by overall mortality and stroke type (ischemic vs hemorrhagic). Bivariate analyses were performed using the Mann-Whitney U test and Chi-square or Fisher's exact test, with a 5% significance level.

### RESULTS

Of 56 patients, 17 (30%) were excluded due to non-stroke diagnoses. Among 39 included patients, 20 (51%) were men, median age 75 years [64-78]. No significant sex differences in stroke presentation, but mortality differences were significant (p=<0.00001). Overall mortality was 23%, with 87% ischemic strokes.
The results of patients who survived the event vs deceased were: creatinine (0.91mg/dL [0.70-1.04] vs 0.96 [0.75-1.01]; p=0.8493); GFAP (39.50pg/mL [22.55-49.48] vs 395.50 [65.70-926.20]; p=0.0005) and UCH-L1 (247.25pg/mL [182.08-627.73] vs 609.00 [245.30-934.50]; p=0.1141).
The values of patients who suffered an ischemic event vs those who had a hemorrhagic event were: creatinine (0.91mg/dL [0.72-1.03] vs 1.01 [0.63-1.05]; p=0.8493); GFAP (44.95pg/mL [26.23-59.50] vs 926.20 [744.70-7052.20]; p=0.0005) and UCH-L1 (245.40pg/mL [184.40-620.85] vs 934.50 [429.80-1964.80]; p=0.0139).

### CONCLUSIONS

Elevated GFAP levels in suspected stroke patients may be an early marker for predicting stroke type and mortality. UCH-L1 may help predict stroke type. High levels of both markers suggest a higher likelihood of hemorrhagic stroke. Larger studies are needed to find a cutoff point for the markers that helps in the classification of the type of event and its early therapeutic management.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0886

## GAMMA-GLUTAMYL TRANSPEPTIDASE AS A BIOMARKER FOR ADVANCED FIBROSIS IN NON-ALCOHOLIC FATTY LIVER DISEASE: EMERGING INSIGHTS

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### BACKGROUND-AIM

Chronic liver diseases with fibrosis pose a significant global health burden. Liver fibrosis involves excessive fibrous tissue replacing normal liver tissue, disrupting liver structure and function. Progression to cirrhosis, a severe and irreversible stage, is linked to critical liver dysfunction. Early fibrosis detection is essential for timely intervention and improved outcomes. This study evaluates the efficacy of non-invasive biomarkers and algorithms for fibrosis screening in primary care.
Gamma glutamyl transferase (GGT), vital in glutathione metabolism, is traditionally used to assess liver function in conditions like cholestasis. Beyond its known role, this study explores GGT and its ratio to platelets (GPR) as promising non-invasive biomarkers for early fibrosis detection, offering new pathways for proactive liver health management.

### METHODS

The study included 325 primary care patients with glycohemoglobin requests and FIB-4 values between 1.3–2.6, undergoing routine analysis of liver biomarkers (AST, ALT, and GGT). Transitional elastography (Fibroscan), bioimpedanciometry, and clinical data collection were performed. Fibrosis stages were categorized by Fibroscan readings: F1 (5–7 KPa), F2 (7.7–9 KPa), and F3 (9.5–11 KPa). Biomarker sensitivity and specificity analyses were conducted for ALT, AST, GGT, platelets, and indexes like AAR, APRI, GPR, and FIB-4 at each fibrosis stage. Diagnostic performance was assessed via the area under the curve (AUC).

### RESULTS

Results indicated increased sensitivity and specificity at advanced fibrosis stages. At 5 KPa, AUC values for ALT, AST, GGT, AAR, APRI, FIB-4, platelets, and GPR were 0.6032, 0.5769, 0.6347, 0.5301, 0.5731, 0.5566, 0.5226, and 0.6365, respectively. At 11 KPa (advanced fibrosis), AUC values rose to 0.6280, 0.7233, 0.8448, 0.6651, 0.7469, 0.8317, 0.5523, and 0.8662, with GGT and GPR showing the highest diagnostic performance.

### CONCLUSIONS

These findings highlight the potential clinical utility of non-invasive biomarkers for fibrosis screening. GGT and GPR outperformed traditional liver enzymes at higher fibrosis stages, emphasizing their relevance in advanced fibrosis detection. Routine integration of these markers may improve accuracy in diagnosing fibrosis, enabling timely interventions and better management.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0887

## SEPTIN6 SUPPRESSES β-CATENIN/TCF4-MEDIATED TRANSCRIPTION VIA PHASE SEPARATION AND IDENTIFIES SEPTIN6 AS A PROMISING BIOMARKER FOR EARLY COLORECTAL CANCER

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### BACKGROUND-AIM

Colorectal cancer (CRC) has become the third most common malignant tumor in the world, with the second-highest mortality rate among all cancers. Recent reports support that β-catenin can form transcriptional condensates in the nucleus via liquid-liquid phase separation (LLPS), which is essential for Wnt/β-catenin pathway activation and tumor epithelial-mesenchymal transition (EMT). Investigating the mechanism LLPS condensate formation may provide molecular targets for therapeutic intervention in CRC.
Our previous work found that Septin6 is a novel binding partner for β-catenin, as identified through proteomic analyses during epithelia polarization. Additionally, purified Septin6 proteins can form protein condensates in vitro, exhibiting properties of LLPS. Thus, this work provides new insights into the role of Septin6 in suppressing β-catenin-mediated transcription via phase separation and its potential as a biomarker for CRC.

### METHODS

1.To induce LLPS in vitro, Purified proteins were diluted to indicated concentrations in buffer followed by imaging.
2.Fluorescence recovery after photobleaching (FRAP) was used to assess the flow ability of condensate.
3.Caco-2 3D cell cultures and organoid models were used to detect the tumor EMT ability.
4.RNA-sequencing and CUT&TAG sequencing was performed to detect the consequences of TCF4-mediated downstream signaling pathways.

### RESULTS

1.Both mRNA and protein expression levels of septin 6 was lower in CRC patients compared with para-carcinoma tissues.
2.Suppressing septin6 resulted in EMT in Caco-2 3D cell culture and colon organoid models.
3.Septin6 can undergo LLPS both in vivo and in vitro.
4.The intrinsically disordered region (IDR) of septin6 is critical for driving β-catenin into condensates.
5.Suppressing septin6 leads to increased accumulation of β-catenin in the cell nucleus and enhances the interaction between TCF4 and β-catenin, resulting in the promotion of TCF4-mediated transcription and EMT.
6.Overexpression of septin6, but not the non-phase-separated mutant, can rescue tumor EMT.

### CONCLUSIONS

In conclusion, our findings unravel a novel role for septin 6 in suppressing β-catenin/TCF4-mediated transcription via phase separation. Additionally, this study identifies septin 6 as a promising biomarker for the early diagnosis of colorectal cancer.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0888

## MACHINE LEARNING-BASED DNA METHYLATION MARKERS FOR PERIPHERAL BLOOD MONONUCLEAR CELLS TO ESTIMATE GASTRIC CANCER RISK IN A CHINESE AT-RISK POPULATION: A NATIONAL, MULTI-COHORT, PROSPECTIVE STUDY

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### BACKGROUND-AIM

Gastric cancer (GC) is one of the most common cancers worldwide, and nearly half of new cases and deaths in the world occur in China. Therefore, a GC risk prediction rule as an initial prescreening tool to identify individuals with a high risk prior to gastroscopy is urgently needed.

### METHODS

This was a nationwide multicentre cross-sectional study. Individuals aged 40-80 years who went to hospitals for a GC screening gastroscopy were recruited. DNA methylation markers derived from peripheral blood mononuclear cells, serum pepsinogen (PG) I, PG II, gastrin-17 (G-17) and anti-Helicobacter pylori IgG antibody concentrations were tested prior to endoscopy. Eligible participants (n=1678) were randomly assigned into the derivation and validation cohorts, with a ratio of 2:1, and a prospective cohort (n=2234) to validate their effectiveness in screening patients at high risk of GC.

### RESULTS

The novel GC risk prediction rule comprised ten variables (age, sex, PG I/II ratio, G-17 level, and 5 DNA methylation markers), with scores ranging from 0 to 1. In the testing set, the AUROC of the final model was 0.920 (95% CI 0.897 to 0.957) and the average precision was 0.482 (0.470 to 0.494). If the model-defined moderate-risk and high-risk groups were referred for endoscopy, the sensitivity was 92.5% (95% CI 86.8 to 95.5), specificity was 90.9% (90.2 to 91.5), and the predictive positive value was 18.4% (15.6 to 21.6), and 90.3% of endoscopies could be avoided. Further validation in patients who went to hospitals for a GC screening gastroscopy showed that the AUROC of the model was 0.924 (95% CI 0.900 to 0.960), and 90.8% of endoscopies could be avoided after risk stratification.

### CONCLUSIONS

We developed a prediction tool with favourable performance for identifying individuals at a higher risk in a Chinese high-risk population. This approach could prevent the need for gastroscopy screening in many low-risk individuals and ensure resource optimisation by prioritising high-risk individuals.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0889

## CLINICAL DIAGNOSTIC VALUE OF AUTOMATIC CHEMILUMINESCENCE ASSAY FOR DETECTING ANTI-PLA2R

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### BACKGROUND-AIM

Anti-M-type phospholipase A2 receptor (anti-PLA2R) antibody is a major biomarker for primary membranous nephropathy discovered in 2009, with a sensitivity of up to 70%. At present, the detection methods of anti-PLA2R is mainly manual or semi-automatic. The objective of this study was to verify the clinical diagnostic value of automatic chemiluminescence assay (CLIA) for detecting anti-PLA2R.

### METHODS

The positive or negative of 144 serum samples were achieved by Enzyme-Linked Immunosorbent Assay (Euroimmun Medizinische Labordiagnostika AG). The anti-PLA2R CLIA Microparticles Assay were provided by Autobio Diagnostics Co., Ltd. and detected on full-automatic immunoassay analyzer (AutoLumo A2000 Plus). Key performance testing including precision (EP5), limit of quantitation (LoQ) (EP17) were assessed per Clinical and Laboratory Standards Institute (CLSI) protocols.

### RESULTS

Compared to ELISA, the total coincidence rate of Autobio anti-PLA2R IgG CLIA Microparticles was 96.53% and the Kappa value was 0.913. Intra-assay CVs were 2.32% at 13.02 AU/mL, 2.10% at 56.60 AU/mL and 2.08% at 118.98 AU/mL. Inter-assay CVs were 2.52% at 13.02 AU/mL, 2.39% at 56.60 AU/mL and 2.84% at 118.98 AU/mL. The LoQ was 2.0 AU/mL.
Inter-assay CVs of ELISA provided by the manufacturer's specification were 4.2% at 28 RU/mL, 6.4% at 99 RU/mL and has no LOQ information.

### CONCLUSIONS

Results of this verification confirmed that Autobio anti-PLA2R assay (automatic CLIA) has similar analytical and clinical diagnostic compared to the Euroimmun anti-PLA2R assay (manual or semi-automatic ELISA). In addition, the automatic analysis method can improve the turnaround time and increase laboratory efficiency.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0890

**DEVELOMENT OF CHEMILUMINESCENT MICROPARTICLE IMMUNOASSAY KIT FOR S100 PROTEIN DETECTION**

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**BACKGROUND-AIM**

S100 is associated with Melanoma and brain damage. Clinical determination of S100 is used for dynamic monitoring of patients, disease progression or treatment determination of central nervous system tumors. The objective of this study is to develop Chemiluminescent Microparticle Immunoassay Kit for S100 Protein Detection in human serum.

**METHODS**

The S100 protein detection kit was based on sandwich method. The streptavidin coated microparticles, biotin-labeled S100 antibodies together with Enzyme Conjugate prepared by HRP-labeled S100 antibodies, react with the S100 antigens to produce and measure a chemiluminometric signal which is proportional to the amount of S100 in the sample.The S100 serum reference interval was established using 646 healthy volunteer samples.The performance of the S100 test kit was evaluated by detecting the, blank limit, linear range, repeatability, stability, and drug interference resistance.A total of 170 samples, including 100 cases of central nervous system tumors, 30 cases of melanoma, 10 cases of brain injury, 30 cases of interference were analyzed and compared using the developed S100 kit and the commercially available S100 kit.

**RESULTS**

Chemiluminescent Microparticle Immunoassay Kit for S100 Protein Detection was successfully developed. The normal range of ≤0.11 ng/mL (95th percentiles), the blank limit of the S100 test kit is ≤0.02ng/ml, the linear range is 0.05-40ng/ml, the repeatability CV value is 2.36%-2.99%, the shelf life stability at 2-8°C for 12 months; it has strong anti-interference ability against 20 common anticancer drugs. The correlation between the two evaluated kits, and the linear correlation coefficient R between them was 0.9980, which indicated the developed S100 kit was well correlated with commercially available S100 kit.

**CONCLUSIONS**

The developed Chemiluminescent Microparticle Immunoassay Kit for S100 Protein Detection provides a reliable, fast, and convenient detection method for quantitative detection of S100 protein in human serum.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0891

## DEVELOPMENT OF CHEMILUMINESCENT MICROPARTICLE IMMUNOASSAY KIT FOR HUMAN EPIDERMAL GROWTH FACTOR RECEPTOR 2 DETECTION

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### BACKGROUND-AIM

High serum human epidermal growth factor receptor 2 (HER-2/neu) levels suggest high tumor aggressiveness. The determination of HER-2/neu is widely used for dynamic monitoring of breast cancer patients to assist in judging disease process or treatment effect. Compared with immunohistochemistry, magnetic particle chemiluminescence has significant advantages in sensitivity, stability and ease of operation, which make it one of the international mainstream immunodiagnostic techniques. The aim of this study was to establish a magnetic particle chemiluminescence kit for quantitative detection of HER-2/neu in human serum.

### METHODS

The established HER-2/neu detection kit was based on sandwich method. 845 samples from patients with breast cancer, 61 samples from patients with benign breast diseases and 125 samples from patients with other cancers were compared with the estabilished detection kit and the commercially available kit. In addition, the blank limit, linear interval, specific interference, repeatability, stability and other properties of the kit were evaluated.

### RESULTS

According to statistical analysis, the HER-2/neu measurement value of 95% healthy women was ≤15.0 ng/mL. The comparison between the kit and commercially available oneshowed that the slope was 1.0079, the intercept was 0.05084, and the correlation coefficient was 0.9984. There were statistically significant differences between breast cancer and other cancers. The blank limit was ≤0.5 ng/mL, the linear interval was 2.0-350.0 ng/mL, the repeatability was 1.37-2.36%. It has strong anti-interference ability against 29 common anticancer drugs, including Herceptin and Perjeta, and the detection is not interfered by structural analogues HER-1, HER-3 and HER-4. The kit can be stably stored for 18 months at 2-8°C.

### CONCLUSIONS

The established kit is specific, stable and reliable, which can quantitatively detect serum HER-2/neu levels in breast cancer patients.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0892

## SERUM EXOSOMAL MICRORNA-1258 MAY AS A NOVEL BIOMARKER FOR THE DIAGNOSIS OF ACUTE EXACERBATIONS OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE

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### BACKGROUND-AIM

Acute exacerbation chronic obstructive pulmonary disease (AECOPD) has a high mortality rate.However, there is no efciency biomarker for diagnosing AECOPD. The purpose of this study was to fnd biomarkers that can quickly and accurately diagnose AECOPD.

### METHODS

45 normal controls (NC), 42 patients with stable COPD (SCOPD), and 66 patients with AECOPD were enrolled in our study. Serum exosomes were isolated by ultracentrifuge and verifed by morphology and specifc biomarkers. Fluorescent quantitation polymerase chain reaction (qRT-PCR) was used to detect the expression of micro RNAs (miRNAs), including miR-660-5p, miR-1258, miR-182-3p, miR-148a-3p, miR-27a-5p and miR-497-5p in serum exosomes and serum. Logistic regression and machine learning methods were used to constructed the diagnostic models of AECOPD.

### RESULTS

The levels of miR-1258 in the patients with AECOPD were higher than other groups ($p < 0.001$). The ability of exosomal miR-1258 (AUC = 0.851) to identify AECOPD from SCOPD was superior to other biomarkers, and the combination of exosomal miR-1258 and NLR can increase the AUC to 0.944, with a sensitivity of 81.82%, and specifcity of 97.62%. The cross-validation of the models displayed that the logistic regression model based on exosomal miR-1258, NLR and neutrophil count had the best accuracy (0.880) in diagnosing AECOPD from SCOPD. The three most correlated biomarkers with serum exosome miR-1258 were neutrophil count ($r = 0.57$, $p < 0.001$), WBC ($r = 0.50$, $p < 0.001$) and serum miR-1258 ($r = 0.33$, $p < 0.001$).

### CONCLUSIONS

In conclusion, serum exosomal miR-1258 is associated with infammation, and can be used as a valuable and reliable biomarker for the diagnosis of AECOPD, and the establishment of diagnostic model based on miR-1258, NLR and neutrophils count can help to improving the accuracy of AECOPD diagnosis.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0893

## DAB2+ MACROPHAGES MODULATE THE DIFFERENTIATION OF NAIVE CD4+ T CELLS THROUGH GALECTIN SIGNALING PATHWAY IN TUMOR MICROENVIRONMENT OF HEPATOCELLULAR CARCINOMA

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### BACKGROUND-AIM

To elucidate the interactions between different cell types within the tumor microenvironment (TME) of Hepatocellular Carcinoma (HCC) patients, analyze the key signaling pathways regulating tumor immune responses therein, comprehensively construct a cellular communication map of TME during HCC disease progression, and provide new insights and directions for understanding the mechanisms of HCC progression and exploring novel targets for diagnosis and therapy.

### METHODS

Adjacent liver cirrhosis and tumor tissues from four patients with Hepatitis B Virus (HBV)-related HCC, were collected. Single-cell sequencing was employed to construct a single-cell atlas of TME in HCC patients. Protein mass spectrometry analysis was conducted to identify exosome-carrying proteins in TME. scMappr v1.0.10, clusterProfiler v4.4.0 and Monocle v2.22.0 were utilized to analyze the exosome secretion capability, functional enrichmentint and potential mechanisms of pathways.

### RESULTS

By constructing a cellular communication map of TME in HCC patients, our results revealed that T cells occupy a central position in the TME cellular interaction network. During the progression of HCC, the main interaction partners of T cells shift from NKT cells to endothelial cells, hepatic stellate cells, hepatocytes/liver progenitor cells, and macrophages. Specific ligand-receptor interaction relationships also undergo changes. Different cell types exhibit varying exosome secretion capabilities, and differential exosome proteins originating from different cell types participate in distinct biological processes. In the interaction between ligands LGALS9 and LAMA4, cell interactions mediated by exosomes may predominate. DAB2+ macrophages may influence the differentiation direction of Naive CD4+ T cells via the Galectin signaling pathway, promoting the formation of an immunosuppressive state in HCC patients' TME.

### CONCLUSIONS

This study comprehensively analyzed the cellular communication map of TME in HCC patients from the perspectives of cell interaction and signaling molecules by integrating single-cell sequencing and exosome proteomics. It is expected to provide new cellular targets, molecular targets, and treatment strategies to improve the prognosis of HCC patients.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0894

## FREQUENCY OF AUTOANTIBODIES AND THEIR ASSOCIATED CLINICAL CHARACTERISTICS AND OUTCOMES IN PATIENTS WITH DILATED CARDIOMYOPATHY: A SYSTEMATIC REVIEW AND META-ANALYSIS

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**BACKGROUND-AIM**

Dilated cardiomyopathy (DCM) is a prevalent myocardial disorder characterized by impaired cardiac function affecting either the left ventricle or both ventricles. Accumulating evidence suggests that autoimmunity represents a key mechanism implicated in its pathogenesis. This study aimed to elucidate the prevalence of certain autoantibodies in patients with DCM compared to that in HCs and patients with ICM, as well as to evaluate their correlation with clinical characteristics and outcomes.

**METHODS**

A comprehensive literature search of the PubMed, Web of Science, EMBASE, the Cochrane Library, and Scopus was conducted up to March 26, 2024, and any article that fulfilled our inclusion criteria was reviewed. A meta-analysis was then conducted, using both random- and fixed-effects models.

**RESULTS**

A total of 38 studies met the inclusion criteria and were pulled for this analysis. Significantly higher prevalence rates of autoantibodies targeting the anti-β1 adrenergic receptor (β1-AR; odds ratio [OR] = 4.96, p = 0.000), M2 muscarinic receptor (M2-R; OR = 4.07, p = 0.000), adenine nucleotide translocator (ANT; OR = 21.18, p = 0.001) and myosin (OR = 12.26, p = 0.000) were observed in patients with DCM compared to HCs. Moreover, patients with DCM exhibited a significantly higher frequency of positive ANT Abs (OR = 34.52, p = 0.005) compared to those with ICM. Regarding clinical characteristics and outcomes, seropositivity for β1-AR Abs was found to be significantly correlated with New York Heart Association (NYHA) classification (standardized mean difference [SMD] = 0.78, p = 0.006), left ventricular ejection fraction (LVEF) (SMD = −1.38, p = 0.001), and heartbeat (HB) (SMD = 1.505, p = 0.022). Seropositivity for anti-calcium channel Abs was significantly associated with sudden cardiac death (SCD; OR = 3.17, p = 0.000) and all-cause mortality (OR = 2.06, p = 0.008), while anti-troponin I (TnI) Abs were associated with atrial fibrillation (OR = 0.21, p = 0.042).

**CONCLUSIONS**

This study represents the first comprehensive meta-analysis regarding autoantibody prevalence and DCM and may thus potentially guide the clinical management of such patients.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0895

## TUMOR SPECIFIC PROTEIN 70 IS A POTENTIAL BIOMARKER FOR DIFFERENTIAL DIAGNOSIS OF THYROID NODULES

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### BACKGROUND-AIM

To investigate the diagnostic value of tumor specific protein 70 (SP70) in malignant thyroid nodules.

### METHODS

Patients at the Thyroid Surgery Department of the First Affiliated Hospital of Nanjing Medical University were enrolled from October 2017 to June 2019. A total of 373 subjects were included, including 164 differentiated thyroid carcinoma (DTC) patients, 104 benign thyroid nodule (BTN) patients, 50 other types of thyroid disease but without thyroid nodules (OTD) patients and 55 health controls (HC). The Thyroid Imaging Reporting and Data System (TI-RADS) Committee of the American College of Radiology (ACR) was used to classify thyroid nodules based on ultrasonography characteristics. Serum samples before treatment were collected to measure the concentrations of SP70, thyroglobulin (Tg), anti-thyroglobulin antibody (TgAb) and thyroid stimulating hormone (TSH). The diagnostic value was assessed by ROC analysis and nomogram.

### RESULTS

SP70 is highly expressed in malignant thyroid tissues (87.9%, 51/58), while none expressed in benign tissues (0/15). The serum SP70 level in the DTC group was significantly higher than that in BTN, OTD, and HC groups (all $P<0.001$). However, commonly used tumor markers (Tg, TgAb and TSH) have no significant differences between BTN and DTC groups (all $P>0.05$). Serum SP70 level was closely related to tumor size and bilateral distribution (all $P<0.05$), presenting a sensitivity of 58.5% and specificity of 81.7% at cut-off value of 9.3 ng/mL (AUC: 0.742, 95%CI: 0.684-0.801), while TI-RADS has a similar AUC of 0.772 (95%CI: 0.718-0.827, SP70 vs. TI-RADS: $\chi 2=0.540$, $P=0.464$). In addition, the combination of serum SP70 and TI-RADS showed the best diagnostic performance for malignant thyroid nodules (AUC: 0.847, 95%CI: 0.800-0.894) which is obviously superior to each single index.

### CONCLUSIONS

SP70 is a valuable biomarker for differential diagnosis of thyroid nodules. It improved the diagnosis efficacy of malignant thyroid nodules prominently while combined with B-ultrasound examination. The potential benefits of incorporating SP70 into thyroid cancer diagnosis could lead to more efficient patient management and fewer unnecessary interventions which may change the consensus or guideline of thyroid nodule diagnosis and treatment in the future.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0896

## DIAGNOSTIC UTILITY OF METALLOPROTEINASE 7 (MMP-7) IN OVARIAN CANCER PATIENTS

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### BACKGROUND-AIM

Ovarian cancer is the commonest cause of gynaecological cancer-associated death. The disease typically presents in postmenopausal women, with a few months of abdominal pain and distension. In its early stage, no symptoms emerge, a that is why, it is called a sillent killer.
Matrix metalloproteinases (MMPs) are a group of over twenty proteases, operating chiefly extracellularly to cleave components of the extracellular matrix, cell adhesion molecules, cytokines etc. The purpose of this study, was to evaluate the plasma level and diagnostic utility of MMP-7 in comparison to the CA125 marker in ovarian cancer patients and in relation to the healthy subjects.

### METHODS

Tested group consisted of 30 ovarian cancer patients (stage II-III in FIGO, endometrioid ovarian cancer) and the control group included 30 healthy volunteers. Plasma levels of MMP-7 were determined using immunoenzyme assay (ELISA), CA125 concentrations by chemiluminescent microparticle immunoassay (CMIA).

### RESULTS

Plasma levels of MMP-7 (median 4,650 pg/ml) and CA125 (237.1 U/ml) were significantly higher in ovarian cancer patients compared to healthy individuals (0.8180 pg/ml; 123.5 U/ml, respectively). When assessing their diagnostic performance, MMP-7 outperformed CA125. MMP-7 exhibited a diagnostic specificity of 93%, sensitivity of 65.23%, negative predictive value (NPV) of 61%, and positive predictive value (PPV) of 92.25%. In contrast, CA125 showed lower values: specificity of 62.55%, sensitivity of 62.74%, NPV of 41.19%, and PPV of 80.87%. This indicates that MMP-7 is more accurate in identifying both healthy individuals and those with ovarian cancer.
The combined use of both markers improved the diagnostic sensitivity to 84% and increased the NPV to 72,3%, suggesting a better ability to detect cancer and rule out healthy individuals. Additionally, MMP-7 demonstrated a higher area under the receiver operating characteristic (ROC) curve (AUC of 0.9622) compared to CA125 (AUC of 0.6024).

### CONCLUSIONS

Obtained results could suggest that MMP-7 may be considered as a new marker in diagnostic of ovarian cancer, especially in combined use with CA125.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0897

## THE EVALUATION OF MMP-7 AND MMP-26 IN ENDOMETRIAL CANCER PATIENTS

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### BACKGROUND-AIM

Endometrial cancer is the most common malignant tumor of the gynecological malignancies. It ranks fourth in terms of morbidity among malignant tumors in women. Therefore, it is crucial to identify additional markers in this cancer, apart from the commonly used CA125, to facilitate early-stage diagnosis.
Matrix metalloproteinases (MMPs) play an important role in cancer cell invasion and metastasis by degrading the extracellular matrix. In this study, we investigated the plasma levels of matrilysins (MMP-7 and MMP-26) in comparison to the classical tumor marker CA125 in endometrial cancer patients and healthy subjects.

### METHODS

Tested group included 30 epithelial endometrial cancer patients (stage II-IV in FIGO, adenocarcinoma endometrioides). The control groups consisted of 30 healthy volunteers. Plasma levels of MMP-7 and MMP-26 were determined using immunoenzyme assay (ELISA), CA125 concentrations tested by chemiluminescent microparticle immunoassay (CMIA).

### RESULTS

Plasma levels of MMP-7 (median 4,361 ng/ml), MMP-26 (13,17 ng/ml) and CA125 (19,85 U/ml) were significantly higher in endometrial cancer patients as compared to the healthy subjects (0,8180 ng/ml, 3,281 ng/ml, 14,67 U/ml, respectively). MMP-7 and MMP-26 diagnostic specificities received higher values (93%, 66,47%) than CA 125 (62,45%). In addition diagnostic sensitivity, the negative predictive values (NPV) and positive predictive value (PPV) were highest for MMP-7 (93,96%, 90%, 96,45%, respectively) than for MMP-26 (76%, 72.56%, 90%) also than compared marker CA125 (69,93%, 55,52%, 83%, respectively) The combined use of tested MMP-7 or MMP-26 with CA 125 resulted in the increase of the sensitivity and NPV range (both equal 95%). The higher areas under the ROC curve (AUC) were observed for MMP-7 (0,9556) and MMP-26 (0,8567) than the AUC of CA125 (0,7156).

### CONCLUSIONS

These results suggest a potential usefulness of MMP-7 and MMP-26 in diagnostic of endometrial cancer patients, especially in combined use with CA125.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0898

## NEXT GENERATION PROTEIN BIOMARKER SIGNATURE IN BLOOD FOR EARLY DETECTION OF COLORECTAL CANCER

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### BACKGROUND-AIM

Colorectal cancer (CRC) is the second-leading cause of cancer-related mortality in Europe and the United States, but early detection boosts the 5-year relative survival rate to 91%. While colonoscopy remains the gold standard for screening, its invasiveness reduces adherence. Although less invasive stool-based and blood-based biomarker tests have advanced screening efforts, additional strategies are needed to enhance accuracy, particularly for early stage CRC and advanced adenomas (AA). In this study, part of the Horizon-funded DIOPTRA project for Mission Cancer, a blood-based protein biomarker approach to improve early detection was investigated.

### METHODS

A prospective clinical study was conducted to collect blood samples from individuals undergoing colonoscopy (N=260). Participants were categorized into four groups: Healthy, Non-AA (NAA), AA, and CRC based on the colonoscopy findings and subsequent histopathological diagnosis. Each sample was analyzed using Olink's next-generation proteomics platform, based on the proximity extension assay technology, measuring 3,072 proteins in blood. Bioinformatic analysis, utilizing machine learning algorithms and differential expression methods, identified a 45-protein signature capable of distinguishing the four study groups.

### RESULTS

In a 5-fold cross-validation scheme, the linear combination of these proteins achieved a sensitivity of 90.7% (95% CI: [79.7%, 96.9%]) for CRC detection and a specificity of 90.0% (95% CI: [73.5%, 97.9%]) for advanced neoplasia (calculated by combining the Healthy and NAA groups). Notably, the model's sensitivity for stage I/II CRC was 95.8% (95% CI: [78.9%, 99.9%]) and for AA was 62.0% (95% CI: [56.2%, 67.5%]), demonstrating the potential of protein signatures in blood to detect early stage cancer and advanced precancerous lesions.

### CONCLUSIONS

Future work is focused on developing multiplex immunoassays for these biomarkers to orthogonally validate the findings and assess the signature's analytical and clinical performance in a large participant cohort from the DIOPTRA validation studies (N=1600 participants). This protein biomarker signature could pave the way for more accurate, patient-friendly CRC screening methods that detect both cancer and its precursors at earlier, more treatable stages.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0899

## ASSOCIATION OF SERUM FERROPORTIN CONCENTRATION WITH CARDIOMETABOLIC RISK FACTORS IN PRESUMABLY HEALTHY SUBJECTS - A PRELIMINARY STUDY.

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### BACKGROUND-AIM

Ferroportin (FPN) is an iron exporting membrane protein that is essential for physiological regulation of cellular iron. The expression of FPN is suppressed by liver hepcidin (HEP) in response to increased iron levels or inflammatory stimulation. The aim of this study was to evaluate the relationship between serum FPN concentration and selected cardiometabolic risk factors in presumably healthy subjects.

### METHODS

The study included 120 non-diabetic, non-smoking subjects, aged 25-40 years (66 women, 54 men). Basic anthropometric indices (weight, waist circumference, BMI, WHR) and blood pressure measurements were performed in all subjects. Following laboratory tests: complete blood count, plasma glucose, serum lipid profile, C-reactive protein (hs-CRP), iron, total bilirubin (T-Bil) and glycated hemoglobin were measured on Architect ci8200 analyzer (Abbott Laboratories, IL, USA). Serum FPN and HEP concentrations were determined by enzyme-linked immunosorbent assay (ELISA) using commercially available kits (Sunred Biological Technology Co. Ltd., China; DRG International, NJ, USA).

### RESULTS

Serum FPN was significantly lower in women compared with men (48.7 vs. 31.2 ng/mL; p=0.003). Significant negative correlations were found between FPN and HEP, BMI, hs-CRP and glucose, while positive relationship was observed for FPN with T-Bil and HDL-cholesterol. Multivariable regression analysis showed that FPN concentration is influenced by HEP ($p<0.001$), overweight (BMI >25 kg/m$^2$; $p<0.001$), increased hs-CRP (>3 mg/L; p=0.001) and glucose (p=0.02). In subjects with lower FPN concentration (<21.4 ng/mL, 1$^{st}$ tertile) abdominal obesity and dyslipidemia occurred almost 2-fold and 40% more frequently, respectively, compared to subjects with higher FPN (>64.2 ng/mL, 3$^{rd}$ tertile).

### CONCLUSIONS

Serum FPN concentration is associated with the occurrence of cardiometabolic disorders in presumably healthy individuals, which may be related to the disturbance of iron homeostasis.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0900

## POLYMORPHISMS OF NCOA7, DRD2, AND SHBG ARE ASSOCIATED WITH THE RISK OF FEMALE BREAST CANCER IN A CHINESE POPULATION

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### BACKGROUND-AIM

Breast cancer has become the most common cancer in the world, accounting for 11.7% of new cancer cases. Breast cancer is induced by multiple risk factors, including genetics, environmental exposures, hormones, and behaviors, among which genetic factors are particularly important. Several genes, such as CHEK2, PTEN, BRCA2, and BRCA1, have been identified as being related to an increased risk of breast cancer, and single-nucleotide polymorphisms (SNPs) have also been claimed to be associated with breast cancer. Therefore, to assess the contribution of the SNPs in three genes (NCOA7 rs9375411, DRD2 rs10891556, SHBG rs1641537) to breast cancer risk, we conducted a case-control association study in a Chinese female population.

### METHODS

A population-based case-control study involving a total of 439 breast cancer patients and 439 age-matched healthy controls was carried out. We adopted Sequence MASS array to identify genotyping and used immunohistochemistry to test the expression of estrogen receptor (ER), progesterone receptor (PR), and human epidermal growth factor receptor-2 (HER-2) in tumor tissue.

### RESULTS

We found that NCOA7 rs9375411 (AG vs. GG: adjusted OR=0.72, 95% CI: 0.54-0.95; AG/AA vs. GG: adjusted OR=0.76, 95% CI: 0.58-0.99) and SHBG rs1641537 AA genotype (AA vs. GG: adjusted OR=0.62, 95% CI: 0.41-0.96) were associated with a decreased risk of breast cancer. In addition, stratified analysis revealed that DRD2 rs10891556 (TT vs. GG: adjusted OR=2.12, 95% CI: 1.18-3.81) was more common in premenopausal breast cancer patients. Furthermore, in terms of the pathological characteristics of tumors as well as the expression of ER, PR, and HER-2, NCOA7 rs9375411 and SHBG rs1641537 were also related to the breast cancer risk. This study revealed that NCOA7 rs9375411, DRD2 rs10891556, and SHBG rs1641537 were potentially associated with breast cancer risk.

### CONCLUSIONS

In this case-control study, we concluded that NCOA7 rs9375411, DRD2 rs10891556, and SHBG rs1641537 were potentially associated with breast cancer risk.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0901

## DEVELOPMENT OF A LC-MS/MS METHOD FOR THE QUANTIFICATION OF BRAIN CHOLESTEROL METABOLITES IN NEURODEVELOPMENTAL DISORDERS

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### BACKGROUND-AIM

Several neurodevelopmental disorders, such as Smith-Lemli-Opitz syndrome, Fragile X syndrome, and autism spectrum disorders, are associated with defects in peripheral and cerebral cholesterol homeostasis. Oxidized derivatives of brain cholesterol, known as oxysterols, hold a crucial biological role due to their ability to cross the blood-brain barrier. The quantification of these oxysterols in plasma offers a non-invasive approach to assess cerebral cholesterol homeostasis in these disorders. However, their low plasma concentrations and their structural similarities present significant analytical challenges, with only a few methods available for their simultaneous analysis.
Objective: We aim to develop and validate a sensitive and specific method using liquid chromatography coupled with tandem mass spectrometry (LC-MS/MS) for the analysis of 18 compounds: 5 cholesterol precursors, 5 auto-oxidized oxysterols, and 8 enzyme-derived oxysterols.

### METHODS

The LC-MS/MS method was developed using an Acquity UPLC system coupled with a Xevo TQ-S micro mass spectrometer (Waters). The ionization source was electrospray ionization in positive mode. Stable deuterium-labeled analogs were used as internal standards for each compound.

### RESULTS

The Multiple Reaction Monitoring (MRM) acquisition mode was employed. Specific transitions were designated for the 18 oxysterols and their respective internal standards. Isocratic separation of oxysterols was obtained at 62.5% acetonitrile with 0.1% formic acid at 0.3 mL/min. The best separation was achieved with a C8-silica column, with a total run time of 17.5 minutes.

### CONCLUSIONS

Mass spectrometry, ionization, and chromatographic separation parameters were optimized. The validation will be performed according to Clinical & Laboratory Standards Institute (CLSI) C62 guidelines. Oxysterols will then be quantified in individuals with neurodevelopmental disorders. This method will be implemented in clinical laboratories to support potential diagnostic applications and prognostic monitoring of cholesterol-related neurodevelopmental disorders.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0902

## SERUM SOLUBLE PROGRAMMED DEATH-1: A PROMISING PROGNOSTIC BIOMARKER FOR NSCLC PATIENTS UNDERGOING IMMUNE CHECKPOINT INHIBITOR THERAPY

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**BACKGROUND-AIM**

Soluble programmed death-1 (sPD-1) has emerged as a novel prognosis immune biomarker in infectious diseases and cancers. Previously, we established an automated, rapid fluorescent immunoassay to quantify serum sPD-1. This study aimed to evaluate whether sPD-1 could predict the clinical outcomes of non-small cell lung cancer (NSCLC) patients treated with immune checkpoint inhibitors (ICIs).

**METHODS**

This prospective study included 27 NSCLC patients treated with ICIs at Nanjing Drum Tower Hospital in Nanjing, China. Serum samples were collected before, during, and after ICI treatment. Serum sPD-1 levels were measured using the recently developed Pylon sPD-1 assay (EThealthcare, China). Progression-free survival and disease progression were analyzed. Kaplan-Meier curves for PFS were evaluated using the log-rank test, and multivariable analyses of PFS and disease progression were performed using Cox proportional hazard regression models.

**RESULTS**

Of the 27 NSCLC patients, 13 were at stage IV, 14 at stage III. The median sPD-1 level was 156.7 pg/mL (IQR 130.6–200.7), significantly higher than in healthy controls (108.8 pg/mL, IQR 92.8–135.0). sPD-1 levels were positively correlated with biomarkers such as CA153 ($r = 0.474$, $P = 0.034$). There was a trend toward higher sPD-1 levels in patients with distant metastases compared to those without (193.4 pg/mL [IQR 135.9–241.1] vs. 138.1 pg/mL [IQR 130.8–168.5], $P = 0.105$). Following anti-PD-1 therapy, serum sPD-1 levels significantly decreased (156.7 pg/mL [IQR 119.6–202.2] vs. 2.8 pg/mL [IQR 2.8–45.5], $P = 0.026$). During follow-up, 12 patients (44.4%) experienced advanced disease progression, and 2 patients (7.4%) died. The overall PFS was 20 months. Patients with pre-treatment sPD-1 levels in the upper tertile had shorter PFS (8 months [95% CI 1–11] vs. 20 months [95% CI 6–20]) and a higher event rate (60% vs. 35.2%) compared to the other patients ($P = 0.086$). Cox regression analysis indicated that patients with pre-treatment sPD-1 in the upper tertile had a hazard ratio (HR) of 2.58 (95% CI 0.822–8.08, $P = 0.1046$) for disease progression.

**CONCLUSIONS**

Serum sPD-1 levels were elevated in NSCLC patients and significantly decreased following ICIs therapy. sPD-1 shows promise as a novel prognostic immune biomarker associated with PFS in NSCLC patients.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0903

## THE ROLE OF IL6 AND OTHER BLOOD BIOMARKERS TO SAFELY DISCHARGE CHILDREN WITH MILD TRAUMATIC BRAIN INJURY.

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### BACKGROUND-AIM

Mild traumatic brain injury (mTBI) can affect anyone, with children being particularly vulnerable. Even mild, these traumas can lead to intracranial injuries (ICI) requiring prompt identification and monitoring of symptoms evolution at the emergency department (ED). The use of blood biomarkers for the management of these children is still to be explored.
The objective of our study was to evaluate the performances of combined blood biomarkers, in discriminating between mTBI children who had ICI (CT+) and mTBI children without ICI (either CT- or without CT but with long in-hospital-observation stay). The aim is to safely rule out ICI in children with mTBI in the ED.

### METHODS

A multicenter prospective cohort study was conducted in 5 pediatric EDs in Switzerland. Newborns to teenagers (≤ 16 years old) with mTBI were included. Blood was drawn at admission (≤ 24h) and 6 blood biomarkers (S100b, GFAP, HFABP, NfL, NTproBNP and IL6) were measured by immunoassay. Their performances to identify patients with ICI were evaluated through ROC curves, where sensitivity was set at 100%. All the single and duplex combinations of blood-biomarkers were tested. Biomarker age correlation was assessed in a healthy group of children aged 0-16 years.

### RESULTS

Blood samples of 419 children with mTBI and 99 healthy children were analyzed. 23 % (n=97/419) of children had CT scan examination, while all the others (n=322/419) were kept in observation at the ED for more than 6 hours. 19 % (n=18/97) of the children who underwent a CT scan had ICI, corresponding to 4 % of all mTBI included patients. IL6 was present in the three best combinations reaching 100% sensitivity (SE) and with the highest associated specificity (SP). IL6 + NfL yielded 61% SP, followed by IL6 + NTproBNP with 60% SP, and IL6 + GFAP with 57% SP, all with 100% negative predictive value. Neither IL6 nor NTproBNP were found to be age correlated.

### CONCLUSIONS

This study demonstrated that IL6 can significantly aid in the management of mTBI patients in the ED by avoiding unnecessary CT scans and reducing the length of stay for children and their families. Blood panels incorporating IL6 have the potential to transform clinical decision-making for the acute management of pediatric mTBI. Further external studies are needed to validate these findings.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0904

## INFLUENCE OF PRIOR ANTIBIOTIC USE ON THE DIAGNOSTIC ACCURACY OF MEMED®BV FOR BACTERIAL INFECTIONS

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### BACKGROUND-AIM

Evaluating patients in the Emergency Department (ED) with suspected infection is a common challenge. Many have previously received antibiotics, either for unresolved infections or due to self-medication without prescription.
Diagnostic tools like MeMed®BV help optimize rational antibiotic use by classifying the infection's etiological origin. MeMed scores>65 strongly suggest bacterial infection. It's based on three biomarkers: C-reactive protein(CRP), which rises in bacterial infections; interferon gamma-induced protein 10(IP-10); and TNF-related apoptosis-inducing ligand(TRAIL), both elevated in viral infections.
Understanding how prior antibiotic use affects these biomarkers is key to interpreting results accurately.
Our objective is to asses whether prior antibiotic use affects the diagnostic accuracy of MeMed as an indicator of bacterial infection in patients with suspected infection in the ED.

### METHODS

Data were collected from 244 patients in the ED with suspected infection between November 2023 and February 2024. Etiological suspicion (bacterial (ba) or non-bacterial (nb)), prior antibiotic use in the past month, and the MeMed score (LiasonXL®) were recorded.
Patients were grouped based on prior antibiotic use, and MeMed results were compared using Student's t-test. Sensitivity, specificity, and AUC were calculated for each group using SPSS®.

### RESULTS

Student's t-test, with $\alpha$=0.05, showed no significant differences in MeMed results based on antibiotic use in the previous month (p=0.487)
No Antibiotics (N=152): Sensitivity:0.731, Specificity:0.909, AUC:0.892(0.834–0.949)
Yes Antibiotics (N=92): Sensitivity:0.594, Specificity:0.833, AUC:0.737(0.607–0.867)

### CONCLUSIONS

Results indicate that while there are no significant differences in MeMed values based on prior antibiotic use, a decrease in sensitivity, specificity, and AUC was observed for diagnosing bacterial infection in patients who had taken antibiotics in the previous month. These findings highlight the importance of conducting thorough clinical interviews in the ED to correctly interpret infection biomarker results. Prior antibiotic use may modulate the immune response, affecting the expression of diagnostic proteins such as CRP, TRAIL, and IP-10.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0905

**CEREBROSPINAL FLUID LEVELS OF CHROMOGRANIN-A ARE INCREASED IN ALZHEIMER DISEASE PATIENTS.**

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**BACKGROUND-AIM**

Chromogranin-A (CgA) is a peptide from the granin family that has been found in the secretory vesicles of neurons and in neuroendocrine cells such as chromaffin cells. CgA is present in the brain (cerebral cortex) and seems to play a neuroinflammatory role, mainly acting on microglial inducing neuronal damage. It has been proposed that this peptide may play a role in some neurodegenerative diseases. In this context it has been described the presence of CgA in amyloid deposits characteristic of Alzheimer disease (AD) which are surrounded by activated glia. There are some studies indicating that CgA might be detected by mass spectrometry in cerebrospinal fluid (CSF). Results concerning CSF CgA levels in AD are controversial showing both increased or decreased CgA concentrations. In the present study we want to measure CgA levels in CSF from subjects with suspected cognitive impairment in order to test its possible role as AD biomarker.

**METHODS**

56 patients with suspected cognitive impairment were subjected to lumbar puncture in order to measured AD biomarkers. LCR samples were collected in low adherence tubes and frozen until assays. Beta-amyloid (βA) (isoforms 40 and 42) and Tau proteins (total and 181-phosphorylated) were analysed by CLIA (Lumipulse, Fujirebio). AD diagnosis criteria: βA42/ βA40 <0.069; tTau >404 pg/mL; pTau>56.5pg/mL. CgA was measured by an immunofluorescence assay based in TRACE technology (Kryptor Gold, Thermofisher Scientific). Results are shown as mean±SD. Statistical study (t-test and ROC curves) was performed by MedCal program.

**RESULTS**

22 patients were AD compatible (AD) showing βA42/ βA40: 0.042±0.009; tTau: 1766±3014 pg/mL; pTau: 190±129 pg/mL; 25 subjects were non-AD compatible (nAD): βA42/ βA40: 0.095±0.01; tTau: 318,4±160,7 pg/mL; pTau: 40.7±21 pg/mL and 9 subjects showed inconclusive results (did not meet all diagnostic criteria). In AD patients, CSF CgA levels were significantly higher than those measured in n-AD subjects (39.6±17.5 and 20.9±7.2 ng/mL, respectively; P<0.001). ROC curve for CgA levels in AD: AUC: 0.847; p<0.0001; Sensitivity: 72.7. Specificity: 84.6; CgA criterion: >26,62ng/ml.

**CONCLUSIONS**

Our results indicate that CSF CgA concentrations might be an additional biomarker in Alzheimer disease.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0906

**CANCER TESTIS ANTIGEN 45 AS A DIAGNOSTIC AND PROGNOSTIC MARKER IN OVARIAN CANCER**

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**BACKGROUND-AIM**

Ovarian cancer (OC) is the deadliest gynecological cancer. CT45 reacts with platinum to prolong the overall survival.

**METHODS**

In 62 cases of high-grade serous carcinoma (HGSC), pre-therapy serum and intraoperative tumor tissues were collected. We had 35 upfront surgeries and 27 neo-adjuvant chemotherapy cases.
A cutoff for the serum level of CT45 was established to differentiate between cancer and healthy (N = 25) individuals as 0.77 ng/mL. A cut-off of fold change 1.00 was used for tissue expression in qPCR.

**RESULTS**

CT45 expression in ovarian tissue (N = 62): Out of 62, 22 (35%) cases had high expression, and 40 cases had low expression (65%). In low-expression cases, 14/40 (35%) cases showed recurrence. The median fold change in recurrent vs. non-recurrent cases was -3.59 and 0.23, respectively. Among high-expression cases, 6/22 (27.2%) had recurrence. The median fold change in recurrence and non-recurrence cases was 7.56 and 111.8, respectively. Looking at the difference, a cut-off of 9.51 was established to differentiate between recurrent and non-recurrent cases ($p<0.0001$) using ROC curve analysis at a sensitivity and specificity of 89% and 88.24%, respectively. Above this value, no case showed recurrence till at least 2 years. Among all 62 cases of HGSC, 28 (45%) had a fold change of >9.51.
Serum level of CT45 (N = 31): The serum level of CT45 was measured in 31 patients. The high and low values were seen in 16/31 (51.6%) and 15/31 (48.3%), respectively. Recurrence was seen in 12/31 cases. The mean serum CT45 in recurrent cases was 1.11 ng/mL (median 0.83 ng/mL), while in non-recurrent cases it was 0.60 ng/mL (median 0.17 ng/mL).

**CONCLUSIONS**

Patients with high CT45 showed no recurrence and a better prognosis in all the cases. This is the first study on CT45 expression in ovarian cancer, showing a cutoff of 9.51 for the prediction of recurrence following platinum-based chemotherapy.
Key words: CT45-expression, ovarian cancer, recurrence

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0907

## COMPARATIVE ANALYSIS OF THREE METHODS FOR FAECAL CALPROTECTIN MEASUREMENT

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### BACKGROUND-AIM

Faecal calprotectin (FC) is a cytosolic protein found in neutrophils, notable for its resistance to bacterial degradation within the colon, resulting in a uniform distribution in faeces. It is therefore used as a biomarker for diagnosing and monitoring inflammatory bowel disease. Consequently, several commercial assays have been developed for FC quantification. The aim of this study is to assess the interchangeability of three different methods of FC measurement.

### METHODS

A total of 54 stool samples were analysed by fluoro-enzymeimmunoassay (EliA Calprotectin2, Phadia250, ThermoFisher), a method used in our laboratory, in parallel with chemiluminescence (Liaison XL, DiaSorin) and turbidimetry (Bühlmann fCAL® turbo, Palex; adapted from Optilite, Binding site) techniques. All samples were stored frozen until analysis and FC extraction was performed in duplicate using the respective devices from each manufacturer. Statistical analysis was performed using Stata software. The cut-off values recommended by the manufacturers were applied: <50 ug/g for ThermoFisher and Diasorin, and <80 ug/g for Palex.

### RESULTS

The Passing-Bablok test resulted in the following equations: ThermoFisher = -18,944 [95%CI: -34.545 to -8.384] + 2.087 [95%CI: 1.691 to 2.520]*Diasorin, indicating both systematic and proportional differences with a moderate correlation coefficient (r = 0.558); and ThermoFisher = -26.289 [95%CI: -34.576 to -15.075] + 0.916 [95%CI: 0.802 to 1.001]*Palex, showing systematic differences and a moderate correlation coefficient (r = 0.620). Bland-Altman analysis revealed a mean bias of 95.880 [95%CI 54.003 to 137.757] between ThermoFisher/Diasorin, and -47.265 [95%CI -99.661 to 5.131] between ThermoFisher/Palex. The kappa concordance index was 0.637 (82% agreement) for ThermoFisher/DiaSorin and 0.596 (80% agreement) for ThermoFisher/Palex.

### CONCLUSIONS

Statistical analysis revealed systematic differences, moderate correlations and notable biases. Consequently, these methods should not be considered interchangeable, and any changes in methodology should be communicated to clinicians. The differences observed may be attributed to variations in the methodologies employed and the compositions of the sampling devices used. These results highlight the need for standardised FC measurement techniques.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0908

**IMPORTANCE OF HIGH FLUORESCENCE CELL ANALYSIS IN TUMOR PATHOLOGY SCREENING THROUGH BIOLOGICAL FLUIDS.**

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**BACKGROUND-AIM**

High fluorescence cells (HF-BF) are those detected by flow cytometry due to their higher nucleus-to-cytoplasm ratio and increased nucleic acid content. These characteristics are common to a variety of cell types, including neoplastic cells, which has led to the proposal that their quantitative analysis in biological fluids could be useful for early detection of malignant neoplasms. According to Labaere, cytomorphological study is considered relevant when the HF-BF percentage in a serous fluid exceeds 2.1%, with a sensitivity of 86% and specificity of 46%.
Objective: To assess the role of the laboratory in screening for tumor pathology in biological fluids.

**METHODS**

An observational, retrospective, and descriptive study was conducted using the Laboratory Information System (Modulab®) and the Pathology program (Patwin®), analyzing biological fluids from May 1, 2023, to May 31, 2024, with the Sysmex® XN-350 analyzer. Fluids with an HF-BF percentage greater than 2.1% were selected. Demographic data, HF-BF percentages, and pathology results (including tumor type) were recorded.

**RESULTS**

A total of 924 biological fluids were reviewed, of which 68 met the inclusion criteria. The mean patient age was 68.12 years, with a slight male predominance (57.35%). Of the fluids, 85.29% were pleural, 13.24% were peritoneal, and 1.47% were pericardial. Pathology studies were conducted in 89.71% of the cases, and 32.35% of fluids with high HF-BF values tested positive for tumor pathology, with pulmonary (40.91%) and ovarian (22.73%) tumors being the most common.

**CONCLUSIONS**

The high percentage of positive tumor pathology results (32.35%) following detection of high HF-BF values underscores the importance of clinical laboratories in the early diagnosis of cancer. However, since HF-BF counts may include both benign and neoplastic cells, it is essential to confirm findings with cytology.
Collaboration between services is critical to achieving early diagnosis and improving patient care.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0909

## ANALYSIS OF IGG SUBCLASSES IN PATIENTS WITH DIFFERENT MULTIPLE SCLEROSIS PHENOTYPES

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### BACKGROUND-AIM

Multiple sclerosis (MS) is a chronic neurodegenerative disease. The disease course is classified into relapsing-remitting forms (RRMS) and progressive forms (primary progressive, PPMS, and secondary progressive, SPMS). The pathogenic mechanism of MS is primarily mediated by elevated levels of the IgG1 and IgG3 subclasses, which may play a significant role in disease activity. Furthermore, elevated levels of IgG3 can predict the development of MS according to different studies, but most of these studies have been carried out in patients with RRMS.
The aim of this study was to study the IgG subclass profile in the different MS phenotypes.

### METHODS

Patients with MS were retrospectively selected according to diagnostic criteria, who underwent lumbar punction as a complementary diagnostic test between February 2010 and November 2020. Exclusion criteria: Patients under 14 years of age, patients with monoclonal gammopathy and patients over 80 years of age (N=9). For the control group, diseases with non-demyelinating characteristics. IgG1, IgG2, IgG3, IgG4 were determined in serum by turbidimetry technique (Binding Site Ltd SPA PLUS).
SPSS Statistics v.25 was the software used.

### RESULTS

The final cohort consisted of 278 patients: 164 patients in the control group, 58 with RRMS, 24 with SPMS and 27 with PPMS. The mean age at lumbar punction was 49.9 years (SD±16.2) in the control group versus 37.8 years (SD±10.3) in the RRMS group, 46.4 (SD±11.0) in SPMS and 51.4 years (SD±8.0) in the PPMS group (p-value<0.05).
The median of the control group for IgG1, IgG2, IgG3 and IgG4 subclasses were 562.5, 400.5, 52.5 and 30.0, respectively. RRMS: IgG1, IgG2, IgG3 and IgG4 subclasses were 490.0, 383.1, 52.7 and 24.0 respectively. PPMS: 451.0, 472.0, 66.0 and 19.0, respectively. SPMS: 541.5, 358.1, 68.8 and 21.3, respectively. There were statistically significant differences in IgG4 subclass levels between PPMS vs RRMS and between PPMS vs control group (p-value Mann-Whitney test 0.022 and 0.016, respectively).

### CONCLUSIONS

Our results show significant differences in IgG4 subclass levels in PPMS with the control group and RRMS, in addition to higher levels of the IgG3 subclass in progressive phenotypes. These differential characteristics could help the prognosis of the disease.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0910

## MR-PROADM IMPROVES TO CANONICAL BIOMARKERS AND MASCC SCORE FOR RISK STRATIFICATION IN ONCOLOGIC PATIENTS WITH FEBRILE NEUTROPENIA

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### BACKGROUND-AIM

Cancer patients with chemotherapy-induced FN are a heterogeneous group with a significant risk of severe complications. According to international guidelines, Multinational Association for Supportive Care in Cancer (MASCC) score is the recommended tool for risk-stratification. However, adherence to those guidelines is low, resulting in unnecessary hospital admissions of low-risk patients and over-prescription of intravenous antimicrobial therapy.
In this study, we aimed to analyze the role of mid-regional pro-adrenomedullin (MR-proADM) to stratify risk in patients with solid tumors attended in an emergency department for FN after chemotherapy, in comparison to canonical biomarkers, such as C-reactive protein (CRP) and procalcitonin (PCT), and MASCC score.

### METHODS

This was an single-center and prospective observational study enrolling patients with solid tumors and FN after chemotherapy admitted to the ED. In all patients, admission CRP, PCT and MR-proADM levels were measured and MASCC score was calculated. The main outcome was the development of serious complications.
To evaluate the discrimination ability of the tested variables, area under the receiver operating characteristic curve (ROC AUC) were calculated and optimal cut-offs were calculated through Youden index.

### RESULTS

Population study included 173 episodes of FN. A serious complication occurred in 55 episodes (31.8%). MR-proADM was the variable with highest accuracy (ROC AUC: 0.90), significantly higher (p of comparison < 0.05, according to DeLong test) than those of PCT (0.83), CRP (0.79) and MASCC score (0.74). This accuracy was not improved by combining MR-proADM with the other tested variables.
Optimal cutoff for MR-proADM was 1.33 nmol/L, achieving a sensititivity of 76.4%, specificity of 86.4%, positive predictive value of 72.4% and negative predictive value of 88.7%, that increased to 96.5% for a cutoff of 0.87 nmol/L, previously recommended to rule-out complications in patients with suspected infection.

### CONCLUSIONS

A single measurement on admission to ED of MR-proADM outperforms to MASCC score and canonical biomarkers to predict serious complications in patients with solid tumors and chemotherapy-induced FN and can be a useful tool for risk stratification

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0911

**FOCUSSING ONLY ON FREE LIGHT CHAINS: ARE WE MISSING THE FOREST FOR TREES?**

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**BACKGROUND-AIM**

There have been quite a few studies on serum FLC (sFLC) ratios. Most guidelines recommend measuring sFLC as a part of the diagnostic work-up for multiple myeloma and other plasma cell dyscrasia. There is considerable variability in terms of the normal ranges and performances of different sFLC kits available in the market.
Therefore, we wanted to analyse the diagnostic utility and capabilities of both free and total light chain ratios in plasma cell dyscrasia.

**METHODS**

We analysed the data of tests done in our laboratory, on newly diagnosed patients of plasma cell dyscrasia over a period of 6 months (Jan 2024 to June 2024). Patients were tested for Myeloma Panel {(Serum Protein Electrophoresis (SPE), Serum Immunofixation Electrophoresis (sIFE), quantification of serum immunoglobins}. Patients were also tested for routine biochemistry. Patients' who were found to have signs of any renal impairment (serum Creatinine > 2.0 mg/dL) were excluded from the data analysis.
Statistical analyses were done to study how frequently an abnormal sFLC ratio, or an abnormal sTLC ratio is associated with the presence of monoclonal band (M-band).

**RESULTS**

Out of 1355 patients analysed, 564 patients had a M-band on SPE & sIFE. An abnormal Total Light chain (TLC) ratio (normal range: 0.8-2.1) showed the best sensitivity of 73.94%, specificity of 78.76%, Positive Predictive value (PPV) of 71.28% and Negative Predictive value (NPV) of 80.91%. Whereas an abnormal sFLC ratio (normal range: 0.26- 1.65) showed a sensitivity of 67.02%, specificity of 68.65%, Positive Predictive value (PPV) of 60.38% and Negative Predictive value (NPV) of 74.49%. ROC curves of: sFLC= 0.55, TLC= 0.60 & (sFLC + TLC) = 0.76.

**CONCLUSIONS**

Our findings suggest that measuring both serum TLC and FLC significantly increases the diagnostic power of detecting an M-band in serum than only measuring sFLC.
Therefore, in all patients of plasma cell dyscrasia both (sTLC & sFLC) should be measured.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0912

**ASSOCIATION BETWEEN SUPEROXIDE DISMUTASE ENZYME AND MORTALITY IN HYPEROXEMIC SEPTIC SHOCK PATIENTS BASED ON AN IN VITRO MODEL OF ENDOTHELIAL DYSFUNCTION.**

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**BACKGROUND-AIM**

Sepsis is the leading cause of admission to intensive care units (ICUs). Oxygen administration is necessary due to the inability of cells to consume oxygen and excessive production of oxidants. Determining what arterial partial pressure of oxygen (PaO2) is adequate to avoid harmful effects is a controversial issue. The aim of this work is to show how an in vitro model of endothelial dysfunction based on plasma treatment of critically ill patients can describe the fatal outcome of PaO2 above 120 mmHg during the management of septic shock patients.

**METHODS**

This single-center observational study included a total of 100 adult patients admitted to the ICU after major surgery at the Hospital Clínico Universitario de Valladolid (Spain). According to the qSOFA score, patients were classified into patients without complications after surgery, non-infectious organ failure, sepsis and septic shock. The study variable was established as hyperoxaemia group (PaO2 ≥ 120 mmHg), or normoxaemia group (PaO2 < 120 mmHg). Clinical and analytical data were recorded, and plasma aliquots were used to treat endothelial cells. Several oxidative stress parameters of the treated cells were quantified by spectrophotometry and the data were analyzed with SPSS, version 29.0.2.0.

**RESULTS**

Superoxide dismutase (SOD) enzyme was associated as a risk factor (OR=6.48, 95% CI 2.11-19.93; p<0.001) for hyperoxaemia condition. SOD was significantly elevated only in the septic shock group. Values above the cut-off value of 0.878 U/mL SOD (AUC 0.679, 95% CI 0.502-0.857; p=0.048), determined as a function of mortality, has hyperbilirubinemia and hyperkalemia as risk factors, which has also a 20% higher mortality (HR: 5.89, 95% CI 1.39-24.92; p=0.016). Notably, when comparing the patient groups according to the SOD cut-off value, we observed significant differences in lactate (p=0.023) and SOFA (p=0.007) score in favour of patients with high mortality.

**CONCLUSIONS**

PaO2 level above 120 mmHg is associated with increased mortality due to increased SOD activity during endothelial dysfunction that occurs in septic patients with hyperbilirubinaemia and hyperkalaemia. Our findings highlight the use of endothelial cell cultures as a future tool in clinical laboratories to determine mortality-related parameters in septic patients.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0913

## DIAGNOSTIC UTILITY OF SERUM BIOMARKERS S100B, GFAP, AND VWF IN PATIENTS WITH ACUTE STROKE

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### BACKGROUND-AIM

Acute stroke is a non-communicable disorder that results in high mortality and morbidity worldwide. Thus, accurate and timely differentiation between ischemic stoke and hemorrhagic stroke is vital for initiating appropriate treatment.This study evaluates the diagnostic utility of serum S100B, GFAP and vWF to improve early stroke diagnosis and differentiation between ischemic and hemorrhagic stroke.

### METHODS

This is a case control study and includes 80 acute stroke patients with 80 age- and sex-matched controls. Blood samples were collected within 12 hrs of symptom onset. Biochemical markers i.e. serum S100B, GFAP and vWF were measured using enzyme-linked immunosorbent assay (ELISA) and results were analyzed. Serum lipid profile and plasma glucose levels were also analyzed to assess any co-morbidity.

### RESULTS

The average levels of serum S100B were notably higher in patients with ischemic stroke (434.14 ± 430.85 pg/ml) and hemorrhagic stroke (504.03 pg/ml ± 314.77 pg/ml) compared to healthy controls (99.18 ± 49.89 pg/ml). On the other hand, GFAP levels were elevated in patients with hemorrhagic stroke (13.58 ± 5.05 ng/ml) when compared to those with ischemic stroke (2.71 ± 1.13 ng/ml) and healthy controls (1.84 ± 1.38 ng/ml). Ischemic stroke patients had significantly higher vWF levels(17.47 ± 22.34 ng/ml) when compared to patients with hemorrhagic stroke (4.72 ± 4.68 ng/ml) and controls (3.08 ± 1.58 ng/ml).
Hence, our results were that serum S100B protein levels were significantly higher in all stroke patients (both ischemic and hemorrhagic stroke) compared to the controls ($p<0.01$) , while serum GFAP was raised significantly in hemorrhagic stroke patients as compared to ischemic stroke patients and controls ($p<0.01$) and serum vWF levels are significantly increased in patients with ischemic stroke as compared to hemorrhagic stroke patients and controls ($p<0.01$).

### CONCLUSIONS

Serum S100B, GFAP and vWF are promising biomarkers for identifying Acute Stroke and also aid in differentiating between ischemic and hemorrhagic stroke. The use of a panel of serum biomarkers to aid in the diagnosis of Acute Stroke will significantly enhance the diagnosis and treatment strategies, thereby improving patient outcome.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0914

**THE ROLE OF HOMOCYSTEINE IN BONE AND CARTILAGE REGENERATION**

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**BACKGROUND-AIM**

The aim of study is to investigate the role of homocysteine as a modern diagnostic biomarker that has a prognostic value in metabolic and repair processes occurring in bone and cartilage tissue in osteoporosis and osteoporotic fractures. Homocysteine (Hcy) is an indicator of prognostic value in monitoring regenerative processes in osteoporosis and osteoporotic fractures. The osteoporosis is known to be a serious health and economic problem, especially for women in the postmenopausal period.

**METHODS**

The study was carried out on patients 45-83 years old divided into 3 groups: group I – 14 patients with osteoporosis , group II – 15 patients with non-osteoporotic fractures, group III – 25 patients with osteoporotic fractures. The control group consisted of practically healthy 14 people. A blood sample was taken at 3 stages to monitor the dynamics of Hcy level: on the 1st day before treatment, on the 10th day of treatment and 1 month after it. Blood levels of Hcy were determined at a wavelength of 450 nm by the ELISA (Cloud Clone Corp., USA ). The statistical evaluation was performed by using SPSS 26.0 program (IBM SPSS Inc., USA).

**RESULTS**

The results showed that on the 1st day before the treatment Hcy concentration was statistically increased 2.7 times(Pu = 0.108) in group I, 5.6 times Pu <0.001) in group II and 6.5 times (Pu <0.001) in group III compared to the control group. Thus, the average value of HCY in group I was 1.76 ± 0.56 μg/ml; in group II – 3.57 ± 0.62 μg/ml; in group III – 4.2 ± 0.50 μg/ml.

**CONCLUSIONS**

Hcy level increases more sharply after fractures,especially in osteoporotic patients. In treatment period Vitamin D plays an important role in synthesis of the Cystathionine β-synthase enzyme, which regulates Hcy metabolism2,4. Increased Hcy levels could lead to an increase in the risk of fracture through the interference in collagen cross-linking5.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0915

**PERFOMANCE STUDY OF SERUM GFAP AND UCH-L1 IN MILD TRAUMATIC BRAIN INJURY: A TOOL TO REDUCE CT SCANS**

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**BACKGROUND-AIM**

Mild traumatic brain injuries (mTBI) are common and have significant public health implications. Diagnosis primarily relies on clinical criteria and computed tomography (CT) scans. Recently, Glial fibrillary acidic protein (GFAP) and Ubiquitin Carboxyl-terminal hydrolase L1 (UCH-L1) have emerged as potential mTBI biomarkers. This study evaluates their serum concentration's diagnostic accuracy relative to CT findings.

**METHODS**

This prospective monocentric study was conducted at Sahloul University Hospital, Sousse, Tunisia. Patients presenting to the emergency department for head trauma within 12 hours, with a Glasgow Coma Scale (GCS) score ≥13 and requiring a CT scan, were included. Pregnant women, malignant melanoma patients, and non-consenting individuals were excluded. GFAP and UCH-L1 levels were measured using VIDAS® TBI tests. Sensitivity (Sn), specificity (Sp), positive predictive value (PPV), and negative predictive value (NPV) were determined based on predefined cut-offs: GFAP (22 pg/ml) and UCH-L1 (327 pg/ml).

**RESULTS**

Among 233 patients, intracranial injuries were detected on CT in 27 cases. The ROC curve for GFAP yielded an AUC of 0.667 (95% CI: 0.588–0.747, p=0.005), with 100% Sn and 56.3% Sp at a 21.8 ng/L cut-off. For UCH-L1, the AUC was 0.686 (95% CI: 0.578–0.793, p=0.002), with 88.9% Sn and 66.5% Sp at 203.05 ng/L. Using predefined cut-offs, GFAP showed 100% Sn, 58.25% Sp, 100% NPV, and 21.1% PPV, while UCH-L1 showed 85.1% Sn, 43.6% Sp, 96.8% NPV, and 18.8% PPV. Combining both biomarkers improved accuracy. If either test was positive, sensitivity reached 100%, specificity was 44.8%, NPV 100%, and PPV 4.7%. When both tests were positive, sensitivity remained 100%, specificity increased to 51.5%, NPV was 100%, and PPV rose to 27%. This approach could reduce CT scans by 31.5% when both tests were negative (65 scans avoided).

**CONCLUSIONS**

The high sensitivity and NPV of combined GFAP and UCH-L1 testing could aid mTBI diagnosis, particularly to exclude patients who do not need CT scans. Multicentric studies are needed to refine their clinical application.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0916

**BIOMARKERS FOR ALZHEIMER DISEASE DIAGNOSIS IN HIGH AND NON-HIGH BETA AMYLOID PRODUCERS SUBJECTS.**

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**BACKGROUND-AIM**

Alzheimer's disease (AD) is the most common neurodegenerative dementia. In AD, central deposition of β amyloid (βA) leads to a reduction in their CSF levels and neuronal damage to an increase in CSF axonal Tau proteins levels. In an earlier study we validated the diagnostic value of CSF βA (βA40 and βA42) and Tau levels and added these biomarkers to our laboratory's tests catalogue. We have seen great variability in βA levels indicating that there are high and normal amyloid producer subjects, a point that should be considered to carry out a correct data interpretation. We want to evaluate the incidence of high amyloid (hβA) vs non-high amyloid (nhβA) producer subjects for AD classification.

**METHODS**

215 subjects with suspected cognitive impairment were included. CSF levels of βA40, βA42, and total Tau (tTau) and 181-phosphorylated Tau (pTau) were tested by CLIA (Lumipulse, Fujirebio). Reference values: βA40:7755-16751pg/mL; βA42>599pg/mL; tTau<404 pg/mL; pTau<56.5pg/mL. To minimize differences between hβA or nhβA producing subjects, AD classification was made by βA42/βA40 ratio (42/40; cut-off:0.069). Subsequently, AD patients were divided in two groups: hβA (βA40>16751 pg/ml) and nhβA (βA40≤16751 pg/ml). Results (means±SD) were compared by Student t test

**RESULTS**

AD compatible patients (N=117): 42/40: 0.049±0.01; tTau:621±33.6; pTau:125±5.7; Non-AD (N=76):42/40:0.109±0.013; tTau:280.1±15.8; pTau:36.9±1.9. Inconclusive group (N=32): 42/40: 0.085±0.22; tTau: 338.7±199.8; pTau: 50.5±32.3. Most AD patients were nhβA (βA40:11507±279 pg/ml) but 18% of AD group were hβA (βA40:19114±70.4 pg/mL; p<0.0001 vs nhβA). hβA patients showed higher levels of βA42 (791±43 vs. 448±13 pg/ml; p<0.001). 42/40 were comparable in both AD groups (hβA: 0.051±0.003 vs 0.054±0.002 in nhβA; p=0.43). CSF Tau proteins were significantly (p<0.001) higher in hβA vs nhβA (tTau:1045±92 vs 698±35 pg/mL and pTau:178±15 vs113±5 pg/mL).

**CONCLUSIONS**

Our results reinforce the importance of using 42/40 to classify AD patients and minimize differences between high or low amyloid producer subjects. In AD, hβA patients also showed higher levels of Tau proteins, thus suggesting higher neuronal damage. Follow-up of both patient's groups may provide information on the role of βA in AD progression.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0917

## CARDIOMETABOLIC INDEX IS INDEPENDENTLY ASSOCIATED WITH CHRONIC KIDNEY DISEASE IN A KOREAN POPULATION

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### BACKGROUND-AIM

Dyslipidemia and obesity are strongly associated with chronic kidney disease. The cardiometabolic index (CMI), which consists of obesity and lipid parameters, has been proposed as a novel predictive tool for diabetes, hypertension, and cardiovascular diseases. Currently, it remains unclear that CMI is independently associated with CKD in general Korean population. The aim of this study was to investigate the association between the CMI and CKD in the Korean population.

### METHODS

This study consisted of 70,711 Korean adults underwent biochemical testing at a comprehensive health promotion center. The CKD was defined by a low eGFR below 60 mL per minute per 1.73 m2 body surface area. The diagnostic performance of CMI was analyzed by receiver operating characteristics curve. The association between CMI and MAFLD were evaluated using multivariate logistic regression.

### RESULTS

A total of 650 (1%) individuals had CKD. The level of CMI was higher in the population with CKD than in the counterparts ($P < 0.0001$). The area under the curve of the CMI was 0.702 (95% confidence interval: 0.698 - 0.706) in females and 0.612 (95% confidence interval: 0.566 to 0.658) in males ($P=0.0001$). The multivariate logistic regression analysis showed that CMI was independently associated with CDK (odds ratio = 1.4102, 95% confidence interval: 1.2360 - 1.6089, $P < 0.0001$).

### CONCLUSIONS

This study demonstrated that CMI is independently associated with CKD in the general Korean population. The CMI could be an alternative predictor of an increased risk of the CKD.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0918

## KAPPA FREE LIGHT CHAIN INDEX IS EFFICIENT FOR THE DIAGNOSIS OF MULTIPLE SCLEROSIS: A SINGLE CENTER COHORT STUDY IN SHANGHAI

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### BACKGROUND-AIM

The kappa free light chain (KFLC) index has become an important diagnostic biomarker in multiple sclerosis (MS) patients, as a quantitative alternative to oligoclonal bands (OCBs).
To evaluate whether KFLC index has similar diagnostic value to identify MS patients compared to OCBs, and to determine optimal cut-off value for KFLC index in Chinese cohort. To explore the correlation of KFLC index with demographics and other clinical indicators.

### METHODS

We performed a prospective, observational study involving 295 patients: 121 MS, 18 neuromyelitis optica spectrum disorders (NMOSD), 32 myelin oligodendrocyte antibody associated disease (MOGAD), 62 other inflammatory neurological disorders (OIND), and 62 non-inflammatory neurological disorders (NIND). KFLCs were measured by nephelometry in paired cerebrospinal fluid (CSF) and serum samples. Receiver operating characteristic (ROC) curve was used to define a cut-off for KFLC index. Spearman correlation analysis was used to evaluate the relationship between clinical parameters and KFLC index.

### RESULTS

The median (range) KFLC index was significantly higher in MS patients [18.9 (0.9, 388.9)] than in NMOSD [4.2 (1.5, 46.4), p = 0.029], MOGAD [4.5 (0.7, 28.6), p = 0.001], OIND [2.6 (0.6, 17.0), p = 0.000], and NIND [1.6, (0.6, 9.2), p = 0.000]. The optimal cut-off for KFLC index to identify MS patients from entire nonselective controls was 5.8. For MS patients, the sensitivity of KFLC index was lower than that of OCBs (0.74 vs 0.79, p=0.383), and its specificity was slightly lower than OCBs (0.84 vs 0.89, p=0.210), but the overall accuracy of KFLC index was similar to OCBs (0.79 vs 0.84, p = 0.880). KFLC index was positively correlated with IgG index (r=0.743, p<0.0001), the number of T2 infratentorial lesions (r=0.27, P=0.002) and paramagnetic rim lesions (PRLs) (r=0.203, p=0.026), negatively correlated with age (r=-0.265, p=0.003). KFLC index correlated poorly with other indicators (sex, disease duration, Expanded Disability Status Scale (EDSS), or contrast-enhancing lesions).

### CONCLUSIONS

KFLC index had similar diagnostic value in MS as OCBs. The age and the number of T2 infratentorial lesions and PRLs were significantly correlated with KFLC index.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0919

## VALIDATION AND IMPLEMENTATION OF QUANTITATIVE DRIED BLOOD MICROSAMPLING TECHNOLOGY FOR SELF-TESTING IN ORGANIZED PROSTATE CANCER TESTING IN SWEDEN

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### BACKGROUND-AIM

In Sweden, men ≥50 years of age are offered participation in Organized Prostate cancer Testing (OPT) by monitoring of prostate-specific antigen (PSA). Currently, the participation rate is 35%.
The aim of this study was to validate an at-home sampling procedure for PSA monitoring. The long-term aim is to investigate the effect on the OPT participation rate when offering this at-home sampling as an alternative to in-hospital normal routine blood sampling.
This at-home sampling is based on a quantitative dried blood spot disc device, named Capitainer®B (qDBS), allowing sampling of a precise volume of blood via a capillary finger-prick. The device is then mailed to a clinical laboratory for PSA quantification.

### METHODS

The developed method was based on extraction of blood from qDBS discs in PBS for 1h in room temperature during shaking. The extracts were then analyzed on Siemens Atellica. The validation focused on comparison to PSA reference method, in anonymized venous plasma samples. Also, precision and limit of quantification (LOQ) were validated. Next part of method validation is an ongoing clinical study, where capillary blood on qDBS are sampled in parallel to routine venous plasma.

### RESULTS

An excellent correlation (R=0.998, n=106) between PSA-concentrations in qDBS extracts of venous blood versus the reference method in plasma was demonstrated. The concentration range was 0.3-307 µg/L (median 3.2). The regression line equation was used to recalculate qDBS concentrations to corresponding plasma concentration. The action limit cut-off for PSA in the OPT is 3.0 µg/L in plasma. Applying this cut-off for the recalculated qDBS concentrations resulted in 98% sensitivity and 100% specificity. The method coefficient of variance (CV) was 4, 6, 12 % in the low, mid and high PSA concentration range, and the LOQ was 0.3 µg/L. In an interim analysis of the ongoing clinical study, promising results were obtained, showing similar statistics for capillary blood on qDBS.

### CONCLUSIONS

The results show that the qDBS method delivers satisfactory analytical performance supporting implementation as an alternative sampling method for monitoring of PSA. Next steps are to complete the ongoing clinical study, followed by a randomized clinical study within the OPT program.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0920

**EVALUATION OF ANTI-CENP REACTIVITY IN SAMPLES WITH CENTROMERE HEP-2 PATTERN AND CORRELATION WITH SYSTEMIC SCLEROSIS CLINICAL FEATURES.**

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**BACKGROUND-AIM**

Anti-centromere antibodies are associated with limited cutaneous Systemic Sclerosis (lcSSc) and, in general, with a more favorable prognosis for SSc. Centromere pattern (AC-3; www.anapatterns.org) observed in the immunofluorescence assay in HEp-2 cells (HEp-2 IFA) suggests the presence of antibodies against CENP antigens, mainly CENP-B. In this study, we evaluated the frequency of reactivity to CENP-B and CENP-A in samples from patients with lcSSc with an AC-3 pattern on the HEp-2 IFA test and correlated these findings with the demographic and clinical characteristics of the disease.

**METHODS**

Samples from 38 lsSSc patients with AC-3 pattern were included and evaluated for reactivity to CENP-B and CENP-A by line-blot and indirect ELISA. As controls, 48 lcSSc without the AC-3 pattern (Non-AC-3 group) were included. Clinical characteristics were recovered for 68 patients, 20 with AC-3 and 48 Non-AC-3.

**RESULTS**

Out of 38 samples with AC-3, 32 (84.2%) were reactive against CENP-B and 31 (81.6%) were reactive against CENP-A using the line-blot assay. Using anti-CENP-B ELISA, 35 (92.1%) AC-3 samples were positive for anti-CENP-B. There was 78.9% concordance for CENP-B reactivity between ELISA and line-blot. Using the immunoblot assay, 26 (68.4%) of the samples with AC-3 were reactive against both CENP-B and CENP-A, and one sample was positive only for CENP-A. Altogether, 37 samples (97.3%) were reactive against CENP-B by at least one method and all 38 samples (100%) were positive for either CENP-B or CENP-A in at least one of the two methods. Regarding the clinical features, interstitial lung disease was less frequent in patients with AC-3 pattern compared to the Non-AC-3 group (10.5% versus 54.2%; p=0.001). Other organ involvement parameters had similar frequencies between the groups.

**CONCLUSIONS**

Anti-CENP-B was the predominant autoantibody in samples yielding the AC-3 pattern, but anti-CENP-A reactivity was also prevalent and exclusive anti-CENP-A reactivity was also observed. Among lcSSc patients, anti-centromere reactivity was associated with less frequent lung involvement, suggesting that the presence of anti-centromere antibodies further differentiate a subgroup of lcSS patients with more favorable prognosis.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0921

## DIAGNOSTIC AND PROGNOSTIC UTILITY OF PERIOSTIN AND GALECTIN-3 AS BIOMARKERS IN INFLAMMATORY BOWEL DISEASES

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### BACKGROUND-AIM

Inflammatory bowel diseases (IBD), including Crohn's disease (CD) and ulcerative colitis (UC), are chronic disorders characterized by immune dysregulation and extracellular matrix (ECM) remodeling. These pathological processes, driven by increased proteolytic activity and altered ECM turnover, contribute to complications such as fibrosis and intestinal damage. Among potential non-invasive IBD biomarkers, matricellular protein periostin (POSTN) and galectin-3 (Gal-3) have been identified as key mediators of inflammation and fibrosis. This study aimed to evaluate their diagnostic and prognostic utility in distinguishing IBD subtypes and assessing disease activity.

### METHODS

Serum levels of POSTN and Gal-3 were quantified using enzyme-linked immunosorbent assay (ELISA) in 49 newly diagnosed CD or UC patients, as well as in 30 healthy controls. Diagnostic performance was assessed using receiver operating characteristic (ROC) curve analysis. Correlations with clinical indicators of disease activity and inflammatory markers such as C-reactive protein (CRP), were also analyzed.

### RESULTS

POSTN levels were significantly reduced in both CD and UC patients compared to controls, demonstrating high diagnostic accuracy. AUC values for POSTN were 0.91 (CD vs. controls) and 0.89 (UC vs. controls), with NPVs of 100% and 95.5%, respectively. Sensitivity and specificity for POSTN were 100% and 75% in CD and 97% and 75% in UC, with Youden indices of 0.75 (CD) and 0.72 (UC).
In contrast, Gal-3 levels were significantly elevated in IBD patients. AUC values were 0.88 (UC vs. controls) and 0.84 (CD vs. controls), with NPVs of 93% (UC) and 86% (CD). Gal-3 correlated positively with CRP levels in CD patients ($r = 0.68$, $p < 0.01$), reflecting its association with systemic inflammation, while POSTN showed no such correlation.

### CONCLUSIONS

This study highlights the potential of POSTN and Gal-3 as complementary non-invasive biomarkers in IBD. POSTN's high NPV and robust AUC values make it a reliable exclusion marker, while Gal-3's correlation with CRP and robust AUC values supports its utility in assessing inflammatory activity. Together, these findings support integrating POSTN and Gal-3 into diagnostic and monitoring strategies for IBD.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0922

## GM-CSF AND TGF-β3 ARE IMPLICATED IN THE BIOLOGY OF MENINGIOMAS AND SHOW POTENTIAL AS DIAGNOSTIC BIOMARKERS

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### BACKGROUND-AIM

Meningiomas are the most common primary intracranial tumors, originating from the meninges. Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF) plays a role in modulating the immune response in tumors, including meningiomas. Transforming Growth Factor-beta (TGF-β) isoforms (TGF-β1, TGF-β2, TGF-β3) are key drivers of tumor progression, immune suppression, angiogenesis, and invasiveness in meningiomas, making them important therapeutic targets. Since growth factors are specifically involved in promoting cell growth, differentiation, and regeneration, the aim of this study was to evaluate whether circulating levels of GM-CSF, TGF-β1, TGF-β2, and TGF-β3 are elevated in patients with meningeal tumors compared to healthy control individuals.

### METHODS

The study group was composed of 31 patients with tumors of the meninges (21 females, 10 males, median age 64 years) and 18 healthy control individuals (9 females, 9 males, median age 50 years). GM-CSF, TGF-β1, TGF-β2, and TGF-β3 concentrations were measured with commercially available ELISA kits.

### RESULTS

The median GM-CSF concentration was significantly higher in the meningioma group (8.68 pg/mL; interquartile range: 5.68-11.20 pg/mL) compared to control (2.35 pg/mL; interquartile range: 1.39-3.27 pg/mL) ($p<0.0001$). Similarly, the median TGF-β3 concentration was significantly elevated in the meningioma group (453.14 pg/mL; interquartile range: 393.53-522.63 pg/mL) compared to control individuals (418.58 pg/mL; interquartile range: 302.23-472.93 pg/mL) ($p=0.0138$). The area under the ROC curve (AUC) for both parameters was significantly greater than 0.5, indicating their diagnostic utility in differentiating meningiomas patients from healthy control individuals.

### CONCLUSIONS

GM-CSF and TGF-β3 are implicated in the biology of meningiomas and show potential as diagnostic biomarkers. Both proteins demonstrate the ability to differentiate meningioma patients from healthy control individuals with reasonable accuracy. Additionally, they represent promising targets for further research into diagnostic tools and therapeutic interventions for meningiomas. Nonetheless, further studies are required to validate these findings and fully explore their clinical applications.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0923

## IDENTIFICATION AND EVALUATION OF POTENTIAL MICRORNA MARKERS FOR DIAGNOSTICS OF ALZHEIMER'S DISEASE AND PARKINSON'S DISEASE AND CORRELATION WITH OTHER BIOCHEMICAL MARKERS

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### BACKGROUND-AIM

The present study aimed to identify microRNA (miRNA) targets with the greatest potential for effective distinction and differentiation of neurodegenerative diseases, and to analyse the correlations between selected miRNAs across different diagnostic groups.

### METHODS

This study analyzed 126 patients (75 women, 51 men) categorized into five diagnostic groups: Alzheimer's disease, non-Alzheimer's dementia, movement disorder, combined dementia and movement disorder, and healthy controls. Circulating RNA was extracted using the iCatcher Circulating cfRNA 1000 Kit with the iCatcher 12 automated isolator. MicroRNA levels were measured by TT-qPCR using the CFX96™ Real-Time Detection System (Bio-Rad). Concentrations of CSF and serum/plasma biomarkers were determined via ELISA. Statistical data were analyzed using MS Excel and MedCalc® software.

### RESULTS

The selection of microRNAs (miRNAs) for this study was based on primary screening and data from published literature, with a focus on the following targets: hsa-miR-23a-3p, hsa-miR-29c-3p, hsa-miR-30b-5p, hsa-miR-142a-5p, hsa-miR-146a-5p, and hsa-miR-151a-3p. Statistically significant correlations were identified between hsa-miR-29c-3p and hsa-miR-30b-5p, hsa-miR-30b-5p and hsa-miR-151a-3p, as well as between hsa-miR-23a-3p and hsa-miR-29c-3p. Furthermore, significant correlations were identified between hsa-miR-142a-5p and hsa-miR-146a-5p, and between hsa-miR-146a-5p and hsa-miR-151a-3p. The Kruskal-Wallis test revealed significant differences in hsa-miR-23a-3p and hsa-miR-29c-3p across different diagnostic groups. Furthermore, significant correlations were observed between the plasma amyloid-β peptide 42 and the following microRNAs: hsa-miR-29c-3p, hsa-miR-142a-5p, hsa-miR-146a-5p, and hsa-miR-151a-3p, when compared to classical dementia biomarkers. A similar correlation was also noted with the plasmatic amyloid-β peptide 42/40 ratio.

### CONCLUSIONS

The most promising microRNAs for distinguishing neurodegenerative diseases are hsa-miR-23a-3p and hsa-miR-29c-3p. Notably, hsa-miR-29c-3p shows a correlation with amyloid-β peptide levels and the amyloid-β 42/40 ratio. Although further large-scale studies are required, this miRNA holds potential for future therapeutic applications.
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Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0924

**VALIDATION OF ADAPTED CUT-OFFS FOR S100B, GFAP AND UCH-L1, IN A MTBI BELGIAN REAL-LIFE SETTING PROSPECTIVE STUDY: THE MITICBRAIN COHORT**

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**BACKGROUND-AIM**

Studies on biomarkers of mild traumatic brain injury (mTBI) have been carried out in different countries with comparable results but data in the Belgian population were still expected. This study evaluates the accuracy of the mTBI biomarkers in a mTBI Belgian Multicentric cohort, the MiTicBraIn cohort

**METHODS**

The MiTicBraIn cohort is a prospective study composed of 78 mTBI patients recruited in several Walloon hospitals (CHU de Liège, Godinne, Clinique Saint-Pierre Ottignies and Tivoli). Inclusion criteria were fulfilled if the mTBI patient was aged from 18 years old, got a CT scan and signed an informed consent. S100B, GFAP and UCH-L1 were measured in each patient.

**RESULTS**

In the MiTicBraIn cohort, the mean time-interval between the head trauma and the blood sample is of 9.9 hours. In this cohort, GFAP, S100B and UCH-L1 possessed areas under the curve of 0.813 ($p<0.001$), 0.747 ($p=0.001$) and 0.732 ($p=0.008$), respectively.
In the entire MiTicBraIn cohort, the “GFAP+UCH-L1” mTBI test had a sensitivity and NPV of 100% and a specificity of 42% and S100B had a sensitivity of 89%, a NPV of 100% and a specificity of 54%.
In adults from 65 years (42 individuals), all biomarkers revealed significantly reduced specificities. Indeed, the “GFAP +UCH-L1” mTBI test had a sensitivity of 100% and a specificity of 11.76% with 4 patients correctly ruled-out and S100B had a sensitivity of 87.5%, a NPV of 99.9% and a specificity of 26.47%.

**CONCLUSIONS**

The measurement of S100B within the manufacturers’ time recommendations seems unfeasible in Walloon hospitals in a real-life setting. The “GFAP+UCH-L1” mTBI test has a high sensitivity for mTBI in the Walloon population with still a significantly decreased specificity in the older population.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0925

## INFLAMMATORY AND NUTRITIONAL MARKERS AS INDICATORS FOR DIAGNOSING AND ASSESSING DISEASE ACTIVITY IN MS AND NMOSD

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**BACKGROUND-AIM**

Inflammation and nutritional markers have recently gained recognition for their roles in the fabrication of cognitive control centers demyelinating illnesses. Inflammatory indices such as the neutrophil-to-lymphocyte ratio (NLR), monocyte-tolymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), systemic immune-inflammatory index (SII), and systemic inflammatory response index (SIRI), along with nutritional markers like albumin (ALB), hemoglobin (HB), and body mass index (BMI), may predict disease occurrence. However, their potential in evaluating diseases such as multiple sclerosis (MS) and neuromyelitis optica spectrum disorder (NMOSD) remains unexplored.

**METHODS**

We retrospectively evaluated 249 NMOSD patients, 244 MS patients, and 249 healthy controls (HC), calculating MLR, NLR, PLR, SII, and SIRI, and measuring ALB, HB, and BMI levels. Logistic regression and ROC curves were used to develop and validate models for diagnosing and differentiating MS and NMOSD. Further, 35 MS patients, 38 NMOSD patients, and 85 matched HC were recruited for validation, and marker changes were monitored over six months.

**RESULTS**

Comparing MS and NMOSD groups with HC, MLR, NLR, SII, and SIRI were significantly greater, while ALB levels were lower ($P<0.05$). NMOSD patients exhibited higher MLR, NLR, SII, and SIRI, and lower HB and ALB levels contrasted with MS patients ($P<0.05$). These markers correlated negatively with total T lymphocytes and positively with C-reactive protein, the Expanded Disability Status Scale (EDSS), and MRI T2 lesion count. Following remission, NLR, SII, and SIRI decreased, while ALB increased over six months ($P<0.05$). Diagnostic models based on these markers showed AUCs of 0.840 (95% CI:0.806–0.875) for MS and 0.905 (95% CI:0.877–0.933) for NMOSD. Differential diagnosis between MS and NMOSD showed an AUC of 0.806 (95% CI: 0.750–0.863).

**CONCLUSIONS**

Inflammatory and nutritional markers are promising for assessing disease activity in MS and NMOSD. Diagnostic models based on these markers enhance the accuracy and clinical value of differentiating between the two conditions.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0926

**THE ROLE OF PRESEPSIN IN DIAGNOSING AND PREDICTING SEPSIS OUTCOMES: A MULTICENTER PROSPECTIVE STUDY**

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**BACKGROUND-AIM**

Sepsis, characterized by a systemic inflammatory response syndrome resulting from infection, poses significant challenges due to high morbidity and mortality rates, as well as the lack of consensus on effective diagnostic and prognostic tools. This study aims to evaluate the diagnostic and prognostic prediction capabilities of biomarkers, including procalcitonin (PCT), interleukin-6 (IL-6), and soluble CD14 subtype (Presepsin), in sepsis.

**METHODS**

This multicenter, prospective study was conducted from December 2023 to December 2024. A total of 132 patients with sepsis (with 88 survivors and 44 deceased at the end of a 28-day follow-up) were recruited from the intensive care units of three medical centers. Additionally, 70 patients with infection were enrolled controls. PCT, IL-6, and Presepsin levels of the participants were measured. Kaplan-Meier survival analysis and the log-rank test were employed to evaluate the 28-day survival rate of patients with sepsis. The receiver operating characteristic (ROC) curve was utilized to assess the diagnostic and prognostic performance of the biomarkers. Binary logistic regression analysis was carried out to analyze the risk factors for sepsis prognosis.

**RESULTS**

Presepsin levels were significantly higher in sepsis patients compared to controls ($p<0.001$). Among the three biomarkers, Presepsin exhibited the highest diagnostic (AUC=0.84, $p<0.01$) and prognostic prediction (AUC=0.81, $p<0.01$) efficacy. Binary logistic regression analysis indicated that PCT, IL-6, and Presepsin were significant risk factors for sepsis prognosis, with odds ratios (OR) of 1.24, 1.095, and 5.61, respectively. The 28-day Kaplan-Meier curve results showed that sepsis patients with Presepsin levels < 3617 pg/ml had significantly longer the survival times compared to those with levels >3617 pg/ml ($p<0.001$).

**CONCLUSIONS**

Presepsin is an effective biomarker for early diagnosis and prognosis of sepsis, highlighting its potential role in improving sepsis management and patient outcomes.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0927

**ELEVATED SERUM REVERSE T3 AS A PROGNOSTIC BIOMARKER IN SEPSIS: A MULTICENTER PROSPECTIVE STUDY**

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**BACKGROUND-AIM**

Euthyroid sick syndrome is characterized by low plasma triiodothyronine levels, elevated trans-triiodothyronine (rT3) levels, and no corresponding rise in thyroid stimulating hormone, which is closely associated with critical illness. This study aims to explore the prognostic value of plasma rT3 levels in predicting outcomes in sepsis patients.

**METHODS**

This multicenter, prospective study enrolled 79 sepsis patients without thyroid disease history from December 2023 to December 2024 across intensive care units of three medical centers. Forty patients diagnosed with infection were enrolled as controls. Data collected included rT3 levels, other laboratory results, acute physiology and chronic health evaluation II (APACHE II) score, and sequential organ failure assessment (SOFA) score. Sepsis patients were followed for 28 days and categorized into survival and death group according to the outcomes. Binary Logistic regression was used to analyze the risk factor for sepsis prognosis, and receiver operating characteristic was used to assess the predictive efficacy.

**RESULTS**

Compared with infection patients, sepsis patients had significantly higher rT3 levels and lower thyroxine concentrations (both $p<0.05$). Additionally, sepsis patients showed significantly higher SOFA score, APACHE II score, and serum levels of procalcitonin, interleukin-6, and presepsin compared to controls (all $p<0.05$). A total of 54 patients had follow-up results, including 38 survivors and 16 non-survivors. Binary logistic regression analysis showed that rT3 levels (OR: 4.445, 95%CI: 1.671–11.828, p=0.003), SOFA score (OR: 1.213, 95%CI: 1.040–1.415, p=0.014), and APACHE II score (OR: 1.151, 95%CI: 1.039–1.276, p=0.007) were risk factors for sepsis prognosis. Compared with other thyroid hormones, rT3 had the highest prognosis predictive efficacy (AUC=0.766, p=0.002). Multi-indicator combined analysis revealed that APACHE II combined with rT3 had the highest prediction efficacy for sepsis prognosis (AUC=0.839).

**CONCLUSIONS**

Serum rT3 levels are elevated in sepsis patients and serve as a risk factor for sepsis prognosis. The combination of rT3 with APACHE II score enhances the predictive value for sepsis outcomes, offering a potentially valuable tool for early risk stratification in critical care.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0928

**EXPLORING THE DIAGNOSTIC POTENTIAL OF MICRORNA146A IN GALLBLADDER CANCER: A PILOT STUDY**

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**BACKGROUND-AIM**

Gallbladder cancer (GBC) is a rare but aggressive disease with high mortality. One of the major challenges in managing GBC is its poor prognosis, primarily due to the absence of reliable early diagnostic markers, which often results in the cancer being detected at an advanced stage. This late detection significantly limits treatment options and reduces survival rates, underscoring the urgent need for research focused on identifying new diagnostic tools and strategies to improve patient outcomes. This study seeks to investigate the potential of microRNA146a (miR146a) as a novel diagnostic biomarker for GBC, with the hope of facilitating earlier detection and improving prognosis for affected individuals.

**METHODS**

This observational analytical study includes a total of 80 participants, consisting of individuals from three distinct groups: patients diagnosed with GBC, patients with cholelithiasis, and controls. Concurrent tissue and plasma samples were obtained from patients of GBC, cholelithiasis and controls. miR146a expression was assessed using real time polymerase chain reaction (qPCR) and analysed using unpaired student t-test. The diagnostic potential of these miRs was subsequently evaluated using receiver operating characteristic (ROC) analysis. Chi-square analysis was carried out to investigate the association between these miRs and clinical factors of GBC patients.

**RESULTS**

miR146a exhibited notably elevated expression levels in gallbladder cancer (GBC) when compared to other groups. A strong positive correlation was observed between miR146a expression in plasma and tissue samples, with a correlation coefficient of r=0.693 and a statistically significant p-value of 0.0007. Moreover, miR146a demonstrated excellent diagnostic performance for GBC, with a sensitivity of 100.0% and a specificity of 90.0%, indicating its potential as a reliable biomarker for detecting the disease.

**CONCLUSIONS**

miR146a showed remarkable sensitivity and specificity as a GBC diagnostic biomarker in both tissue and plasma samples. Future research should aim to elucidate the precise role of miRNAs in the pathogenesis of GBC, thereby enabling their utility not only as biomarkers, but also as therapeutic agents.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0929

## CYTOKINE PROFILES AND THEIR CORRELATION WITH TREATMENT RESPONSE IN SCHIZOPHRENIA

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### BACKGROUND-AIM

Schizophrenia is a complex neuropsychiatric disorder that is characterized by symptoms such as hallucinations and delusions. Treatment-resistant schizophrenia (TRS) is a severe subtype that is resistant to typical antipsychotic medications, and it contributes significantly to the morbidity. While immune dysregulation has been extensively implicated in the underlying causes of schizophrenia, its association with treatment response, particularly in North Indian populations, remains underexplored. Therefore, the current study was designed to investigate the correlation between cytokine imbalance and treatment response in schizophrenia.

### METHODS

The study recruited 54 patients diagnosed with schizophrenia (SCZ) and 30 healthy control participants, after obtaining informed consent. Patients were diagnosed based on the criteria in the Diagnostic and Statistical Manual of Mental Disorders, 5th edition (DSM-5) and evaluated using the Positive and Negative Syndrome Scale (PANSS). The SCZ patients were further divided into two groups: treatment responders and treatment-resistant cases, based on their clinical response. Serum levels of interleukins (IL-6, IL-10, IL-17, IL-22) were measured using ELISA technique.

### RESULTS

IL-10 levels were significantly increased in responders, when compared to resistant cases and controls ($p<0.0001$). IL-6 levels were found to be increased in both responders and resistant. cases compared to controls. However, significant increase was recorded only in TRS, with a median (IQR) of 53.38 (102.81) pg/mL compared to controls 5.7 (3.50) pg/mL ($p<0.0001$). IL-17 exhibited a significant elevation predominantly in the resistant group (84.49 (83.24) pg/mL, $p<0.0001$), with no significant change between the responders and controls. No significant differences were observed between any two groups in IL-22 levels.

### CONCLUSIONS

The study found that treatment-resistant schizophrenia (TRS) cases had elevated levels of the pro-inflammatory cytokines IL-6 and IL-17, as well as decreased levels of the anti-inflammatory cytokine IL-10. These findings highlights a potential role of immune-related mechanisms in the development of treatment-resistant schizophrenia.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0931

## ADVANCING SERUM M-PROTEIN QUANTIFICATION: COMPARISON BETWEEN ELECTROPHORETIC AND EXENT® MASS SPECTROMETRY MEASUREMENTS

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### BACKGROUND-AIM

Reproducible and accurate quantification of M-proteins is imperative for managing monoclonal gammopathies. Conventionally, this is achieved by serum protein electrophoresis (SPEP) using the perpendicular drop (PD) or tangent skimming (TS) method, or by immunochemical isotype measurements. Recently, mass spectrometry (MS)-based assays were introduced as more sensitive alternatives. This study compares M-protein quantification by SPEP (PD and TS method) and EXENT®, which measures M-protein by MALDI-TOF MS.

### METHODS

Left-over serum samples (n=90) with confirmed M-protein by SPEP (excluding biclonal gammopathies with different isotypes) were stored (-20°C) and analysed by EXENT®. SPEP quantification (PD and TS; integration using total protein data) was conducted by a single operator to minimise variability, while EXENT® utilised its automated IQ-software (integration using immunochemical isotype data).

### RESULTS

SPEP was complicated for 12/90 (13%) samples due to the presence of >1 M-spike; EXENT® resolved 11/12 samples as single M-proteins (polymerization confirmed) (1/12 samples biclonal gammopathy with same isotype).
For IgG (n=47), IgA (n=20) and IgM (n=23) M-proteins, both proportional and/or systematic errors were evident when comparing SPEP (TS or PD) and EXENT® M-protein quantification.
M-proteins ≥10 g/L migrating in the γ-region on SPEP (n=33) were on average 13% (4,4 g/L) lower by SPEP/PD compared to EXENT®; SPEP/TS values on average 35% (8,1 g/L) lower compared to EXENT®. M-proteins <10 g/L migrating in the γ-region on SPEP (n=32) were on average 40% (1,9 g/L) higher by SPEP/PD compared to EXENT®; SPEP/TS values on average 76% (1,2 g/L) lower compared to EXENT®. Similar trends were observed for M-proteins migrating in the ß or ß-γ region (n=25).

### CONCLUSIONS

M-protein quantification by SPEP methods (PD and TS) showed significant discrepancies compared to more objective and automated EXENT® results, regardless of M-protein level or migration region. These findings underlie the limitations of rather subjective SPEP quantification methods, including complex cases with multiple M-spikes. The adoption of MS-based quantification of M-proteins in clinical laboratories could enhance diagnostic precision and streamline patient monitoring.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0932

**INTERFERENCE OF BISPECIFIC ANTIBODIES ON SERUM M-PROTEIN ANALYSIS WITH EXENT® MASS SPECTROMETRY**

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**BACKGROUND-AIM**

Bispecific antibodies (BsAbs) have shown promising efficacy in multiple myeloma by targeting specific antigens on myeloma cells and T-cell CD3 co-receptors. Recently, teclistamab (anti–BCMA x CD3) and talquetamab (anti–GPRC5D x CD3) received regulatory approval in the USA and Europe for relapsed/refractory myeloma. This study evaluates the potential interference of these BsAbs in serum M-protein measurement using EXENT®, a mass spectrometry-based assay measuring intact immunoglobulin light chains (LC).

**METHODS**

To obtain the BsAbs unique mass-to-charge ratio (m/z), left-over teclistamab (90 mg/mL) and talquetamab (40 mg/L) were obtained through the hospital pharmacy. The stock solution was diluted (5 g/L) and spiked (0,5 g/L) into a patient sample with IgG κ M-protein. Diluted stock solution and spiked-in samples were analysed in duplicate using EXENT®. Next, frozen (-20°C) left-over serum of patients treated with teclistamab (n=2) and talquetamab (n=2) in which immunofixation electrophoresis was routinely performed were subsequently analysed using EXENT®.

**RESULTS**

Mean m/z values for teclistamab were 11302,2 and 11316,5 (both λ LC; theoretical m/z 11312 respectively 11318). For talquetamab, mean m/z values were 11302,3 (λ LC) and 11818,9 (κ LC) (theoretical m/z 11312 respectively 11821). Spiking teclistamab into a patient sample with IgG κ M-protein did not significantly affect the M-protein concentration (difference 6%), but talquetamab did (difference 17%). Additionally, in the spike-in experiment, EXENT® IQ software misclassified the κ LC of talquetamab (m/z 11818,9) as λ LC and instead flagged the κ peak as antibody-independent binding. In both patient samples, teclistamab (Cmax ~0,023 g/L) was detectable, while talquetamab (Cmax ~0,004 g/L) was not.

**CONCLUSIONS**

The implementation of mass spectrometry approaches to measure serum M-protein in clinical trials and in routine setting necessitates to know potential interference by novel therapeutic monoclonal and BsAbs. The sensitivity of EXENT® (limit-of-detection 0,015 g/L) enables detection of teclistamab but not talquetamab in patients samples. Integrating BsAbs unique m/z into EXENT® IQ software is a useful tool to adequately interpret patient samples.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0933

## HEAD-TO-HEAD COMPARISON OF THE FULLY AUTOMATED ELECSYS PTAU217 PLASMA ASSAY AND THE LUMIPULSE PTAU217 PLASMA ASSAY

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### BACKGROUND-AIM

Blood tests are a non-invasive and cost-effective method for detecting Alzheimer's disease pathology, including amyloid deposits. The Elecsys® Phospho-Tau 217 plasma prototype immunoassay (Roche Diagnostics International Ltd, Rotkreuz, Switzerland) has received United States Food and Drug administration Breakthrough Device Designation. The Lumipulse G pTau217 plasma assay is a research use only assay from Fujirebio.

### METHODS

This head-to-head, blinded, method comparison study compared plasma pTau217 levels measured using the Elecsys and Lumipulse pTau217 assays in samples from a subset of patients from the amyloid screening population of the CREAD2 study (NCT03114657). Amyloid status was determined by amyloid-positron emission tomography imaging with visual read or by the Elecsys CSF pTau181/Ab42 ratio. A dual cutoff approach assessed the cutoffs at sensitivity and specificity of 90%. Positive predictive values (PPV) and negative predictive values (NPV) were calculated. The Pearson correlation coefficient between the two assay results was calculated.

### RESULTS

This analysis included samples from 264 patients. Mean age was 71.3 years, 146 were female, 34 carried 2 copies of Apolipoprotein E4, and the mean Mini-Mental State Examination score was 24.7. Baseline demographics were consistent across amyloid-positive and negative subgroups. The AUC for pTau217 with respect to amyloid status was 0.907 with Elecsys and 0.862 with Lumipulse. For the Elecsys assay, at the 90% sensitivity cutoff, the PPV was 91.7% and the NPV was 78.3%; at the 90% specificity cutoff, the PPV was 94.8% and the NPV was 65.5%; 10.2% were in the intermediate zone. For the Lumipulse assay, at the 90% sensitivity cutoff, the PPV was 87.4% and the NPV was 75.7%; at the 90% specificity cutoff, the PPV was 93.1% and the NPV was 48.6%; 28.0% were in the intermediate zone. Plasma pTau217 levels between the Elecsys and Lumipulse assays were positively correlated (Pearson's r=0.883).

### CONCLUSIONS

The Elecsys pTau217 assay detects amyloid pathology with high accuracy and is highly correlated with the Lumipulse pTau217 assay. The fully automated Elecsys and Lumipulse pTau217 assays have clinical potential for detecting amyloid pathology. However, the assays need to be fully validated and approved by regulatory bodies before clinical use.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0934

## ATHEROGENIC COMBINED INDEX IS AN INDEPENDENT PREDICTOR OF METABOLIC- ASSOCIATED WITH FATTY LIVER DISEASES IN A KOREAN POPULATION

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**BACKGROUND-AIM**

Lipid metabolism abnormalities are one of the major risk factors for metabolic-associated fatty liver diseases (MAFLD) and cardiovascular diseases. A number of lipid parameters have used to predict coronary artery diseases (CAD). The atherogenic combined index (ACI) has been proposed as a novel predictive tool for the presence and severity of CAD. Currently, there is a lack of studies on the relationship between ACI and MAFLD in a Korean population. The aim of this study was to evaluate the diagnostic performance of the ACI and to investigate the association between the ACI and MAFLD in the Korean population.

**METHODS**

This study consisted of 22,103 Korean adults underwent abdominal ultrasonography and biochemical testing at a comprehensive health promotion center. The MAFLD was defined as having hepatic steatosis by abdominal ultrasonography and the presence of overweight/obesity, type 2 diabetes, or the evidences of metabolic dysregulation. The diagnostic performance of ACI was analyzed by receiver operating characteristics curve. The association between ACI and MAFLD were evaluated using multivariate logistic regression.

**RESULTS**

A total of 6,984 (32%) individuals had MAFLD. The level of ACI was higher in the population with MAFLD than in the counterparts ($P < 0.0001$). The area under the curve of the ACI was 0.778 (95% confidence interval: 0.771 - 0.784) at a cutoff of 5.603 with a sensitivity of 71%, and a specificity of 72%. The multivariate logistic regression analysis showed that ACI was independently associated with MAFLD (odds ratio = 2.2135, 95% confidence interval: 2.0961 - 2.3374, $P < 0.0001$).

**CONCLUSIONS**

This study demonstrated that ACI is independently associated with MAFLD in the Korean population. The ACI could be an alternative predictor of an increased risk of MAFLD.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0935

**THE USEFULNESS OF GOLGI PROTEIN-73 (GP73) AS A NEW BIOMARKER OF LIVER DISEASE SEVERITY.**

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**BACKGROUND-AIM**

The Golgi protein-73 (GP73) is a transmembrane protein expressed by epithelial cells of bile duct in the normal liver. In patient with liver diseases, high serum levels of GP73 have been detected, and its measurement has been suggested as a potential biomarker for liver fibrosis staging. We performed a cohort study to evaluate the diagnostic accuracy of GP73 in patients with NAFLD and for liver fibrosis staging.

**METHODS**

We collected serum of consecutive patients who were submitted to liver biopsy. Additionally, we collected serum of 15 healthy volunteers as negative controls. We collected demographic and clinical data. Serum GP73 was measured for all serum samples on Maglumi X8 (Snibe Co., Ltd, Shenzhen, Cina) platform using a CLIA technology according to manufacturers' instructions. Results were expressed as mean and standard deviation (SD). Sensitivity (SE), specificity (SP), the area under the receiver operating characteristic curve (AUROC) and the optimal cut-off value were calculated. Data were considered as statistically significant when $P<0.05$. Analyses were performed using MedCalc v.23.0.9 (MedCalc Software Ltd., Ostend, Belgium) software.

**RESULTS**

We included 84 patients, of which 60 were biopsy-confirmed NASH. The mean serum GP73 concentrations in patients' samples (NAFLD 30±12 ng/ml and NASH 32±12 ng/ml respectively) were significantly higher than that of control group (19±30 ng/ml, $p<0.05$). We observed a gradual increase of GP73 serum levels from F0 (25.37±8.9 ng/ml) to F1 (29.06±11.9 ng/ml), F2 (27.7±10.6 ng/ml), F3 (33.8±14.7 ng/ml) and F4 (32.6±13.6 ng/ml). However, GP73 levels were higher in patients with significant (F2+F3+F4, mean 32±14 ng/ml) and advanced (F3+F4, mean 33±14 ng/ml) fibrosis, than controls and no significant fibrosis (F0+F1, mean 27±10) ($p>0.05$). The optimal cut-off value for identify NAFLD patients was 15.7 ng/ml, with corresponding AUROC of 0.85 (95%CI 0.76-0.91), SE of 90.5% and SP of 73%. To identify patients with NASH, significant or and advanced fibrosis, the optimal cut-offs were 22.6 ng/ml, 31.1 ng/ml and 31.1 ng/ml, with the corresponding AUROC as 0.75, 0.7, and 0.67, respectively.

**CONCLUSIONS**

GP73 may be a useful serological marker to identify patients with NAFLD, NASH and advanced fibrosis.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0936

## META-ANALYSIS OF BIOMARKERS IN SEPSIS: PRESEPSIN AS A PROMISING DIAGNOSTIC TOOL

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### BACKGROUND-AIM

Sepsis is a severe clinical condition that requires early diagnosis and continuous monitoring. Biomarkers assist in identifying and managing sepsis. This study compares the diagnostic efficacy of presepsin, procalcitonin (PCT), and C-reactive protein (CRP) based on a meta-analysis that included various studies. To compare the sensitivity, specificity, and area under the curve (AUC) of presepsin, PCT, and CRP in the early diagnosis of sepsis.

### METHODS

A meta-analysis was conducted with studies published between 2010 and 2023, in English and Portuguese, from PubMed, Scopus, and Web of Science databases. Eighteen studies were included, covering different age groups with suspected sepsis. The analysis combined weighted averages for sensitivity, specificity, and AUC.

### RESULTS

Presepsin showed the highest combined sensitivity (84.01%; 95% CI: 78.5%-89.2%) and specificity (75.47%; 95% CI: 70.1%-80.6%), standing out as the most promising biomarker for sepsis diagnosis. It demonstrated superiority in differentiating sepsis from non-infectious inflammatory conditions, with an AUC of 0.88 ($p < 0.01$) compared to PCT and CRP. Procalcitonin presented a sensitivity of 79% (95% CI: 74.3%-83.7%) and specificity of 76% (95% CI: 71.8%-80.1%), making it useful in intermediate-risk situations. CRP, with a sensitivity of 72% (95% CI: 67.1%-76.8%) and specificity of 75% (95% CI: 70.3%-79.5%), was less effective in early diagnosis, showing greater variation depending on the clinical context. The data suggest that presepsin is the biomarker with the best overall performance, particularly in critical patients, as it provides faster and more specific responses, which can directly influence clinical management and the early initiation of appropriate treatment.

### CONCLUSIONS

Presepsin emerged as the most effective biomarker for early sepsis diagnosis, surpassing PCT and CRP in sensitivity and specificity. This result suggests that presepsin can be incorporated as an important tool for managing septic patients.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0937

## DETERMINATION OF 24,25 OH2 VITAMIN D3, A USEFUL MARKER OF VITAMIN D BODY RESERVES, BY LC/MS METHOD

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### BACKGROUND-AIM

Vitamin D and its optimal levels play a critical role in many aspects of human health. It is essential for the proper bone functioning, the immune system, and there are studies indicating its potential protective role against cancer, cardiovascular diseases and other conditions.
Advances in understanding vitamin D metabolism and its interactions with proteins, such as Vitamin D Binding Protein (VDBP) or albumin, new and more reliable markers of vitamin D reserves in the body are being searched. A very promising marker is the Vitamin D Metabolite Ratio (VMR), which is the ratio of 24,25-dihydroxyvitamin D3 to 25 hydroxyvitamin D3. Unlike the total 25-hydroxyvitamin D3 levels, VMR is unaffected by fluctuations in VDBP levels in the body that can vary due to medication use, acute conditions, and other factors.

### METHODS

The determination of 25-hydroxyvitamin D3 has become routine with the availability of immunoassay and LC/MS-based IVDR methods, there is currently no routine method for determining 24,25-dihydroxyvitamin D3. Due to its low concentration levels, in-house methods using LC/MS techniques are being developed, offering sufficient sensitivity.

### RESULTS

In our laboratory, we successfully developed an LC/MS method with a straightforward sample preparation process, involving protein precipitation and purification of phospholipids using column with specific sorbent, followed by derivatization with PTAD (4-Phenyl-1,2,4-triazoline-3,5-dione). The method was implemented on Agilent 1290 Infinity II UHPLC system combined with the 6495C Triple Quadrupole MS system (Agilent, USA), using dynamic MRM mode. Our measurement procedure detects 24,25 dihydroxyvitamin D3 levels starting from 0.25 ng/mL (LOD, Limit of Detection) and allows reliable quantification starting from 0.5 ng/mL (LOQ, Limit of Quantification). The intra-assay precision of our method ranges from 3–12%, and we achieved inter-assay precision ranging between 8–13%. The accuracy of the method was verified through three cycles of external quality control (DEQAS), with recovery values ranging between 90–101%.

### CONCLUSIONS

We have developed methods for the determination of 24,25-dihydroxyvitamin D3, which is needed to calculate the Vitamin D Metabolite Ratio (VMR). This ratio can serve as an independent indicator of the body's Vitamin D supply.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0938

## ANALYTICAL AND CLINICAL VALIDATION OF A PLASMA FGF21 ELISA KIT USING AN AUTOMATED PLATFORM IN STEATOTIC LIVER DISEASE

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**BACKGROUND-AIM**

Metabolic dysfunction-associated steatotic liver disease (MASLD) is a global health challenge that requires reliable and non-invasive diagnostic biomarkers. Fibroblast growth factor 21 (FGF21), an endocrine hormone linked to metabolic regulation, has shown potential as a biomarker of hepatic steatosis. This study aimed to validate the analytical and clinical performance of a commercial FGF21 enzyme-linked immunosorbent assay (ELISA) kit using an automated immunoassay analyzer.

**METHODS**

The FGF21 plasma level was measured using a Quantikine ELISA Human FGF-21 Immunoassay (DF2100; R&D Systems Inc., Minneapolis, USA) on an Evolis automated immunoassay analyzer (Bio-Rad, Germany). Validation included intra- and inter-assay precision, dilution linearity, spike recovery, lower limit of quantification (LLOQ), interference testing, and sample stability analysis. Clinical evaluation involved 97 patients undergoing abdominal ultrasound-based attenuation imaging (ATI) for the diagnosis of hepatic steatosis. The correlation between the FGF21 level and the ATI-derived attenuation coefficient (hepatic fat deposition) was determined.

**RESULTS**

The assay demonstrated high analytical reliability, with intra- and inter-assay coefficients of variation <15% and an LLOQ of 3.260 pg/mL. Dilution linearity, spike recovery, and interference tests confirmed the robustness of the assay, whereas stability tests highlighted the minimal impact of freeze-thaw cycles and storage conditions. Clinically, the FGF21 level correlated with body mass index ($r = 0.33$, $p < 0.001$) and the attenuation coefficient ($r = 0.44$, $p < 0.001$). The diagnostic performance indicated 84% sensitivity and 81% specificity at the defined FGF21 thresholds for detection of hepatic steatosis.

**CONCLUSIONS**

This study confirms the robust analytical and clinical performance of the FGF21 ELISA kit, reinforcing its potential as a diagnostic biomarker of hepatic steatosis. Automated immunoassay systems further enhance the precision and reliability of the assays, thereby supporting their adoption in clinical practice. Future studies should explore combinatory biomarker strategies to improve the diagnostic accuracy of hepatic steatosis.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0939

## CA15-3 IN BENIGN DISEASES

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### BACKGROUND-AIM

Tumor markers can help in the diagnosis of cancer. In this scenario, a differential diagnosis should be made with other diseases with similar symptoms and sometimes comorbidities that may affect the metabolism of tumor markers.
The aim of this study is to determine pathological conditions leading to false positives.

### METHODS

A total of 2271 consecutive patients from the rapid cancer diagnostic units of our hospital were studied over the course of two years, from January 2017 to December 2018. Of these patients, 1062 (46.8%) were female, with a mean age of 69±15 years.
CA15-3 was determined by an electrochemiluminescent method on a COBAS e801 multiparametric analyzer

### RESULTS

The patients were classified according to their pathology and final diagnosis, with 747(33%) cases of cancer and 1524(671%) cases of benign disease. Those patients with cancer had a significantly higher concentration ($p < 0.001$) of CA15-3 [mean±SD;median(IQR)] [72±404;21(19)] U/mL compared to patients with benign disease [21±12;18(11)] U/mL. The percentage of false positive for upper reference limit (URL) CA15-3>30U/mL (FP%) were calculated per benign disease group: No associated pathology (N;FP%)[mean±SD;median(IQR)] (418;8%)[18±9;17(11)], pancreatitis (30;10%) [19±8;18(14)], liver diseases (71;14%) [22±11;21(13)], cholestasis (57;21%)[22±10;20(15)], diabetes mellitus type 2 (84;16%) [19±9;18(11)], renal failure (208;12%) [19±10;19(10)], gynecological diseases (93;14%) [19±9;16(11)], digestive diseases (e.g., gastritis, diverticulitis) (64;14%)[19±10;17(15)], pneumopathies (188;18%)[21±18;20(15)], smokers (170;11%)[19±8;20(11)], pulmonary diseases and smoking (130;16%)[19±10;18(11)] and macrocytic anemia (11;100%) [67±29;64(35)].

### CONCLUSIONS

We conclude that 12% of patients exhibited values that exceeded the URL, while only 1% showed values that surpassed twice the URL. Of particular relevance is the observation that pulmonary pathology and macrocytic anemia were the most prevalent pathologies associated with false positive results, underscoring the importance of considering these pathologies in patients to ensure the accurate interpretation of this marker.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0940

## ANALYSIS OF POTENTIAL PREDICTIVE AND/OR PROGNOSTIC VALUE OF BIOMARKERS IN EXTENSIVE-STAGE SMALL CELL LUNG CANCER TREATED WITH CHEMO/IMMUNOTHERAPY

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### BACKGROUND-AIM

Small cell lung cancer (SCLC) accounts for 15% of all lung cancer cases, representing the most aggressive subtype with the poorest prognosis. Its neuroendocrine differentiation is associated with increased expression of neuropeptides and neuroendocrine tumor markers, including ProGRP (pro-gastrin-releasing peptide) and NSE (neuron-specific enolase). Evidence supports the utility of these markers in the diagnosis, prognosis, and monitoring of SCLC patients with limited-stage (LS) and extensive-stage (ES) disease treated with chemo and/or radiotherapy. However, their role in the context of immunotherapy, currently the first-line treatment for SCLC combined with chemotherapy, remains unexplored.

### METHODS

This prospective observational study analyzes the potential predictive and/or prognostic value of combined ProGRP and NSE assessments in ES-SCLC patients treated with chemo/immunotherapy since January 2024 at the University Hospital of Jerez de la Frontera. Both biomarkers were quantified using chemiluminescent microparticle immunoassay (CMIA).

### RESULTS

A total of 20 patients have been studied so far. Of these, 10 (50%) were included in the biomarker analysis, while the remaining 10 (50%) were excluded due to Performance Status ≥3. Among the included patients, 70% were male, with a median age of 65.5 years and 100% were smokers with a mean pack-year index of 51.
In 90% of patients who received at least three cycles of chemo/immunotherapy, a correlation was observed between ProGRP reduction (average 85%) and NSE normalization (100%) with radiological response (90% partial response and 10% stable disease) based on Response Evaluation Criteria in Solid Tumors versión 1.1. In this ongoing study, only 4 patients have not experienced disease progression, with a median of 4 treatment cycles. Among the remaining 6 patients, one died due to an infectious complication after the first cycle and 5 showed disease progression after a median of 6 cycles, coinciding with increased tumor marker levels: 100% ProGRP and 20% NSE.

### CONCLUSIONS

Our study highlights the potential predictive value of combined ProGRP and NSE analysis for treatment response and/or relapse risk in the chemo/immunotherapy context for ES-SCLC. Ongoing patient inclusion will further determine the prognostic value of these biomarkers.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0941

**PROADRENOMEDULLIN (MR-PROADM) IN THE ASSESSMENT MORTALITY RISK IN COMMUNITY-ACQUIRED PNEUMONIA**

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**BACKGROUND-AIM**

Biomarkers of systemic inflammation have shown their usefulness for diagnosis and the assessment of severity and mortality risk in community-acquired pneumonia (CAP). Our aim was to determine the usefulness of MR-proAD M at admission for predicting 30- and 90-day mortality in patients hospitalized due to CAP.

**METHODS**

Five hundred and fifty one patients with CAP were recruited at admission to the Emergency Department (ED). The severity of the disease was determined within the first 24h, using the CURB65 score (confusion, urea ≥20 mg/dL, respiratory rate ≥30 breaths/min, blood pressure <90 mmHg systolic or <60 mmHg diastolic, and age ≥65 years. MR-proADM levels were assessed at admission to the ED with TRACE technology (Time Resolved Amplified Cryptate Emission) using an immunoassay sandwich (Kryptor Compact Plus Analyzer, BRAHMS, Hennigsdorf Germany), (detection limit of 0.05 nmol/L). Risk categories for the MR-proADM were identified. An adjusted logistic regression models was created, the performance compared with the CURB65 scale. DeLong test was used to assess whether the differences in area under curves, considering $p<0.05$ significant.

**RESULTS**

Median MR-proADM was 0.95 nmol/L (25-75th interquartils 1.49- 11.84). MR-pro-ADM followed an upward trend, increasing with the increase of severity of CAP assessed by CURB65. Mortality at 30 and 90 days increased in parallel with the MR-proADM values. In patients with MR-proADM > 1.66 nmol/L mortality at 30 and 90 days was significantly higher ($p<0.001$); subjects with MR-proADM <0.83 nmol/L at admission had almost no mortality at 30 and 90 days. CURB65 showed similar predictive capacity (AUC 0.80, 95% confidence interval CI 0.70-0.89) to MR-proADM (AUC 0.83, 95% CI 0.75-0.93) for 30-day mortality, $p=0.05$. MR-proADM had a greater predictive capacity for 90-day mortality than CURB65 score with AUC 0 .75 (CI 95% 0.65-0.85) significantly higher than the AUC of 0.67 (95% CI 0.58-0.77) obtained by the score (<0.001). A cut-off point 1.8 nmol/ L had a sensitivity of 78.1 %, specificity of 75.2 %.

**CONCLUSIONS**

MR-proADM could represent a valid tool in the clinical practice to timely identify those patients with CAP at higher risks of mortality when admitted to the ED.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0942

## SD-V-MO, A CELLULAR POPULATION DATA INDICATING THE HETEROGENEITY OF MONOCYTE VOLUME, AS A RAPID TOOL TO IDENTIFY PATIENTS WITH POSITIVE BLOOD CULTURE IN THE EMERGENCY DEPARTMENT

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### BACKGROUND-AIM

Monocyte distribution width (MDW), approved by the FDA for sepsis diagnosis, is derived from the standard deviation of the volume of monocytes (SD-V-Mo), one of the cellular population data used by the haematology DxH 800 analysers for differential. The aim of the study was to analyse whether SD-V-Mo could be of interest to discriminate patients from the emergency department (ED) with a positive blood culture (BC+) from patients with negative BC (BC-)

### METHODS

SD-V-Mo were extracted from the DxH 800.

### RESULTS

From the January 2023 to September 2024, 281 patients had a positive BC, median SD-V-Mo was 24.9 (25th percentile: 22.6 – 75th percentile: 27.6). It was significantly increased ($p < 0.001$) in comparison to 280 BC- patients randomly chosen [SD-V-Mo = 21.5 (18.8 – 23.8)] or in comparison to 318 healthy controls [SD-V-Mo = 18.8 (17.9 – 19.9); $p < 0.001$]. In 68 cases, a contamination of BC was suspected, SD-V-Mo was 22.4 (19.7 – 24.6), similar to that of BC- patients ($p = 0.192$) and significantly lower than that of BC+ patients ($p < 0.001$). ROC curve analysis showed that a cut-off of 22.9 could discriminate BC+ from BC- patients [Area Under the Curve (AUC) = 0.776; sensitivity (Se) = 72.2; specificity (Sp) = 69.6)]. White blood cell (WBC) and neutrophil (PMN) counts were significantly ($p < 0.001$) higher in BC+ patients [12.9 (9.1 – 17.8) x109/L for WBC and 10.6 (7.3 – 16.0) x109/L for PMN] than in BC- patients [10.5 (7.9 – 13.5) x109/L for WBC and 8.1 (5.6 – 11.0) x109/L for PMN] but were not discriminant (AUC = 0.616 for WBC and 0.648 for PMN). C-reactive protein was significantly higher ($p < 0.001$) in BC+ than in BC- patients [141.6 (60.8 – 228.7) vs 42.9 (8.3 -109.7) mg/L, respectively). A cut-off of 96.6 mg/L could discriminate patients with positive from negative BC (AUC = 0.727; Se = 71.5; Sp = 64.1). AUCs between SD-V-Mo and CRP were not significantly different ($p = 0.093$), but combination of both parameters increased the specificity to 84.5 %. Interestingly, patients with gram negative bacteria (n = 170) had a higher ($p < 0.001$) SD-V-Mo [25.6 (23.2 – 28.6)] than the 111 patients with gram positive BC [24.2 (22 – 26.1].

### CONCLUSIONS

In conclusion, SD-V-Mo, obtained costless when complete blood count is performed, could constitute a help to identify quickly BC+ patients in the ED.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0943

## ADVANCING FIBROSIS SCREENING IN PRIMARY CARE: INSIGHTS FROM EVALUATING NON-INVASIVE BIOMARKERS AND ALGORITHMS

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### BACKGROUND-AIM

Chronic liver diseases with fibrosis are a significant global health concern. Fibrosis, characterized by excessive fibrous tissue accumulation replacing normal liver tissue, often arises as a response to chronic liver injury or inflammation. Progression to cirrhosis, an advanced and irreversible stage, is linked to severe liver dysfunction. Early fibrosis detection is critical for timely intervention and better outcomes. This prospective study evaluates the efficacy of non-invasive biomarkers and algorithms for fibrosis screening in primary care.

### METHODS

We included 325 patients with glycohemoglobin requests and FIB-4 values between 1.3–2.6, evaluating biomarkers such as Hyaluronic Acid (HA), procollagen type III N-terminal peptide (PIIINP), tissular inhibitor of metalloproteinase 1 (TIMP-1), and the Enhanced Liver Fibrosis (ELF) index, alongside FIB-4 and Fibrometer. Fibroscan, bioimpedanciometry, and clinical data were also collected. Fibrosis stages were categorized by Fibroscan readings: F1 (5–7 KPa), F2 (7.7–9 KPa), and F3 (9.5–11 KPa). Sensitivity and specificity analyses and area under the curve (AUC) calculations were performed for all biomarkers.

### RESULTS

As fibrosis stage increased, sensitivity and specificity improved. At 5 KPa, AUC values for ELF, FIB-4, PIIINP, TIMP-1, HA, and Fibrometer were 0.6366, 0.5655, 0.6166, 0.6623, 0.6191, and 0.6067, respectively. At 9 KPa, these values rose to 0.7986, 0.7101, 0.8075, 0.8207, 0.7127, and 0.6215. At 11 KPa, AUC values were highest: 0.8896 for ELF, 0.8337 for FIB-4, 0.8525 for PIIINP, 0.8996 for TIMP-1, 0.8164 for HA, and 0.6969 for Fibrometer, underscoring their diagnostic power for advanced fibrosis.

### CONCLUSIONS

Non-invasive markers and imaging techniques offer significant promise for primary care fibrosis screening. PIIINP, TIMP-1, HA, and ELF outperformed FIB-4 and Fibrometer, particularly at advanced fibrosis stages. Integrating these markers into routine clinical practice could improve diagnostic accuracy, enabling earlier interventions and enhanced patient management, ultimately reducing the burden of chronic liver diseases.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0944

## ATYPICAL IMMUNOGLOBULIN STRUCTURE IN A PATIENT WITH MULTIPLE MYELOMA AND CRYOGLOBULINEMIA OBSERVED BY THE EXENT® IMMUNOGLOBULIN ISOTYPE ASSAY WITH CONFIRMATION VIA FRACTIONATED DIGEST LC-MS ANALYSIS

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### BACKGROUND-AIM

A sample from a patient diagnosed with multiple myeloma, type I cryoglobulinemia and progressive proteinuria was evaluated with the EXENT® Immunoglobulin Isotype Assay (EXENT GAM). An IgG kappa M-protein was identified with two additional potential IgG kappa monoclonal components, that were not identified in the initial workup of this patient. We hypothesised that these additional peaks in IgG and total kappa specificities were related to fragments of the intact immunoglobulin light chain.

### METHODS

The sample was evaluated with EXENT GAM under reducing and non-reducing conditions to determine if the potential fragments were related to the intact immunoglobulin. The suspected fragment peaks were further analysed using a fractionated digest approach, coupled with LC-MS (Liquid Chromatography- Mass Spectrometry) technology. The EXENT eluate was injected onto a LC system and fractions were collected every 30 seconds. These fractions were then spotted onto MALDI-MS (Matrix Assisted Laser Desorption Ionisation Mass Spectrometry) plates and the purity of the fractions confirmed. The isolated component fractions were then reduced, alkylated, and digested using trypsin. Digests were run via LC-MS and screened vs databases to confirm whether the suspected fragments were light-chain related.

### RESULTS

The EXENT GAM assay showed an IgG kappa M-protein at m/z ~11655 ($[M+2H]^{2+}$) and two peaks at m/z ~10220 and ~13105 ($[M+H]^{+}$). Eluting in acidic but non-reducing conditions released only the suspected fragment peak at m/z ~10220. The intact IgG kappa light chain at m/z ~11657 and the peak at m/z ~13105 were only detected when the sample was treated with a reducing agent. Analysis by LC-MS confirms that both fragments are related to the IgG kappa monoclonal protein.

### CONCLUSIONS

Fractionated LC-MS digest analysis confirms that peaks seen at m/z ~10220 and m/z ~13105 via EXENT GAM are kappa light chain fragments. The fragment at m/z ~13105 is attached via a disulphide bond, but the suspected fragment at m/z ~10220 is not. These fragments appear to be directly related to the intact immunoglobulin species observed in the EXENT GAM, only being observed once reducing and/or eluting conditions are employed.The potential pathology of these fragments warrants further investigation.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0945

## ACCURATE AND EARLY DETECTION OF COLORECTAL CANCER USING A MULTILOCUS DNA METHYLATION MARKERS-BASED TESTING IN PERIPHERAL BLOOD MONONUCLEAR CELLS

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### BACKGROUND-AIM

An effective blood-based method for the diagnosis of colorectal cancer has not yet been developed. Molecular alterations of immune cells occur early in tumorigenesis, providing the theoretical underpinning for early cancer diagnosis based on immune cell profiling. Therefore, we aimed to develop an effective detection method based on peripheral blood mononuclear cells (PBMC) to improve the diagnosis of colorectal cancer.

### METHODS

Candidate DNA methylation markers were first identified from PBMCs using the Infinium MethylationEPIC array in the discovery phase (Shandong cohort I, n=100) and further validated via pyrosequencing and targeted bisulfite sequencing in validation phase (Shandong cohort II, n=202). Then, a single-tube multiplex methylation-specific quantitative PCR assay (multi-msqPCR) for simultaneous detection of five markers was established in a pilot study. After that, a CRC prediction model (CPM) based on DNA methylation and multi-msqPCR method was construct and its diagnostic performance were evaluated using the area under the receiver operating characteristic curve (AUROC) in our multicenter cohort (n=595).

### RESULTS

Five discriminative DNA methylation markers identified by Illumina 850K microarray were successfully validated to diagnose early-stage CRC. Multi-msqPCR showed a better discriminative performance and 10-time lower detection limit than single-molecule detection in early-stage CRC. The cross-validated AUROC for CPM for early-stage CRC was 0.91 (sensitivity=81.18%; specificity=89.39%), significantly higher than CEA (AUROC =0.62). CPM assay also yielded a high degree of discrimination for advanced adenoma (AA) cases (AUROC=0.85; sensitivity=63.04%; specificity=89.39%). Besides, detecting CPM in multiple cancer types implied a CRC-specific diagnostic value. Our follow-up data also demonstrated that CPM could detect early-stage CRC up to 2 years before current traditional diagnostic methods.

### CONCLUSIONS

CPM, in combination with epigenetic biomarkers and the multi-msqPCR method, was promising, cost-effective, and easily implementable for routine clinical diagnosis of early-stage CRC.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0946

## ABERRANT EXPANSION OF CD177+ NEUTROPHILS PROMOTES ENDOTHELIAL DYSFUNCTION IN SYSTEMIC LUPUS ERYTHEMATOSUS VIA NEUTROPHIL EXTRACELLULAR TRAPS

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### BACKGROUND-AIM

Aberrant neutrophil activation is implicated in the pathogenesis of systemic lupus erythematosus (SLE) and its related comorbidities. We found that CD177 was one of the most highly up-regulated genes at the transcriptional level in purified neutrophils from SLE patients. In this study, we aimed to explore the role of CD177+ neutrophils in the pathogenesis of SLE.

### METHODS

Expression of CD177 was analyzed by neutrophil transcriptome and flow cytometry. CD177+ neutrophils and CD177- neutrophils were isolated to determine the role of neutrophils-derived NETs in endothelium dysfunction. Wild type and CD177-/- murine model of lupus were analyzed for organ involvement, endothelium-dependent vasorelaxation, serum autoantibodies, and innate and adaptive immune responses in an imiquimod (IMQ)-induced lupus model.

### RESULTS

$CD177^{MFI\text{-}hi}$ neutrophils and $CD177^{MFI\text{-}hi}$ low-density granulocytes (LDGs) were expanded in active SLE, which were weakly but significantly associated with disease activity. CD177+neutrophils displayed enhanced production of reactive oxygen species (ROS) and NETs, which impaired the murine aortic endothelium-dependent vasorelaxation and induced endothelial cell apoptosis. Moreover, CD177-/- mice exposed to IMQ showed alleviated splenomegaly, endothelium-dependent vasorelaxation, and renal immune complex deposition.

### CONCLUSIONS

Our findings indicated that $CD177^{MFI\text{-}hi}$ may serve as a potential biomarker for monitoring disease activity in SLE. Further, CD177+ neutrophils may play a vasculopathic role in cardiovascular disease (CVD) via NETs formation, suggesting that specific targeting CD177+ neutrophil subset may have therapeutic effect in SLE by reducing the levels of NETs-prone neutrophils.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0947

## DIAGNOSTIC VALUE OF CEACAM6 AND HE4 FOR MALIGNANT PLEURAL EFFUSION

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### BACKGROUND-AIM

This study aimed to assess the reliability and accuracy of carcinoembryonic antigen-related adhesion molecules (CEACAM6) and human epididymis protein 4 (HE4) in diagnosing pleural fluid for malignant pleural effusion (MPE).

### METHODS

This study was a prospective study. Pleural levels of CEACAM6 and HE4 were determined in two independent cohorts. The test cohort included 182 patients with exudative pleural effusions (123 malignant and 59 benign) and the validation cohort comprised 117 patients with exudative pleural effusions (65 malignant and 52 benign). The receiver operating characteristic (ROC) curve was plotted to evaluate the diagnostic value of CEACAM6 and HE4 for MPE.

### RESULTS

The levels of CEACAM6 and HE4 were significantly higher in MPE compared to benign pleural effusion (BPE) in both two cohorts ($p < 0.001$). In test cohort, CEACAM6 and HE4 for distinguishing MPE from BPE showed AUC values of 0.862 (0.804-0.909) and 0.826 (0.763-0.878), sensitivities of 73.2% (64.4-80.8) and 61.8% (52.6-70.4), and specificities of 93.2% (83.5-98.1) and 96.6% (88.3-99.6), respectively. The combination of CEACAM6 and HE4 resulted in a higher area under the curve (AUC) value (0.938 (0.893-0.968)) than either marker alone. In differentiating lung cancer-related malignant pleural effusion (LC-MPE) from BPE, CEACAM6 and HE4 exhibited AUC values of 0.922 (0.869-0.958) and 0.847 (0.782-0.899), respectively. The combination of CEACAM6 and HE4 demonstrated an even higher AUC value of 0.967 (0.926-0.989). In validation cohort, the levels of PE HE4 or CEACAM6, as assessed through receiver operating characteristic (ROC) analysis, also demonstrated good performance in distinguishing between MPE and BPE, as well as between LC-MPE and BPE. In addition, incorporating CEA into the CEACAM6 and HE4 combination slightly improved the AUC value.

### CONCLUSIONS

Pleural effusion CEACAM6 and HE4 levels could significantly distinguish MPE from BPE, and the combination of CEACAM6, HE4 and CEA are valuable biomarkers for MPE diagnosis.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0949

## DIAGNOSTIC SIGNIFICANCE OF SERUM ANGIOPOIETIN-LIKE 4 PROTEIN CONCENTRATION IN COLORECTAL CANCER PATIENTS

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### BACKGROUND-AIM

Colorectal cancer (CRC) is classified as a neoplasm that poses a significant socio-economic challenge globally. The identification of novel, non-invasive biomarkers is essential for the development of effective screening methods for CRC, particularly due to the convenience associated with blood sample collection. A considerable proportion of non-hereditary cancers exhibit genetic mutations during the early stages of carcinogenesis. Tumorigenic cells derived from these evolving neoplasms possess the capability to secrete various proteins, which can be detected in serum. This study aims to evaluate the utility of serum Angiopoietin-like 4 (ANGPTL4) protein concentration as a potential biomarker for CRC, comparing its efficacy to that of routinely utilized tumor markers and C-reactive protein (CRP).

### METHODS

We investigated the serum concentrations of ANGPTL4, CEA, CA 19-9, CRP in 75 individuals (45 CRC patients and 30 healthy controls). The concentration of ANGPTL4 was determined using Luminex 200, following the manufacturer protocols. Classical tumor markers levels were measured by CMIA, while CRP by immunoturbidimetric method. Statistical analysis was conducted using Statistica 14.0. The differences between groups were evaluated by Mann–Whitney U test. The diagnostic performance of each protein was assessed through the calculation of sensitivity (SE), specificity (SP), positive and negative predictive values (PPV, NPV), accuracy (ACC), and the area under the receiver operating characteristic curve (AUC). The cut-off points for each biomarker were determined using Youden's index, with p-values $<0.05$ being considered statistically significant.

### RESULTS

Based on the results obtained from the study, it can be concluded that serum concentrations of ANGPTL4 are significantly elevated in patients with CRC compared to controls. Furthermore, ANGPTL4 exhibited the highest diagnostic utility among all parameters assessed. The ANGPTL4 AUC at the established cut-off value (187,304.00 pg/mL) was found to be 0.910, with SE=86.7%, SP=80%, PPV=74.3%, NPV=90%, and ACC=82.7%.

### CONCLUSIONS

Our findings indicate the potential utility of ANGPTL4 as a diagnostic biomarker for CRC, highlighting its relevance in both clinical applications and diagnostic settings.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0950

## THRESHOLD DETERMINATION OF TRIGLYCERIDE-GLUCOSE INDEX (TYG) AS A PREDICTIVE MARKER FOR DIABETIC NEPHROPATHY IN TYPE 2 DIABETES PATIENTS: A CROSS-SECTIONAL STUDY

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**BACKGROUND-AIM**

The triglyceride-glucose (TyG) index has been identified as a reliable marker for insulin resistance and is increasingly recognized for its association with diabetic nephropathy (DN) in patients with type 2 diabetes (T2D). However, the specific threshold values that effectively predict DN have yet to be fully established. This cross-sectional study aims to establish a threshold for the TyG index as a predictive marker for diabetic nephropathy in patients with T2D, thereby enhancing early identification and management strategies

**METHODS**

This cross-sectional study included 1013 patients with T2D referred to the Teaching Hospital of Mazandaran University of Medical Sciences, Sari, Iran from May 2022 to August 2024. Receiver operating characteristic (ROC) curve analysis was utilized to determine the optimal cut-off value for the TyG index, while logistic regression models assessed the relationship between the TyG index and DN. Sensitivity and specificity metrics were calculated to evaluate diagnostic performance.

**RESULTS**

From the 1013 diabetic patients, 432 (42.6%) were diagnosed with DN, whereas 581 (57.4%) did not have the condition. The study identified a significant association between elevated TyG index levels and the presence of DN (OR 0.792 (0.638 - 0.983), P=0.03). The cut-off value of 8.96 yielded a sensitivity of 43% and specificity of 64%, indicating moderate diagnostic accuracy. Patients with a TyG index exceeding this threshold demonstrated a higher risk of developing DN, highlighting the potential of the TyG index as an effective marker for identifying individuals at risk.

**CONCLUSIONS**

The findings substantiate that the TyG index is associated with the risk of developing DN in patients with type 2 diabetes. Despite its moderate sensitivity and specificity, utilizing a cut-off value may aid clinicians in early identification and management of patients at risk for DN, thereby potentially improving clinical outcomes in this population.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0951

**DNA METHYLATION MARKERS FOR EARLY DETECTION OF HEPATOCELLULAR CARCINOMA**

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**BACKGROUND-AIM**

Hepatocellular carcinoma (HCC) occurs in a well-defined high-risk patient population, but better screening tests are needed to improve the survival rate of patients. Therefore, we investigated the use of circulating tumour DNA (ctDNA) as a screening test.

**METHODS**

Candidate markers were selected from GSE136319 dataset in GEO database through bioinformatics analysis . We enrolled 180 patients from a medical centre including 89 HCC and 91 LC to examine methylation rates by methylation-specific polymerase chain reaction (MSP). A HCC risk prediction model was developed to combine multiple traditional biomarkers as a screening test.

**RESULTS**

Methylated GSTP1 and SFRP2 were selected as the model markers. The methylation rates of GSTP1 and SFRP2 in HCC patients were significantly higher than those in LC patients($P<0.01$).The combination of GSTP1 and SFRP2 (sensitivity 60.32%, specificity 88.89%) is superior to single-gene testing for HCC (GSTP1: sensitivity 95.24%, specificity 36.51%; SFRP2: sensitivity 60.32%, specificity 68.25%). GSTP1 and SFRP2, combined with four additional indicators—smoking history, MRI, AFP, and PIVKA-II—were integrated to construct a comprehensive prediction model, which effectively discriminates between conditions (the training set:C-index 0.962, 95% CI 0.936-0.988, AUC 0.962; the validation set: C-index 0.955, 95% CI 0.907-0.963, AUC 0.955).

**CONCLUSIONS**

Our findings strongly suggested the combination of methylated GSTP1 and SFRP2 in ctDNA enhanced the diagnostic value in HCC. The HCC risk prediction model can be used as a potential non-invasive HCC screening test.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0952

**WOMEC: A NOVEL DIAGNOSTIC TEST FOR THE DETECTION OF ENDOMETRIAL CANCER IN UTERINE FLUID**

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**BACKGROUND-AIM**

Endometrial cancer (EC) is the first most common gynecological cancer. Abnormal vaginal bleeding is the main symptom to initiate the multistep EC diagnostic process. Current diagnosis relies on the observation of tumor cells in a pipelle biopsy specimen, but this fails to diagnose up to 30% of patients, leading to further invasive tests. In this study, we used the liquid fraction of pipelle biopsies, the uterine fluid, to develop WomEC, an immunoassay-based EC diagnostic test.

**METHODS**

EC diagnostic biomarkers were discovered and verified in four independent clinical case-control retrospective cohorts including 291 patients. Targeted mass spectrometry was used for protein identification and statistical analysis permitted to develop 2 and 3-protein panels using logistic models. Out of the most accurate biomarkers, we selected 7 proteins for validation in an independent case-control retrospective cohort of 152 patients. We measured the concentration of these 7 proteins in uterine fluid samples using commercial and proprietary immunoassays.

**RESULTS**

Among 106 proteins studied by mass spectrometry in uterine fluid samples from 291 patients, 58 proteins had significant EC diagnostic potential. Among those, a 3-protein panel permitted to diagnose EC patients with a negative predictive value (NPV) 97% and Sensitivity 99%.
In a new validation phase, a total of 7 proteins were studied in uterine fluids from 152 patients (76 EC, 76 non-EC) using commercial and proprietary immunoassays. The best 3-protein combination achieved a diagnostic performance of NPV 95% and Sensitivity 97%.

**CONCLUSIONS**

This study validates the use of immunoassays to diagnose EC in uterine fluid samples by measuring 3 protein biomarkers. Based on these results, we are currently developing WomEC, a diagnostic test that could be used in routine clinical laboratories to aid in the diagnosis of EC in women presenting with abnormal vaginal bleeding.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0953

## ASSOCIATION BETWEEN URINE GENE EXPRESSION OF KRT7 AND KRT20 AND BLADDER CANCER

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**BACKGROUND-AIM**

The aim of this study was to develop a robust, fully automated diagnostic test for early, non-invasive diagnosis of bladder cancer (BC) by gene expression (GE) assay targeting genes previously identified as diagnostic markers for BC (KRT7, KRT20 and TERT).

**METHODS**

A total of 121 urine samples were collected from BC patients (n=41) and controls (n=80). Samples were preserved by adding guanidine thiocyanate and stored at -20°C until analysis. The Oncotrack kit (Nurex Srl) and the Kairos instrument were used to achieve fully automated mRNA extraction and Real time-PCR plate preparation starting from small amount of urine (200 µL). GE of KRT7, KRT20 and TERT were concluded in <3 hours.

**RESULTS**

The combination of KRT7 and KRT20 GE analysis allows to discriminate positive from negative samples with a sensitivity of 75%, a specificity of 96%, a positive predictive value of 91% and a negative predictive value of 88.5%. Receiver Operating Characteristics (ROC) curve analysis yielded an area under the curve (AUC) of 0.87 for KRT7 (95%CI: 0.78-0.95) and 0.85 for KRT720 (95%CI: 0.77-0.93), respectively. Despite extensive literature supporting its involvement in early disease onset, TERT was not significantly expressed in samples from BC patients.

**CONCLUSIONS**

Gene expression analysis of KRT7 and KRT20 effectively discriminates BC patients from negative controls. The next step will involve validating this method on larger sample sets, incorporating additional key targets involved in BC signalling pathways (e.g., IGF2 and BIRC5), which showed promising results in preliminary tests on cell lines and pools of positive samples.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0954

## STUDY OF THE COST-EFFECTIVENESS OF THE MTBI TEST, THE CANADIAN CT HEAD RULE AND THE CT SCAN IN AN ADULT POPULATION

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### BACKGROUND-AIM

New biomarkers to diagnose mild traumatic brain injury (mTBI) have emerged and multiple studies demonstrated their efficacy in ruling-out mTBI. Still, studying the cost-effectiveness of mTBI biomarkers was required before including the biomarkers in clinical practice.

### METHODS

Decision tree models of 10 000 individuals were created to assess the cost-effectiveness of the mTBI test (GFAP+UCH-L1) compared to the cost-effectiveness of sending every patient to the CT scan or using the Canadian CT Head Rule (CCTHR) to rule patients out of the CT scan. This study is based on the population of the CHU of Liège (2022) using costs of the INAMI (2024).

### RESULTS

When the mTBI test was used to rule patients out of the CT scan compared to performing a CT scan to all patients, 3 784 CT scans were spared for 234 extra hospitalisations and costs of 349 909€ per 10 000 patients. The mTBI test scenario spared 407 CT scans compared to the CCTHR scenario with extra 534 hospitalisations for an added cost of 1 010 802.392€ per 10 000 patients.
In younger adults, the mTBI test scenario spared 7 053 CT scans while saving 481 228.316€ per 10 000 patients compared to the CT scan scenario. The CCTHR scenario spend additional 3 444 CT scans and 75 hospitalisations for additional 500 253€ compared with the mTBI test scenario. In older adults, when the mTBI test was used to rule patients out the CT scan, 1896 CT scans were spared for 660 extra hospitalisations and extra costs of 1 104 079€ per 10 000 patients compared to the CT scan scenario.

### CONCLUSIONS

In the entire population, the mTBI test scenario spares CT scans while inducing extra-costs and hospitalisations whereas in younger adults the mTBI test scenario is cost-effective, saving both scans and money. Increasing the mTBI test specificity in older adults might increase the cost-effectiveness of the mTBI scenario.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0955

## ALLERGEN-SPECIFIC IGE AND IGG4 SIGNATURES IN IGG4-RELATED DISEASE REVEALED BY A LARGE-SCALE PHIP-SEQ STUDY

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### BACKGROUND-AIM

IgG4-related disease (IgG4-RD) is characterized by elevated serum IgG4 levels, multi-organ involvement, and a high frequency of allergic/atopic manifestations. However, the full breadth of allergen-specific signatures in this disease remains poorly understood. Therefore, we detected allergen-specific IgE and IgG4 levels in IgG4-RD patients to understand the proposed association between allergy/atopy and the pathogenesis of IgG4-RD.

### METHODS

In total, 826 plasma samples from 370 IgG4-RD patients and 354 age- and sex- matched healthy controls from Peking Union Medical College Hospital were used to perform Phage Immunoprecipitation Sequencing (PHIP-Seq) as an approach to pan allergen-specific IgE and IgG4 antibody testing. Of these patients, 102 additionally underwent plasma sample collection at a mean follow-up time of 3 years after the initial collection. Allergen-specific IgE and IgG4 responses were compared between cases and controls, and machine learning (XGBoost) was used to identify key allergen peptides associated with IgG4-RD.

### RESULTS

Abnormal IgE and IgG4 allergen reactivity was observed in IgG4-RD patients. Stronger IgE or IgG4 responses against certain allergens such as Apis mellifera and Arachis hypogaea were found to be more common among cases, in addition to being potentially linked with clinical organ involvement. Longitudinal samples indicated that overall IgE/IgG4 reactivity against the majority of top allergens declined over time, with some responses shifting from IgE- to IgG4-dominant.

### CONCLUSIONS

The study was the largest systematic screen of pan allergen-specific IgE and IgG4 antibody reactivity conducted to date in IgG4-RD patients, highlighting that aberrant allergic responses may influence disease pathogenesis and organ involvement.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0956

## BULK T-CELL RECEPTOR SEQUENCING CONFIRMS CLONALITY IN OBSTETRIC ANTIPHOSPHOLIPID SYNDROME AND MAY AS A POTENTIAL BIOMARKER

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### BACKGROUND-AIM

The heterogeneity of the T cell receptor (TCR) repertoire critically influences the autoimmune response in obstetric antiphospholipid syndrome (OAPS) and is intimately associated with the prophylaxis of autoimmune disorders. Investigating the TCR diversity patterns in patients with OAPS is thus of paramount clinical importance.

### METHODS

This investigation procured peripheral blood specimens from 31 individuals with OAPS, 21 patients diagnosed with Systemic Lupus Erythematosus (SLE), and 22 healthy controls (HC), proceeding with TCR repertoire sequencing. Concurrently, adverse pregnancy outcomes in the OAPS cohort were monitored and documented over an 18-month timeframe. We paid particular attention to disparities in V/J gene utilization and the prevalence of shared clonotypes amongst OAPS patients and the comparative groups.

### RESULTS

When juxtaposed with observations from healthy controls and SLE patients, immune repertoire sequencing disclosed irregular T- and B-cell profiles and a contraction of diversity within the OAPS group. Marked variances were found in the genomic rearrangements of the V gene, J gene, and V/J combinations. Utilizing a specialized TCRβ repertoire, we crafted a predictive model for OAPS classification with robust discriminative capability (AUC=0.852).

### CONCLUSIONS

Our research unveils alterations in the TCR repertoire among OAPS patients for the first time, positing potential covert autoimmune underpinnings. These findings nominate the TCR repertoire as a prospective peripheral blood biomarker for the clinical diagnosis of OAPS and may offer valuable insights for advancing the understanding of OAPS immunologic mechanisms and prognostic outcomes.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0957

## INVESTIGATING MIRNA-33A, MIRNA-133A AND MIRNA-125 AS BIOMARKERS OF DIABETES, OBESITY AND DYSLIPIDEMIA IN AN HIV INFECTED SOUTH AFRICAN POPULATION

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### BACKGROUND-AIM

MicroRNAs are gaining interest as potential biomarkers of cardio-metabolic diseases including type 2 diabetes (T2D) and obesity in the general populations. However, such investigations are lacking in people living with HIV (PLWH) who constitute about 13% of the South African population. This study therefore investigated miRNA-125, miRNA-139 and miRNA-33a as potential biomarkers of T2D and obesity in an HIV infected South African population.

### METHODS

The study included 696 male and female HIV infected South Africans aged 18 years and above. Demographic and lifestyle information was recorded, and biochemical parameters were measured. MiRNA-125, miRNA-139 and miRNA-33a were quantified by real time quantitative polymerase chain reaction. Correlations and regression analysis were conducted to depict the microRNAs associated with diseases and traits.

### RESULTS

MiRNA 133a was negatively correlated with waist–to-hip ratio (r = -0.106, p=0.013). MiRNA 33a was negatively correlated with BMI (r = -0.098, p=0.010), waist–to-hip ratio (r = -0.114, p=0.003), waist-to-height ratio (r = -0.120, p=0.002), glycated haemoglobin (r = -0.240, p=0.001), highly sensitive c-reactive peptide (r = -0.115, p=0.003) and positively correlated with waist circumference (r = 0.109, p=0.004). Similarly, logistic regression analysis showed a potential association between miRNA 33a with obesity, T2D and hypertriglyceridaemia (all p<0.05). MiRNA 133 was significantly associated with elevated low-density lipoprotein cholesterol (p = 0.014) while no significant association was observed with miRNA 125. While these three miRNAs were poor predictors of T2D (all AUC < 0.590) and obesity (all AUC < 0.550) separately, they were observed to increase the prognostic potential of T2D by Fasting Plasma Glucose (FPG) (AUC FPG = 0.874 vs AUC FPG + miRNAs = 0.949) and 2-hour glucose (2HG) (AUC 2HG = 0.864 vs AUC 2HG + miRNAs = 0.922).

### CONCLUSIONS

miRNA 133a and miRNA 33a are potential predictors of T2D, obesity and dyslipidaemia. Moreover, they increase the prognostic potential of T2D when combined with conventional diagnostic markers such as FPG and 2-hours oral glucose tolerance test in HIV infected South Africans. Further studies to confirm these findings and explore other miRNAs are warranted to identify new prognostic markers.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0958

## DIAGNOSIS OF SSEPTIC AND NON-SEPTIC SHOCK USING MIRNAS DERIVED FROM EXTRACELLULAR VESICLES

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### BACKGROUND-AIM

Early identification of septic shock is crucial but challenging, especially due to its similarity to non-septic shock. MicroRNAs (miRNAs) present in extracellular vesicles could be used as biomarkers to differentiate septic from non-septic shock, allowing a more accurate diagnosis in patients who have undergone surgery. This study aims to determine whether miRNAs derived from extracellular vesicles can differentiate septic shock from non-septic shock in post-surgical patients, which would enable specific diagnosis and, consequently, improve decision-making accuracy.

### METHODS

A prospective, multicenter study was conducted on miRNA profiles in patients with shock. Samples from two cohorts were formed from the Intensive Care Units of two hospitals in Spain: a discovery cohort with 109 patients and a validation cohort with 53 patients. Plasma samples were obtained within 24 hours of shock diagnosis and analyzed by high-throughput miRNA sequencing in order to identify differentially expressed miRNAs. Our findings were validated using qPCR in the validation cohort.

### RESULTS

Thirty microRNAs were found to be differentially expressed between septic and non-septic shock patients. Of these, miR-100-5p, miR-484, miR-10a-5p, miR-148a-3p, miR-342-3p, and miR-451a showed strong potential to predict septic shock with an area an area under the curve over 0.7. Moreover, the combination of miR-100-5p, miR-148a-3p, and miR-451a resulted in an area under the curve of 0.894 in the discovery cohort, with qPCR validation in the validation cohort yielding an area under the curve of 0.960.

### CONCLUSIONS

This study highlights extracellular vesicle-derived miRNAs as promising biomarkers to differentiate septic from non-septic shock. The three miRNA signatures identified have great potential to improve the diagnosis of septic shock, which would facilitate timely and appropriate treatment in post-surgical patients.

Disease specific biomarkers: autoimmune, bone, cardiac, cancer, diabetes, neurological, sepsis, traumatic brain injury, …

P0959

## AUTOANTIBODY PROFILING IN REVEALING PAN-DISEASE AND PHENOTYPE-SPECIFIC BIOMARKERS FOR BEHçET'S SYNDROME

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### BACKGROUND-AIM

Behçet's Syndrome (BS) lacks autoantibody (AAb) biomarkers reflecting its diverse phenotypes and disease course, impeding its diagnosis and treatment priority. Herein, we utilized high-density protein array to identify broad spectrum and phenotype specific AAbs of BS.

### METHODS

A total of 840 sera samples from 495 BS, 227 disease controls (DCs) and 118 healthy controls (HCs) were collected for two-step microarray screening, validation and ELISA verification. Machine learning (ML) was employed for optimizing and building AAb panels for pan-BS diagnosis. Differential analyses, pathway enrichment and clustering algorithm were used to elucidate the importance of phenotype-specific, severity-relevant AAbs underlying distinct pathophysiology of organ/tissue damage. Immunochemistry staining were performed to detect the autoantigens (AAgs) on patient tissues. Mendelian randomization was conducted to verify the causal relationships between the corresponding genes of AAgs and clinical manifestations of BS.

### RESULTS

Platelet degranulation, chaperone mediated autophagy and neutrophil activation were significantly enriched by 626 differentially expressed AAbs (DEAAbs) of BS/HC comparison from primary screening. ML model comprising 19 AAb candidates from focused array achieved 0.82 diagnostic value in differentiating BS from HC and DC. Anti-HBS1L antibody was verified as a reliable marker for pan-BS diagnosis, while anti-PPP1R13L was promising for severity assessment. Anti-p017 was verified as phenotype-specific antibody among gastrointestinal involved BS. CCDC140, expressed mainly in cytoplasmic matrix as well as interior mucus on colon tissues of BS, was main target of AAbs leading to gastrointestinal lesions, which is also potential for discerning gastrointestinal phenotype of BS from inflammatory bowel disease. We also delineated an underlying interim status of BS transitioning from autoinflammatory to autoimmune onset, where major gastrointestinal involvement was dominant in AAb profiling of BS.

### CONCLUSIONS

Our findings provide autoantigenomic view into BS immunopathogenesis as well as potential AAb candidates for the clinical diagnosis of broad-spectrum and phenotypic BS.