Virchows Arch (2016) 469 (Suppl 1):S1–S346
DOI 10.1007/s00428-016-1997-7

ABSTRACTS

Abstracts

XXXI International Congress of the IAP and 28th Congress of the ESP

Oral Free Paper Sessions

Monday, 26 September 2016, 08.30–12.00, Conference Room 5
OFP-01 Digestive Diseases Pathology - GI

OFP-01-001
Comparison of KRAS, NRAS and PIK3CA mutational status in Poorly Differentiated Clusters (PDC) and corresponding main tumour mass of colon cancer
V. Barresi*, L. Reggiani Bonetti, S. Bettelli, A. Maiorana
*Policlinic G. Martino, Dept. of Human Pathology, Messina, Italy

Objective: To assess and compare the mutational status of KRAS, NRAS and PIK3CA in poorly differentiated clusters (PDC) of neoplastic cells and corresponding main tumour tissue in colon cancer (CC).
Method: Twenty-five CCs with KRAS mutation and at least 10 PDC in a 20× microscopic field were considered. Tumour cells forming PDC and main tumour mass were separated by laser microdissection and KRAS, NRAS and PIK3CA mutational status was analyzed in each of the two components by using mass spectrometry.
Results: In 20 cases PDC had the same biomolecular profile as the main tumour, but in 2 cases they had WT KRAS and in 3 cases they had additional PIK3CA mutations not observed in the main tumour. Cases with PIK3CA mutations in PDC but not in the main tumour had higher frequency of nodal metastases ($P = 0{,}07$), high pTNM stage ($P = 0{,}07$) and LVI ($P = 0{,}07$), although statistical significance was not reached.
Conclusion: Intra-tumour heterogeneity in biomolecular profile of CC may depend upon different histological aspects. Since PDC reflect epithelial mesenchymal transition and they are likely to produce metastatic disease, their molecular status, if different from that of the main tumour, may be relevant for prediction of response to targeted therapies.

OFP-01-002
Characterization of MEK1 and DIAPH3 expressions in colorectal mucinous and non-mucinous carcinomas with relation to clinicopathological parameters and prognosis
A. A. Foda*, M. Ahmed, M. Sami, H. Wagih
*University of Mansoura, Dept. of Pathology, Egypt

Objective: The exact role of MEK1 and DIAPH3 in colorectal carcinogenesis is not yet well known. This study aims to investigate expression of MEK1 and DIAPH3 in colorectal mucinous adenocarcinoma (MA) and non-mucinous adenocarcinoma (NMA), and their relation to clinicopathological and survival data.
Method: Tumour tissue specimens from 75 patients with colorectal MA and 75 NMA were included in the study. All clinicopathological data of these 150 cases were revised with re-examination of all their slides. Three high density manual tissue microarrays were constructed and immunohistochemistry for MEK1 and DIAPH3 was done.
Results: Cytoplasmic MEK1 and DIAPH3 were overexpressed in 74 and 73 CRC cases (49.3 and 48.6 % respectively). NMA showed significantly higher MEK1, but not DIAPH3, expression than MA. MEK1 overexpression was significantly associated with positive lymphovascular emboli in the NMA group and with old age in MA group. DIAPH3 overexpression was not significantly associated with any of the tested variables. MEK1 overexpression was associated with better overall survival.
Conclusion: MEK1 and DIAPH3 have a significant interrelated role in colorectal carcinogenesis, especially in the non-mucinous type. Unlike DIAPH3, MEK1 overexpression is associated with better survival. Patients with non-mucinous carcinomas, and not mucinous ones, can benefit from MEK1 and DIAPH3 targeted therapies.

OFP-01-003
Combining digital image analysis with ngTMA construction: Lessons from a study analyzing CDX1 and CDX2 in colorectal cancer
S. Nolte*, I. Zlobec, A. Lugli, W. Hohenberger, R. Croner, S. Merkel, A. Hartmann, C. Geppert, T. Rau
*Institute of Pathology, FAU Erlangen-Nuremberg, Germany

Objective: Immunohistochemical biomarker evaluation on TMAs is a standard technique. Until now, few attempts have been made to retrieve the maximum information from digital pathology during construction of TMAs and their subsequent analysis. As CDX2 (and CDX1) may have potential predictive power as colorectal cancer biomarkers, we aim to assess their robustness in terms of pre-analytics, tumour heterogeneity and effects of different intensity-percentage combinations on patient selection and prognosis.
Method: Next-generation tissue microarrays (ngTMA) of 636 colorectal cancer patients with cores covering tumour center and invasive front were immunostained for CDX1 and CDX2, scanned and analysed using Tissue Studio software (Definiens) Pre-analytical variables analysed included storage and fixation times. Three different types of heterogeneity were defined and investigated; prognostic relevance was determined.
Results: A complete ngTMA-DIA workflow can optimize on-target punching and leads to less core-loss. Pre-analytically both biomarkers were stable. Over 7 million epithelial cells of finally 612 accessible patients were labelled. Tumour heterogeneity was only slightly detectable as a mosaic, but excluded for the targeted differences between center and front as well as for occurrence of haphazard hot/cold spots. CDX1 and CDX2 protein loss are independent biomarkers of worse prognosis in multivariate analysis. Two-dimensioned intensity-percentage graphs can highlight the differences in cohort stratification and patient selection.
Conclusion: Tumour heterogeneity of CDX1 and CDX2 is minimal and protein expression is stable over different fixation and storage times. Both markers are prognostically relevant. However, we recommend that CDX2 loss be evaluated as percentaged complete negativity. New standards for digital image analysis are needed.