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O-1

The epithelial-to-mesenchymal transition protein periostin is associated with higher tumour stage and grade in non-small cell lung cancer

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Background: The epithelial-to-mesenchymal transition (EMT) is vital for morphogenesis and has been implicated in cancer invasion. EMT of carcinoma cells can be defined by morphological trans-differentiation, accompanied by permanent cytosolic overexpression of mesenchymal proteins, which are normally expressed in the peritumoural stroma. We aimed for correlating the expression levels of the EMT indicator proteins periostin and vimentin with clinico-pathological parameters of non-small cell lung cancer (NSCLC). Method: 538 consecutive patients with surgically resected NSCLC were enrolled in the study and a high density tumour tissue micro-array, containing 2 cores per tumour, was constructed. Immunohistochemistry with antibodies against periostin and vimentin was performed and the protein expression levels in either stroma or cytoplasma were measured by semi-quantitative scores 0 to 3+. EMT was defined as cytoplasmic overexpression with score 2+ to 3+. Results: Of the 538 patients, 384 (71%) were men and 154 (29%) women; the median age being 64 years. Adenocarcinoma was diagnosed in 245 (46%), squamous cell carcinoma in 275 (51%) and adenosquamous carcinoma in 18 (3%) cases. EMT was observed in 30% (periostin) and 12.5% (vimentin) of all tumours, respectively. Overexpression of periostin in both stroma and cytoplasm was significantly associated with the squamous cell carcinoma subtype, a higher pT-stage, a higher histological tumour grade and an increased tumour size of >4 cm (p-values<0.05). Overexpression of stromal periostin only was associated with a higher pN-stage and a higher clinical stage (p-values<0.05). For vimentin, overexpression of cytoplasmic protein only was associated with a higher histological grade (p-value<0.05). Conclusion: To define EMT in NSCLC, the expression levels of the mesenchymal proteins periostin and vimentin have to be measured in both peritumoural stroma and carcinoma cell cytoplasm. Overexpression of periostin is closely associated with increasing TNM stage and grade.

O-2

Squamous cell carcinoma of the lung: polysomy of chromosome 7 and wild type of exon 19 and 21 were defined for the EGFR gene

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BACKGROUND: The use of tyrosine kinase inhibitors after first line chemotherapy, induced several studies to determine molecular characteristics in non-small-cell lung cancer to predict the response to those drugs.
The present study was delineated to clarify the status of *EGFR* gene by Fluorescence *in situ* Hibridization(FISH), Polimerase Chain Reaction (PCR) and Immunohistochemical protein expression in 60 cases of squamous cell carcinoma of the lung after surgical resection of tumours in stages IIb/IIIa.
METHOD: Representative sections were selected and submitted to tissue microarray construction for determination of EGFR protein expression by applying the antibody Mouse anti-EGFr, Clone 31G7 (Zimed Laboratories) and *EGFR* gene copy number was searched with LSI EGFR/CEP 7 probe (Vysis, Abbot Molecular). Also LP34, CK7, Chromogranin A and CD56 antibodies were applied to correctly define the squamous differentiation of each tumour. Genomic DNA was extracted from selected malignant cells by microdisection in 40 cases. PCR was performed to verify deletions in exon 19 and the pontual mutation in exon 21 of *EGFR* gene, assessed by capillary electrophoresis and restriction fragment length polymorphism (RFLP), respectively.
RESULTS: Immunohistochemical EGFR protein overexpression was identified in 35 cases, by the application of Hirsh scoring system. Increased gene copy number was observed in 32 cases by FISH, according to Cappuzzo method. Through capillary electrophoresis, the deletion in exon 19 of EGFR gene was detected in 3 cases; the exon 21 of *EGFR* was expressed in its wild type by RFLP, in all cases.
CONCLUSIONS: Our study concerning only cases of squamous cell carcinoma of the lung in surgical stages is the first to be done, to the best of our knowledge, after reviewing the published medical literature. In published studies performed in non-small-cell lung cancer in advanced stages, the cases of squamous cell carcinoma referred, expressed