Clinical significance of the expression of membrane receptors of the alternative nuclear factor-kappaB pathway in non-small cell lung cancer

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Background: During the last decade, the alternative pathway of Nuclear Factor-kappaB (NF-κB) has gained importance due to its implication in cancer initiation and development where it has been shown to be deregulated. It is mainly activated through the membrane receptors Lymphotixin β Receptor (LTβR), CD40, B-cell activating factor receptor (BAFFR) and Receptor Activator of NF-κB (RANK), having an important role in immune response and multiple cancer cell functions.

Methods: Immunohistochemical analysis of the expression of these 4 receptors was performed on 150 tumour and adjacent non-neoplastic formalin fixed and paraffin embedded tissue samples from patients with non-small cell lung cancer (NSCLC).

Results: CD40 and BAFFR expression was higher in neoplastic compared to adjacent non-neoplastic tissue (P = 0.006 and 0.001, respectively) while no such differences were observed for RANK and LTβR. Moreover, CD40 levels in tumour infiltrating lymphocytes (TILs) correlated with development of metastases in adrenals (P = 0.003), liver (P < 0.001) and in brain (P = 0.048), while CD40 levels in stromal cells correlated with liver metastasis (P = 0.013). Cytoplasmic BAFFR expression in cancer cells was associated with T status while BAFFR levels in stromal cells were related to 2-year survival (P = 0.034). Cytoplasmic RANK expression was associated with membrane levels in cancer cells (P < 0.001) but was independent of any clinicopathological characteristics. Finally, nuclear detection of LTβR was related to histological subtypes with squamous cell carcinoma having higher levels compared to adenocarcinomas (P = 0.026).

Conclusions: Protein levels of CD40 and BAFFR are altered in NSCLC in agreement with a deregulation of the alternative NF-κB pathway previously shown by our team. CD40, BAFFR and LTβR tissue protein levels appear to constitute biomarkers for specific clinicopathological parameters including survival, stage and histological subtype.

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