Abstracts

PO-358 CELF2 AT THE CORE OF A PROGNOSTIC ALTERNATIVE SPLICING SIGNATURE IN COLORECTAL CANCER

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Introduction Colorectal carcinoma (CRC) is a common malignancy, being the fourth cause of cancer-related deaths worldwide. Disregulation of alternative splicing (AS) is a molecular hallmark of cancer, having been associated with initiation and development of CRC. However, the global patterns of deregulation of AS and its association to prognosis in CRC remain largely unexplored.

Material and methods Clinically annotated tumour transcriptomes from The Cancer Genome Atlas (TCGA) were analysed in order to identify AS events with prognostic value in CRC. DNA methylation patterns in their vicinity were explored using TCGA methylation array data. A local CRC patient sample cohort and CRC cell lines were used in the experimental validation of the TCGA-derived AS prognostic signatures.

Results and discussions We revealed a novel gene expression-independent AS signature, with prognostic value additional to that assigned to pathological stage and age, dominated by three AS events in the mRNA complement of CELF2, a gene encoding for RNA-binding proteins and reportedly an oncogene. Those events relate to the expression of three isoforms with alternative promoter usage and potentially distinct sub-cellular localization and functions in RNA processing, namely AS regulation, mRNA edition and translation inhibition. We corroborated the prognostic value of alterations in CELF2 isoform expression using clinically annotated CRC samples from the local biobank. Further analyses in primary tumour-derived and metastasis-derived colon cancer cell lines confirmed those alterations as markers of increased tumour malignancy. Moreover, analyses of CRC TCGA DNA methylation profiles revealed significant differences in methylation in the vicinity of the three prognostic AS events in CELF2 associated with expression levels of the involved isoforms in matched patients.

Conclusion Our analyses suggest that a switch in the relative expression of CELF2 isoforms associates with prognosis in CRC. That switch dominates a gene expression-independent AS signature with prognostic value in CRC, representing a novel biomarker potentially usable in the prospective selection of patients for adjuvant therapy. We hypothesise that modifications in the dynamic balance between nuclear and cytoplasmic activities is the functional link between AS and the CELF2 prognostic value. This may be explained, at least in part, by local epigenetic alterations, given the observed changes in promoter methylation patterns in tumour samples from patients with poorer prognosis.

ESMO Open 2018;3(Suppl 2):A1–A463

Poster Presentation: Tumour Immunology

Tumour Immunology

PO-359 MACROPHAGE POLARISATION AND SQUAMOUS CELL CARCINOMA

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Introduction Macrophages comprise most of the infiltrating cells associated with solid tumours, and affect various aspects of tumour progression such as matrix remodelling, angiogenesis, dissemination and invasion. An important feature of macrophages is their functional plasticity in response to environmental signals. Macrophages and related cell types in mouse and human tumours generally have an M2 phenotype, which might promote tumour growth and suppress adaptive immunity.

Material and methods Therefore, we aimed to evaluate the presence of M1 and M2 macrophages in mouse and human squamous cell carcinoma.

Results and discussions Tumor-associated macrophages (TAMs), independently of their M1/M2 polarisation profile, were