The role of tumour microenvironment in phenotype regulation of disseminated cancer cells in breast cancer patients

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Metastatic disease constitutes the cause of vast majority of cancer deaths, thus, it is perceived the central clinical challenge of solid tumour oncology. Tumour dissemination is a complex process that involves a specific interplay between cancer cells and the surrounding microenvironment. Despite the extensive research, the exact mechanism of metastatic spread still remains elusive. Understanding of metastasis formation is of particular importance in breast cancer (BCa) – the most frequently diagnosed and the second leading cause of cancer death in women worldwide.

Our previous research provided a detailed clinical, pathological and molecular characterization of a group of early BCa patients, with the particular interest in cancer cells phenotype at following steps of metastasis formation – in the primary site, in lymph nodes and in circulation (circulating tumour cells; CTCs). We demonstrated that mesenchymal phenotype of tumour cells present in lymph node metastases (LNM) and blood (CTCs) correlated with poor clinical outcome, while it had no prognostic significance in primary tumour (PT)[1,2]. Consequently, we hypothesized that microenvironment in primary tumour and lymph node affects aggressiveness of cancer cells in a different manner.

The current project aims at exploring the role of tumour microenvironment in breast cancer cell dissemination. We are going to analyse and compare the expression of numerous immune-associated factors (nCounter® PanCancer Immune Profiling Panel) in stromal cells in matched pairs of PT and LNM, with regard to CTC status and clinical outcome. So far we have optimized a protocol of RNA isolation from Formalin-Fixed Paraffin-Embedded (FFPE) tumour specimens and its pre-amplification for multi-target gene expression analysis using NanoString technology. We have employed the precise laser capture microdissection approach to ensure the non-malignant character of the analysed material. Using a multiplex immunoassay (Immune Monitoring 65-Plex Human ProcartaPlex™ Panel) we measured levels of multiple cytokines/chemokines in sera of previously characterized patients to provide a deeper insight into the mechanisms of communication between normal and tumour cells in BCa. Stroma of analysed patients was also profiled for expression of the following markers: CD68, CD163, vimentin, α-SMA, CD34 and podoplanin.

1. Markiewicz A et al., Expression of epithelial to mesenchymal transition-related markers in lymph node metastases as a surrogate for primary tumor metastatic potential in breast cancer, J Transl Med, 2012; 10:226
2. Markiewicz A et al., Mesenchymal phenotype of CTC-enriched blood fraction and lymph node metastasis formation potential, PLoS One 2014; 9(4):e93901