The role of tumor microenvironment in phenotype regulation of disseminated cancer cells in breast cancer

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Tumor microenvironment is considered to play key role in the carcinogenesis, tumor dissemination and metastasis formation. It includes various cell types, such as fibroblasts, immune cells, endothelial cells, and mesenchymal stem cells. One of the most abundant components in tumor stroma are tumor-associated macrophages (TAMs) which play a critical role at each stage of cancer progression. Mostly, TAMs resemble the alternatively activated macrophages - M2, which promote tissue repair, angiogenesis and favor tumor progression. However, some TAMs, even within the same tumor, can be classified as classically activated M1-type macrophages that are pro-inflammatory and promote anti-tumor immune responses. Breast cancer (BC) is the most frequently diagnosed and the second leading cause of cancer related death in women worldwide. Despite advances in early detection and comprehensive treatments approximately 30% of patients with early-stage breast cancer still experience recurrence of the disease. Understanding interactions between tumor and stroma cells would allow to use breast cancer microenvironment as a prognostic factor as well as a potential therapeutic target and facilitate development of therapies allowing to control and treat the disease more effectively.

Project aims to investigate the influence of tumor microenvironment (macrophages) on phenotype and behavior of breast cancer cells assigned to different BC molecular subtypes. We will use triple-negative cell line (HCC-1806) which do not express receptors for estrogen, progesterone and HER2 protein, ER-positive (MCF-7), PR and HER2-positive (BT474), HER2 positive cell line (SKBR3) and non-cancerous cell line (HB2). As tumor microenvironment we will test polarized macrophages (M1 and M2) derived from different sources: THP1 cell line (human leukemia monocytic cell line) and human peripheral blood mononuclear cells. Conditioned media from M1 and M2 macrophages will be used to analyze migration, invasion and anchorage independent growth of BC cell lines as well as changes in phenotypes of these cells. We will also test influence of particular cytokines/chemokines secreted by macrophages on BC cell lines. Selected cytokines/chemokines correlated with poor clinical outcome, stroma content or levels of blood components in the group of previously characterized non-metastatic breast canacer patients.

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EUROPEAN UNION
EUROPEAN
SOCIAL FUND

Project co-funded by European Union under the European Social Fund