Introduction Tumor-associated macrophages (TAMs) choreograph various aspects of the tumour microenvironment. Macrophages exhibit cellular plasticity and can be polarised to M1 or M2 subtypes in the presence of different microenvironmental signals. Annexin A1 (ANXA1), an anti-inflammatory protein is highly expressed in the metastatic breast cancer. Many studies have found that the TAMs exhibit a higher pro-tumorigenic and anti-inflammatory, M2 phenotype.

Material and methods Gene Expression Omnibus (GEO) and ArrayExpress were used to assess the association between TAMs and breast cancer in the patients. Percentage of M2 macrophages was evaluated using flow cytometry in the breast tumours from the MMTV mice and the mammary fat pad of the control mice. Macrophage education by breast cancer was assessed by ex vivo differentiation of bone-marrow derived macrophages (BMDMs) in the presence or absence of breast cancer conditioned media by flow cytometry, ELISA, and mRNA expression.

Results and discussions Clinically, we found that the M2 TAMs were highly enriched in the claudin-low breast cancer subtype and was strongly associated with ANXA1 gene expression. In the MMTV mouse model, M2 TAMs were higher in the breast tumours as compared to the mammary tissues along with higher expression of ANXA1 and other M2 markers. Additionally, BMDMs were skewed to a more M2 TAM-like phenotype upon co-culture with the breast cancer cells, with enhanced migratory and invasive properties and phagocytic potential, which was reduced in the ANXA1-deficient BMDMs. In another in vivo mouse model employed in our study, we found that the pro-tumorigenic M2 macrophages were significantly reduced in the breast tumours isolated from the ANXA1-deficient mice as compared to the wild type, when 4T1 had been injected orthotopically in them.

Conclusion Collectively, our data describe a novel regulatory role of Annexin A1 in promoting macrophage polarisation to a more M2 phenotype in the breast tumour microenvironment both ex vivo and in vivo, thus presenting itself and its associated receptor as a potential drug target. Furthermore, our secretome data has also revealed some interesting results and Affymetrix microarray profiling and RNA sequencing studies are underway to explore the unique signature molecules and the signalling mechanism involved in governing this dynamic process.
rate. Recent studies indicate that the tumour microenvironment (TME) plays an important role in all stages of tumorigenesis in PaCa. Therefore, both tumour cells and their TME should be targeted for an effective treatment. Eukaryotic elongation factor 2 kinase (EF2K) is an enzyme which is overexpressed in cancer cells and plays a key role in cancer cell survival under stress conditions. There is no study that has shown the relationship between EF2K and TME. Thus, we investigated that the effects of EF2K expression on PaCa cell line (PANC1) and the TME.

**Material and methods** PANC1 cells were cocultured with mononuclear THP-1 cells and macrophages were polarised from THP-1 cells. The changes in EF2K expression, cell migration and invasion were analysed using western blot, migration and invasion assays, respectively. The effects of coculture on monocyte chemoattractant protein-1 (MCP-1) levels, which is one of the most important chemokines in TME were analysed using ELISA. The role of MCP-1 on both EF2K and migration of PANC1 cells were investigated. The role of MCP-1 on monocyte-macrophage differentiation was also investigated. To determine the relationship between EF2K and MCP-1, EF2K was stably overexpressed in PANC1 cells and MCP-1 levels were measured using western blot. Then, EF2K was silenced using siRNA and the changes in MCP-1 expression levels, the ability of colony formation, migration and invasion of PANC1 cells were investigated. Pancreatic orthotopic tumour model was used to determine the in vivo effects of EF2K inhibition. In tumour tissues, the changes in expression levels of MCP-1 was measured using western blot and the presence of tumour-infiltrated pro-tumorigenic macrophages were shown using immunohistochemical staining.

**Results and discussions** The interaction between PANC1 cells and macrophages caused an increase in EF2K and MCP-1 proteins and this interaction accelerated cell migration and invasion. In addition, it was found a bidirectional interaction between MCP-1 and EF2K. MCP-1 also caused differentiation of monocytes to pro-tumorigenic macrophages. In vitro silencing of EF2K decreased MCP-1 expression, cell invasion and migration. In vivo inhibition of EF2K also decreased MCP-1 expression, tumour volume and the number of tumour-infiltrated pro-tumorigenic macrophages.

**Conclusion** Targeting both tumour cells and macrophages through EF2K inhibition might be a promising strategy for PaCa treatment.

**PO-290**

**ONCOSTATIN M SIGNALLING MEDIATES THE CROSSTALK BETWEEN CANCER CELLS AND TUMOUR MICROENVIRONMENT AND PROMOTES BREAST CANCER PROGRESSION**

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**Introduction** Cytokines are important players in inflammation, a process highly associated with tumour initiation, tumour growth, angiogenesis and metastasis. Oncostatin M Receptor (OSMR) is a membrane receptor belonging to the interleukin 6 (IL6) receptor family and it has been shown to play a role in inflammation, angiogenesis and tumour progression. In breast cancer it has been associated with the EMT process, key component in cancer progression. While it is clear that cancer cells express the receptor OSMR it seems that the ligand Oncostatin M (OSM) is mainly secreted by the tumour stroma suggesting a possible existence of paracrine signalling between the tumour microenvironment and cancer cells. We previously showed that OSMR is frequently copy-number gained and over-expressed in squamous cell carcinoma, where it induces migration, invasion and metastasis. We now investigate the role of OSMR in breast cancer progression and its importance in mediating the communication with the tumour microenvironment.

**Material and methods** To address this issue we used a wide array of tools including in vivo models and in vitro cell cultures of breast cancer cell lines together with co-cultures of stromal cells such as cancer-associated fibroblasts and macrophages. The role of OSMR in oncogenesis and metastasis was studied by generating a mouse line that expresses the PyMT oncogene after the MMTV promoter and lacks OSMR. To address the importance of OSMR pathway in the tumour microenvironment context, we injected murine cells in the mammary gland of OSMR KO and control mice.

**Results and discussions** The receptor OSMR is expressed by breast cancer cells while the ligand OSM seems to be mainly produced by cancer associated macrophages and fibroblasts. Depletion of OSMR delays tumour onset, decreases tumour growth and generation of lung metastasis in MMTV-PyMT mice model. Orthotopic injections of murine TS1 cells in OSMR deficient mice shows a decrease in tumour growth compared to control mice, suggesting that OSMR signalling is also important in tumour stroma.

**Conclusion** Our results support that OSMR pathway has an important role in the initiation and progression of breast cancer and that it is important in preparing the tumour microenvironment to facilitate tumourigenesis. OSMR could be blocked by antibody based inhibition, strategy that has had a major impact on breast cancer which makes it a promising candidate for therapeutic targeting.

**PO-291**

**THE DISBALANCE OF THE BASIC CYTOKINES OF THE IMMUNE SYSTEM IN PATIENTS WITH OVARIAN CANCER ON THE BACKGROUND OF IMMUNOTHERAPY**

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**Introduction** The violation of the balance in the cytokine system is considered as an important mechanism for the development of cancer processes and ovarian cancer (OC). According to scientific confirmation, in the process of neogenesis occurs an imbalance between the production proneoplasticheskih (IL-6) and anti-neoplastic (IFN-γ, TNF-α) cytokines. Despite the improvement of diagnosis, OC treatment remains one of the urgent problems of oncogynecology.

**Material and methods** The aim of the study was to evaluate the relations of the main cytokines of the immune system in patients with ovarian cancer stage II-III in the combined treatment on the background of immunotherapy. A total of 174 patients with stage T2–3N0–1M0 OC were examined and treated at oncogynecology and chemotherapy departments. Depending on the application of immunotherapy methods (EIPHT with the use of the thymus immunotrophic drug (thymalin),