Conclusion B16F10 cells have a functional TGF-β pathway and are able to colonise the liver.

PO-186 IN VITRO AND CLINICAL STUDIES OF THE ROLE OF MHC CLASS II INvariant CHAIN (CD74) IN BREAST CANCER

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Introduction The major histocompatibility complex (MHC) class II invariant chain (CD74) is a protein which functions as a chaperone for MHC class II in antigen-presenting cells. Furthermore, it acts as a receptor for the cytokine macrophage migration inhibitory factor (MIF), mediating downstream signalling. Many clinical studies have determined that CD74 is overexpressed at the protein level in a subset of human breast tumours. However, there are discrepant findings regarding its correlation to clinical parameters. In some reports, CD74 has been correlated to triple-negative (TN) status and increased presence of metastases, but in separate studies it correlated with better overall survival. In vitro studies of CD74’s molecular functions in cancer cells have generally supported that it has a cancer-promoting effect through stimulating proliferation, invasion and autophagy.

Material and methods Human breast cancer cell lines MDA-MB-231 and MDA-MB-436 were transfected with siRNA targeting CD74 or a negative control. Cells were then subjected to in vitro analysis of proliferation or invasion through matrigel. Lysates of transfected cells were analysed by immunoblot for protein levels of cell survival and autophagy markers.

A tumour microarray (TMA) containing 651 human breast tumour cores was stained by immunohistochemistry (IHC) for CD74 protein expression. Staining intensity was manually scored for each sample in a blinded fashion. Statistical analysis was performed in R.

Results and discussions siRNA knockdown of CD74 in MDA-MB-231 and MDA-MB-436 resulted in reduced proliferation and invasiveness. Furthermore, survival signalling through Akt was decreased. These findings replicate previously published in vitro studies of CD74’s functions in cancer cells. Furthermore, a novel finding was that CD74 knockdown resulted in reduced levels of markers of autophagy.

The correlations between CD74 IHC staining of TMA samples and TN status, lymph node status and overall survival were examined. In contrast to previous studies we observed no correlation between expression of CD74 and TN status or cancer spread to the lymph nodes. Instead, survival analysis revealed increased overall survival for cancers with moderate or high CD74 intensity.

Conclusion Our results from cell lines support that CD74, when studied in vitro, has functions that stimulate cancer cells to proliferate and invade. However, results from clinical samples show a correlation of CD74 expression with increased survival.

PO-187 LIQUID-PHASE POLARITY FACILITATES ATTACHMENT, ADHESION AND METASTASIS OF TUMOUR CELLS

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Introduction Tumour metastasis is the major cause for mortality in cancer patients. Novel strategies to prevent metastatic dissemination are therefore needed to provide curative treatment options for patients with metastatic cancer. Therapeutic targeting of circulating tumour cells (CTCs) may offer new strategies for the prevention or reduction of metastasis.

One common aspect of metastasis is dynamic de- and repolarisation of tumour cells throughout the metastatic cascade. Whether tumour cells are polarised in circulation and during other phases of detachment and if such polarisation plays a role in metastatic seeding has not been investigated previously. In this comprehensive study, we have identified and characterised a novel type of liquid-phase (lp) polarity of single cells and demonstrated its role in metastasis.

Material and methods Lp polarity of tumour cells was investigated and characterised in cells from various tumour entities in vitro, in vivo and in liquid biopsies from cancer patients. The role of lp polarity during attachment, adhesion and metastatic seeding of tumour cells was explored in vitro, in vivo, ex vivo and in silico.

Results and discussions We have identified a novel type of single-cell polarisation termed liquid-phase (lp) polarity. We show that lp polarity is a generic feature of cell lines from different tumour entities and CTCs isolated from cancer patients. We have demonstrated that lp polarity favours attachment and adhesion of tumour cells and thereby contributes to metastatic seeding. The extent of lp polarisation correlated with the metastatic capacity of CTCs in mice and the metastatic potential of cell lines. Importantly, inhibition of lp polarity by different methods reduced metastatic seeding in in vivo models, indicating that lp polarity may constitute a targetable feature of metastasising tumour cells.

Conclusion Our research shows that lp polarity is a generic feature of tumour cells in liquid phase constituting a metastatic quality of CTCs that can be targeted to reduce metastatic spreading. Clinical evaluation and further research into molecular regulators of lp polarity may thus enable novel, broad therapeutic strategies against metastatic cancers.