

Profiling changes in the metastatic potential of breast cancer cells exposed to flow

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Abstract

Most cancer related deaths can be directly attributed to blood borne metastasis. Metastasis is the process by which tumor cells leave the initial tumor travel through the circulatory or lymphatic system to distant sites where secondary tumors are formed. One important part of metastasis is epithelial to mesenchymal transition (EMT), in which cells lose their epithelial cell morphology and gain a mesenchymal morphology. This transition causes enhanced migratory capacity, invasiveness, and resistance to cell death, creating a more metastatic cell. In this study we used a parallel plate flow chamber to create conditions that would encourage EMT in breast cancer cells. Several breast cancer cell lines were exposed to high shear stress (10 dyn/cm²) for 20 hours. RNA was collected from static and flow exposed cells. RT-qPCR was used to compare the expression of four genes known to be related to EMT or cell invasiveness. We found that TSP-1 gene expression was strongly upregulated, MMP-14 was slightly upregulated, ICAM-1 was slightly downregulated, and TGFR1 gene expression did not change. TSP-1 has been shown to increase tumor cell migration and invasiveness and MMP-14 has also been associated with increased tumor cell invasiveness. ICAM-1 is an intercellular adhesion molecule that plays different roles in cell to cell adhesion. The loss of ICAM-1 and the up regulation of TSP-1 and MMP-14 show that the cells exposed to flow lose some intercellular interaction and gain increased mobility and invasiveness, all of which is indicative of EMT. These results show for the first time that fluid forces can upregulate genes involved in cancer cell EMT. This will be used in future studies to investigate more about the metastatic potential of breast cancer cells.
