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Effects of group X secretory phospholipase A_2 overexpression on proliferative and invasive properties of breast cancer cells MDA-MB-231

Phospholipases A_2 (PLA_2) catalyse the first step in the arachidonic acid (AA) metabolism that leads to synthesis of eicosanoids (prostaglandins, leukotrienes, lipoxins), important mediators of inflammation. Elevated levels of prostaglandins and the key enzymes in the AA pathway, including secretory PLA_2 ($sPLA_2$), have been linked to the development of several cancers. The aim of our work is to elucidate the role of $sPLA_2$ in breast cancer.

By means of quantitative real-time PCR (qPCR) we determined the expression profile of the complete set of all 10 human $sPLA_2$s ($hsPLA_2$) in seven breast epithelial and cancer model cell lines. $hsPLA_2$s from groups IIA, IIF, III, V in X were found to be differentially expressed in these cell lines. In order to determine the impact of $hsPLA_2$s on the proliferative and invasive properties of breast cancer cells, we performed gain of function studies by overexpressing $hsPLA_2$ in breast cancer cells. The highly invasive breast cancer cell line MDA-MB-231, which displays undetectable levels of $hsPLA_2$-X expression, was transfected with a plasmid carrying the group X $hsPLA_2$ ($hsPLA_2$-X) cDNA. Stable transfectants were generated by clonal selection and overexpression of $hsPLA_2$-X was confirmed by qPCR.

The B1/C10 clone, which displayed the highest level of $hsPLA_2$-X overexpression, had a significantly lower proliferation rate than non-transfected cells, as determined by the MTT viability assay. However, the preliminary results obtained by the Click-It EdU proliferation assay suggest that B1/C10 cells have a higher proliferation rate than non-transfected cells. Exogenously added recombinant $hsPLA_2$-X caused a significant decrease in the proliferation rate of MDA-MB-231 cells as determined by the MTT and Click-It EdU proliferation assay. The invasive properties of transfected and non-transfected cell lines were compared using an optimized *in vitro* invasion assay using Matrigel. The B1/C10 clonal cell line overexpressing $hsPLA_2$-X had a significantly lower invasive potential than its non-transfected counterpart.

Our results show that overexpression of $hsPLA_2$-X in the highly invasive MDA-MB-231 breast cancer cells as well as exogenously added $hsPLA_2$-X have an influence on their proliferation rate. In addition, overexpression of $hsPLA_2$-X decreases the invasive potential of MDA-MB-231 cells.