ABSTRACT NO. 16

INCREASED INVASION THROUGH BASEMENT MEMBRANE BY CXCL7-TRANSFECTED BREAST CELLS

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Introduction: Although usually associated with inflammation, some members of the CXC chemokine family have additional roles in breast cancer. CXC chemokines and their receptors may modify breast cancer cells and the surrounding extracellular matrix in order to facilitate metastasis. One member, CXCL7, is heparin-binding and is a ligand to a G-protein linked receptor (CXCR1/2). The purpose of this study was to determine the effect of CXCL7 on invasion, a critical step in metastasis.

Methods: Two isogenic cell lines of increasing malignancy were used from the MCF 10 model of progressive human breast cancer. The malignant MCF10CA1a.cl1 cells were previously shown to invade significantly more frequently through Matrigel than premalignant MCF10AT cells. The CXCL7 gene expression was determined by both RT-PCR and protein expression by Western blot normalized to beta-actin, and expressed as a fold difference between the two cell lines. Premalignant MCF10AT cells were transfected with CXCL7 plasmids and cell invasion assays were performed in BioCoat Matrigel invasion chambers. An antibody to CXCL7 (specific Ab) was used to inhibit invasion. The secretion of CXCL7 in the transfectants was quantified by using the CXCL7 ELISA kit (R&D).

Results: CXCL7 mRNA and protein expression was significantly higher in malignant MCF10CA1a.cl1 cells than in premalignant MCF10AT cells. The secretion of CXCL7 by MCF10AT transfected with CXCL7 was significantly higher than MCF10AT and MCF10CA1a.cl1 cells. At 48 hours, 33.8% of CXCL7-transfected MCF10AT cells invaded through Matrigel, compared to 5.9% of premalignant MCF10AT cells. Antibody to CXCL7 inhibited invasion of CXCL7-transfected MCF10AT cells.

Conclusions: The malignant MCF10CA1a.cl1 cells express more CXCL7 mRNA and protein than premalignant MCF10AT cells. CXCL7-transfected MCF10AT cells are as invasive as malignant breast cancer cells. Transfection of CXCL7 confers substantially increased ability to invade through basement membrane to MCF10AT cells.