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“Exogenous treatment with an inflammatory cytokine, Tumor Necrosis Factor Alpha, increases invasiveness in highly and weakly metastatic breast cancer cells MDA-MB-231 and MCF-7”

Background: Breast cancer is a chronic disease characterized by uncontrolled growth of abnormal breast cells. It comprises 24.2% of total cancers and is the second leading cause of cancer mortality amongst women worldwide, constituting a complex public health problem. Recent studies reveal that inflammatory signals contribute to the initiation and developmental progression of cancer. Inflammation is a natural signaling response to an internal or external injury to protect the body. However, it is also a factor that promotes tumor progression in its microenvironment. In either case of an external or internal injury, the body produces inflammatory mediators, such as cytokines, to promote repair of damaged tissue and cellular proliferation at the site of an injury. Tumor necrosis factor alpha (TNF α) is a multifunctional pro-inflammatory cytokine that regulates immune and inflammatory responses as well as tissue remodeling. In cancer, TNF α is a prominent inflammatory mediator due to its ability to promote cancer cell invasion and metastasis, resulting in tumor promotion.

Methods: Invasiveness is an *in vitro* marker for metastasis. In this assay, we presume to see increased invasiveness in highly metastatic MDA-MB-231 cells as compared to weakly metastatic MCF-7 cells. Having established these differences in invasiveness that correlate to metastatic behavior, we will further study the effect of the inflammatory mediator TNF α . This study aims to quantitatively compare the effect of TNF α treatment on cell invasiveness between MDA-MB-231 and MCF-7 breast cancer lines.

To measure invasiveness, a gel matrix was made mixing a 1% agarose gel with supplemented medium at a 1:1 ratio. 40,000 cells were seeded in a punch made in the center of this gel. In this experiment, invasiveness of MDA-MB-231 and MCF-7 cells was evaluated under two conditions: cells were seeded in agarose gel with no additives or with 14.14ng/mL TNF α . Cells were then incubated for seven days to allow an optimal amount of time for cells to invade through the pores of the agarose. Each well was then fixed and stained, allowing measurement of cell invasion following the incubation period.

Results: In concluding this experiment, we discovered our hypothesis to be true. Highly metastatic MDA-MB-231 cells had increased invasiveness compared to MCF-7 cells. We also observed that TNF α increased the invasiveness in the breast cancer lines, particularly the weakly metastatic MCF-7 cells. MDA-MB-231 followed a similar pattern, but the data gathered did not show a significant difference, so further studies of the MDA-MB-231 cell line are needed to provide a concrete conclusion.

Conclusion: Overall, this investigation provides evidence that inflammation is positively correlated with the metastasis of breast cancer. Understanding inflammation's impact on metastasis allows us to examine in further studies how targeting pro-inflammatory cytokines and ameliorating inflammation may suppress metastatic progression in cancer.