Mesenchymal Stem Cell Stimulation of Breast Cancer Proliferation is Dependent on Both Stem Cell Source and Tumor Type

Background: Stem cell based reconstructive strategies are growing in popularity for breast cancer patients. While the injection of stem cell enriched autologous fat grafts offers a minimally invasive option for the reconstruction of lumpectomy and mastectomy defects there are significant concerns regarding the oncological safety of the procedure. Current studies report conflicting findings of both stimulatory and inhibitory effects of stem cells on breast cancer cell growth.
We hypothesise that the effect of MSCs on breast cancer cell proliferation may differ according to the origin of the stem cell and the molecular profile of the breast cancer cell. In this study we examine these important variables under controlled conditions.

Methods: Mesenchymal stem cells were isolated from human bone marrow and abdominal adipose tissue from multiple donors. Phenotype and differentiation to adipogenic, chondrogenic and osteogenic lineages were confirmed. Bone marrow and adipose derived stem cells were indirectly co-cultured with breast cancer cell lines in transwell plates. Cell lines from three different breast cancer molecular subtypes were evaluated: triple negative mesenchymal (MDA-MB231), triple negative epithelial (BT-20) and estrogen positive (MCF-7). Proliferation of breast cancer cell lines was determined after 48 hours using flow cytometry.

Results: Adipose derived stem cells showed greater stimulatory effect than bone marrow derived stem cells resulting in increased cell growth in all three cell lines, while bone marrow MSCs only stimulated growth of the estrogen positive cell line. The MCF 7 cell line was most sensitive to the stimulatory effect of stem cells showing a significant increase in proliferation when co-cultured with either bone marrow or adipose derived MSCs ($p<0.001$).

Conclusion: This study demonstrates that adipose derived stem cells have a greater stimulatory effect on breast cancer cell proliferation when compared to bone marrow derived MSCs. This indicates that findings from previous studies using bone marrow MSCs cannot necessarily be extrapolated to fat derived stem cells. In addition, estrogen positive cell lines show greater sensitivity to the stimulatory effects of adipose derived stem cells when compared to other cancer subtypes. These findings may help identify patient sub-groups at increased risk of tumor recurrence following stem cell based reconstructive therapies.

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