ADIPOSE TISSUE DERIVED MESENCHYMAL STEM CELLS: INVASION, DIFFERENTIATION AND APPLICATION IN TARGETED DELIVERY OF DRUGS TO BONE METASTASIZED PROSTATE CANCER.

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Background: Human bone marrow derived multipotent mesenchymal stem cells (hBM-MSCs) are a promising autologous source for producing biological agents locally at tumor sites. However, their therapeutic use has been limited essentially because collection of bone marrow is a painful procedure. Moreover, there is always a potential risk that the patient’s cancer cells may already be in circulation in the bone marrow. Human adipose derived MSCs (hADSCs) on the other hand are easy to procure from liposuction aspirates and are capable of differentiating along multiple lineages at least in vitro. Thus a thorough understanding of their biology can be applied towards the ultimate goal of using these cells for various forms of therapy and tissue engineering. However, use of these cells particularly as delivery vehicles requires the knowledge of factors that regulate their invasive behavior and differentiation potential towards the desired cell fate. Accordingly, present study first compared to see if invasive and differential potential of ADSCs is comparable to that of currently used BM-MSCs to establish their suitability as delivery vehicle for treating bone metastasized prostate cancer.

Methods: Our initial studies were geared to assess the importance of growth factors and tumor microenvironment specific factors in the recruitment of hADSCs to tumors using in vitro invasion of MSCs through Matrigel-coated inserts. To further evaluate their differentiation potential towards osteogenic and adipogenic lineages, differentiation of hADMSC was assessed in response to prostate cancer cell line specific conditioned media.

Results: Here we report that hADMSCs were able to traverse through the matrigel inserts (percent invasion 98% - 104% for different donors) as well as the hBM-MSCs (percent invasion 99% - 105%). In addition, serum deprivation and conditioned media (CM) from prostate cancer cell lines particularly the PC3-CM marginally augmented (2.2 fold & 1.01 – 1.07 fold respectively) their invasive behavior. Studies to assess their differentiation potential demonstrated a trend towards osteogenic differentiation in the presence of PC3 conditioned media. Detailed temporal analyses of the invasive and differentiation programs are in progress. Finally in order for us to enrich for the invasive population of ADMSCs, influence of bone marrow endothelial barrier on the invasive behavior of ADMSCs is also being evaluated.

Conclusions: Our preliminary findings are relevant for devising enrichment strategies for tumor tropic ADMSCs. Understanding how pathways mediating the differentiation between osteoblasts and adipocytes are regulated should be of relevance for the development of tumor tropic ADMSCs that can be utilized for the therapeutic control of bone metastasized prostate cancer.

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