Effects of Alginate Encapsulation on the Vertebral Bone-Adherent Mesenchymal Stromal Cell Paracrine Secretome

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Background/Objectives:
Mesenchymal stromal cells (MSCs) are spindle-shaped multipotent cells that can be found in any vascularized organ especially bone marrow, adipose tissue, and cord blood. MSCs have potent angiogenic and myogenic properties which have been proposed as a potential treatment for preventing limb amputations in patients with critical limb-threatening ischemia due to peripheral artery disease and diabetes mellitus. Allogeneic MSCs from a young healthy donor may decrease the risk of amputation by promoting angiogenesis and muscle regeneration. However, their efficacy could be limited by host immune reactions to allogeneic cells. Encapsulating MSCs in a hydrogel such as alginate may help to protect transplanted MSCs from the immune system of the host. Additionally, encapsulation could enhance the secretion of anti-inflammatory and angiogenic molecules from MSCs. Some of the cytokines and growth factors involved in fighting inflammation and promoting angiogenesis include interleukin (IL)-10, IL-33, hepatocyte growth factor (HGF), vascular endothelial growth factor (VEGF), and angiopoietin-1.

Methods:
For the encapsulation group, MSCs were centrifuged in a 2% alginate solution through a needle and into a calcium chloride bath. Both unencapsulated and encapsulated MSCs were incubated for 48 hours in various conditions including normoxia, normoxia with high glucose (diabetic mimic), hypoxia, and hypoxia with high glucose. The media was then harvested and analyzed using enzyme-linked immunosorbent assays (ELISAs) (R&D Systems, MN) for IL-10, HGF, VEGF, and angiopoietin-1.

Results:
No detectable levels of IL-10, HGF, or angiopoietin-1 were found in either unencapsulated or encapsulated cell media samples. VEGF levels were significantly elevated in hypoxic high glucose conditions compared to normoxic and normoxic high glucose conditions within the unencapsulated group.

Discussion:
These results demonstrate that hypoxic high glucose conditions emulating ischemic diabetic muscle amplify MSC VEGF secretion. The next step is to run a VEGF ELISA on the encapsulated cell media group and compare the results to the unencapsulated group.