Differentiation of Human Bone Marrow Mesenchymal Stem Cells on Decellularized Extracellular Matrix Materials

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Statement of Purpose: Mesenchymal bone marrow stromal cells may be a source of cells to pre-seed decellularized biologic mesh materials for improved cellularization and promote a more physiologic tissue after remodeling. Spontaneous differentiation of mesenchymal stromal cells on the decellularized material would be undesirable. Conversely induced differentiation of mesenchymal stem cells (MSC) on the material would suggest that these materials have promise as scaffold materials for bone, cartilage or adipocyte formation. This initial study of MSCs on biologic materials explores growth characteristics of the cells on the material and the spontaneous and induced differentiation of MSCs into bone, adipose and cartilage tissue.

Methods: Two sources of mesenchymal cells, primary human bone marrow derived MSCs and Lonza human bone marrow derived MSCs (Lonza, Walkersville, MD), were evaluated for induced differentiation in control wells. These MSCs were also evaluated for spontaneous or induced differentiation on decellularized porcine dermis, referred to as dermis ECM, basal lamina mesothelium, referred to as mesothelium ECM BL, and preperitoreal mesothelium, referred to as mesothelium ECM PP materials (DSM Biomedical, Exton, PA). Osteogenic differentiation was assessed using Alizarin red staining, adipogenic differentiation was analyzed with lipoprotein lipase staining, and chondrogenic differentiation was evaluated with Safranin-O staining.

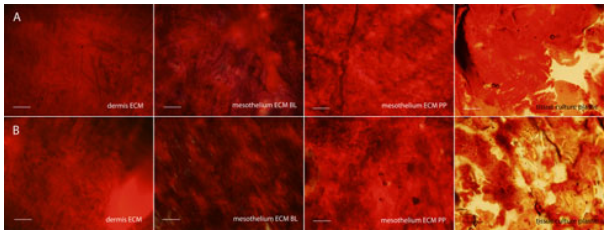

Figure 1. Osteogenic differentiation of harvested (A) and commercially obtained (B) MSCs. Scale bars = 200 μm.

Results: Primary bone marrow harvested MSCs and commercially obtained MSCs were induced into osteoblasts and adipocytes on the decellularized dermis and mesothelium materials as shown in Figs. 1 and 2 respectively. The MSCs were able to be induced into chondrocytes in pellet form but not when grown as a monolayer on the materials as seen in Fig. 3. The MSCs did not undergo spontaneous differentiation into of the three cell types when grown on the materials for up to three weeks.

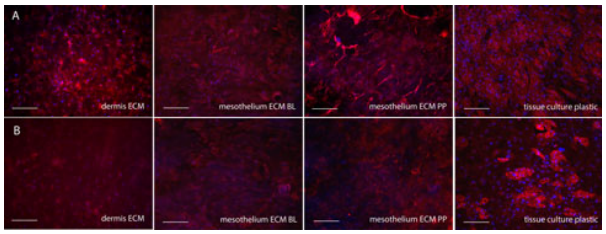

Figure 2. Adipogenic differentiation of harvested (A) and commercially obtained (B) MSCs. Scale bars = 200 μm.

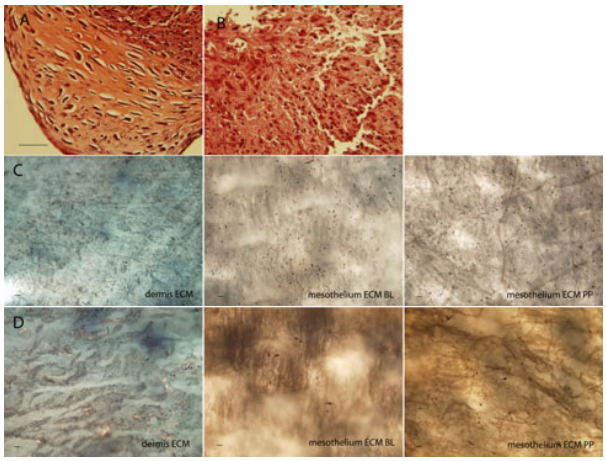

Figure 3. Chondrogenic differentiation of harvested and commercially obtained MSCs grown as pellets (A, B respectively) and lack of differentiation on materials (C, D respectively). Scale bars = 50 μm.

Conclusions: Mesenchymal stem cells grown on decellularized porcine dermis or mesothelium do not spontaneously differentiate despite the biological activity of these materials[1,2]. Induced MSCs will differentiate into osteoblasts or adipocytes on the ECM materials. Bone marrow derived MSCs may serve as a source of autologous cells for pre-seeding these extracellular matrix materials prior to implantation.

References:

[1]Hoganson DM. Biomaterials. 2010;31:6730-6737.
[2]Hoganson DM. Biomaterials. 2010;31:6934-6940.