Title: Stem cell-derived live bone mimics for superior spinal arthrodesis.
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Background: Due to the increasing awareness of significant complications related to the use of bone morphogenetic protein, there is a strong demand for new, safer, graft substitutes that do not require potentially morbid iliac crest harvest. At the same time, surgeons desire more biologically active alternatives that can achieve the excellent rates of bone healing seen with the use of recombinant proteins. One possible way to achieve similar or improved rates of healing to autograft, without the disadvantages of harvesting the iliac crest, is to create a living analog of bone tissue. Our lab has done this by seeding osteogenically enhanced human mesenchymal cells (OEhMSC’s) onto a scaffold that has been bioconditioned with extracellular matrix (ECM) produced from these same cells. By placing the cells in a three dimensional scaffold that contains enriched sources of osteogenic proteins, a biomimetic tissue (BMT) can be created to enhance spinal fusion.

Purpose/Rationale: To evaluate the bone healing potential of a combination of OEhMSC’s seeded on a scaffold conditioned with ECM for posterolateral arthrodesis in the athymic rat.

Study Design/Methods: In vitro cell culture assays were performed using plastic adherent hMSCs cultured from human bone marrow. OEhMSC/lymphocyte co-culture was performed using peripheral blood from human donors, OEhMSC/macrophage co-culture was performed using a murine macrophage cell line. Osteogenicity was enhanced by reducing the activity of the transcription factor peroxisome proliferator-activated receptor gamma. The bioconditioned scaffold (BCS) was generated by culture of OEhMSCs on gelatin foam followed by enzymatic and solvent-mediated decellularization. Posterolateral lumbar fusion L5-L6 was performed in athymic nude rats (n=10) and allowed to proceed for 8 weeks. Negative controls (decorticated only) were compared with syngeneic bone graft, BCS alone, BCS/OEhMSC constructs, and BCS seeded with whole human bone marrow.


Results: BCS/OEhMSCs did not cause cytotoxicity when incubated with immunologically mismatched lymphocytes and OEhMSCs actually inhibited lymphocyte expansion in mixed lymphocyte assays. OEhMSCs also inhibited secretion of inflammatory cytokines by macrophages activated with lipopolysaccharide. BCS/OEhMSC constructs induced profound bone growth at fusion sites in vivo with a comparable rate of fusion to syngeneic bone graft (negative (0/10), bone graft (7/10), BCS/OEhMSC (10/15)). A similar rate of fusion was also observed when BCS was administered with whole human bone marrow (8/8). BCS alone did not spontaneously induce fusion when administered without OEhMSCs or bone marrow cells (0/10).

Conclusions: Collectively, these studies demonstrate that BCS/OEhMSC constructs possess low immunogenicity and drive vertebral fusion with efficiency matching syngeneic bone graft in rodents. We also demonstrate that BCS serves as an excellent scaffold for spine fusion when combined with unfractionated human bone marrow too. Work on cryopreservation of the BMT is ongoing, which could allow for future use of this technology as an off the shelf alternative to autologous bone or BMP’s for spinal fusion.