A NOVEL METHOD FOR TREATING DEGENERATIVE MUSCULOSKELETAL CONDITIONS USING MESENCHYMAL STEM CELLS IN A BILAMINAR CELL PELLET

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BACKGROUND

Stem cell based musculoskeletal tissue-engineering presents the unique opportunity to repair or replace dysfunctional cells in degenerating tissue. In this context, one goal of tissue engineering is to propagate stem cells that can then be reintroduced into the degenerating tissue to repair or replace dysfunctional cells, restore the physical and biochemical properties of the tissue, and re-establish normal function. In particular, mesenchymal stem cells (MSC) are useful in the treatment of musculoskeletal degenerative conditions such as degenerative disc disease and osteoarthritis. MSCs are abundant, relatively easy to isolate, and can differentiate into a variety of cell types. However, the ischemic and inflammatory environment characteristic of injured tissues proves hostile for the direct introduction of MSCs, which often do not survive in this setting. While growth factors are commonly used to pre-differentiate MSCs into chondrocytes prior to their use, this can cause terminal differentiation and cell hypertrophy that leads to inferior extracellular matrix material properties. Instead, pellet culture systems are better suited for tissue engineering because they can mimic certain embryonic microenvironments that stimulate stable cell differentiation and better support the regenerative process.

TECHNOLOGY DESCRIPTION

Investigators at UCSF have developed a novel bilaminar cell pellet (BCP) system that is significantly better suited to repair inflammatory degenerative conditions of the musculoskeletal system because it overcomes two major limitations of tissue engineering: limited supply of cells needed for tissue regeneration and generation of new cells without hypertrophy. In addition, BCPs do not seem to be negatively affected by inflammatory and hypoxic conditions. The BCP is a sphere of MSCs enclosed in a shell of differentiated cells that can be manufactured simply by successive centrifugation. By varying the cellular composition of the bilayers, BCPs can be potentially induced to differentiate into many other tissue types including cartilage, bone, tendon, muscle or other musculoskeletal tissues.

In particular, the investigators have validated the use of different BCPs in two models of musculoskeletal degenerative conditions: spinal disc degeneration and articular cartilage damage. BCPs containing MSCs surrounded by nucleus pulposus cells, which contain chondrocytes-like cells, resulted in significantly more cell proliferation compared to pellets with a single cell type or those

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OTHER INFORMATION

CATEGORIZED AS

- Medical
  - Disease: Musculoskeletal Disorders
  - Stem Cell
  - Therapeutics

RELATED CASES

2008-142-0

with random organization resulting in increased chondrocyte production[1]. When placed in a bioreactor designed to simulate inflammatory and painful disc conditions, this BCP made 25% more glycoasminoglycans per cell than MSCs alone and 57% more than the nucleus pulposus cells cultured alone[2]. When tested in an *in vivo* model of inflammatory disc degeneration, BCP treatment produced better outcomes as assessed by several measures of disc well-being such as disc quality and height, qualitative histology, levels of cytokines and proteoglycan, and the retention of implanted cells[3]. Similarly, a second type of BCP consisting of MSCs surrounded by juvenile chondrocytes produced mature chondrocytes in the absence of growth factors. These BCPs, unlike MSCs in suspension, do not cause hypertrophy making them ideal for therapeutic restoration of articular cartilage damage[4].

APPLICATIONS

- Tissue engineering
- Mesenchymal stem cell propagation for reintroduction into the damaged or degenerating tissue
- Induction of differentiation of MSC progenitors into a variety of musculoskeletal cell types

ADVANTAGES

- **Significantly more proliferation** than single cell pellets
- **Enhanced differentiation of MSCs** into other cell types
- **Enhanced survival** in inflammatory conditions
- **Effective** in ameliorating inflammatory disc degeneration **in an in vivo mode**l
- **Effective** in replenishing a variety **of differentiated musculoskeletal cell types**

RELATED MATERIALS

▶ 1. Structured co-culture of mesenchymal stem cells and disc cells enhances differentiation and proliferation. Allon AA, Butcher K, Schneider RA, Lotz JC. Cells Tissues Organs. 2012; 196(2): 99-106.

▶ 2. Structured bilaminar co-culture outperforms stem cells and disc cells in a simulated degenerate disc environment. Allon AA, Butcher K, Schneider RA, Lotz JC. Spine. 2012 May 1; 37(10): 813-8.

▶ 3. Structured co-culture of stem cells and disc cells prevent disc degeneration in a rat model. Allon AA, Aurouer N, Yoo BB, Liebenberg EC, Buser Z, Lotz JC. Spine J. 2010 Dec; 10(12): 1089-97.

▶ 4. Structured three-dimensional co-culture of mesenchymal stem cells with chondrocytes promotes chondrogenic differentiation without hypertrophy. Cooke ME, Allon AA, Cheng T, Kuo AC, Kim HT, Vail TP, Marcucio RS, Schneider RA, Lotz JC, Alliston T. Osteoarthritis Cartilage. 2011 Oct; 19(10): 1210-8.

PATENT STATUS

Country	Type	Number	Dated	Case
United States Of America	Issued Patent	8,603,819	12/10/2013	2008-142

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