Preparation and Delivery of Clinically Relevant Numbers of Stem Cells Using 3D Hydrogels

Grant Award Details

Preparation and Delivery of Clinically Relevant Numbers of Stem Cells Using 3D Hydrogels

Grant Type: Tools and Technologies II

Grant Number: RT2-01938

Project Objective: The objective of the project (which is only Aim 1 of the originally submitted proposal) is to develop a hydrogel that can be used to improve the efficiency of stem cell transplantion by injection. Specifically, the project will develop a protein-based self-assembling biomaterial to achieve greater than 95% viability of transplanted stem cells by direct injection.

Investigator:

Name:	Sarah Heilshorn
Institution:	Stanford University
Type:	PI

Human Stem Cell Use: Adult Stem Cell

Cell Line Generation: Adult Stem Cell

Award Value: $600,695

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Grant Application Details

Application Title: Preparation and Delivery of Clinically Relevant Numbers of Stem Cells Using 3D Hydrogels

Public Abstract: A critical bottleneck to translate the promise of regenerative medicine to the clinic is the ability to efficiently harvest, expand, and deliver sufficient numbers of viable stem cells. While relatively large numbers of patient-specific, multipotent human adipocyte stem cells (hASC) can be harvested from adults, these cells must be re-delivered to the patient (either with or without intervening culture steps) in sufficient quantity for functional regeneration. We propose development of a clinically translatable biomaterial that is used both to improve the efficiency of stem cell expansion and to enhance the effectiveness of stem cell delivery. Current in vitro stem cell expansion protocols are time-, space-, energy-, and cost-intensive and often result in the spontaneous loss of self-renewal in addition to a heterogeneous population of differentiated cells. Furthermore, the most non-invasive method of stem cell delivery to the patient, direct cell injection, commonly results in less than 5% cell viability. Our specific aims demonstrate the flexibility of a single biomaterial to address these bottlenecks in three different clinical paradigms: 1) direct re-injection of hASC immediately following cell isolation from the patient, 2) ex vivo expansion and differentiation of hASC prior to transplantation, and 3) in vitro reprogramming of hASC into induced pluripotent stem cells (iPSC). Due to the urgency of translational outcomes and the complementary, non-overlapping experimental design, the following aims will be pursued in parallel:

Aim 1. Utilize a novel, protein-based, self-assembling biomaterial to achieve greater than 95% viability of transplanted hASC by direct injection. Injection protocols will be optimized in vitro and validated in vivo using a subcutaneous mouse model with non-invasive bioluminescence imaging. We hypothesize that cell delivery within a biomaterial will significantly improve viability by providing flow-protection during injection, localization at the target site, and scaffolding to promote cell adhesion.

Aim 2. Improve efficiency of hASC expansion and differentiation using a three-dimensional (3D) niche mimic for bone tissue regeneration. Biomaterial delivery of bone morphogenetic protein 2 (BMP2) and hydroxy apatite (HA) nanoparticles will be optimized ex vivo to enhance osteogenic differentiation and validated in vivo using a mouse cranial critical defect model. We hypothesize that customization of the biomaterial for optimal mechanics, BMP2 delivery, and HA content will enhance 3D bone tissue formation.

Aim 3. Optimize materials and methods for reprogramming of hASC into iPSC using a 3D in vitro culture environment and nonviral minicircle DNA. Recently, hASC have demonstrated enhanced iPSC reprogramming efficiency compared to other cell types. We hypothesize our 3D cultures will greatly reduce reagent, space, and cost requirements and improve efficiency of iPSC preparation compared to traditional 2D culture methods.

Statement of Benefit to California: A critical bottleneck in translating the promise of regenerative medicine to the clinic is (i) the efficient preparation and (ii) the successful delivery of sufficient numbers of stem cells. While relatively large numbers of patient-specific, human adipocyte (i.e., fat-derived) stem cells (hASC) can be harvested from adults, these cells must be re-delivered to the patient in sufficient quantity for functional regeneration. We propose development of a clinical biomaterial that can be used both to improve the efficiency of stem cell expansion and to enhance the effectiveness of stem cell delivery. Current stem cell expansion protocols are time-, space-, energy-, and cost-intensive. Furthermore, the most non-invasive method of stem cell delivery to the patient, direct cell injection, commonly results in death for more than 95% of the transplanted cells. We hypothesize that an optimized biomaterial scaffold will greatly reduce the time-, space-, energy-, and cost-requirements for stem cell culture, resulting in a great cost-savings for California. We further hypothesize that these biomaterials will improve the efficiency of stem cell transplantation, enabling the transplantation of more than 95% living, functional cells, resulting in greatly improved clinical outcomes for California patients.

Source URL: https://www.cirm.ca.gov/our-progress/awards/preparation-and-delivery-clinically-relevant-numbers-stem-cells-using-3d