

## Gene Targeting to Endogenous Stem Cells for Segmental Bone Fracture Healing

### Grant Award Details

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Gene Targeting to Endogenous Stem Cells for Segmental Bone Fracture Healing

**Grant Type:** Early Translational IV

**Grant Number:** TR4-06713

**Project Objective:** The objective of this DC award project is to achieve a development candidate consisting of ultrasound-mediated transfection of plasmid-encoded BMP to endogenous MSCs for bone repair. Segmental bone defects are caused by trauma, infection and cancer and do not heal spontaneously. The therapeutic approach is a collagen scaffold implanted at the injury site which then recruits endogenous MSCs which are targeted for BMP expression by injection of the plasmid DNA with microbubbles medium and transdermal sonoporation to transfect the cells at the injury site. They aim to get to a pre-pre-IND meeting with FDA by the end of the 3 year award period

**Investigator:**

<b>Name:</b>	Dan Gazit
<b>Institution:</b>	Cedars-Sinai Medical Center
<b>Type:</b>	PI

<b>Name:</b>	Hyun Bae
<b>Institution:</b>	Cedars-Sinai Medical Center
<b>Type:</b>	Co-PI

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**Disease Focus:** Arthritis, Bone or Cartilage Disease

**Human Stem Cell Use:** Adult Stem Cell

**Cell Line Generation:** Adult Stem Cell

**Award Value:** \$5,121,514

**Status:** Closed

### Progress Reports

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<b>Reporting Period:</b>	Year 1
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**Reporting Period:** Year 2

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**Reporting Period:** Year 4 (NCE)

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## Grant Application Details

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**Application Title:** Gene Targeting to Endogenous Stem Cells for Segmental Bone Fracture Healing

**Public Abstract:** Segmental bone fractures are a complex medical condition. These injuries cause great suffering to patients, long-term hospitalization, repeated surgeries, loss of working days, and considerable costs to the health system. It is well known that bone grafts taken from the patient (autografts) are considered the gold-standard therapy for these bone defects. Yet these grafts are not always available, and their harvest often leads to prolonged pain. Allografts, are "dead" bone grafts, which are readily available from tissue banks, but have very low potential to induce bone repair. We have previously shown that stem cells from human bone marrow, engineered with a bone-forming gene, can lead to complete repair of segmental fractures. However, such an approach requires several steps, which could complicate and prolong the pathway to clinical use. An alternative approach would be to gene-modify stem cells that already reside in the fracture site. We were the first to show, in a rodent model, that a segmental bone defect can be completely repaired by recruitment stem cells to the defect site followed by direct gene delivery. In the proposed project we aim to further promote this approach to clinical studies. The project will include the development of a direct gene delivery technology, based on ultrasound. We will test the efficiency of the method in repairing large bone defects and its safety. If successful, we will be able to proceed to FDA approval towards first-in-human trials.

**Statement of Benefit to California:** Segmental bone defects are a complex medical problem that often requires bone grafting. Autografts are considered the gold standard for these defects, but their usage is limited by availability and donor-site morbidity and supply. Allografts are more available but often fail to integrate with the host bone. Thus there is an unmet need in the field of orthopedic medicine for novel therapies for segmental bone fractures. We propose to develop a novel approach for the treatment of such fractures without the need for a bone graft. Specifically, we will utilize ultrasound to deliver a bone-forming gene to stem cells that will be recruited to the defect site. As we have already shown, the gene would trigger the cells to regenerate the bone that had been lost due to trauma or cancer. If successful, this project could lead to the development of a simple treatment for massive bone loss. Such a treatment will benefit the citizens of California by reducing loss of workdays, duration of hospital stays, and operative costs, and by improving quality of life for Californians with complex segmental bone fractures.

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