Enhancing healing via Wnt-protein mediated activation of endogenous stem cells

Grant Award Details

Enhancing healing via Wnt-protein mediated activation of endogenous stem cells

Grant Type: Early Translational I

Grant Number: TR1-01249

Project Objective: To develop therapeutics for bone regeneration particularly in the aged by using autologous bone marrow treated with human recombinant Wnt3A stabilized by a liposomal formulation

Investigator:

Name:	Jill Helms
Institution:	Stanford University
Type:	PI

Disease Focus: Bone or Cartilage Disease

Human Stem Cell Use: Adult Stem Cell

Award Value: $6,464,126

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: Year 4 (NCE)

View Report

Reporting Period: Year 5 (Bridge)

View Report

Reporting Period: Year 6/ExtrSupp

View Report

Grant Application Details

Application Title: Enhancing healing via Wnt-protein mediated activation of endogenous stem cells

Public Abstract: All adult tissues contain stem cells. Some tissues, like bone marrow and skin, harbor more adult stem cells; other tissues, like muscle, have fewer. When a tissue or organ is injured these stem cells possess a remarkable ability to divide and multiply. In the end, the ability of a tissue to repair itself seems to depend on how many stem cells reside in a particular tissue, and the state of those stem cells. For example, stress, disease, and aging all diminish the capacity of adult stem cells to self-renew and to proliferate, which in turn hinders tissue regeneration.

Our strategy is to commandeer the molecular machinery responsible for adult stem cell self-renewal and proliferation and by doing so, stimulate the endogenous program of tissue regeneration. This approach takes advantage of the solution that Nature itself developed for repairing damaged or diseased tissues, and controls adult stem cell proliferation in a localized, highly controlled fashion. This strategy circumvents the immunological, medical, and ethical hurdles that exist when exogenous stem cells are introduced into a human. When utilizing this strategy the goal of reaching clinical trials in human patients within 5 years becomes realistic.

Specifically, we will target the growing problem of neurologic, musculoskeletal, cardiovascular, and wound healing diseases by local delivery of a protein that promotes the body's inherent ability to repair and regenerate tissues. We have evidence that this class of proteins, when delivered locally to an injury site, is able to stimulate adult tissue stem cells to grow and repair/replace the deficient tissue following injury. We have developed technologies to package the protein in a specialized manner that preserves its biological activity but simultaneously restricts its diffusion to unintended regions of the body. For example, when we treat a skeletal injury with this packaged protein we augment the natural ability to heal bone by 350%; and when this protein is delivered to the heart immediately after an infarction cardiac output is improved and complications related to scarring are reduced. This remarkable capacity to augment tissue healing is not limited to bones and the heart: the same powerful effect can be elicited in the brain, and skin injuries.

The disease targets of stroke, bone fractures, heart attacks, and skin wounds and ulcers represent an enormous health care burden now, but this burden is expected to skyrocket because our population is quickly aging. Thus, our proposal addresses a present and ongoing challenge to healthcare for the majority of Californians, with a novel therapeutic strategy that mimics the body's inherent repair mechanisms.

Statement of Benefit to California:

Californians represent 1 in 7 Americans, and make up the single largest healthcare market in the United States. The diseases and injuries that affect Californians affect the rest of the US, and the world. For example, stroke is the third leading cause of death, with more than 700,000 people affected every year. It is a leading cause of serious long-term disability, with an estimated 5.4 million stroke survivors currently alive today. Symptoms of musculoskeletal disease are the number two most cited reasons for visit to a physician. Musculoskeletal disease is the leading cause of work-related and physical disability in the United States, with arthritis being the leading chronic condition reported by the elderly. In adults over the age of 70, 40% suffer from osteoarthritis of the knee and of these nearly 80% have limitation of movement. By 2030, nearly 67 million US adults will be diagnosed with arthritis. Cardiovascular disease is the leading cause of death, and is a major cause of disability worldwide. The annual socioeconomic burden posed by cardiovascular disease is estimated to exceed $400 billion annually and remains a major cause of health disparities and rising health care costs. Skin wounds from burns, trauma, or surgery, and chronic wounds associated with diabetes or pressure ulcer, exact a staggering toll on our healthcare system: Burns alone affect 1.25M Americans each year, and the economic global burden of these injuries approaches $50B/yr. In California alone, the annual healthcare expenditures for stroke, skeletal repair, heart attacks, and skin wound healing are staggering and exceed 700,000 cases, 3.5M hospital days, and $34B.

We have developed a novel, protein-based therapeutic platform to accelerate and enhance tissue regeneration through activation of adult stem cells. This technology takes advantage of a powerful stem cell factor that is essential for the development and repair of most of the body's tissues. We have generated the first stable, biologically active recombinant Wnt pathway agonist, and showed that this protein has the ability to activate adult stem cells after tissue injury. Thus, our developmental candidate leverages the body's natural response to injury. We have generated exciting preclinical results in a variety of animals models including stroke, skeletal repair, heart attack, and skin wounding. If successful, this early translational award would have enormous benefits for the citizens of California and beyond.
