Generation of inner ear sensory cells from human ES cells toward a cure for deafness

Grant Award Details

Generation of inner ear sensory cells from human ES cells toward a cure for deafness

Grant Type: Comprehensive Grant

Grant Number: RC1-00119

Investigator:

Name:	Stefan Heller
Institution:	Stanford University
Type:	PI

Disease Focus: Hearing Loss

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $2,330,371

Status: Closed

Progress Reports

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: Year 4

View Report

Grant Application Details

Application Title: Generation of inner ear sensory cells from human ES cells toward a cure for deafness

Public Abstract:

Hearing loss is the leading birth defect in the United States with ~3 children in 1,000 born with partial to profound compromise of auditory function. Debilitating hearing loss is estimated to affect ~4% of people under 45 years of age, and 34% of those 65 years or over.

A major cause of why acquired hearing loss is permanent in mammals lies in the incapacity of the sensory epithelia of the inner ear to replace damaged mechanoreceptor cells, or hair cells. Sensory hair cells are mechanoreceptors that transduce fluid movements generated by sound into electrochemical signals interpretable by the brain. Degeneration and death of hair cells is causal in >80% of individuals with hearing loss

In this grant application, we propose to explore, in comparative manner, the potential of at least five human ESC lines to develop into hair cells. We strive to use recently derived human embryonic stem cells for this purpose to avoid problems caused by potential chromosomal abnormalities and nonhuman or viral contaminants, which greatly restrict the use of these stem cells and render their derivatives unacceptable for in vivo studies. Federal funding cannot be used for research with these embryonic stem cell lines.

The most exciting long-term goal of the proposed experimentation is to provide an abundant source of human inner ear progenitor cells that can be tapped in the future to routinely create human hair cells for in vitro and in vivo experiments and for clinical studies aimed to repair damaged ears. Having access to human hair cells in vitro offers, for the first time, the opportunity for detailed cell-biological studies of this cell type. We envision that human ESC-derived inner ear progenitor cells can be used to screen for drugs that lead to increased hair cell differentiation. Equally exiting with regard to possible clinical applications are studies aimed at differentiating functional human hair cells in vitro, in organ culture, and in vivo after transplantation of the cells into the cochleae of deaf animal models and potentially into human patients. In the more distant future, we envisage that our proposed research will result in novel treatment strategies to cure deafness and potentially other inner ear diseases such as tinnitus caused by malfunctioning sensory hair cells, and vestibular disorders.

Statement of Benefit to California:

Hearing loss affects about 30 million Americans and consequently about 3 million Californians suffer from debilitating hearing problems, making this condition one of the most common chronic disorders. Degeneration and death of hair cells, and potentially their associated spiral ganglion neurons, is causal in >80% of individuals with hearing loss. The functional replacement of hair cells represents the ultimate treatment modality for deafness.

Clinically, the functionality of lost hair cells can be partially restored by electrical stimulation of the auditory nerve achieved with implantation of electronic devices; for example cochlear implants can provide a subset of suitable deaf patients with a form of treatment to improve hearing. In the long-term and for the benefit of patients not suitable for existing treatment, other avenues of therapy need to be explored, for example stimulation of hair cell regeneration after damage.

It has recently been shown that it is possible to generate hair cells from mouse embryonic stem cells and the herein proposed experiments aim to extend this research toward generating human hair cells from embryonic stem cells. Having devised a way to coax human embryonic stem cells into hair cells via an intermediate cell type, the inner ear progenitor cell will be a major advance for developing novel treatment strategies to cure deafness and possibly other inner ear disorders. Beside the immediate and obvious benefit for patients, we envision that technological advances that are applicable to millions of patients alone in California, but even more worldwide, bears an enormous commercial potential. Californians could consequently benefit possibly from the first biological treatments for hearing loss offered through local hospitals and the State of California could possibly benefit from local commercialization of novel biotechnology that has a global demand.