A hNSC Development Candidate for Huntington's Disease

Grant Award Details

A hNSC Development Candidate for Huntington's Disease

Grant Type: Preclinical Development Awards

Grant Number: PC1-08117

Project Objective: The project objective is to have a successful pre-IND meeting and be ready to initiate pivotal IND-enabling studies for hESC-derived NPC, injected to the brain for HD.

Investigator:

Name:	Leslie Thompson
Institution:	University of California, Irvine
Type:	PI

Disease Focus: Huntington's Disease, Neurological Disorders

Human Stem Cell Use: Embryonic Stem Cell

Award Value: $4,951,623

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Grant Application Details

Application Title: A hNSC Development Candidate for Huntington's Disease

Public Abstract:

Huntington's disease (HD) is a devastating degenerative brain disease with at least a 1 in 10,000 prevalence that inevitably leads to death. These numbers do not fully reflect the large societal and familial cost of HD, which requires extensive care-giving. HD has no effective treatment or cure and symptoms unstoppably progress for 15-20 years, with onset typically striking in midlife. Because HD is genetically dominant, the disease has a 50% chance of being inherited by the children of patients. Symptoms of the disease include uncontrolled movements, difficulties in carrying out daily tasks or continuing employment, and severe psychiatric manifestations including depression. Current treatments only address some symptoms and do not change the course of the disease, therefore a completely unmet medical need exists. Human embryonic stem cells (hESCs) and their derivatives offer a possible long-term treatment approach that could relieve the tremendous suffering experienced by patients and their families. HD is the 3rd most prevalent neurodegenerative disease, but because it is entirely genetic and the mutation known, a diagnosis can be made with certainty and clinical applications of hESCs may provide insights into treating brain diseases that are not caused by a single, known mutation. Trials in mice where protective factors were directly delivered to the brains of HD mice have been effective, suggesting that delivery of these factors by hESCs may help patients. Transplantation of tissue in HD patients suggests that replacing neurons that are lost may also be effective. The ability to differentiate hESCs into neural populations offers a powerful and sustainable alternative to provide neuroprotection to the brain with the possibility of cell replacement. We have assembled a multidisciplinary team of investigators and consultants with expertise in basic, translational and clinical development and have identified a lead developmental candidate, ESI-017 neural stem cells, that have disease modifying activity in HD mice with sufficient promise to perform systematic efficacy and safety studies in HD mice with cells generated for this project. We will utilize the collaborative research team, additional preclinical and clinical investigators, stem cell experts and FDA consultants to finalize work that will lead to a productive pre-IND meeting with the FDA and a path forward for clinical trials with the neural stem cell development candidate.

Statement of Benefit to California:

The disability and loss of earning power and personal freedom resulting from Huntington's disease (HD) is devastating and creates a financial burden for California. Individuals are struck in the prime of life, at a point when they are their most productive and have their highest earning potential. As the disease progresses, individuals require institutional care at great financial cost. Therapies using human embryonic stem cells (hESCs) have the potential to change the lives of hundreds of individuals and their families, which brings the human cost into the thousands. For the potential of hESCs in HD to be realized, we have brought together a team of investigators highly experienced in HD basic science and preclinical development, stem cell research, HD clinical trials and FDA regulatory activities to evaluate a human stem cell derived neural stem cell line, ESI-107 NSC in HD mouse models. This selection of this development candidate is based on efficacy in behavioral and electrophysiology measurements in a rapidly progressing mouse model of HD. HD is the 3rd most prevalent neurodegenerative disease, but because it is entirely genetic and the mutation known, a diagnosis can be made with certainty and clinical applications of NSCs may provide insights into treating brain diseases that are not caused by a single, known mutation. We have assembled a strong team of California-based investigators to carry out proposed studies to move ESI-017 NSCs to the point of a productive pre-IND meeting with the FDA to ultimately move this clinical product into Investigative New Drug-enabling (IND) activities with the goal of performing clinical trials in HD subjects. Anticipated benefits to the citizens of California include: 1) development of new human stem cell-based treatments for HD with application to other neurodegenerative diseases such as Alzheimer's and Parkinson's diseases that affect thousands of individuals in California; 2) improved methods for following the course of the disease in order to treat HD as early as possible before symptoms are manifest; 3) transfer of new technologies and intellectual property to the public realm with resulting IP revenues coming into the state with possible creation of new biotechnology spin-off companies; and 4) reductions in extensive care-giving and medical costs. It is anticipated that the return to the State in terms of revenue, health benefits for its Citizens and job creation will be substantial.

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