

Banking transplant ready dopaminergic neurons using a scalable process

Grant Award Details

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Grant Type: Early Translational II

Grant Number: TR2-01856

Project Objective: Develop a scalable GMP compatible process for production of clinical grade dopaminergic neurons from hESCs and/or hiPSCs to support the development of a therapeutic cell candidate for Parkinson's disease (PD), and generate sufficient supporting data from scalable culture to make a case to move to pre-clinical development work.

Investigator:

Name: Xianmin Zeng
Institution: Buck Institute for Age Research
Type: PI

Name: Larry Couture
Institution: City of Hope, Beckman Research Institute
Type: Co-PI

Disease Focus: Neurological Disorders, Parkinson's Disease

Collaborative Funder: Maryland

Human Stem Cell Use: Embryonic Stem Cell

Award Value: \$4,983,013

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3 + NCE

View Report

Grant Application Details

Application Title: Banking transplant ready dopaminergic neurons using a scalable process

Public Abstract: Parkinson's disease (PD) is a devastating movement disorder caused by the death of dopaminergic neurons (a type of nerve cells in the central nervous system) present in the midbrain. These neurons secrete dopamine (a signaling molecule) and are a critical component of the motor circuit that ensures movements are smooth and coordinated.

All current treatments attempt to overcome the loss of these neurons by either replacing the lost dopamine, or modulating other parts of the circuit to balance this loss or attempting to halt or delay the loss of dopaminergic neurons. Cell replacement therapy (that is, transplantation of dopaminergic neurons into the brain to replace lost cells and restore function) as proposed in this application attempts to use cells as small pumps of dopamine that will be secreted locally and in a regulated way, and will therefore avoid the complications of other modes of treatment. Indeed, cell therapy using fetal tissue-derived cells have been shown to be successful in multiple transplant studies. Work in the field has been limited however, partially due to the limited availability of cells for transplantation (e.g., 6-10 fetuses of 6-10 weeks post-conception are required for a single patient).

We believe that human embryonic stem cells (hESCs) may offer a potentially unlimited source of the right kind of cell required for cell replacement therapy. Work in our laboratories and in others has allowed us to develop a process of directing hESC differentiation into dopaminergic neurons. To move forward stem cell-based therapy development it is important to develop scale-up GMP-compatible process of generating therapeutically relevant cells (dopaminergic neurons in this case).

The overall goal of this proposal is to develop a hESC-based therapeutic candidate (dopaminergic neurons) by developing enabling reagents/tools/processes that will allow us to translate our efforts into clinical use. We have used PD as a model but throughout the application have focused on generalized enabling tools. The tools, reagents and processes we will develop in this project will allow us to move towards translational therapy and establish processes that could be applied to future IND-enabling projects. In addition, the processes we will develop would be of benefit to the CIRM community.

Statement of Benefit to California: Parkinson's disease affects more than a million patients United States with a large fraction being present in California. California, which is the home of the Parkinson's Institute and several Parkinson's related foundations and patient advocacy groups, has been at the forefront of this research and a large number of California based scientists supported by these foundations and CIRM have contributed to significant breakthroughs in this field.

In this application we and our collaborators in California aim propose to develop a hESC-based therapeutic candidate (dopaminergic neurons) that will allow us to move towards translational therapy and establish processes that could be applied to future IND-enabling projects for this currently non-curable disorder. We believe that this proposal includes the basic elements that are required for the translation of basic research to clinical research. We believe these experiments not only provide a blueprint for moving Parkinson's disease towards the clinic for people suffering with the disorder but also a generalized blueprint for the development of stem cell therapy for multiple neurological disorders including motor neuron diseases and spinal cord injury. The tools and reagents that we develop will be made widely available to Californian researchers. We expect that the money expended on this research will benefit the Californian research community and the tools and reagents we develop will help accelerate the research of our colleagues in both California and worldwide.

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