Developmental Candidates for Cell-Based Therapies for Parkinson's Disease (PD)

Grant Award Details

Developmental Candidates for Cell-Based Therapies for Parkinson's Disease (PD)

Grant Type: Early Translational I

Grant Number: TR1-01267

Project Objective: Is to evaluate and identify the optimal stem cell therapy type for therapy for Parkinson's Disease(PD) using an animal model of PD

Investigator:

Name: Evan Snyder

Institution: Sanford Burnham Prebys Medical Discovery Institute

Type: PI

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Name: Clare Parish

Institution: Howard Florey Institute

Type: Partner-PI

Disease Focus: Neurological Disorders, Parkinson's Disease

Collaborative Funder: Victoria, Australia

Human Stem Cell Use: Adult Stem Cell, Embryonic Stem Cell, iPS Cell

Award Value: $5,190,752

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Reporting Period: NCE

View Report

Grant Application Details

Application Title: Developmental Candidates for Cell-Based Therapies for Parkinson's Disease (PD)

Public Abstract: Parkinson's Disease (PD) is a devastating disorder, stealing vitality from vibrant, productive adults & draining our health care dollars. It is also an excellent model for studying other neurodegenerative conditions. We have discovered that human neural stem cells (hNSCs) may exert a significant beneficial impact in the most authentic, representative, & predictive animal model of actual human PD. Interestingly, we have learned that, while some of the hNSCs differentiate into replacement dopamine (DA) neurons, much of the therapeutic benefit derived from a stem cell action we discovered a called the "Chaperone Effect" – even hNSC-derived cells that do not become DA neurons contributed to the reversal of severe Parkinsonian symptoms by protecting endangered host DA neurons & their connections, restoring equipoise to the host nigrostriatal system, and reducing pathological hallmark of PD. While the ultimate goal may someday be to replace dead DA neurons, the Chaperone Effect represents a more tractable near-term method of using cells to address this serious condition. However, many questions remain in the process of developing these cellular therapeutic candidates. A major question is what is the best (safest, most efficacious) way to generate hNSCs? Directly from the fetal brain? From human embryonic stem cells? From skin cells reprogrammed to act like stem cells? Also, would benefits be even greater if, in addition to harnessing the Chaperone Effect, the number of stem cell-derived DA neurons was also increased? And could choosing the right stem cell type &/or providing the right supportive molecules help achieve this? This study seeks to answer these questions. Importantly, we will do so using the most representative model of human PD, a model that not only mimics all of the human symptomatology but also all the side-effects of treatment; inattention to this latter aspect plagued earlier clinical trials in PD. A successful therapy for PD would not only be of great benefit for the many patients who now suffer from the disease, or who are likely to develop it as they age, but the results will help with other potential disease applications due to greater understanding of stem cell biology (particularly the Chaperone Effect, which represents "low hanging fruit") as well as their potential complications and side effects.

Statement of Benefit to California:	Not only is Parkinson's Disease (PD) a devastating disease in its own right-- impairing typically vibrant productive adults & draining our health care dollars -- but it is also an excellent model for studying other neurodegenerative diseases. We have discovered that stem cells may actually exert a beneficial impact independent of dopamine neuron replacement. As a result of a multiyear study performed by our team, implanting human neural stem cells (hNSCs) into the most authentic, representative, and predictive animal model of actual human PD, we learned that the cells could reverse severe Parkinsonian symptoms by protecting endangered host dopaminergic (DA) neurons, restoring equipoise to the cytoarchitecture, preserving the host nigrostriatal pathway, and reducing alpha-synuclein aggregations (a pathological hallmark of PD). This action, called the "Chaperone Effect" represents a more tractible near-term method of using cells to address an unmet medical need. However, many questions remain in the process of developing these cellular therapeutic candidates. A major question is what is the best (safest & most efficacious way) to generate hNSCs? Directly from the fetal brain? From human embryonic stem cells? From human induced pluripotent cells? Also, would benefits be even greater if, in addition to harnessing the Chaperone Effect, the number of donor-derived DA neurons was also increased? And could choosing the right stem cell type &/or providing the right supportive molecules help achieve this? This study seeks to answer these questions. Importantly, we will continue to use the most representative model of human PD to do so, a model that not only mimics all of the human symptomatology but also all the side-effects of treatment; inattention to this latter aspect plagued earlier clinical trials in PD. Because of the unique team enlisted, these studies can be done at a fraction of the normal cost, allowing for parsimony in the use of research dollars, clearly a benefit to California taxpayers. Not only might California patients benefit in terms of their well-being, and the economy benefit from productive adults re-entering the work force & aging adults remaining in the work force, but it is likely that new intellectual property will emerge that will provide additional financial benefit to California stakeholders, both citizens & companies.
