Using patient-specific iPSC derived dopaminergic neurons to overcome a major bottleneck in Parkinson's disease research and drug discovery

Grant Award Details

Using patient-specific iPSC derived dopaminergic neurons to overcome a major bottleneck in Parkinson's disease research and drug discovery

Grant Type: Early Translational I

Grant Number: TR1-01246

Investigator:

Name: J. William Langston

Institution: Parkinson's Institute

Type: PI

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Name: Thomas Jovin

Institution: Max-Planck Institute, Goettingen

Type: Partner-PI

Disease Focus: Neurological Disorders, Parkinson's Disease

Collaborative Funder: Germany

Human Stem Cell Use: iPS Cell

Cell Line Generation: iPS Cell

Award Value: $3,698,646

Status: Closed

Progress Reports

Reporting Period: Year 1

View Report

Reporting Period: Year 2

View Report

Reporting Period: Year 3

View Report

Grant Application Details

Application Title: Using patient-specific iPSC derived dopaminergic neurons to overcome a major bottleneck in Parkinson's disease research and drug discovery

Public Abstract: The goals of this study are to develop patient-specific induced pluripotent cell lines (iPSCs) from patients with Parkinson's disease (PD) with defined mutations and sporadic forms of the disease. Recent groundbreaking discoveries allow us now to use adult human skin cells, transduce them with specific genes, and generate cells that exhibit characteristics of embryonic stem cells, termed induced pluripotent stem cells (iPSCs). These lines will be used as an experimental pre-clinical model to study disease mechanisms unique to PD. We predict that these cells will not only serve an 'authentic' model for PD when further differentiated into the specific dopaminergic neurons, but that these cells are pathologically affected with PD.

The specific objectives of these studies are to (1) establish a bank of iPSCs from patients with idiopathic PD and patients with defined mutations in genes associated with PD, (2) differentiate iPSCs into dopaminergic neurons and assess neurochemical and neuropathological characteristics of PD of these cells in vitro, and (3) test the hypothesis that specific pharmacologic agents can be used to block or reverse pathological phenotypes.

The absence of cellular models of Parkinson's disease represents a major bottleneck in the scientific field of PD, which, if solved in this collaborative effort, would be instantly translated into a wide range of clinical applications, including drug discovery. This research is highly translational, as the final component is aimed at testing lead compounds that could be neuroprotective, and ultimately at developing a high-throughput drug screening program to discover new disease modifying compounds. This is an essential avenue if we want to offer our patients a new therapeutic approach that can give them a near normal life after being diagnosed with this progressively disabling disease.

Statement of Benefit to California:	Approx. 36,000-60,000 people in the State of California are affected with Parkinson's disease (PD), a common neurodegenerative disease that causes a high degree of disability and financial burden for our health care system. It is estimated that the number of PD cases will double by the year 2030. We have a critical need for novel therapies that will prevent or even reverse neuronal cell loss of specific neurons in the brain of patients. This collaborative proposal will provide real benefits and values to the state of California and its citizens in providing new approaches for understanding disease mechanisms, diagnostic tools and drug discovery of novel treatment for PD. Reprogramming of adult skin cells to a pluripotent state is the underlying mechanism upon which this application is built upon and offers an attractive avenue of research in this case to develop an 'authentic' pre-clinical model of PD. The rationale for the proposed research is that differentiated pluripotent stem cells from patients with known genetic forms of PD will recapitulate in vitro one or more of the key molecular aspects of neural degeneration associated with PD and thus provide an entirely novel human cellular system for investigation PD-related disease pathways and for drug discovery. The impact of this collaborative research project, if successful, is difficult to over-estimate. The scientific field has been struggling with the inability to directly access cells that are affected by the disease process that underlies PD and therefore all research and drug discovery has relied on "best guess" models of the disease. Thus, the absence of cellular models of Parkinson's disease represents a huge bottleneck in the field.