Human iPSC-based personalized cell therapy of PD

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Principal Investigators

KIM, KWANG-SOO

Institution

MCLEAN HOSPITAL

Contact information of lead PI
Country

USA

Title of project or programme

Human iPSC-based personalized cell therapy of PD

Source of funding information

NIH (NINDS)

Total sum awarded (Euro)

€ 3,030,610.09

Start date of award

01/06/2010

Total duration of award in years

5

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

Cell Therapy, induced pluripotent stem cell, Parkinson Disease, Midbrain structure, epigenetic memory

Research Abstract

? DESCRIPTION (provided by applicant): Parkinson’s disease (PD) is a synucleinopathy whose motor syndrome is caused by progressive and selective degeneration of midbrain dopamine

(mDA) neurons. PD is the most frequent movement disorder, affecting 1-2% of the population over the age of 65. With our aging population, it is anticipated that the burden on our health care system will escalate. Currently, there are no treatments that can halt or slow down the progression of Parkinson’s disease. Because the loss of a specific cell type (i.e., A9 mDA neurons in the substantia nigra) is the main cause of motor PD, it is one of most promising target diseases for cell-based therapy. Indeed, numerous clinical and preclinical studies demonstrated the proof-of-principle that cell transplantation is a viable therapeutic regimen for PD treatment once a limitless, functional, and safe cell source can be established. Among various potential cell sources, we speculate that patient-derived induced pluripotent stem cells (iPSCs) represent the most promising cell source and may lead to personalized cell therapy without immune rejection and ethical issues such as embryo destruction. In support of this, during the last funding cycle, we have made significant progress such as the establishment of mechanism-based novel reprogramming strategies that efficiently generate high quality iPSCs, identification and purification of authentic mDA progenitors, chemical methods to eliminate remaining undifferentiated cells, and novel and efficient differentiation methods. Based on these promising data, we propose to further establish generation of clinical grade iPSCs from sporadic PD fibroblasts, including their characterization, their in vitro differentiation, and the purificaton of mDA progenitors. Furthermore, we will analyze and compare in vivo functional outcomes of mDA progenitors derived from human ESCs and iPSCs using both rodent and primate models of PD. Biological and behavioral outcomes of these transplantation studies will be systematically investigated in a long-term scale. Our proposal will address practical and major issues of patient-specific cell therapy by comparing the functional efficacies of hESC- and hiPSC-derived mDA cells both in vitro and in vivo and will provide invaluable insights and stepping-stones, eventually leading to a new generation of cell replacement therapy for PD.

Lay Summary

PUBLIC HEALTH RELEVANCE: The “”induced pluripotent stem cell (iPSC)”” technology is a promising method that can revolutionize customized cell-based therapies of intractable human diseases such as PD. To realize the potential of using iPSCs in personalized cell-based therapy for PD, we propose to establish and characterize clinically viable iPSC lines by our novel reprogramming methods, to optimize their differentiation and purification of midbrain dopamine cells, and to test their functionality in rodent and primate models. This proposal will provide important stepping-stones for realistic development of a personalized cell-based therapy of PD and will lead to a new generation of cell replacement therapy of PD.

Further information available at:

Types:
Investments > €500k

Member States:
United States of America

Diseases:
Parkinson's disease & PD-related disorders

Years:
2016

Database Categories:
N/A

Database Tags:
N/A