Transgenic marmosets for translational stem cell research

https://neurodegenerationresearch.eu/survey/transgenic-marmosets-for-translational-stem-cell-research/

Principal Investigators

GOLOS, THADDEUS G

Institution

UNIVERSITY OF WISCONSIN-MADISON

Contact information of lead PI
Country

USA

Title of project or programme

Transgenic marmosets for translational stem cell research

Source of funding information

NIH (NINDS)

Total sum awarded (Euro)

€ 2,464,431.19

Start date of award

01/05/2015

Total duration of award in years

3

The project/programme is most relevant to:

Parkinson's disease & PD-related disorders

Keywords

Callithrix, Callithrix jacchus jacchus, Stem Cell Research, LRRK2 gene, induced pluripotent stem cell

Research Abstract

DESCRIPTION (provided by applicant): Nonhuman primates (NHP) offer the most appropriate experimental model for many areas of human biomedical research, particularly in reproductive

medicine, immunology and transplantation, and neurological disease. Furthermore, monkey induced pluripotent stem cells (iPSCs) are envisioned as a valuable renewable resource of cells for preclinical testing of personalized regenerative medicine approaches. Based on initial advances in common marmoset assisted reproductive technologies (ARTs) developed at the Wisconsin National Primate Research Center (WNPRC), the production of transgenic common marmosets expressing green fluorescent protein, including the demonstration of germline transmission, has been reported. Marmoset monkeys present several advantages for transgenic approaches, including the ability to routinely carry multiple offspring (rapidly increasing cohort size), facile reproductive management, and a shorter lifespan, which facilitates the study of age-related diseases such as diabetes, arthritis and Parkinson's disease (PD). In regards to PD, identification of specific alleles of the leucine rich repeat kinase 2 (LRRK2) in familial and sporadic cases of PD supports the development of a NHP model expressing these variants, as proof-of-principle for the contribution of human alleles to disease pathophysiology. We propose to advance the development of animal disease models for stem cell-based therapeutic applications with two Specific Aims: Specific Aim 1. To optimize reprogramming of iPSCs from common marmoset fibroblasts, to use transgene expression and genomic editing to define the effect of alleles associated with PD on in vitro neural differentiation in isogenic iPSC lines, and to use genomic editing tools to define the feasibility, efficiency and accuracy of genomic editing in IVF-derived common marmoset embryos. Specific Aim 2. To produce transgenic marmoset monkeys carrying wild-type and PD-associated human LRRK2 alleles and evaluate a “”proof-of-principle”” cohort for PD pathophysiology. The long-term goal of this work is to provide investigators with marmoset iPSC lines, and genetically modified common marmosets as platforms for translational research, particularly in the treatment of diseases for which primate species are the most suitable models. Animal experiments will be performed at WNPRC, which is one of the few facilities in North America housing an experimental common marmoset colony, and the only Center where marmosets, primate embryology, and cutting edge neurological translational models are actively being used to test therapies for human disease. The proposed generation and analysis of transgenic monkeys and associated modified iPSCs will provide a platform to create disease specific models and cells, and develop tests of therapeutic approaches, including personalized medicine using engraftment of iPSCs.

Lay Summary

PUBLIC HEALTH RELEVANCE: The profound potential of pluripotent stem cells for personalized regenerative medicine therapies is tempered by a lack of understanding of the safety and efficacy of such cutting-edge procedures. Thus, there is a pressing need for the best available models to study how to realize the promise of regenerative medicine for human patients. Nonhuman primates uniquely fill that need across a wide range of diseases. This proposal will develop advanced approaches to prepare nonhuman models of devastating human diseases using Parkinson's disease as proof-of-principle, in conjunction with induced pluripotent stem cells for testing stem cell therapy approaches for the improvement of human health.

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