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## Identifying Drugs for Alzheimer's Disease with Human Neurons Made From Human IPS cells

### Grant Award Details

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Identifying Drugs for Alzheimer's Disease with Human Neurons Made From Human IPS cells

**Grant Type:** Early Translational III

**Grant Number:** TR3-05577

**Project Objective:** The team proposes to generate a feasible development candidate for Alzheimer's Disease (AD). They propose to discover novel candidates by screening purified human neurons made from human IPS cells (hIPSC) from familial AD patients.

They proposed to identify novel candidates by screening purified human neurons made from human IPS cells (hIPSC) from familial AD patients.

Scope:

1) Scale production of purified human neurons from our existing hIPSC lines from familial AD patients with APP duplications.

2) Miniaturize and optimize a HTS

assay to test for compound-induced decreases of a new and unique phenotype in human neurons, which is phospho-tau:total tau ratios in APP duplication human neurons. HTS will be done in an automated 384-well format in collaboration with a highly qualified academic screening center (the Conrad Prebys Center for Chemical Genomics-CPCCG at the Sanford- Burnham Medical Research Institute-SBMRI).

3) Screen 55,000

carefully selected compounds from a 350,000 compound library.

4) Establish structureactivity

relationships within one novel chemical series.

5) Prioritize lead compound

candidates using in vitro and in vivo pharmacological experiments.

6) Demonstrate in

vivo proof of concept by testing biochemical and pathological efficacy in a suitable human tau transgenic mouse model.

**Investigator:**

<b>Name:</b>	Lawrence Goldstein
<b>Institution:</b>	University of California, San Diego
<b>Type:</b>	PI

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**Disease Focus:** Alzheimer's Disease, Neurological Disorders

**Human Stem Cell Use:** iPS Cell

**Cell Line Generation:** iPS Cell

**Award Value:** \$1,774,420

Status: Closed

## Progress Reports

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Reporting Period: Year 1

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Reporting Period: Year 3

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## Grant Application Details

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**Application Title:** Identifying Drugs for Alzheimer's Disease with Human Neurons Made From Human IPS cells

**Public Abstract:** We propose to discover new drug candidates for Alzheimer's Disease (AD), which is common, fatal, and for which no effective disease-modifying drugs are available. Because no effective AD treatment is available or imminent, we propose to discover novel candidates by screening purified human brain cells made from human reprogrammed stem cells (human IPS cells or hiPSC) from patients that have rare and aggressive hereditary forms of AD. We have already discovered that such human brain cells exhibit an unique biochemical behavior that indicates early development of AD in a dish. Thus, we hope to find new drugs by using the new tools of human stem cells that were previously unavailable. We think that human brain cells in a dish will succeed where animal models and other types of cells have thus far failed.

**Statement of Benefit to California:** Alzheimer's Disease (AD) is a fatal neurodegenerative disease that afflicts millions of Californians. The emotional and financial impact on families and on the state healthcare budget is enormous. This project seeks to find new drugs to treat this terrible disease. If we are successful our work in the long-term may help diminish the social and familial cost of AD, and lead to establishment of new businesses in California using our approaches to drug discovery for AD.

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