Small Molecule Proteostasis Regulators to Treat Photoreceptor Diseases

Grant Award Details

Small Molecule Proteostasis Regulators to Treat Photoreceptor Diseases

Grant Type: Quest - Discovery Stage Research Projects

Grant Number: DISC2-10973

Project Objective: Discover small molecule compounds that correct disease in eyecups (retinal organoids) differentiated from patient iPSCs with photoreceptor diseases.

Investigator:

Name:	Jonathan Lin
Institution:	University of California, San Diego
Type:	PI

Disease Focus: Vision Loss

Human Stem Cell Use: iPS Cell

Award Value: $1,160,648

Status: Active

Progress Reports

Reporting Period: Year 2

View Report

Grant Application Details

Application Title: Small Molecule Proteostasis Regulators to Treat Photoreceptor Diseases

Public Abstract:

Research Objective

We will discover small molecule compounds that correct disease in eyecups (retinal organoids) differentiated from patient iPSCs with photoreceptor diseases.

Impact

Our small molecule agents will provide new treatments for achromatopsia and cone-rod dystrophy. These are rare hereditary blinding diseases with no cures

Major Proposed Activities

- Transcriptomic and proteomic profiling of control and diseased iPSC-differentiated eyecups after ATF6 agonist treatment.
- Define the potential for ATF6 agonists to improve photoreceptor protein folding and function in patient iPSC-differentiated eyecups.
- Demonstrate that ATF6 agonists increase survival of patient iPSC-differentiated eyecups under ER stress and protein misfolding conditions.
- Transcriptomic and proteomic profiling of control and diseased iPSC-differentiated eyecups after XBP1s agonist treatment.
- Define the potential for XBP1s agonists to improve photoreceptor protein folding and function in patient iPSC-differentiated eyecups
- Demonstrate that XBP1s agonists increase survival of patient iPSC-differentiated eyecups under ER stress and protein misfolding conditions.

Statement of Benefit to California:

The proposed research will benefit the citizens of California by identifying new treatments for rare orphan vision loss diseases that currently have no cure. The proposed research will benefit the State of California by improving the visual acuity and color perception of California citizens with these diseases so that they can meaningfully engage in daily activities and pursue career and educational objectives with better quality-of-life outcomes.
