

Grant Title: Development of a Novel Adult Stem Cell-based Drug Discovery Platform at Mayo Clinic

Grant Number: RMM-2016-BB-02

Requestor: Dennis Wigle, MD, PhD

Project Timeline: 6/1/2016 – 5/30/2017

Brief Description of Project: To address a gap in Mayo Clinic's regenerative medicine's translational efforts and to leverage biological assets hosted as part of the CRM Biotrust biobank, the institution has initiated efforts to develop an adult stem cell (iPSC)-based drug discovery platform. This effort by the CRM Biotrust is currently hindered by the lack of an automated drug delivery system and the end-point, biologic monitoring capabilities required for the screening of large drug libraries. To aid us in maintaining the highest quality and reproducibility and aiding in a high-throughput activity, we used the approved funds to purchase a cell imaging system to quantify outcomes of various projects.

The Cytation 5 (BioTek U.S.) is a configurable system that combines automated digital widefield microscopy with conventional multi-mode microplate reading to provide phenotypic cellular information and well-based quantitative data. This single instrument platform can process workflows that would traditionally require multiple instruments (fluorescent and chemiluminescent) and software interfaces. With 40 X magnification, the microscopy module provides high-quality cellular and sub-cellular imaging in fluorescence, brightfield, color brightfield and phase contrast. Image capture, data collection and powerful image and data analysis are managed with Gen5 software, specifically designed for uncomplicated processing of complex assays. The Cytation 5 multi-mode reader allows the CRM Biotrust, with a single piece of equipment, over time and in a single plate, to: 1) monitor the efficiency of iPSC differentiative protocols via automated cell counting capabilities (fluorescence), 2) validate differentiations by immunohistochemistry (fluorescence) and 3) monitor biological outcomes (cell death, chemiluminescence/fluorescence) all in the same well over the length of the treatment period. Importantly, these abilities of the Cytation 5 multi-mode plate reader allow for not only images to be captured, but chemiluminescence and fluorescence quantification to be collected real-time for drug screening activities.

Where did project take place? Mayo Clinic, Rochester, MN

People impacted by the project and where were they from? The majority of the patient-specific iPSC lines used in this drug screening platform were derived solely from Mayo Clinic patients with a large proportion of them being Minnesotans. The outcomes of current and proposed projects (cardiac channelopathies, Type I Diabetes, hereditary eye disease, breast cancer and heart disease) made quantifiable through the use of the shared resource purchased using this funding, will have ongoing implications locally, state and nation-wide.

What is the outcome of the project? To date, the Cytation 5 has been used to screen and validate 85 clones derived from over 35 patients for their ability of iPSC to be differentiated to insulin producing cells. Additionally, we have used the equipment to screen multiple small molecules to determine the ability of these drugs to affect the efficiency of this process. This effort is in support of a proposed, first in human trial to cure Type I Diabetes with an iPSC-based treatment for which we are currently extramurally funded.

Disclosures/Patents: A number of the iPSC validated on the equipment purchased have been licensed by the pharmaceutical industry for use in a variety of studies including cardiac channelopathies and hereditary eye diseases. Also, a novel mammary-like cell differentiation protocol has been developed implementing this device and is currently under review for patentability.

Other grant applications: Development of a Diversified Induced Pluripotent Stem Cell Library for Drug Discovery Applications, Licensing Opportunities and Business Development – Reg Med MN 2017.

Responsible spending: The entirety of the funds was used to purchase the piece of equipment with the difference being covered by the CRM Biotrust's annual budget.