Minnesota Regenerative Medicine
Year 1- Progress Report

Grant Title: Toward Autologous Retinal Cell Replacement Therapy for Age-related Macular Degeneration
Grant Number: MRM 2015 5337
Principal Investigator: Deborah Ferrington, PhD
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Project Timeline: May 1, 2015 - April 30, 2017

Overview of project:
Age-related macular degeneration (AMD) is the leading cause of blindness in the elderly. This disease causes individuals to lose their central vision, which affects activities such as reading, driving, and face recognition, and has a significant negative impact on daily function and quality of life. AMD is especially prevalent among individuals of Northern European heritage and thus of great importance in Minnesota since 32% of the population are of Scandinavian ancestry. A key feature of AMD is the loss of retinal pigment epithelial (RPE) cells. The goal of the proposed work is to develop new clinical strategies that either protect the RPE and slow disease progression, or repair the damage created by the disease. Taking a personalized medicine approach, we envision using induced Pluripotent Stem Cell (iPSC)-derived RPE developed from patient biopsies to either identify drugs that promote RPE survival or as an autologous transplant therapy for RPE cell replacement.

Summary of Progress: To date, we have successfully generated iPSC-derived RPE from conjunctival biopsies of three different human donors. The process involved transducing conjunctival cells with iPSC reprogramming factors using Sendai virus based vectors (Cytotune 2.0™ Invitrogen). The method used to generate RPE from the iPSC-lines included a defined 14-day induction of RPE (Fig. 1A), followed by expansion of iPSC-derived RPE that form pigmented monolayers (Fig. 1B). Initial progression of the differentiation from pluripotent iPSC to RPE is characterized using immunohistochemistry and qRT-PCR. Figure 3C compares qRT-PCR analysis of early RPE gene expression in two iPSC lines from a non-diseased donor (MGS1) and one iPSC line from a donor with AMD (MGS2). As the data indicate, the initial RPE induction protocol is consistent between iPSC lines derived from either the same or different donors. These results indicate that we have been successful in generating iPSC-derived RPE from donors with and without AMD. The RPE induction protocol consistently provides RPE that closely matches the phenotype and gene expression of primary RPE. Furthermore, we have developed these cells under cGMP conditions so that the transition to clinical application should be seamless.

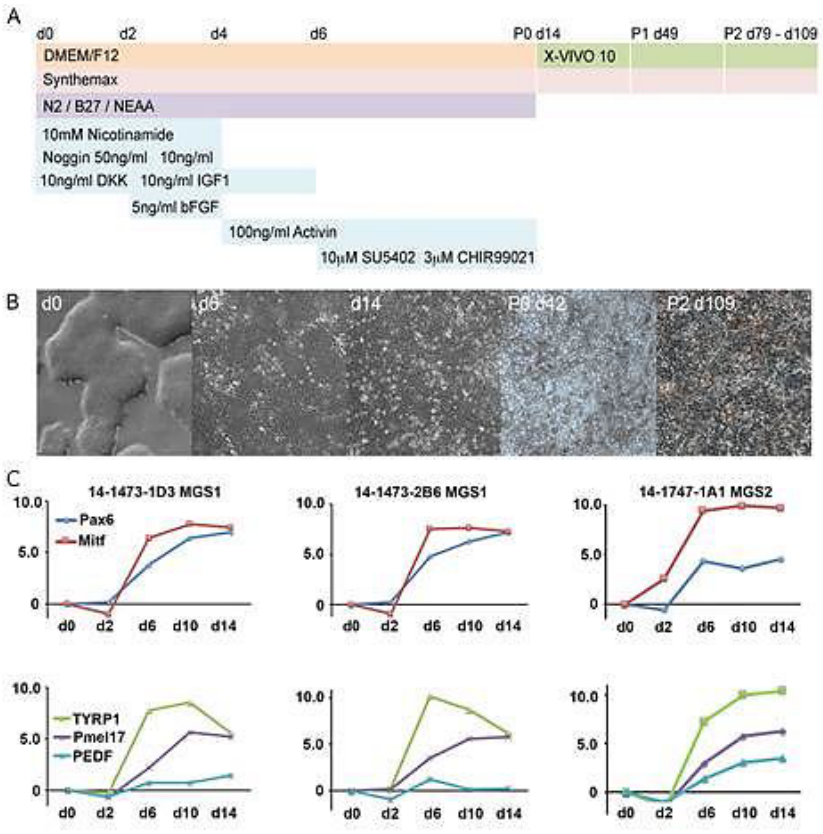

Figure 1 Differentiation of RPE from iPSCs. (A) RPE differential protocol, **(B)** Progression of iPSC to pigmented RPE, **(C)** Induction of RPE gene expression measured by qRT-PCR.