

LCHAD Retinopathy Research Update

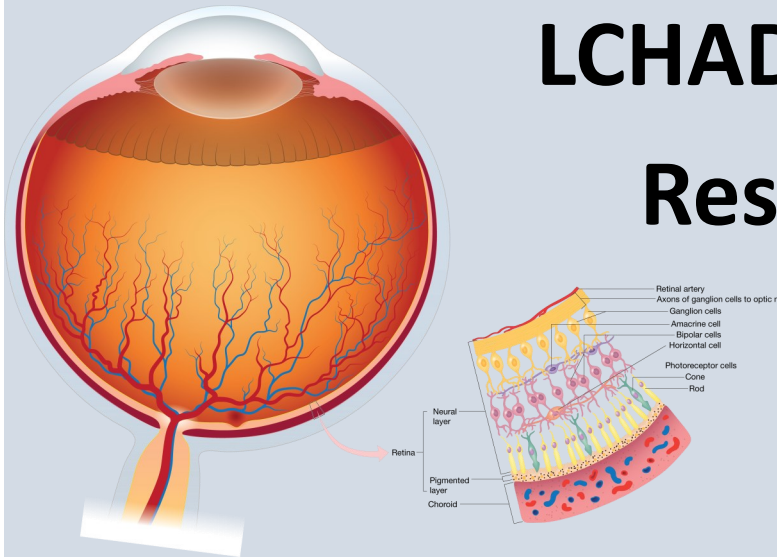


Figure 1: Diagram of the eye with the Retinal Pigment Epithelium layer noted. This is the cell layer that dies first in LCHAD retinopathy (Ophthalmology 2016)

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Our original goal was to develop a cellular model that can mimic LCHAD and simultaneously develop the method and tools needed to introduce a gene therapy treatment. The project included 3 steps: step 1 to make the cell model; step 2 to characterize the cell model and step 3 to test gene therapy in the cells. We have successfully completed step 1 thanks to the generous support of the Peterson/Scully Foundation.

In our last update, we completed the initial step to create an LCHAD-deficient stem cell from skin cells. We have now used those LCHAD-deficient stem cells and programmed them to become retinal pigment epithelium or RPE cells. The RPE cells form a layer of support under the photoreceptors, the cells responsible for vision, in the eye (Figure 1).

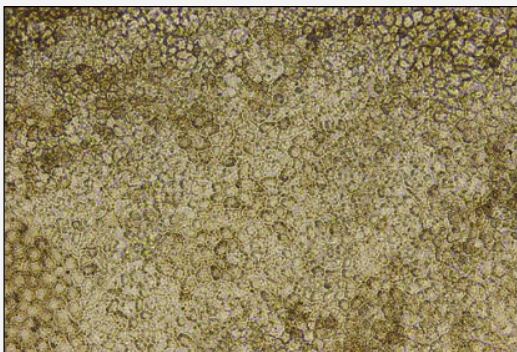


Figure 2: RPE cells derived from LCHAD-deficient stem cells. RPE cells show typical pigmentation (brown coloring)

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They have a unique hexagonal shape (Figure 2) and connect to one another forming tight

junctions (Figure 3). They develop a pigment, a brownish color, across the layer of cell. We believe these cells are the first cells in the retina to become diseased and die in LCHAD-retinopathy (recent publication Boese et al Ophthalmology 2016). The pigment physicians see in the back of the eye in children with LCHAD is large clumps of the relatively uniform pigment pictured here.

Our next goal is to move onto step 2, characterizing our LCHAD-deficient retinal cells. We have started measuring how the LCHAD-deficient RPE cells process fat compared to our control cells.

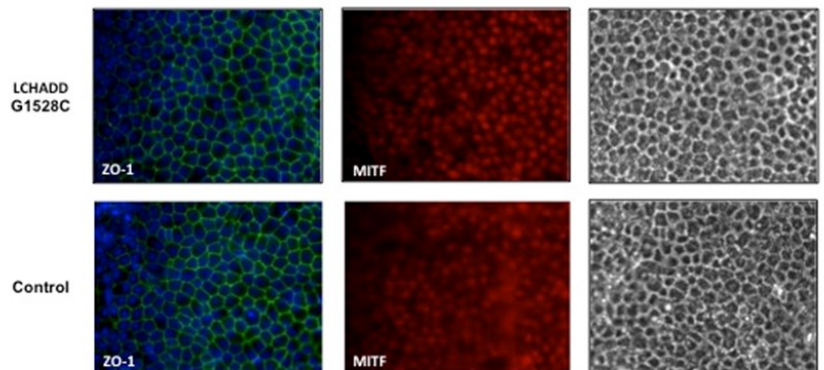


Figure 3: Immunofluorescent staining for Retinal pigment epithelium (RPE). RPE differentiated from patient and control stem cells show expression of RPE specific markers, ZO-1 (green, nuclei are marked by Dapi in blue) and MITF (red). The image on the far right taken using phase contrast light microscopy indicates the differentiated RPE have the typical cobblestone shape.