Project Title: Understanding how dysfunction of energy metabolism in the retinal pigment epithelium contributes to photoreceptor degeneration	**Code: SMS14**

Host School / Institute: Sydney Medical School/ Save Sight Institute	**Address:** Save Sight Institute, 8 Macquarie St, Sydney NSW

Certificates & Clearances required: No

Primary Supervisor: Dr Weiyong Shen

Phone: 0401 956 809	**Email:** weiyong.shen@sydney.edu.au

Co-Supervisor/team: Prof Mark Gillies (Head of the Macular Research Group)

Project Type: Laboratory based

Project Category: Vision; Neuroscience

Skills / Attributes of a successful student: The student needs to understand the principles of Cell Biology, immunohistochemistry and Western blot analysis.

Project Keywords: Age-related macular degeneration; retinal pigment epithelium; photoreceptor cell; glucose metabolism; mitochondrial metabolism

Project Description: Age-related macular degeneration (AMD) is a leading cause of vision loss in people over 50 years of age. The atrophic (dry) form of AMD is characterised by dysfunction or death of monolayer of retinal cells called retinal pigment epithelium (RPE) followed by degeneration of photo-detecting retinal neurons (photoreceptors). However, there is little information about the causal link between a bioenergetic crisis in the RPE and photoreceptor degeneration in the atrophic form of AMD. This project aims to study the effects of selectively knocking down key metabolic genes in the RPE on the health of the mouse retina.

We have performed immunohistochemistry to study expression of key molecules in glucose metabolism in the mouse retina including insulin receptor (IR) and pyruvate dehydrogenase E1α (PDH-E1α), which are important for insulin signalling (IR) and mitochondrial energy metabolism. Our results indicate that RPE cells express IR and PDH-E1α strongly. We have generated transgenic mice to study the consequences of selectively knocking down IR or PDH-E1α in the mouse retina. We found that knocking down IR or PDH-E1α in the RPE resulted in loss of RPE cells and decreased expression of mitochondrial proteins in the RPE as well as photoreceptor degeneration. This summer scholarship offers the student an opportunity to learn techniques including immunohistochemistry, biochemical analyses and Western blots to study how knocking down IR or PDH-E1α in the RPE affects the number and function of mitochondria in the RPE and photoreceptors in our transgenic mice.