**TITLE:** Gene therapy to induce neuroprotection in the retina

**FACULTY MENTOR:** John D. Ash, PhD  
Francis M. Bullard Eminent Scholar Chair Ophthalmology  
Email  jash@ufl.edu  
Phone (353) 273-8328

**RESEARCH PROJECT DESCRIPTION** (brief overview of background, hypothesis, methods, role of medical student, funding and relevant publications)

In this study we are proposing to test AAV-vectors that we have made that express downstream targets of LIF in either photoreceptors or RPE. Our first aim will demonstrate whether increased expression of the transcription factor STAT3 is sufficient to induce protection of photoreceptors or RPE, while our second aim will demonstrate whether increased expression of the protein PIM-1 is sufficient. This project has the potential to impact many forms of inherited retinal degeneration and dry AMD. We have identified both STAT3 and PIM-1 as downstream effectors of the neuroprotective pathways activated by CNTF and LIF, which have been shown to protect photoreceptors from oxidative stress induced by damaging light, and from inherited retinal degeneration caused by opsin mutations. We have also found that STAT3 is necessary to decrease RPE sensitivity to oxidative stress. Therefore, the AAV vectors we have developed for this project have the potential to prevent blindness in many forms of inherited retinal degenerative diseases, and to prevent the death of cones and RPE in the dry forms of age related macular degeneration (dAMD). This project will provide a definitive test of the protective activity of three new gene therapies for the neuroprotection of photoreceptors and RPE. The summer student would participate in the project by performing subretinal injections of AAV vectors and will participate in analysis of retinal function by electroretinograms (ERGs), retinal imaging by optical coherence tomography (OCT), and histology. The lab is well funded by grants from the NIH and the Foundation Fighting Blindness.