James & Esther King Biomedical Research Program

Lewin, Alfred

Molecular Genetics and Microbiology
University of Florida

2010 Program
Research Project Grant
(3-year project)

Project Title: Developing Gene Therapy for Age-Related Macular Degeneration

Project Summary: Age-Related Macular Degeneration (AMD) is a blinding disease affecting as many as 1 in 3 people over 70. Smoking is a major risk factor for developing this disease. This is a project to develop a mouse model of early AMD and to test two novel approaches to gene therapy in that model. Our goals are to better understand the cause of AMD and to develop a treatment for early stages of the disease. We have created a genetically modified mouse strain in which a protective enzyme is missing from one layer of the retina, the part of the eye that absorbs light. In our previous experiments, we observed that reducing levels of the enzyme caused serious structural damage similar to that occurring in early ("dry") AMD. In this project, we will determine the time course of these retinal changes and see if they progress to the "wet" form of AMD, in which leaky blood vessels sprout into the retina causing loss of central vision. We will also attempt to use gene transfer methods to arrest the progression of AMD-like changes. First, we will use a non-harmful virus to deliver genes that prevent the generation of reactive oxygen molecules by an enzyme called NOX. Blocking NOX in patients could slow the progression of AMD. Our second approach will be to restrain the release of a molecular signal that stimulates inflammation in the retina. We believe that blocking inflammation will prevent the damage to the retina seen in AMD.