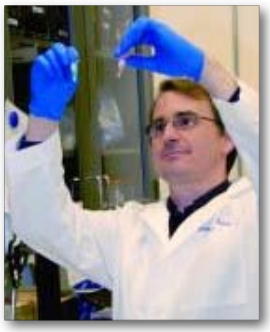

Stem Cells Generate New Retinal Cells Necessary for Vision

Pluripotent stem cells — those, like embryonic stem cells, that give rise to almost every type of cell in the body — can be converted into the different classes of retinal cells necessary for vision, according to a new, RPB-supported study from researchers at SUNY Upstate Medical University in Syracuse, N.Y.

This research points to exciting new possibilities for preventing or reversing the disabling vision loss caused by age-related macular degeneration, diabetic retinopathy, retinitis pigmentosa, glaucoma, and other diseases that damage the retina, the layer of light-sensitive nerve cells that line the back of the eye. The research was presented at Neuroscience 2008, the annual meeting of the Society for Neuroscience and the world's largest source of emerging news about brain science and health. "Vision is lost in these diseases because one or more of the seven retinal cell types die," said Michael Ezra Zuber, PhD, the study's lead author. "Current treatments can slow these diseases' progression, but they can't replace lost retinal cells. Pluripotent cells offer a promising starting point from which to generate new retinal cells."

Zuber (who received a four-year, $200,000 Career Development Award from RPB in 2003 to pursue this investigation) and his colleagues knew that cultured pluripotent cells could

RPB supports entire team that grows functioning eyes

The project was a collaborative effort among three RPB Career Development Awardees [CDA] working at the Center for Vision Research, in the Ophthalmology Department at SUNY Upstate Medical University. "We each brought distinct skill sets, but shared a goal of generating functional retinal cells from pluripotent cells," says Michael Zuber, Ph.D. According to Zuber, instrumental contributions came from Eduardo Solessio, Ph.D. (RPB CDA 1999) and Andrea Viczian, Ph.D (RPB CDA 2005).

Dr. Viczian is a stem cell biologist with expertise in transplantation and retinal cell biology. Dr. Viczian has demonstrated that a single extrinsic factor can transform frog skin cells into retinal

be induced to express some retinal cell genes, but they didn't know if all retinal cell classes could be generated or if the cells would have the ability to form a functioning retina. To test that hypothesis, the scientists turned to pluripotent Xenopus laevis (frog) cells. Under normal conditions, pluripotent frog cells form only skin tissue. The scientists were able, however, to convert the pluripotent cells to retinal cells by forcing them to express the eye field transcription factor (or EFTF) genes. The reprogrammed cells formed all seven classes of retinal cells normally found in the eyes, including the retinal ganglion cells, which have axons (optic nerves) that extend to the brain.

Furthermore, these new cells eventually formed into functioning eyes. When tested, tadpoles used their induced eyes to detect light and to engage in a vision-based behavior. The scientists also found a population of self-renewing cells in the periphery of the induced retinas, suggesting that EFTF-induced cells also formed adult retinal stem cells.

stem/progenitor cells and, further, that the newly made cells could generate an entire functional eye once they were transplanted to host embryos. In order to determine if these retinal cells could form a truly functioning eye, she developed a behavioral assay to test the animals' vision. These experiments clearly showed that the animals could respond to a light stimulus via their induced eyes.

Dr. Solessio is an accomplished electro-physiologist, able to record visual responses in small animals. His initial RPB-funded research was aimed at furthering the vision research community's understanding of the mechanisms underlying macular degeneration, retinitis pigmentosa, and other retinal degenerations. With his expertise, the team was able to demonstrate that the induced retinas were light responsive.

"The goal of regenerative medicine is to replace dead or dying cells," said Zuber. "The retina, like all body organs, contains multiple, distinct cell types. Therefore, successful recovery from blindness due to injury or disease will require the functional replacement of multiple retinal cell types. Our results demonstrate that pluripotent cells can be purposely altered to generate all the functional retinal cell classes necessary for vision."

The research was supported by Research to Prevent Blindness, the E. Matilda Ziegler Foundation for the Blind, The Lions Club of Central New York, and the U.S. National Eye Institute.