Age-related macular degeneration (AMD) and retinitis pigmentosa (RP)

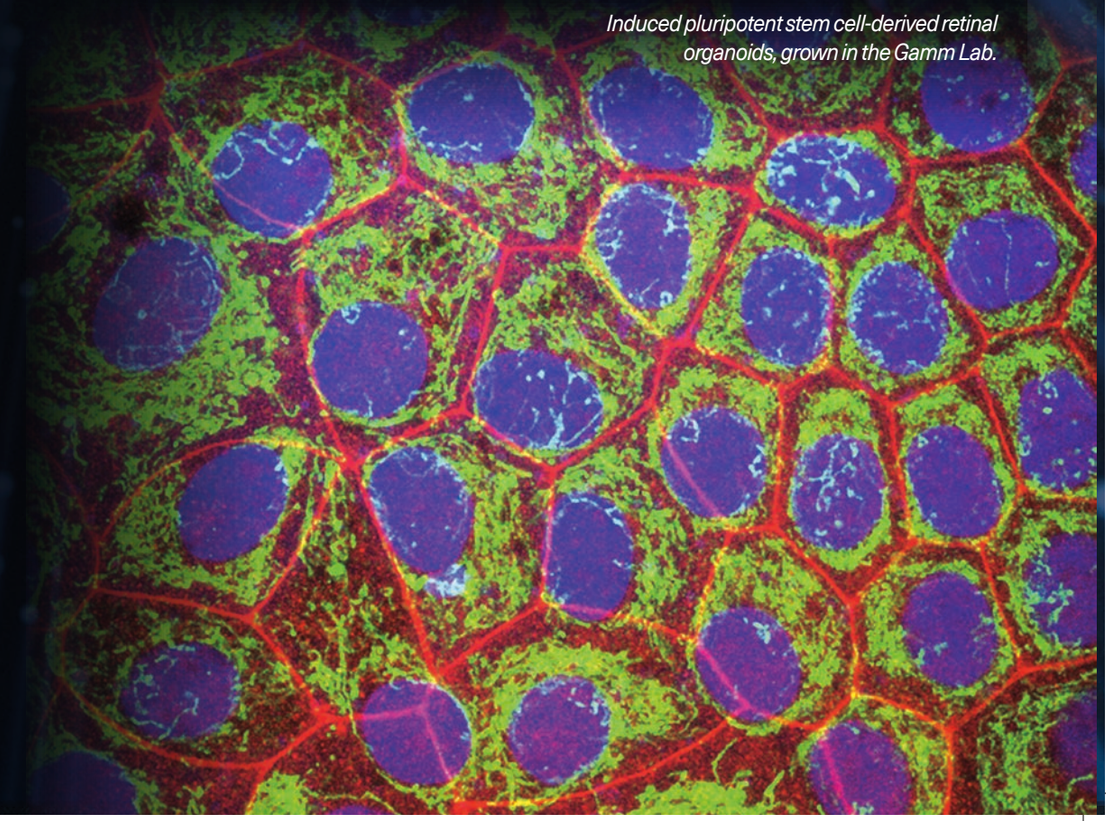
The McPherson ERI Stem Cell Consortium: Looking toward human clinical trials

Until very recently, the idea of replacing the cells in human eyes that initiate vision—the photoreceptors—was considered science fiction. Those who have followed the McPherson ERI's research for the past 10 years, though, know that what was once a fanciful dream is moving towards reality. In the last decade, 1 **David Gamm** (Sandra Lemke Chair in Eye Research) and his lab members, along with multiple collaborating researchers at UW-Madison and around the world, have used induced pluripotent stem cells (iPSCs) to create functional human photoreceptors and other retinal cells in the lab, as well as whole retinal tissues. The McPherson ERI's stem cell team, led by Dr. Gamm, includes biologists, statisticians, engineers, surgeons, and industry leaders.

2022 has seen strong forward movement towards transplantation of photoreceptors for retinitis pigmentosa and RPE (or RPE + photoreceptors) for age-related macular degeneration (AMD). Other inherited diseases that will benefit from these efforts include Usher syndrome, Stargardt disease, and Best vitelliform macular dystrophy, among many others. Pioneering research and patents from the McPherson ERI's stem cell team led to the establishment of Opsis Therapeutics, a subsidiary of FujiFilm Cellular Dynamics Inc. (FCDI), in Madison, WI. In 2021, Opsis and FCDI joined forces with BlueRock Therapeutics (Boston, MA) and Bayer AG (Germany) to take their iPSC-derived photoreceptor and RPE cell technology to patients. At least two human clinical trials are planned in the coming years—the first for retinitis pigmentosa and Usher syndrome, and the second for AMD and other forms of macular disease.

In 2022, two different studies published by McPherson ERI stem cell team members have provided strong evidence that lab-grown photoreceptor cells have "what it takes" to function in the human eye. Early in the year, neuroscientist and David and Nancy Walsh Family Professor 2 **Raunak Sinha** published a study in collaboration with the Gamm Lab showing that stem cell-derived cone photoreceptor cells can respond to light in a very similar way as those in adult non-human primates. An equally important finding came later in the year, when neuroscientist 3 **Tim Gomez's** lab reported that these same stem cell-derived cone photoreceptors have the innate ability to extend "wires"—termed axons—in order to contact other retinal cells. That study, led within the Gomez lab by 4 **Sarah Rempel** in collaboration with the Gamm lab, bolsters confidence that transplanted photoreceptors can forge the links necessary to re-establish vision-generating retinal circuits in patients whose photoreceptors have been terminally damaged.

This past year, the McPherson ERI stem cell team continued to explore innovative ways to deliver photoreceptors and RPE cells to their home in the very back of the eye using the latest engineering advances. Working with Dr. Gamm, the labs of 5 **Sarah Gong** (RRF Edwin and Dorothy Gamewell Professor) and 6 **Jack Ma** have created a 4th generation biodegradable micro-scaffold that can safely and accurately place photoreceptors and/or RPE cells under the thin, delicate retina. The team is now testing these scaffolds in preclinical studies in collaboration with the lab of 7 **Kapil Bharti** with support from the U.S. Department of Defense and the National Eye Institute. Refining the subretinal transplant procedure has also been a major Institute focus in 2022, with key improvements being made by lead retinal surgeon and stem cell team member 8 **Michael Altaweel** (Monroe E. Trout Chair in Eye Research).



Induced pluripotent stem cell-derived retinal organoids, grown in the Gamm Lab.