Point of View
THE EYE RESEARCH INSTITUTE UNIVERSITY OF WISCONSIN–MADISON
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Nurturing Researchers and Retinas

If your father kept a collection of animal brains in jars in the barn when you were a kid, you'd probably grow up with either an interest in or an aversion to such things. For David Gamm, assistant professor of Ophthalmology and Visual Sciences and member of the UW Eye Research Institute, his school psychologist father's passion for both the inner workings of the mind and its physical structure instilled David with a curiosity about the nervous system. Gamm's mother, a nurse, also encouraged an interest in medicine. "I think I managed to blend both parental influences," laughs Gamm, who studied cellular and molecular biology as an undergraduate and then pursued a combined MD degree and PhD degree (in Neuroscience) at the University of Michigan.

Choosing advanced clinical training as a pediatric ophthalmologist was logical for Gamm. In addition to the enjoyment of working with children, ophthalmology directly incorporated Gamm's neuroscience training, since it includes study of the retina, a thin layer of neural (brain) cells lining the back of the eye.

"As a resident, I did research in the lab of Drs. Arthur Polans and Daniel Albert, who now respectively serve as the Associate Director and Director of the UW Eye Research Institute," Gamm explains. "Following my time in their lab, Dr. Albert asked if I had ever considered studying stem cells in the eye, as it was a new area of research that had implications from a basic science as well as clinical standpoint. The idea intrigued me, but I knew I would need more training. And how could I do that while starting my clinical practice?"

Clive Svendsen, PhD, professor of Anatomy and Neurology, was studying ways to repair damaged areas of the brain using stem cells. Gamm met with Svendsen to investigate research options, and Svendsen agreed to become Gamm's mentor and sponsor for a National Institutes of Health K08 grant. The K08 is designed to support the development of outstanding clinician-scientists by providing a 3–5 year period of supervised research experience. "It was a perfect fit for me," says Gamm.

Stem cells: n. Undifferentiated, primitive cells with the ability both to multiply and to differentiate into specific kinds of cells.

The K08 award requires an investigator to devote 75% of his time to the research project. To facilitate this, Gamm's pediatric ophthalmology colleagues arranged his clinical practice schedule to fit the 25% time he would have available. "Without the support of Drs. Tom France, Burton Kushner, Mike Struck and Yasmin Bradfield, I couldn't possibly have balanced the clinical and research requirements."

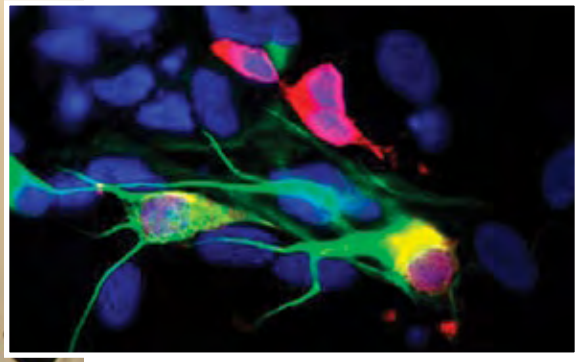
And support came from other quarters. The UW's Waisman Center, whose mission is to advance knowledge about human development, developmental disabilities, and neurodegenerative diseases, stepped forward with lab space for Gamm just down the hall from the Svendsen lab. Marsha Seltzer, Director of the Waisman Center, notes, "We at the Waisman Center were delighted when David Gamm joined our ranks. He is an outstanding scientist, a very skillful surgeon, and a truly wonderful human being. The addition of Dave to the Waisman Center has helped to build a critical mass of stem cell researchers whose work is central to our mission."

In addition, donations to support Gamm's research came from UW Board of Regents member David Walsh and philanthropist William Heckrodt. Stem cell research on the campus receives further backing from the Wisconsin Alumni Research Foundation, and Wisconsin Governor Jim Doyle has worked diligently to expand and support stem cell research in the state. All these factors come together to create a climate favorable for faculty — like Gamm — who wish to work on unlocking stem cells' clues to healing.

Stem cells tantalize scientists because they are a potentially unlimited source of "flexible" cells in the human body which have the ability to differentiate into other cell types. These changes normally

happen during development, when cells are programmed to become eyes, brain, bone, or other body components.

Gamm's work focuses on retinal progenitor cells — cells that can be coerced into becoming specific retinal cells. Gamm needed to develop a technique to grow retinal progenitor cells efficiently in order to have a renewable population of cells available for his studies and, ultimately, for the treatment of retinal disorders. "We are trying to learn whether retinal progenitor cells can be grown in large enough numbers to be therapeutically useful, then to coax them into becoming retinal cells such as ***photoreceptors***, the cells that convert light images into the electrical signal the brain recognizes as sight," says Gamm.



Left: David Gamm, MD, PhD, examines a flask of retinal pigment epithelial cells in culture.

Above: Cultured human retinal progenitor cells mature into retinal neurons (greenish cells), including photoreceptor-like cells (pinkish-purple areas).

The need for carrying out these studies is great. Millions of people suffer from irreversible vision loss from eye diseases related to faulty or damaged photoreceptors like retinitis pigmentosa, macular degeneration or Stargardt macular dystrophy. Over 8 million Americans are at high risk for developing advanced age-related macular degeneration, and of these, 1.3 million are likely to experience vision loss within 5 years. Retinitis pigmentosa and Stargardt's are rarer diseases, but affect more than 1.5 million people worldwide, and tend to affect younger individuals.

Because of his physical proximity to the other scientists in the Stem Cell Research Group, Gamm is now forging new collaborations. For example, he found opportunities to interact with Matt Pankratz, a graduate student in the laboratory of Su-Chun Zhang, MD, PhD. Pankratz has derived forebrain neurons from stem cells, and Gamm realized that the predominant cell type Pankratz had isolated closely resembled the cells that eventually form the eye during development. Dr. Jason Meyer, a post-doctoral student in the Zhang lab, shared Gamm's interest in Pankratz's results.

As Pankratz, Meyer and Gamm began comparing notes, they realized that they might be able to use information obtained from Pankratz's experiments to coax undifferentiated stem cells to become retinal progenitor cells.

As Gamm was developing this line of work, the UW Eye Research Institute had just established a new professorship through the generosity of the Retina Research Foundation and Dr. Alice McPherson, a UW alumna and Houston ophthalmologist. The goal of the professorship is to stimulate collaborative approaches to curing blindness and preventing vision loss by providing funding to investigators doing innovative and interdisciplinary work. Gamm, whose work met these criteria perfectly, was named its first recipient in July 2006.

"The Gamewell Professorship support allowed us to pursue this line of work when the idea came to us, instead of writing a new grant and waiting to receive its funding," he states. "We can move ahead much more quickly with the pilot project, thanks to this support."

Gamm is hopeful about the potential for stem cell technology to produce therapies for blinding disorders. He says, "The amount of useful vision that a person obtains from such treatments will probably be low, at least at first. Treating blindness is like treating cancer — there are hundreds of different reasons for vision loss, and each disease behaves and responds in distinct ways. Just like we don't have a 'cure' for cancer, stem cells are not going to 'cure' blindness, but we are likely to improve visual function in a subset of patients."

Gamm looks forward to the day that stem cell therapies for vision loss are common. With his personal determination, combined with the circle of support uniquely available on the UW campus, Gamm's research will surely bring that day closer.

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