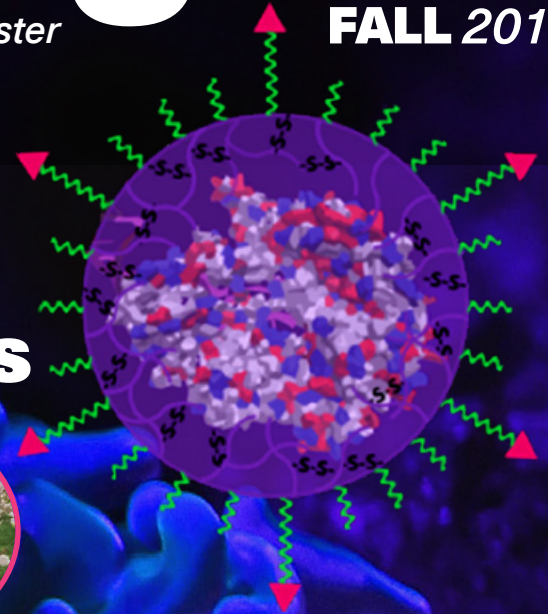


## Developing Ocular Nanodelivery Systems

WITH SHAOQIN SARAH GONG, PH.D.

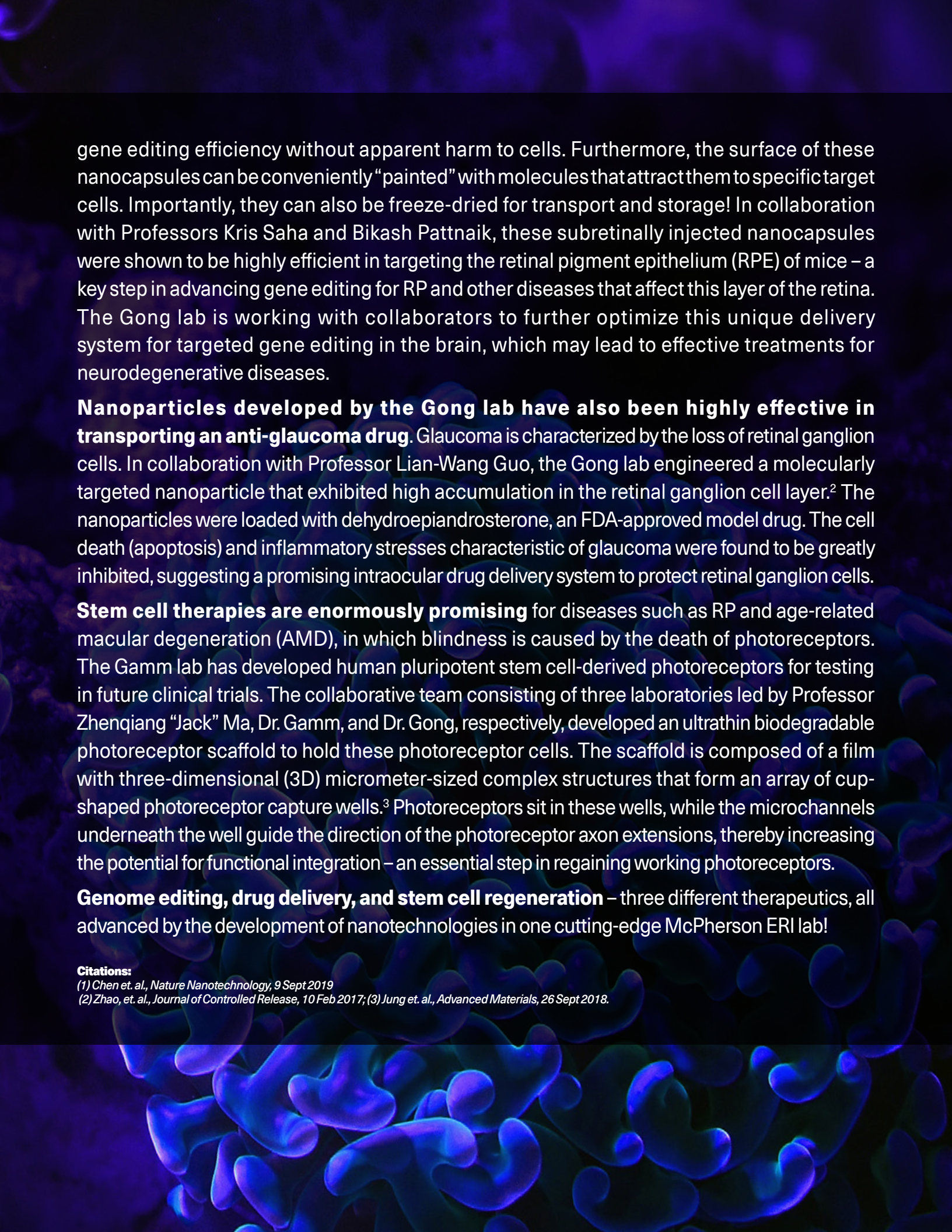


**Advances in genome editing and stem cell therapeutics** are moving forward rapidly at UW-Madison and elsewhere, but share a common challenge: How can therapeutics best be delivered to the diseased cells or tissue that need to be targeted? Biomedical Engineering Professor Shaoqin Sarah Gong and her research group focus on designing and synthesizing novel biomaterials – including nanodelivery systems and tissue engineering scaffolds – for these and other biomedical applications. The Gong lab collaborates with multiple McPherson ERI researchers in need of advanced delivery methods for new ocular therapies.

**Gene editing has the potential to cure many vision diseases**, including various types of the genetic disorder retinitis pigmentosa (RP). The CRISPR-Cas system is a powerful genome-editing tool capable of gene manipulation and repair. But how does one safely and efficiently deliver the CRISPR-Cas genome-editing machinery to diseased cells? Viral vectors are commonly used, as they are efficient at infiltrating and altering cells. They are costly to manufacture, however, and can give rise to immune problems and unanticipated genetic changes. In contrast, non-viral methods may be safer and easier to produce in large batches, but their efficiency remains in question.

**As reported in a recent *Nature Nanotechnology* paper,**<sup>1</sup> Professor Gong's lab has solved many of the problems of non-viral therapeutic delivery by engineering a customizable synthetic nanocapsule (NC), which contains the preassembled Cas9/sgRNA ribonucleoprotein complex which enables gene disruption. These nanocapsules are engineered to stay intact outside of cells and in the bloodstream, but they can disintegrate readily once taken up by the target cells, allowing for a rapid release of the gene-editing tools inside those cells. The nanocapsules have shown great





gene editing efficiency without apparent harm to cells. Furthermore, the surface of these nanocapsules can be conveniently “painted” with molecules that attract them to specific target cells. Importantly, they can also be freeze-dried for transport and storage! In collaboration with Professors Kris Saha and Bikash Pattnaik, these subretinally injected nanocapsules were shown to be highly efficient in targeting the retinal pigment epithelium (RPE) of mice – a key step in advancing gene editing for RP and other diseases that affect this layer of the retina. The Gong lab is working with collaborators to further optimize this unique delivery system for targeted gene editing in the brain, which may lead to effective treatments for neurodegenerative diseases.

**Nanoparticles developed by the Gong lab have also been highly effective in transporting an anti-glaucoma drug.** Glaucoma is characterized by the loss of retinal ganglion cells. In collaboration with Professor Lian-Wang Guo, the Gong lab engineered a molecularly targeted nanoparticle that exhibited high accumulation in the retinal ganglion cell layer.<sup>2</sup> The nanoparticles were loaded with dehydroepiandrosterone, an FDA-approved model drug. The cell death (apoptosis) and inflammatory stresses characteristic of glaucoma were found to be greatly inhibited, suggesting a promising intraocular drug delivery system to protect retinal ganglion cells.

**Stem cell therapies are enormously promising** for diseases such as RP and age-related macular degeneration (AMD), in which blindness is caused by the death of photoreceptors. The Gamm lab has developed human pluripotent stem cell-derived photoreceptors for testing in future clinical trials. The collaborative team consisting of three laboratories led by Professor Zhenqiang “Jack” Ma, Dr. Gamm, and Dr. Gong, respectively, developed an ultrathin biodegradable photoreceptor scaffold to hold these photoreceptor cells. The scaffold is composed of a film with three-dimensional (3D) micrometer-sized complex structures that form an array of cup-shaped photoreceptor capture wells.<sup>3</sup> Photoreceptors sit in these wells, while the microchannels underneath the well guide the direction of the photoreceptor axon extensions, thereby increasing the potential for functional integration – an essential step in regaining working photoreceptors.

**Genome editing, drug delivery, and stem cell regeneration** – three different therapeutics, all advanced by the development of nanotechnologies in one cutting-edge McPherson ERI lab!

**Citations:**

(1) Chen et. al., *Nature Nanotechnology*, 9 Sept 2019

(2) Zhao, et. al., *Journal of Controlled Release*, 10 Feb 2017; (3) Jung et. al., *Advanced Materials*, 26 Sept 2018.



# From the Director



**Dear Friends,**

**We're pleased to highlight in this issue** two research projects (involving half a dozen McPherson ERI labs) that have received significant publicity in recent months. Both of them – Sarah Gong's work with nanocapsule delivery systems and Andreas Velten's innovative "around-the-corner" imaging methods – are outstanding representations of the mission of the McPherson Eye Research Institute. When we were founded in 2005, it was with the goal of increasing the number and quality of meaningful vision research collaborations at UW-Madison, and between UW-Madison and other institutions. "No researcher is an island" could have been our motto.

**Working together also makes us** more efficient and impactful. Research often requires months or years of diligent, precise and often painstaking work before conclusions become clear. While this process cannot move fast enough for those waiting for new therapies, collaboration allows us to work in parallel within our respective areas of expertise. Consequently, the potential for major advances in the diagnosis and treatment of vision-threatening disorders over the next few years has never been greater. Along the way, we keep in mind that the stakes are high, and that technology developed in our labs must be tested thoroughly to assure safety before being used with patients.

**In the work noted in this issue,** you will see progress in therapeutic and diagnostic tools that are likely to move to the clinic in the foreseeable future. There is more work to be done before this happens, but the McPherson ERI will support these efforts every step of the way.

**We're grateful to you for your help, as well.** Please watch for our annual year-end report and calendar next month, and enjoy the holiday season.

A handwritten signature in white ink, reading "David M. Gamm". The signature is fluid and cursive.

**David M. Gamm, MD, PhD**

Emmett A. Humble Distinguished Director, McPherson Eye Research Institute  
Sandra Lemke Trout Chair in Eye Research



# McPherson ERI Updates

## **Trout Family Endowment Major Gift Will Support McPherson ERI's Research, Education & Outreach Activities**



**Dr. Monroe and Sandra Trout** have generously supported the McPherson ERI since 2012, following an event held at the Trout Art Museum in Appleton. Their interest is both personal and visionary – as Monroe told the SMPH Quarterly in 2016, “I have macular degeneration, and I know I might not see the benefits of current research in my lifetime. But we hope we can help researchers find ways to prevent and possibly someday cure a disease that impacts millions of Americans.” The Trouts have been pleased with the depth of retinal research taking place at UW-Madison, Sandy Trout’s alma mater. In recent years, the Trouts established two endowed positions, the Sandra Lemke Trout Chair in Eye Research and the Timothy William Trout Professorship in Eye Research. This fall, the Trouts provided a \$2 million gift to fully endow the Monroe & Sandra Trout Director’s Fund for Vision Research, established in 2016. Proceeds from the Director’s Fund will support the entire range of McPherson ERI research, education, and outreach activities, and greatly aid the Institute’s mission. “It is a transformative gift,” says McPherson ERI Director and Sandra Lemke Trout Chair holder David Gamm, “given by a family that deeply understands how basic research works, and what it needs to succeed. Sandy and Monroe are wonderful people, and our gratitude to them is beyond measure.”





*Photo credit: Andy Manis*

## **Raunak Sinha, PhD, Will Hold New David & Nancy Walsh Family Professorship in Vision Research**

**The David and Nancy Walsh Family Professorship** in Vision Research, announced in 2018, has now been fully endowed through generous support from the Walsh Family and Dr. Alice McPherson, along with a match from John and Tashia Morgridge. The McPherson ERI is delighted to have a professorship in the name of the Walsh family. David, former chair of the Board of Regents and first chair of the McPherson ERI's Advisory Board, drafted the McPherson ERI's founding documentation. According to its mandate, the Walsh Family Professorship must be held by a researcher performing "cutting-edge research," and Raunak Sinha, PhD, Assistant Professor in the Department of Neuroscience, certainly fits that bill. Dr. Sinha, who was profiled in the Fall 2018 McPherson ERI *InSights*, is studying signaling pathways in the fovea, the specialized area in the retina that is largely responsible for its high resolution. Understanding how these pathways operate at a cellular and synaptic level is a vital step towards developing treatments to restore or simulate the function of the fovea – a revolutionary effort.



## Daniel M. Albert Lecture Will Honor the McPherson ERI's Founding Director

**UW-Madison has become a crossroads** for distinguished vision lecturers in recent years, with guest speakers from around the world delivering the spring McPherson Endowed Lecture and the McPherson ERI's annual fall lecture. These talks bring new scientific advances and perspectives on vision to campus, and regularly allow visiting researchers to meet with UW faculty individually or in small groups. In honor of Dr. Daniel M. Albert, the McPherson ERI's Founding Director, the Institute will establish an annual Daniel M. Albert Lecture, which will begin with an inaugural lecture in 2020. The Daniel M. Albert Lecture will be funded by an endowment established by Alice McPherson, MD – the Institute's namesake and Dr. Albert's longtime colleague and friend. Together, Drs. McPherson and Albert created the UW Eye Research Institute in 2005; the Institute was renamed in Dr. McPherson's honor in 2012. With the establishment of this new annual lecture, UW-Madison will become even more of a destination for visiting vision scientists.



## Fall 2019 Walsh Research Travel Awards Announced

**Ryan Donahue and Mengguo Jing** have been awarded McPherson ERI/David G. Walsh Research Travel Awards, which provide funds for graduate students and postdocs from McPherson ERI members' research groups to present vision-related work at scientific conferences. Donahue, a graduate student in Ophthalmology and Visual Sciences (mentored by Rob Nickells) will attend the 2019 International Society for Eye Research (ISER)/Brightfocus Glaucoma Symposium in Atlanta. His presentation is entitled *BclIX gene therapy to prevent RGC degeneration after optic nerve crush and in the DBA/2J mouse model of glaucoma*. Mengguo Jing, a graduate student in Human Development and Family Studies (Heather Kirkorian, mentor), just returned from attending the Cognitive Development Society Biennial Meeting in Louisville. She presented a poster entitled *The effect of comprehensibility on saliency-based gaze prediction for children and adults watching Sesame Street*. Both award recipients will be invited to speak in the McPherson ERI seminar series during the 2020-21 academic year.





# Seeing Around Corners

WITH ANDREAS VELTEN, PH.D



**Along with flying and invisibility,** high on the list of every child's aspirational superpowers is the ability to see through or around walls or other visual obstacles. McPherson ERI member Andreas Velten and his colleagues have now brought that capability a big step closer to reality. Drawing on the lessons of classical optics, they have shown that it is possible to image complex hidden scenes using a projected "virtual camera" to see around barriers.

**Technologies to achieve what scientists call** "non-line-of-sight imaging" have been in development for years, but technical challenges have limited them to fuzzy pictures of simple scenes. Velten, Associate Professor of Biostatistics and Medical Informatics in the UW School of Medicine and Public Health, published his work in a recent *Nature* study. The basic idea of non-line-of-sight imaging revolves around the use of reflected light, a light echo of sorts, to capture images of a hidden scene. Photons from thousands of pulses of laser light are reflected off a wall or another surface into an obscured scene; then the reflected, diffused light bounces back to sensors connected to a camera. The recaptured light particles are used to digitally reconstruct the hidden scene in three dimensions.

**In order to improve the quality of scene regeneration,** Velten and his colleagues had the idea of applying the same math used to interpret images taken with conventional imaging systems or created by the lens of the human eye. These systems interpret light as waves, which are shaped into images by applying well known mathematical formulas. In so doing, Velten and colleagues were able to interpret the waves and reconstruct an image of a hidden scene. In effect, this new method turns any diffuse wall into a virtual camera.

**The potential applications of this technology** are numerous. In medicine, it holds promise for improving surgery inside the eye and other organs by providing a more complete picture to the surgeon. And Velten notes that the technology can be made both inexpensive and compact... meaning real-world applications are just a matter of time.

– by Terry Devitt



# Donate

to the McPherson ERI in  
November and December 2019,  
and **your gift will be matched**  
– up to a total of \$100,000 –  
by Roger & Lynn Van Vreede,  
of Appleton, WI.

Please support us at  
[vision.wisc.edu/giving](http://vision.wisc.edu/giving)



On Display in the  
Mandelbaum & Albert  
Family Vision Gallery  
until December 13th

SAVE THE DATE

**CYCLE FOR SIGHT 2020**

Saturday  
**Mar 7th**  
2020