

VOLUME 20 • NUMBER 4 • 2018

FOR ALUMNI, FRIENDS, FACULTY AND STUDENTS OF THE  
UNIVERSITY OF WISCONSIN SCHOOL OF MEDICINE AND PUBLIC HEALTH

# Quarterly

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David Gamm, MD, PhD (PG '02, '03), oversees his productive laboratory at the UW-Madison Waisman Center.



# Stem Cell Science

## 20 YEARS OF PROGRESS TOWARD CLINICAL APPLICATIONS

**T**wo decades after James Thomson, VMD, PhD—now an investigator of regenerative biology at the Morgridge Institute for Research at the University of Wisconsin-Madison—derived the first human embryonic stem cell lines (ESC) on this campus, his revolutionary discovery is just beginning to emerge on the clinical landscape. To date, a handful of clinical trials of ESC-derived therapies have been completed, with approximately another 16 underway worldwide.



*James Thomson,  
VMD, PhD*

MORGRIDGE INSTITUTE FOR RESEARCH

patients is balanced with realism about the path forward. Responsible science can be a slow, grueling process. But experts in the field feel more optimistic than ever, due to a critical mass of small successes.

Perhaps no field of medicine has as much reason to be hopeful about stem cell therapy as ophthalmology. Of the human trials underway, all but two involve therapies for eye disorders. David Gamm, MD, PhD (PG '02, '03), an associate professor in the Department of Ophthalmology and Visual Sciences at the UW School of Medicine and Public Health (SMPH), attributes this to three factors: practicality, safety and cost.

“Most new stem cell therapies require new surgical techniques and devices, but not always for the eye,” Gamm explains. “That reduces the cost of development and quickens the pace of getting new therapies through the U.S. Food and Drug Administration (FDA) and to patients.”

But Gamm, who also is the Retina Research Foundation Emmett A. Humble Distinguished Director of UW-Madison's McPherson Eye Research Institute and the

Sandra Lemke Trout Chair in Eye Research, understands patients' frustrations. He likens the process of developing stem cell therapies to the first attempts at human flight.

“If the Wright Brothers claimed they could build a plane that would fly across the Atlantic, people would have laughed at them,” Gamm says. “What they were trying to do was glide off a hill safely, with the hope of greater things to come. And that's where this field is right now.”

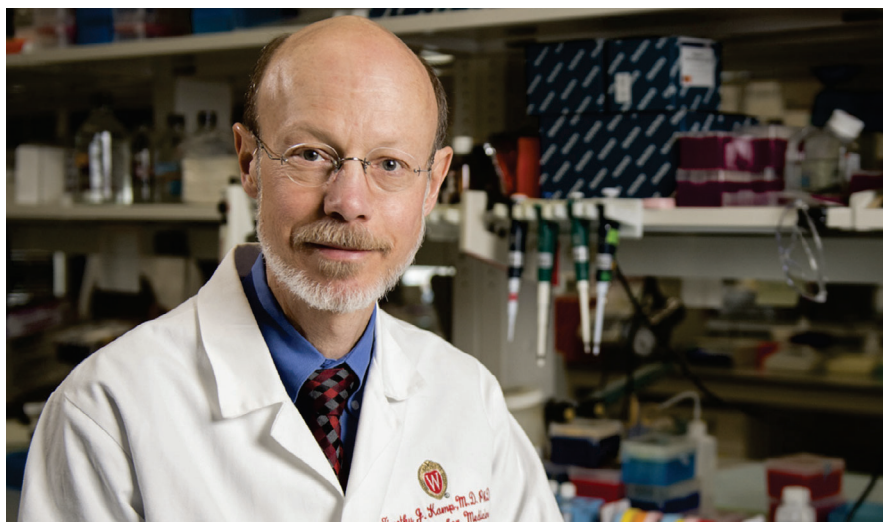
Most of the advances in the field to date have involved the development of human ESC-derived retinal pigment epithelium (RPE). The RPE is a single layer of cells that regulates the transport of nutrients and waste products to and from the retina and is considered to be the part of the eye where macular degeneration begins. In 2012, 18 adults with severe eye disease received transplants created from human embryonic stem cells, and they continue to have no apparent complications. Thirteen of them had an increase in pigmentation, suggesting that the transplanted cells were still alive. Results of the study, reported by researchers at

Advanced Cell Technology in Massachusetts, provided the first evidence of the medium-term to long-term safety and graft survival, and possible biological activity of pluripotent stem cells in individuals with any disease.

Gamm says the numerous stem cell experts at UW-Madison work together, often across disparate disciplines—from cell biology to engineering to ethics.

“This is where Jamie Thomson and UW-Madison have led the way. We have a strong sense of integrity and ethics here, and because we have this multidisciplinary approach to stem cells, we also have a sense of realism,” Gamm says. “So, while we may not have flown far yet, what we have done has allowed us to land safely. And that has allowed us to dust ourselves off, re-evaluate, climb back up that hill and try again.”

Gamm’s company, Opsis Therapeutics, is working with Cellular Dynamics International, founded by Thomson and now owned by Fujifilm, toward clinical trials for retinitis pigmentosa, a group of genetic diseases that



CLINT THAYER/DEPARTMENT OF MEDICINE

*Timothy Kamp, MD, PhD*

lead to blindness at an early age. Currently, there are no treatments for these diseases.

Clinical trials for other conditions—including Parkinson’s disease, diabetes, spinal cord injury and heart disease—likely will use induced pluripotent stem cells (iPSCs), which are adult cells that are converted back into naive stem cells capable of becoming nearly any cell in the body.

Cardiologist Timothy Kamp, MD, PhD, a professor in the SMPH Departments of Medicine and of Cell and Regenerative Biology, and director of the UW Stem Cell and Regenerative Medicine Center (see sidebar), shares Gamm’s cautious optimism.

“Stem cell biology is constantly evolving,” Kamp says. “With every new legitimate effort, though, it’ll get easier for the rest of us to

## Stem Cell and Regenerative Medicine Center Galvanizes Stem Cell Research

*by Jordana Lenon*

Since University of Wisconsin-Madison researcher James Thomson, VMD, PhD, and colleagues derived the first human embryonic stem cells 20 years ago, research universities and biotechnology companies around the globe have worked to unlock their vast potential.

Through the work of the UW Stem Cell and Regenerative Medicine Center (SCRMC), UW-Madison has remained at the forefront of the field. Launched in May 2007, the center serves as an intellectual and collaborative hub for a broad-based, interdisciplinary research community. Today, more than 600 scientists and students in almost 100 SCRMC labs

around campus are working, teaching and studying in the field.

The SCRMC encompasses faculty, staff and students across five schools and colleges, 40 departments, and 10 centers and institutes. It is not housed in a single brick-and-mortar building but is a virtual center with investigators across campus. The center operates under the UW-Madison Office of the Vice Chancellor for Research and Graduate Education and UW School of Medicine and Public Health (SMPH). An executive committee of faculty from across campus provides leadership.

Most SCRMC researchers work on much-needed basic science with both embryonic and induced pluripotent stem cells, while others also are exploring

new cell culture techniques, gene editing methods, and advances in preclinical animal research and human clinical trials.

“The growth of stem cell-related research and educational programs on campus over the past two decades has been amazing,” says SCRMC Director Timothy Kamp, MD, PhD, a professor in the SMPH Departments of Medicine and of Cell and Regenerative Biology. “I’m delighted that the SCRMC has helped bring together center members from diverse disciplines to build collaborative projects that are pushing these discoveries forward.”

For more information, see the Stem Cells@20 coverage on UW-Madison’s web site: [news.wisc.edu/stem-cells/](http://news.wisc.edu/stem-cells/)





*A UW-Madison graduate student, Angela Xie, conducts stem cell research.*

get approval from the FDA and our therapies into patients.”

Kamp cites Geron—the first company to get a stem cell trial approved by the FDA—as an example of how each success helps accelerate progress.

“Geron’s final FDA application was more than 20,000 pages long,” Kamp explains. “It took them many years and millions of dollars, but that initial process educated the FDA and provided answers to some previously unanswered questions. And that was great news for the rest of us.”

Kamp is conducting pre-clinical work with colleagues from Duke University and the University of Alabama on a patch made of contracting heart muscle derived from iPSCs. He and his collaborators hope one day these cells can be used to treat patients who lose heart muscle after a heart attack. Another of Kamp’s collaborators, French researcher Philippe Menasché, MD, PhD, recently completed a phase 1 trial that transplanted ESC-derived cardiac progenitor cells into patients with severe heart failure. That therapy seems to be safe, but it’s too early to tell how effective it was in re-muscularizing damaged parts of the heart.



*Jon Odorico, MD (PG '96)*

Diabetes is another cell-based disease in the cross hairs of SMPH researchers. In early 2018, results of the first human trial of a stem cell-derived beta cell replacement therapy were published. Jon Odorico, MD (PG '96)—a professor in the SMPH Department of Surgery who organized the conference at which the results were presented—says while the findings were not a home run, the trial helped blaze an important trail through the FDA. Conducted by the company Viacyte, the trial was the first involving stem cells and a macroencapsulation device designed to protect the transplanted cells from a

patient’s immune system. A second trial is underway in the same patient population (adult patients with type 1 diabetes and hypoglycemia unawareness), and a handful of others are planned, including one through Odorico’s company, Regenerative Medical Solutions, Inc. He hopes to have a product in clinical trials within the next few years.

“A critical mass of experts is involved in this field, and things are moving a lot faster, with more money and more industry involvement,” Odorico says. “Wisconsin has played a leading role in getting the field to this point, and we are poised to take an even more prominent role, nationally and internationally.”

As for Gamm and his patients, the conversation has begun to shift from one of resignation to one that allows for guarded optimism. He recalls a time when there wasn’t much he could offer patients, and while there are still no approved and proven stem cell therapies on the market, his message has changed dramatically.

“It’s great to be able to tell my patients that they are not forgotten,” Gamm concludes. “I can finally tell them that the hope is real.”