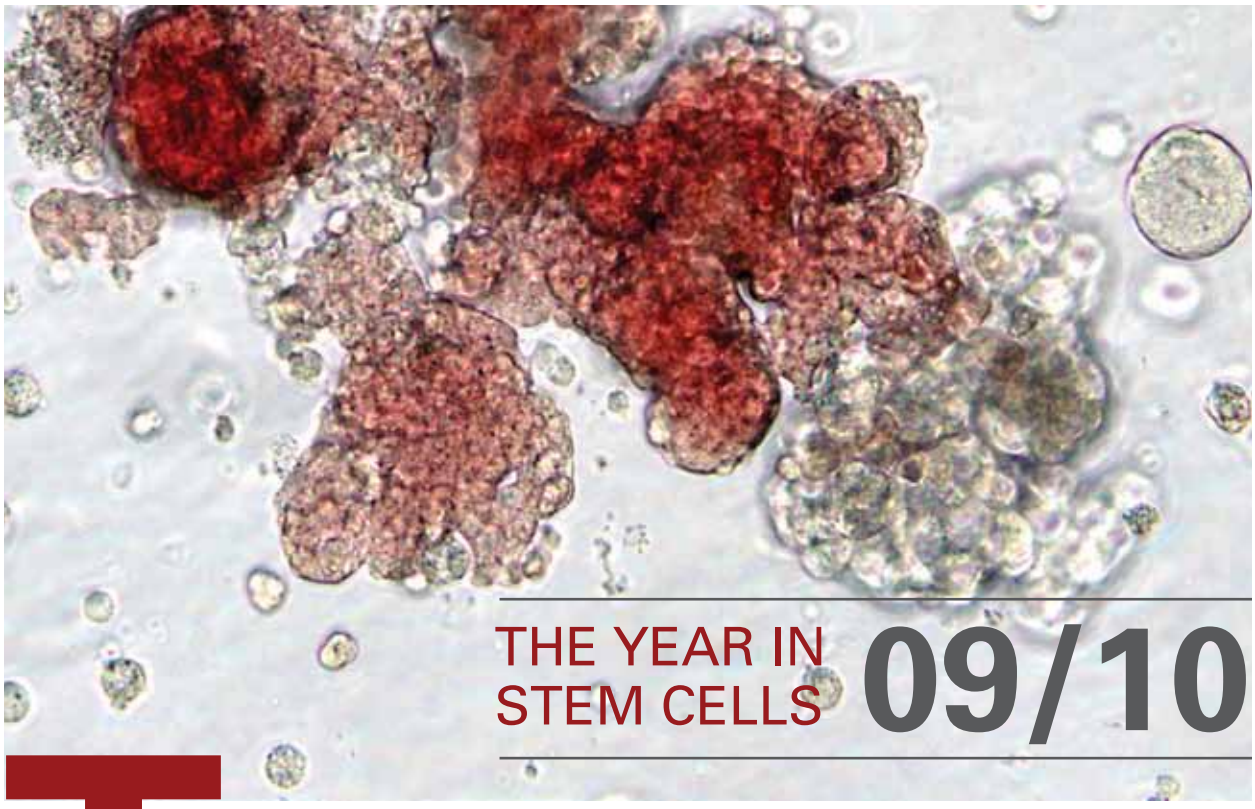
Stem Cell and Regenerative Medicine Center
University of Wisconsin-Madison



THE YEAR IN STEM CELLS 09/10

THE UNIVERSITY OF WISCONSIN-MADISON Stem Cell and Regenerative Medicine Center measures its success in accomplishments.

- Growing retina cells from stem cells, opening the possibility of screening new drugs for eye disease
- Discovering that a single gene is the master regulator that directs stem cells to become all of the various cells in the brain, offering the hope of making cells to treat brain injury
- Transforming stem cells into several kinds of white blood and immune cells, a discovery that could lead to a replacement for bone-marrow transplants

Encompassing 85 researchers from more than 40 departments, the center is dedicated to moving discoveries from the laboratory into patient treatment. This year, researchers received national recognition for their work, ensured widespread access for scientists to critical lines of embryonic and induced pluripotent stem cells, and continued to unravel the mysteries of how stem cells work.

The Stem Cell and Regenerative Medicine Center is pleased to share with you this year's accomplishments that ensure the UW-Madison remains at the forefront of this exciting and promising field.

A research assistant uses a pipette to change media in wells that contain human embryonic stem cells. Photo by Jeff Miller / UW-Madison University Communications.

David Gamm, assistant professor of ophthalmology, above. Photo courtesy of Departments of Ophthalmology and Anatomy.

AUG09

Gamm grows retina cells

A Waisman Center research team successfully grew multiple types of retina cells from two types of stem cells, a discovery announced in the August 24, 2009, edition of the *Proceedings of the National Academy of Sciences*. The study, led by David Gamm, MD, PhD, an assistant professor of ophthalmology and visual sciences in the School of Medicine and Public Health (SMPH), and Jason Meyer, PhD, a SMPH research scientist, suggests cells grown from a patient's own skin may one day be used to repair damaged retinas. In the near future, the discovery will lead to laboratory models for studying genetically linked eye conditions, screening new drugs to treat those conditions and understanding the development of the human eye.

"This is an important step forward for us, as it not only confirms that multiple retinal cells can be derived from human induced pluripotent (iPS) cells using the Wisconsin approach, but also shows how similar the process is to normal human retinal development," Gamm said. "That is quite remarkable given that the starting cell is so different from a retinal cell and the whole process takes place in a plastic dish. … Perhaps this is the way to close the gap between what we know about building a retina in mice, frogs and flies with that of humans."

SEPT09

Slukvin expands stem cell potential

In a discovery that could advance the safety screening of new drugs and could lead to a replacement for bone-marrow transplants, UW-Madison scientists reported in the September 1 edition of *The Journal of Clinical Investigation* a technique to transform embryonic and induced pluripotent stem cells into several types of white blood and immune cells.

Bone-marrow stem cells already are used for drug screening, but the new technique promises to produce large quantities of cells in a dish without requiring cells from donors, said Igor Slukvin, MD, PhD, a SMPH assistant professor of pathology and laboratory medicine based at the Wisconsin National Primate Research Center. Although clinical use is years in the future, cells created through this technique will allow scientists to better study the development and treatment of disease. It could be used to grow specific immune cells to target specific infections, tumors or conditions such as osteoporosis and asthma.

Brenda Ogle, right, an assistant professor of biomedical engineering, holds a rack of media supplements for stem-cell differentiation. Ogle is investigating methods of engineering natural tissues to create blood vessels. Photo by Michael Forster Rothbart / UW-Madison University Communications.

NOV09

Ogle wins NSF Career Award

Stem cells have the potential to develop into many cell types, yet that ability can frustrate researchers trying to study them in their original state. Mechanical, electrical and chemical stimuli can induce differentiation, said Brenda Ogle, PhD, assistant professor of biomedical engineering in the College of Engineering. She received a 2009 National Science Foundation Career award for her work in developing stem cell analysis tools that offer researchers flexibility to study individual cells, multicellular entities and small tissue-engineered constructs.

"Often we don't realize we're inducing these changes, and so the cells have to be constantly monitored," Ogle said. "The large numbers of cells to be analyzed, and the sensitivity of stem cells to external stimuli make this a difficult task."

JAN10

Kimble discovers new way to look at stem cell changes

A new way to look at how stem cells leave their original state and differentiate into other cells was presented by Judith Kimble, PhD, professor of biochemistry and Howard Hughes Medical Institute investigator in the College of Agricultural and Life Sciences, in the January 11 online edition of *Proceedings of the National Academy of Sciences*. Working with scientists from the University of California-Irvine, Kimble and her UW-Madison team discovered a new model of regulating the transition from stem cell to mature cell in the roundworm *Caenorhabditis elegans*.

"Looking in vivo at how a stem cell is controlled to go from one state to another is really important if you want to intervene or engineer," Kimble said. "This provides us a new way of thinking about it." The regulation is important because a disruption in the balance between stem cell and mature cell could lead to tumors or the loss of the ability to maintain healthy tissue. The work could help understand the development of leukemia and other cancers.

Fellowship winners named

Two graduate students received the 2010 Stem Cell and Regenerative Medicine Center Fellowship for 2010. Wei Shen from David Gamm's laboratory in ophthalmology received the postdoctoral fellowship. Maria Mikedis from Karen Downs' laboratory in anatomy received the graduate fellowship award. Each award provides two years of funding for the winners.

Heart healthy advance recognized

The American Heart Association in January named the UW-Madison discovery that proved functional heart muscle cells can be produced from genetically reprogrammed skin cells one of the most important research advances for cardiovascular disease and stroke in 2009.

Tim Kamp, MD, PhD, a SMPH professor of medicine, and stem cell pioneer James Thomson, DVM, PhD, an anatomy professor and director of regenerative biology at the Morgridge Institute for Research, led the team that demonstrated how induced pluripotent stem cells could be differentiated into contracting cardiac cells. The discovery suggests that a patient's own skin cells could someday be used to repair damaged heart tissue.

FEB10

Zhang lab shows all stem cells are not equal

Induced pluripotent stem cells (iPS) perform less efficiently than their embryonic counterparts, a UW-Madison team reported February 15 in the *Proceedings of the National Academy of Sciences*. The study from Su-Chun Zhang's Waisman Center laboratory compared the ability of induced and embryonic cells to differentiate into brain cells.

"The finding that iPS cells are less predictable means there are more kinks to work out before they can be used reliably in a clinical setting," said Zhang, MD, PhD, a SMPH anatomy professor. "Embryonic stem cells can pretty much be predicted," he said. "Induced cells cannot." Scientists see advantages in using iPS cells, including that they do not need to be derived from early stage human embryos.

New stem cell bank emerges

WiCell, host of the former National Stem Cell Bank (NSCB), has transitioned the distribution of the 20 human embryonic stem cell (hESC) lines formerly available through the NSCB to the Wisconsin International Stem Cell Bank (WISC Bank). It also continues to carry its previously banked seven induced pluripotent stem cell lines and six genetically modified hESC lines.

"WiCell has developed a unique track record in developing the expertise, protocols and quality assurance systems for the optimal growth, culture, testing, storage and distribution of these finicky cells," said Executive Director Erik Forsberg, PhD.

APR10

Stem cell lines reapproved

The National Institutes of Health in April reapproved federal funding for research using James Thomson's original embryonic stem cell line, H9, the most used and cited in scientific research. Three other original Wisconsin lines, H7, H13 and H14, also were reapproved in April, following a January reapproval of the H1 line.

Without reapproval, millions of dollars of time-consuming research spent studying the cell lines would have ended or been set back for years.

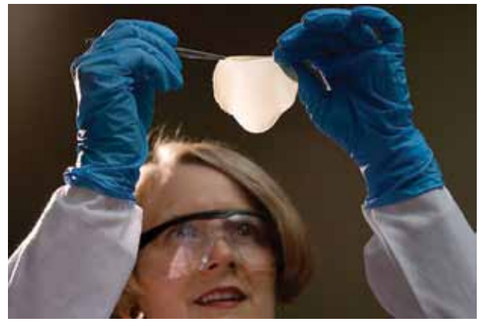
Scientists meet in Madison

World leaders in stem cell research addressed key hurdles to stem cell therapies April 21 at the fifth annual Wisconsin Stem Cell Symposium, "The Road to Stem Cell Applications: Bioprocessing Safety and Preclinical Evaluation," in Madison.

Featured speakers included Raymond Lund of the Oregon Health Science University, Brent McCright of the U.S. Food & Drug Administration, Jane Lebkowski of Geron Corporation, Lynn Allen-Hoffman of Stratatech Corporation and UW-Madison, and Derek Hei, Linda Hogle, Tim Kamp, Amish Raval and Su-Chun Zhang of UW-Madison. They addressed questions such as key issues the Food and Drug Administration will consider when reviewing applications to move cell therapies into early-stage human clinical trials and what safety issues need to be addressed prior to human clinical trials.

New production assistance available for cellular therapies

The Waisman Clinical Biomanufacturing Facility announced its launch of Production Assistance for Cellular Therapies (PACT) during the Wisconsin Stem Cell Symposium. The contract award from the National Heart, Lung and Blood Institute focuses on providing assistance for cellular therapy translational research and the manufacture of cellular therapy products. PACT programs are located at only five facilities in the country.



Professor of pathology Lynn Allen-Hoffmann holds a piece of StrataGraft at the Stratatech Corporation in the UW-Madison's University Research Park. Based on her university research, StrataGraft is a proprietary human skin cell line that forms a fully stratified multilayered human tissue with the physical strength and biological characteristics of intact human skin. Allen-Hoffman founded Stratatech. Photo by Jeff Miller/ UW-Madison University Communications.

JUNE 10

Wisconsin, California agree to collaborate

Governor Jim Doyle and the chairman for the California Institute for Regenerative Medicine signed a symbolic agreement June 17 to encourage collaboration between Wisconsin and California stem cell researchers.

"Wisconsin and California share a strong past and a bright future in stem cell research and technology development," Doyle said at the signing, held during the International Society for Stem Cell Research annual meeting in San Francisco. "This agreement builds on our common strengths and commits to continuing collaboration that will lead the future of innovation, grow our economies and take lifesaving technologies from our laboratories to the marketplace."

Governor Jim Doyle speaks to an audience of biotechnology executives, university administrators and faculty scientists at the Biotechnology Center. Doyle pledged his support to help Wisconsin's biotechnology industry and to blunting legislative attacks on stem cell science. Photo by Jeff Miller / UW-Madison University Communications.

The agreement will make it easier for researchers in California and those at UW-Madison and other Wisconsin scientists to obtain joint funding to broaden the potential pool of expertise that can be applied toward research in any specific area.

"This partnership is great news for those living with some of today's most debilitating diseases," California Governor Arnold Schwarzenegger said. "This revolutionary science has the potential to save millions of lives, and this collaboration will help to bring some of the best minds together to advance stem cell research."

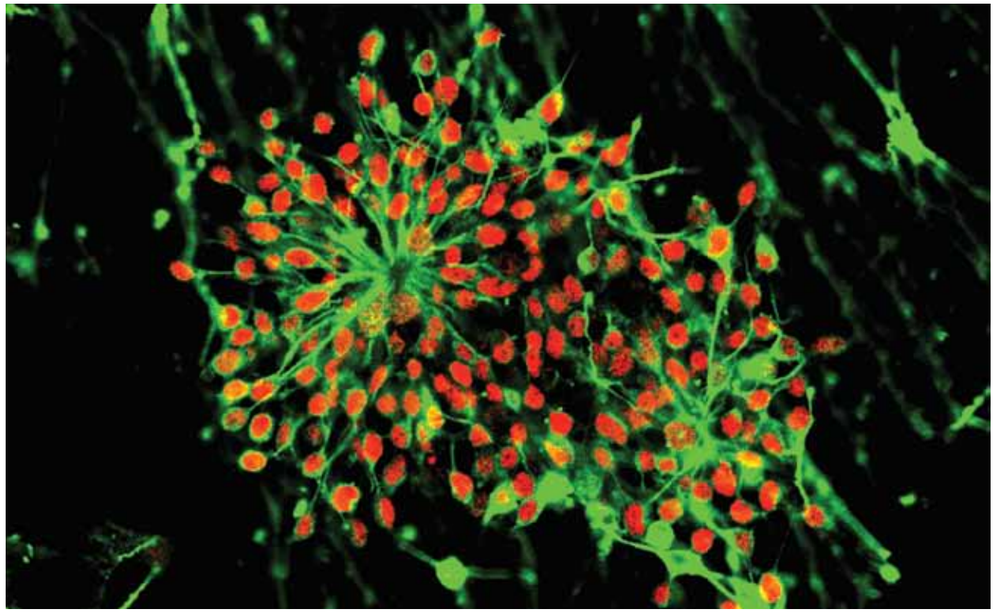
JULY 10

Team identifies brain stem cell regulator

A team of UW-Madison scientists reported in the July 1 *Stem Cell Journal* that a single gene seems to be the master regulator of human brain development, guiding undifferentiated stem cells down tightly defined pathways to become all types of brain cells.

The discovery from the lab of Waisman Center neuroscientist Su-Chun Zhang, MD, PhD, a SMPH anatomy and neurology professor, is a first step toward building customized brain cells in the lab dish for transplant and for modeling diseases of the brain and central nervous system.

The new work reveals the pervasive influence of Pax6 on the neuroectoderm, a structure that arises early in embryonic development and that churns out the two primary forms of brain cells — neurons and glial cells — and the hundreds of cell



Microscopic view of neural cells generated from iPS cells. Photo by Su-Chun Zhang/Baoyang Hu.

subtypes that make up the human brain. "This is a well-known gene," Zhang told the Milwaukee Journal Sentinel. "It's been known for a long time from work in mice and other animals, but what Pax6 does in human development isn't very well known." The finding may help explain why the human brain is larger and, in many respects, more advanced than what is observed in other species.

Generation Acceleration introduces middle school students to stem cells

Two dozen Wisconsin and Alabama middle school students learned to harvest stem cells, perfect their molecular biology lab skills and watch cells that had differentiated into beating heart cells during Generation Acceleration, a summer camp run by the Morgridge Institute for Research, the nonprofit biomedical research institute affiliated with the University of Wisconsin-Madison.

"We want to educate and train the next generation of scientists," Rupa Shevde, director of outreach, told the Milwaukee Journal Sentinel. "Studies have shown when you engage students with science at a younger age, they are more likely to explore a variety of careers later."

Eighth-grader Mariah Ortega-Carr said students attended weekly Saturday meetings to prepare for camp. "I wanted to come here because I knew stem cells are a controversial topic and I wanted to know why some people want to use stem cells and some don't," she said.

Sources: University Communications, UW Health, Milwaukee Journal Sentinel, California Institute for Regenerative Medicine

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Our Mission

The UW–Madison Stem Cell and Regenerative Medicine Center (SCRMC) is an umbrella organization operating under the School of Medicine and Public Health and the Graduate School. The center provides a central point of contact, information and facilitation for all stem cell research activities on campus.

The center's mission is to advance the science of stem cell biology and foster breakthroughs in regenerative medicine through faculty interactions, research support and education.

Our Goals

- Maintain UW-Madison as the leader in stem cell and regenerative medicine research and application
- Foster increased SCRMC communication within campus and beyond its borders
- Support SCRMC research: basic, translational, clinical, bioethics and public policy
- Develop educational, training and outreach programs
- Enhance philanthropic support

Support Stem Cell Research

You can play a vital role in the future of stem cell research. Your investment in the Stem Cell and Regenerative Medicine Center will yield rewards that will change the future of medicine and health care.

Your gift can support

- basic, pre-clinical or clinical research;
- education and training for students and post-doctoral fellows, and/or
- an unrestricted fund that gives the center maximum flexibility to take advantage of new opportunities.

For More Information

Visit our Web site at **www.stemcells.wisc.edu.**

Please contact Barb McCarthy at 608-265-5891 or barb.mccarthy@supportuw.org to learn how you can support stem cell research and regenerative medicine.

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