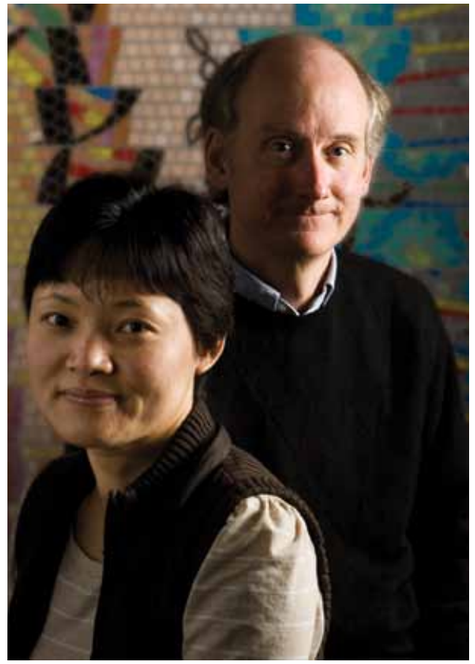
Stem Cell and Regenerative Medicine Center
University of Wisconsin-Madison

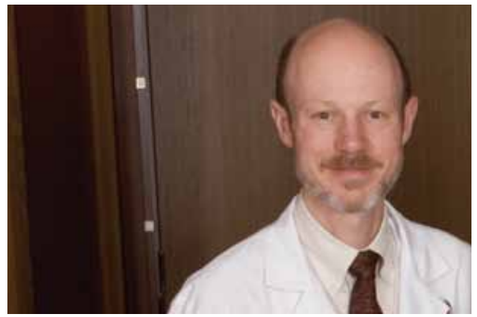
THE YEAR IN STEM CELLS 08/09

As scientists continue to unearth the potential of human embryonic and induced pluripotent stem cells, the University of Wisconsin-Madison remains at the forefront of new discovery. In the last year, University researchers have won national awards and made research breakthroughs that are changing the course of stem cell science and bringing us closer to the treatment for devastating diseases, including ALS, heart failure, blood cancers and Parkinson's disease.

The University of Wisconsin-Madison has been a leader in stem cell research since the mid-1980s, when scientists discovered how to use mouse embryonic stem cells to create the first transgenic mice. In 1995, 1998 and 2007, the University made world headlines as Professor James Thomson and his team were the first to isolate embryonic stem cells from nonhuman primates, the first to isolate human embryonic stem cells and the first to produce induced pluripotent stem cells from adult human skin cells.

The Stem Cell and Regenerative Medicine Center is pleased to share our recent groundbreaking research that helps ensure the UW-Madison remains at the forefront of this exciting and promising field. Here are some of our stories.





Junying Yu, assistant scientist in the Primate Research Center, and James Thomson, professor in the School of Medicine and Public Health, became the first scientists to reprogram skin cells to create cells indistinguishable from embryonic stem cells. Photo by Bryce Richter / UW-Madison University Communications.

Timothy Kamp, above, cardiologist and professor in the School of Medicine and Public Health at the UW-Madison, was awarded the Schuster Prize for his research on ion channels and the use of stem cells to create heart cells. Facing page, heart cell derived from iPS cells. Courtesy of Jianhua Zhang and Timothy Kamp.

APR08

Leading Scientists Attend Annual Wisconsin Stem Cell Symposium

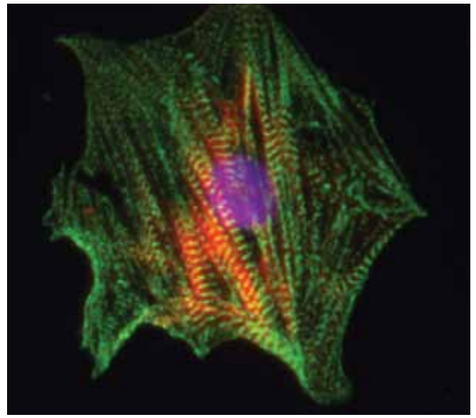
Some of the top names in world stem cell research convened in Madison, Wisconsin, for the Third Annual Wisconsin Stem Cell Symposium. Coordinated by the University of Wisconsin Stem Cell and Regenerative Medicine Center and the BioPharmaceutical Technology Center Institute, the symposium considered the primordial molecular controls of stem cells that could be of clinical significance. Stem cell controls in the embryo, stem cells and cancer and the molecular controls of regeneration were among the topics discussed.

Thomson Elected to the National Academy of Sciences, Receives Other Awards

UW-Madison stem cell pioneer James Thomson was elected in April to the National Academy of Sciences. In 1998, Thomson became the first scientist to isolate and culture human embryonic stem cells. A John D. MacArthur Professor of Anatomy in the UW School of Medicine and Public Health, he continues to study the basic biology of how stem cells can become any cell type in the body. In 2007, Thomson and Junying Yu of the Genome Center of Wisconsin and the Wisconsin National Primate Research Center became the first scientists to reprogram human skin cells to create cells indistinguishable from embryonic stem cells.

Thomson and researcher Shinya Yamanaka from Japan's Kyoto University were included in the 2008 *"Time Magazine 100."*

Thomson also was named director of regenerative biology at the UW-based Morgridge Institute for Research.



"Few people doubt that embryonic stem cells may offer extraordinary opportunities to treat or prevent disease, but few deny either that the politics surrounding the idea has often seemed as complex as the science," Ian Wilmut, who cloned the sheep Dolly using stem cells, reported in *Time.* "All that may have changed last year with the announcement that it was possible to give adult human cells many of the characteristics of embryonic stem cells, avoiding entirely the issue of whether embryos would be destroyed in the process."

In December, Thomson received the 2008 Massry Prize for his work with embryonic and induced pluripotent stem cells. The Meira Massry Prize was established in 1996 to recognize outstanding contributions to the biomedical sciences and the advancement of health. In accepting the prize, Thomson predicted that, within the next 10 years, scientists would be able to make all clinically relevant cells in the body and that getting them into the body in a physiologically useful form would present the biggest challenge and involve every discipline in medicine.

MAY08

Palacek Preserves Stem Cells

Sean Palacek, a UW-Madison chemical and biological engineer, developed an improved way to preserve stem cells. His results were published in the May 2008 issue of the *Biophysical Journal*. Palacek worked closely with biologists to find a method to grow and maintain stem cells so they remain robust, uncontaminated and ready to go to work in a variety of applications — from maintaining long-term cultures to growing elaborate cell and tissue 3-D structures.

Kamp Wins Inaugural Schuster Prize

Timothy Kamp, MD, PhD, a professor of medicine and physiology, was awarded the inaugural Schuster Prize for excellence in advancing cardiovascular medicine in the School of Medicine and Public Health. Kamp's research focuses on ion channels and the use of stem cells to create heart cells. Benjamin Schuster, a UW-Madison alumnus, is the retired medical director of the Kettering Cardiovascular Institute in Dayton, Ohio.

"The Schuster Prize recognizes the work of many students, trainees and researchers working in my lab to advance our understanding of how the electrical system in the heart works and what goes wrong in arrhythmias and heart failure," Kamp said. "Additionally, our research over the last decade has pioneered the use of stem cells as a model system to generate human heart cells both for research applications and for pilot studies of cardiac regeneration of injured or failing hearts."

Rural Wisconsin high school students, above, participate in the Summer Science Camp hosted at the WiCell Research Institute at University Research Park. Photos by Jeff Miller / UW-Madison University Communications.

JUL08

High School Students Explore Stem Cells

Rural Wisconsin high school students assembled at the WiCell Research Institute to study human embryonic stem cells. The students had hands-on experience in their four days at the Summer Science Camp, where they worked with WiCell scientists and researchers from the University of Wisconsin Stem Cell and Regenerative Medicine Center.

AUG08

$8.9 million Project Studies Stem Cell Secrets

A team of UW-Madison researchers received an $8.9 million, five-year grant from the National Institute of General Medical Sciences (NIGMS) to study why stem cells can be reprogrammed into any other body cell while other cells cannot.

The team includes researchers from chemistry, the School of Medicine and Public Health, the Wisconsin National Primate Research Center, the Genome Center of Wisconsin, the Morgridge Institute for Research and the Medical College of Wisconsin. The team will study how cells decide to exit a pluripotent state to become a certain cell type and how, when they're reprogrammed, they return to a pluripotent state.

SEPT08

Madison Hosts World Stem Cell Summit

The World Stem Cell Summit convened September 21-23 in Madison, Wisconsin. Bringing together stem cell experts from around the world, the summit attracted scientists, clinicians, patients and patient advocacy groups, business leaders, entrepreneurs, students, teachers, journalists, bioethicists, politicians and the general public.

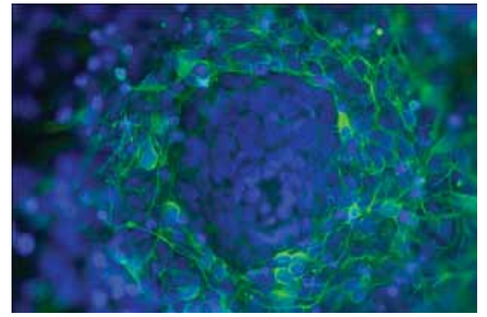
Discussions explored a range of topics, including the new business of stem cell research, the ethics of embryonic stem cells and the future of induced pluripotent cells. Drug testing, gene therapy, cell replacement, tissue engineering and stem cell advances related to patient care also were considered.

Gov. James Doyle, Former Governor Tommy Thompson, James Thomson, Alta Charo, a UW professor of law and bioethics and Peter Kiernan from the Christopher and Dana Reeve Foundation gave keynote addresses.

Engineered Stem Cells Slow ALS in Rats

UW-Madison scientists published work in the September issue of *Molecular Therapy* showing they had successfully used adult stem cells from bone marrow to deliver a nurturing growth factor to atrophied muscles, slowing the progression of amyotrophic lateral sclerosis (ALS), or Lou Gehrig's disease, in rats. The work could lead to treatments for a now untreatable disease, though years of research will be needed before it would be ready for humans.

UW-Madison associate scientist Masatoshi Suzuki, DVM, PhD, of the Waisman Center led the study, which built on previous work showing how motor neurons, the critical cells that connect muscles to the central



Madison was host to the 2008 World Stem Cell Summit, top. "People need to know that stem cells offer hope to millions of patients, just like me," said attendee Richard Gaskin, who was paralyzed after a shooting in 1987. On his right is stem-cell advocate Sabrina Cohen. Photo by Patrick Burly, for the World Stem Cell Summit.

Neural cells, above, from human embryonic stem cells, are used to understand how motor neurons develop and die in ALS. Anatomy professor and Co-director of UW-Madison's Stem Cell and Regenerative Medicine Center Clive Svendsen and UW-Madison associate scientist Masatoshi Suzuki have successfully used adult stem cells from bone marrow to deliver a nurturing growth factor to atrophied muscles, slowing the progression of ALS in rats. Photo by C. Svendsen and A. Ebert, UW-Madison

nervous system, can be protected by stem cells that ferried a key growth factor, glial cell line-derived neurotrophic factor (GDNF). Suzuki and Clive Svendsen, PhD, previously had shown that transplanting neural stem cells to release the growth factor into the spinal cord could protect motor neurons that degenerate in an ALS rat model. The motor neurons, however, still did not effectively connect with the muscles that waste away due to ALS. The new study used the same strategy to pump GDNF directly to the muscle, increasing the number of neuromuscular connections and motor neurons in the spinal cord and delaying progression of the disease.

OCT08

Researchers receive Parkinson's Grant

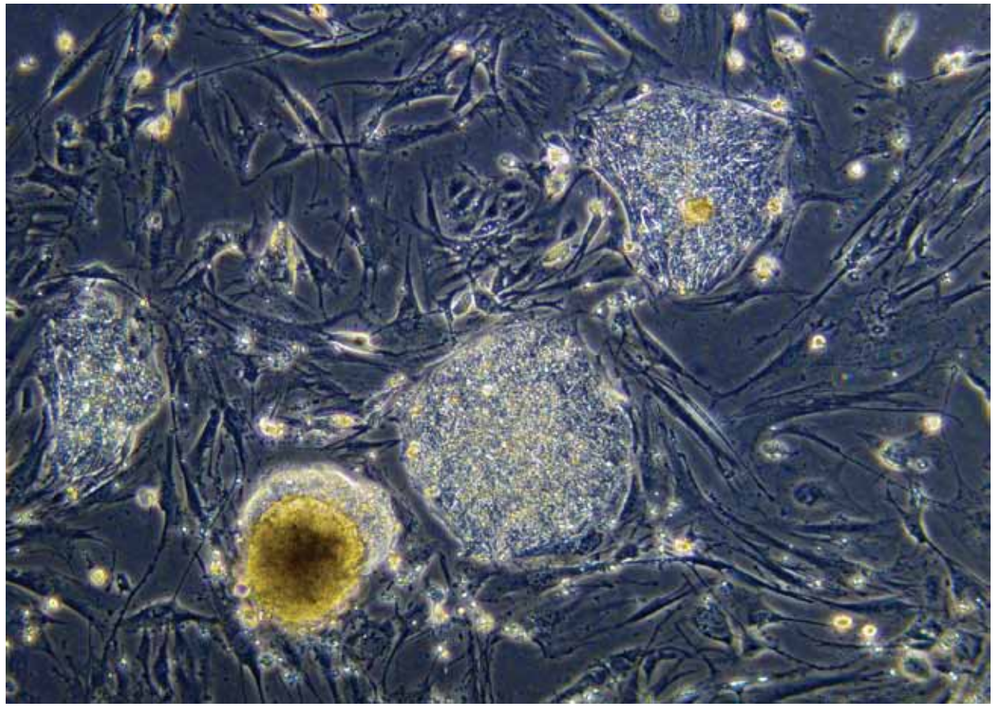
UW-Madison scientists Marina Emborg and Su-Chun Zhang have been awarded a grant from the Parkinson's Disease Foundation to grow and transplant dopaminergic neurons from rhesus-derived iPS cells into monkeys with Parkinson's disease. Emborg and collaborators James Thomson, Clive Svendsen and Zhang previously conducted a pilot study to assess the transplanted cells' viability and safety in monkeys. Results suggested that differentiated human embryonic stem cells provoked an immune response that adversely affected dopaminergic characteristics and survival. The new study will use a personalized medicine approach using iPS cells derived from monkeys. The investigators are collaborating to discover how to direct stem cells into becoming dopaminergic neurons in an effort to treat Parkinson's disease.

NOV08

Human Embryonic Stem Cell Research Celebrates 10th Anniversary

The possibility that all-purpose stem cells could be used to treat human disease arrived 10 years ago, when the November 1998 journal *Science* published "Embryonic Stem Cell Lines Derived from Human Blastocysts." James Thomson, a UW-Madison developmental biologist, showed that the cells, which exist for only a fleeting moment before they become one of the 220 types of cells in the human body, could be controlled in the laboratory. The work was hailed as a biomedical coup, which may revolutionize transplant therapy by making unlimited amounts of cells of all types available for transplant, transform drug discovery and provide a window into the earliest stages of human development.

In the following decade, scientists have directed blank-slate stem cells to become blood cells, neurons and beating heart cells. Stem cells and their derivatives are used in industry as high-throughput screens to test drugs for efficacy and toxicity. Stem cell work has led to dozens of UW-Madison discoveries, the establishment of the Stem Cell and Regenerative Medicine Center, and the creation of hundreds of new jobs.



DEC08

Patient-derived Induced Stem Cells Retain Disease Traits

UW-Madison scientist Clive Svendsen and colleagues reported in the December issue of the journal *Nature* that they had genetically reprogrammed skin cells from a patient with spinal muscular atrophy to create cells with the hallmarks of the devastating neurological disease.

The disease-specific stem cells give scientists an unparalleled opportunity to watch the course of a disease unfold in a lab dish, marking an enormous step forward in the study and development of new therapies for genetic diseases. The work was a collaboration between the UW-Madison and the University of Missouri-Columbia. Spinal muscular atrophy is the most common cause of genetic infant mortality.

The induced pluripotent stem cells allow scientists to replay the disease repeatedly in a lab dish to understand the earliest steps in the disease process.

"If we start to understand more of the mechanism of why the motor neurons specifically affected in the disease are dying, then potentially new therapies can be developed to intervene at particular times early in development," said UW-Madison researcher Allison Ebert, the study's lead author. The approach also could pave the way for modeling other genetic disorders, such as Huntington's disease.

Colonies of undifferentiated stem cells, above, grow on a "feeder layer" in James Thomson's lab. Photo,UW-Madison

Wisconsin State Journal Honors Cezar

UW-Madison stem cell scientist Dr. Gabriela "Gabby" Cezar ('02 PhD ALS), an assistant professor in Animal Sciences and at the Molecular and Environmental Toxicology Center, was named among "Eight Who Had an Eventful 2008" by the *Wisconsin State Journal*.

After studying tissue samples from 20 autistic patients, Cezar is ready to publish her findings on how the brains of people with autism are different. Cezar also is working with Professor Fred H. Gage from the Salk Institute for Biological Studies in La Jolla, California, to create brain cells with the characteristics of amyotrophic lateral sclerosis (ALS). The findings will be used to help screen drugs to better treat ALS patients.

Stemina Biomarker Discovery, the Madison biotech company Cezar co-founded, is ready to release its first product. The test will determine whether newly developed drugs will cause birth defects.

Gabriela "Gabby" Cezar, above, an assistant professor of animal sciences at the UW-Madison, was named among "Eight Who Had an Eventful 2008" by the *Wisconsin State Journal*. Photo by Jeff Miller / UW-Madison University Communications.

Lab manager Jessica Antosiewicz-Bourget, left, in researcher James Thomson's lab at the UW-Madison. Photo by Jeff Miller/UW-Madison, University Communications.

Stem Cell and Regenerative Medicine Center Names Fellowship Winners

The Stem Cell and Regenerative Medicine Center announced five winners in its 2008 Fellowship Competition.

Nathaniel Pope from Emery Bresnick's laboratory, pharmacology, received an honorary graduate fellowship.

Graduate fellowships went to:

- Hongda Li from Qiang Chang's laboratory, genetics
- Josh Selekman from Sean Palecek's laboratory, biochemical engineering

Post-doctoral fellowships were awarded to:

- Sheeny Lan from William Murphy's laboratory, biomedical engineering
- Fang Wan from Aseem Ansari's laboratory, biochemistry

JAN09

Mass Spectrometry Allows Deeper Look into Stem Cells

Mass spectrometry, the new "can-do" super machine of stem cell research, allowed Josh Coon, assistant professor of chemistry and biomolecular chemistry, to identify specially modified proteins that help embryonic stem cells turn into any cell type in the body. In findings published in the January 27 issue of the *Proceedings of the National Academy of Sciences*, Coon identified phosphoproteomes using the highly versatile mass spectrometer, which allows scientists to sift through thousands of different molecules in complex biological soups.

All NIH Stem Cell Registry Lines Deposited in Madison

With the deposit of two human embryonic stem cell lines from a Swedish biotechnology company, the U.S. National Stem Cell Bank (NSCB) has received all 21 stem cell lines from the six providers listed on the National Institutes of Health (NIH) federal registry.

Scientists have access to 16 lines that have completed the NSCB's extensive quality control process. The NIH established the country's first national stem cell bank at the WiCell Research Institute, a private, nonprofit supporting organization to the UW-Madison, in September 2005. Its mission is to obtain, characterize and distribute the 21 embryonic stem cell lines that, when approved, can be used in U.S. federally funded research.

The availability of a variety of human embryonic stem cell lines is critical to advancing the field, said Derek Hei, a UW-Madison researcher and leader of the NSCB. "Now we'll be able to distribute these lines to the worldwide research community," he said. "We'll also be able to generate data unique to these lines that is valuable to the advancement of stem cell research."

WiCell also has begun its own bank, the WiCell International Stem Cell Bank, to study and distribute stem cells that cannot be offered through its current contract with the NIH. It allows WiCell to offer induced pluripotent and other stem cells through a tested operation with an experienced staff, said Erik Forsberg, executive director of WiCell.

FEB09

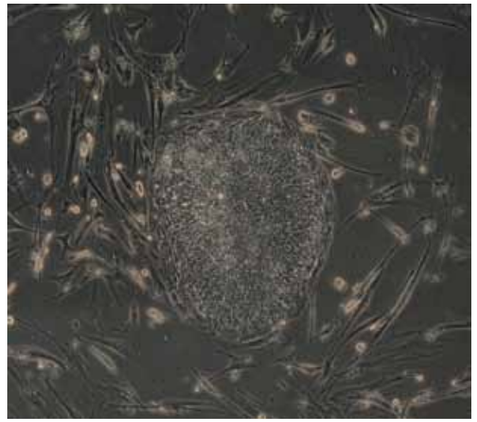
Heart Cells Formed From iPS Cells

UW-Madison scientists published results in *Circulation Research*, a journal of the American Heart Association, showing that induced pluripotent stem cells can be turned into the specialized cells that make up heart muscle.

Timothy Kamp, professor in the School of Medicine and Public Health, and his research team had previously shown that embryonic stem cells could develop into the three major kinds of heart cells. Their new work shows that skin cells that have been turned into induced pluripotent cells (iPS) also can similarly become heart cells.

"It's an encouraging result because it shows that those cells will be useful for research and may someday be useful in therapy," said Kamp, who also is a UW Health cardiologist. "If you have a heart failure patient who is in dire straits—and there are never enough donor hearts for transplantation—we may be able to make heart cells from the patient's skin cells and use them to repair heart muscle. That's pretty exciting."

This work is preliminary, he said. Reprogramming skin cells to an embryo-like state involves using a virus, which could possibly cause cancer. Any treatments from reprogrammed skin cells probably will come after new methods are devised to induce the iPS cells.



Above, cells that have been induced into a pluripotent state—a condition that is essentially the same as that of embryonic stem cells — can be turned into heart muscle blood cells. Photo courtesy of Junying Yu / UW-Madison.

MAR09

Scientists Develop Safer iPS Cells

UW-Madison scientists successfully created induced human pluripotent stem (iPS) cells free of viral vectors and exotic genes – removing key safety concerns about the use of iPS cells in therapeutic settings.

The study, led by geneticist Junying Yu in James Thomson's lab, was reported in the March 26 online issue of the journal *Science*. Instead of using a virus to ferry reprogramming genes into adult cells, the groups work uses a plasmid. The plasmid and the genes it carries do not integrate into the genome of the iPS cells.

Timothy Kamp, Clive Svendsen, James Thomson, U.S. Representative Tammy Baldwin, Derek Hei and Alta Charo, above, White House.

Blood Cells Formed From iPS Cells

Different types of blood cells can be created from iPS cells, UW-Madison scientist Igor Slukvin showed in a paper published in the March 2 issue of the journal *Stem Cells.* Slukvin previously had developed blood cells from embryonic stem cells. Slukvin and Peiman Hematti, another UW-Madison scientist, are researching the potential of using iPS cells as a source for expanded blood products and bone marrow transplants. Bone marrow transplants are among the most effective treatments for blood cancers such as leukemia, lymphoma and multiple myeloma, but not enough matched bone marrow donors are available to meet patient needs.

Obama Ends Stem Cell Ban

On March 9, 2009, University of Wisconsin researchers James Thomson, Clive Svendsen, Timothy Kamp and Derek Hei and R. Alta Charo, professor of law and medical ethics, witnessed President Barack Obama's signing of the executive order that ended a ban on the use of federal funds for disease research that is in any way connected to human embryos.

"With this new executive order comes the possibility that we may now explore all of the most promising avenues toward understanding, and even curing, our most dread diseases," said Charo, who also is a member of the Obama-Biden Transition Project's Health and Human Services Review Team.

Stem Cell and Regenerative Medicine Center
University of Wisconsin-Madison

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
- 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@uwfoundation.wisc.edu to learn how you can support stem cell research and regenerative medicine.

UNIVERSITY OF WISCONSIN FOUNDATION
1848 University Avenue
PO Box 8860
Madison, WI 53708-8860

608. 263. 7003

uwf@uwfoundation.wisc.edu

www.uwfoundation.wisc.edu