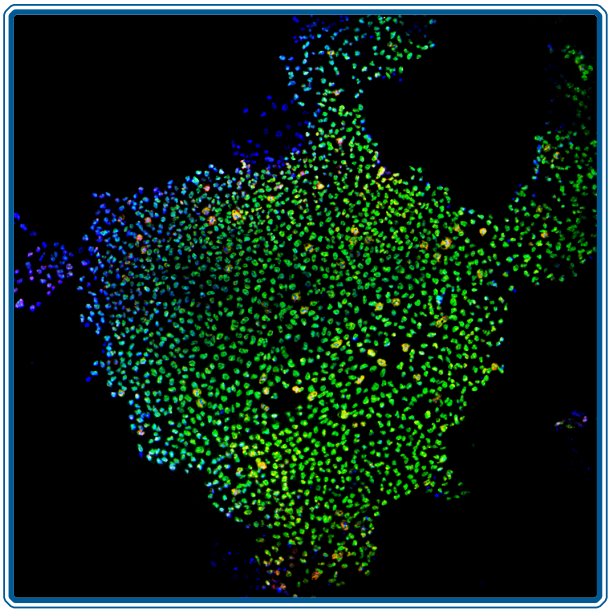
The mission of the UW Stem Cell and Regenerative Medicine Center is to advance the science of stem cell biology and foster breakthroughs in regenerative medicine through faculty interactions, research support and education.

Fall 2010

SCRMC Notes



Induced pluripotent stem cells.
(Photo: courtesy James Thomson)

Inside this issue:

From the Director	1
Featured Researcher: Qiang Chang	2
Year-in-Review	5
SSSCR News	6
Fellowships Available	7
CampusSC Lab Meetings Move to WID	7
WiCell Update	7
Summer Science Camp	8
Reaching Out	9
SCRMC Member Services	10
SCRMC/ICTR Pilot Grants	10
Spring BTCI Stem Cell Symposium	11
Executive Committee Elections	11
2nd Faculty& Staff Retreat	12

FROM THE DIRECTOR

Welcome to your Fall 2010 SCRMC newsletter. Although you are undoubtedly saturated with things to read, you need to read this newsletter to learn about the SCRMC activities, research breakthroughs, and perhaps most importantly opportunities for funding as well as other resources to support your research.

Surprises are not infrequent in stem cell research, but the preliminary federal injunction on federal funding of human embryonic stem cell research issued August 23 by Judge Royce Lamberth truly caught researchers and administrators off guard. The SCRMC worked with campus leaders, SCRO committee, WARF, and the Governor's office to provide information on the adverse impact the federal injunction had on stem cell research as a whole and specifically at UW. Thank you to all SCRMC members who provided specific information for the amicus (friend-of-the-court) brief filed by several groups. The situation has been confusing and difficult to predict; we have dedicated a new page on our website to provide the latest information. Fortunately, the federal appeals court has put a stay on the preliminary injunction, and we are back to the situation as it was before the injunction. However, the story is not over, as Judge Lamberth is now hearing the case and legal experts suggest an injunction is likely to follow some months in the future. Clearly, our work is not over in educating the public and our elected officials about this critical area of research. We will intensify our efforts at public outreach, led by **Jordana Lenon**, SCRMC university relations specialist.

New this year is the initiation of our visiting speaker series the first Tuesday every month during the academic year. Joseph Wu, assistant professor of medicine and

(continued on page 5)

Number 3

FEATURED RESEARCHER



After moving to the United States from China, Chang studied neuroscience at the University of Pennsylvania School of Medicine, neuroregeneration at Harvard University and epigenetic gene regulation at the Whitehead Institute/ Massachusetts Institute of Technology. Chang now serves as the co-director of the Rodent Models Core at the Waisman Center and an assistant professor of genetics and neurology on campus. *(Photo by Marianne English)*

Qiang Chang

by Marianne English

Growing up in Beijing, China, **Qiang Chang** was determined to one day tackle biology's toughest questions—a goal unchallenged by two-hour bike rides to school and then later moving thousands of miles away to study in a foreign country.

Now a UW-Madison assistant professor of genetics and neurology and co-director of the Rodent Models Core at the Waisman Center, Chang still carries similar resolve. After receiving a bachelor of science in biochemistry and molecular biology from Peking University in his hometown of Beijing, China; a Ph.D from the University of Pennsylvania School of Medicine; and postdoctoral appointments at Harvard University and Massachusetts Institute of Technology, Chang reminisces about the ideas that inspired him years ago.

"I was interested in how the brain works," he said, explaining his drive to pursue a post-graduate degree. "I thought it was fascinating, going down to the basic philosophical question: Can the system understand itself?"

Today Chang studies DNA methylation-dependent epigenetic regulation of brain functions. The focus of his research program revolves around MeCP2 (methyl CpG binding protein 2), a key player in recognizing and interpreting epigenetic marks of DNA methylation. Mutations in the *MECP2* gene cause Rett syndrome (RTT), a severe autism spectrum disorder mostly found in females.

Prior to arriving at UW-Madison, Chang sought training in neuroscience as a graduate student at the University of Pennsylvania where he analyzed the development and function of motoneurons and neuromuscular junctions. The formation, maintenance and remodeling of neuronal connections throughout an individual's life piqued Chang's interest—he wanted to understand how environmental stimuli-induced changes in neurons affect a whole organism's ability to survive and thrive.

After earning his Ph.D and completing a 10-month postdoctoral appointment at Harvard studying neuroregeneration, Chang realized he needed a more powerful toolbox to accomplish his future research goals.

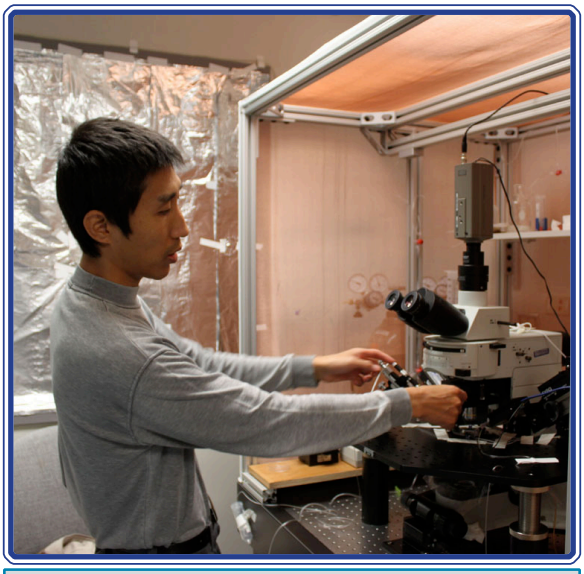
"I think the limitation of a biologist is often what he can do with his existing toolbox, not necessarily what biological questions he wants to answer," Chang said, explaining that scientific progress sometimes depends

more on techniques than ideas.

Chang's desire to expand his skill set brought him in 2001 to the lab of Rudolf Jaenisch, M.D., at the Whitehead Institute for Biomedical Research at MIT, where he studied epigenetic gene regulation. He trained extensively in genetic engineering of mouse embryonic stem cells to create knockout mice for the purpose of pinpointing genetic processes and understanding human diseases.

Chang subsequently began to study the *Mecp2* mutant mouse model, hoping to understand the disease mechanism of RTT and develop treatment for patients with the disease. Because the considerable overlap in clinical features between RTT and autistic spectrum disorders, the lessons learned studying RTT might also benefit the general understanding of autism and other neurological disorders.

In a 2006 study featured in the journal *Neuron*, Chang and colleagues from the Whitehead Institute/MIT and Brandeis University discovered a unique relationship between MeCP2 and a neuronal protein called "brain-derived neurotrophic factor," or BDNF, which plays an important role in neuronal development and function. Chang found lower levels of BDNF in *Mecp2* mutant mice, so he inserted an extra copy of BDNF into them and discovered the resulting increase in the BDNF protein delayed disease progression.



Chang and his team use an electrophysiology recording rig to study synaptic plasticity in brain slices and cell cultures from various genetically engineered mouse lines. By looking at MeCP2 in different phosphorylation states, Chang's lab can better understand the role it plays in Rett syndrome and work to develop treatment for the disease. *(Photo by Marianne English)*

Chang has continued his work on MeCP2 and RTT since coming to UW-Madison in 2007. Combining his experiences with transgenic mice, neuroscience and newer techniques such as induced pluripotent stem (iPS) cells, he has established unique experimental platforms that take advantage of both the *in vivo* and *in vitro* methods.

In addition to juggling multiple appointments, Chang oversees two postdoctoral students, two graduate students, one technician and two undergraduate students in his lab.

Half of the Chang lab studies basic biological functions of MeCP2 while the other half works to develop therapeutic treatment options for RTT patients. The first half is funded by the National Institutes of Health, whereas the other is supported by start-up funding from UW-Madison and the International Rett Syndrome Foundation.

Relating to the first half of the lab's work, Chang said one fascinating phenomenon of MeCP2 is that the protein can be differentially phosphorylated at different positions in response to the same extracellular stimulus. Since MeCP2 is associated with a large number of gene promoters—approximately 30 to 40 percent based on unpublished data from the Chang lab and published studies from other groups in the field, Chang said this posttranslational modification makes MeCP2 a perfect master molecular switch to integrate multiple extracellular stimuli and coordinate appropriate outputs from large scale transcriptional networks. The Chang lab has generated unique *Mecp2* knockin mouse lines that lock MeCP2 at different states of phosphorylation at different sites. This work has begun to reveal the physiological function of stimuli-induced MeCP2 phosphorylation.

Though Chang understands the power of mouse models of human diseases, he is fully aware of the limitations of animal models.

"After all, humans are not mice, flies or worms," he said, which is why the other part of the lab works to develop Rett syndrome treatments with human iPS cells.

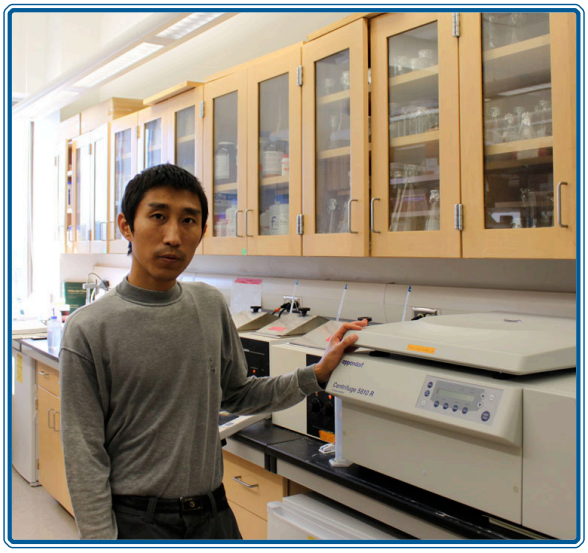
"One of the reasons I came to UW-Madison was because of its strong leadership in stem cell biology," he said. "We feel the need to establish a human cell

(continued from page 3)

culture-based system to validate and extend our findings in mice—that's why I started working with human iPS cells." Concerning the lab's other focus, Chang collaborates with other scientists to obtain skin cells from RTT patients that carry characteristic *MECP2* mutations to derive RTT-specific iPS cells. He also plans to use neurons differentiated from RTT iPS cells to study disease mechanisms and conduct drug screening in the future.

"Looking ahead, the human cell culture-based system and the mouse model will be the two arms of our drug discovery approach or effort," Chang said. "We can go back and forth between human and mouse—between *in vivo* and *in vitro*—to take advantage of both systems."

Marianne English is a graduate student in science journalism at UW-Madison.



Overseeing postdoctoral students, graduate students, a research technician and undergraduates, Chang studies basic biological functions of MeCP2 to help develop treatments for Rett syndrome patients. *(Photo by Marianne English)*

Sources:

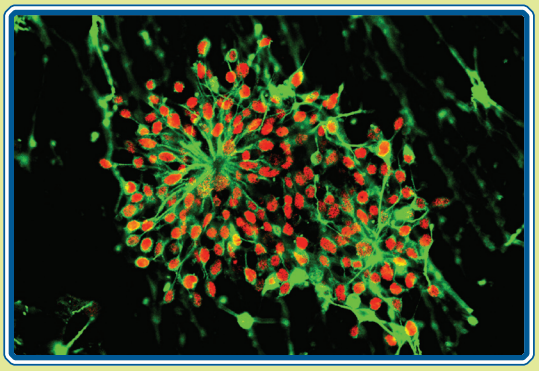
Qiang Chang (website and personal interview)
Rudolf Jaenisch website
MIT Whitehead Institute press release
NIH page on MeCP2

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Year-in-Review Highlights SCRMC Discoveries

Science news highlights from SCRMC members appear in the newly published Year-in-Review Report, published by the UW Foundation. Please contact Barb McCarthy, barb.mccarthy@supportuw.org, for printed copies. *(Photo by Su-Chun Zhang and Baoyang Hu)*

(continued from page 1)

radiology at Stanford University kicked off the series with an excellent presentation on stem cells and the heart. We have been fortunate to attract outstanding speakers for this event with the help of SCRMC faculty hosts. Both the Visiting Speaker series and the Campus Stem Cell Lab meetings will move to the new Wisconsin Institutes for Discovery in 2011.

Also new this year is our ICTR/SCRMC pilot grant program, which awarded $50,000 grants to four SCRMC investigators. Look for the "call for applications" for next year's round.

Our second annual SCRMC retreat took place at the UW Arboretum, with 37 center members, and a number of guests convening on the last day of September. The day provided great opportunities to meet new researchers, establish or strengthen collaborations, and provide future direction to the SCRMC. Among important action items arising from the retreat were goals to establish an easy communication network to share reagents and resources (internet chat-room style), survey members for suggested scientific-focus groups and start forming highest priority groups, and establish an SCRMC education committee. Also highlighted were powerful opportunities available on campus for investigators to translate their preclinical studies to clinical studies, taking advantage of the PACT grant and other technical support.

Another exciting development this fall is the proposal to form a new Department of Cellular and Regenerative Biology. This resulted from the realignment process of basic science departments in the SMPH. I am excited that this new department will be able to enhance and empower the mission of the SCRMC by providing new faculty hiring opportunities, provide a rich academic environment for our members, and lead to establishing educational initiatives relevant to stem cell biology and regenerative medicine. Particularly important is the new "Fundamentals of Stem Cells and Regenerative Biosciences" graduate course targeted for Fall 2011 and led by **Emery Bresnick** and a number of contributing faculty.

Finally, please provide your input and suggestions. The SCRMC is you and exists to empower your academic research, promote related educational programs, and act as a portal to the excitement and power of stem cell and regenerative medicine research at UW-Madison.

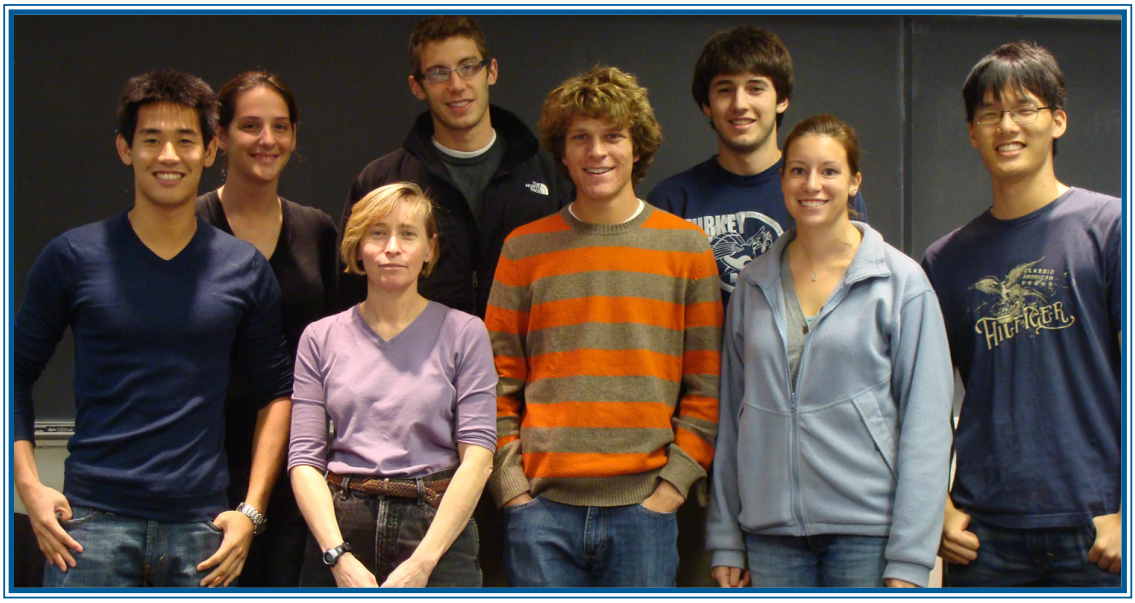
Tim Kamp

Questions about this newsletter? Please contact Sue Gilbert, sggilber@wisc.edu
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Assistant Editor: Marianne English, english2@wisc.edu
Designed by Sue Gilbert
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Student Society for Stem Cell Research (SSSCR) Strengthens Role

The UW-Madison chapter of the Student Society for Stem Cell Research (SSSCR) has kicked off another year and continues to expand its role on campus. In addition to a growing membership pool, the club plans to create a channel for undergraduates to get more involved in research on campus. This project has started with the compiling of various resources, and the club hopes to eventually provide personal assistance and mentoring to those members who are interested in becoming part of a lab. SSSCR has a full schedule for this fall semester. SSSCR faculty advisor **Jayne Squirrell** gave the first presentation to the group at the Biotechnology Center on campus Oct. 4 as a primer for students who want to learn more about stem cell biology. Squirrell is an assistant scientist in the Laboratory for Optical and Computational Instrumentation (LOCI) through the Department of Molecular Biology. Another meeting will be more hands-on; allowing students who may not have any lab experience to explore what lab work is like. Outreach has always been a cornerstone of the UW-Madison chapter of SSSCR, and with the enhanced buzz around stem cell research lately, educating the student and general population is especially critical. Currently, SSSCR is working on a project designed to give children and young people a basic idea of what stem cells are and can they do. SSSCR is always looking for ways to help out and improve. New members can join anytime, so researchers are encouraged to send their undergraduate assistants our way! Visit us at ssscrwisc.weebly.com for our speaker and activities schedule and other updated news about the group.

SSSCR board members, 2010/2011



(Above Photo) Back row, left to right: Meghan Rosenkranz (Outreach Chair), Daniel Walden (Secretary), George Bonadurer (Events Chair), Matthew Tso (Vice President). *Front row, left to right:* Eric Chen (CALS Student Council Representative), Jayne Squirrell (faculty advisor), Ross Pedersen (Treasurer), Melissa Breunig (President).

Fellowships Available for 2011

The SCRMC Fellowship Program is an interdisciplinary pre- and post- doctoral program that aims to support the training of UW graduate students and post-doctoral fellows in interdisciplinary stem cell and regenerative medicine research. The program is funded by the UW SCRMC. We are currently accepting applications until Jan. 1, 2011, for two one-year fellowship positions with the possibility of renewal for a second year. Applications will be reviewed by Jan. 15, 2011. See the website for more details.

WiCell Focuses on Providing Services to SCRMC Members

by Erik Forsberg

In response to recommendations from SCRMC members, WiCell has adjusted its core services and qualified reagents to meetUW-Madison scientists' changing needs. For example, in addition to its regular lineup of pre-qualified core reagents and live cultures, WiCell now offers teratoma and mycoplasma testing services and FGF2 produced at Waisman Biomanufacturing. (https://stemcells.wisc.edu/research/services/WiCell/UW-CORE_ORDER_FORM.July.2010.pdf).

The cytogenetics lab at WiCell has added new services including mouse (in addition to human) karyotyping and array Comparative Genomic Hybridization (aCGH), as well as the *fast*FISH® assay for inexpensive detection (with results in less than two days) of common chromosomal abnormalities in human pluripotent stem cell cultures (wicell.org/cytogenetics). SCRMC users of WiCell's Spring Street facility (which is devoted for use by UW-Madison scientists) have direct access to core supplies, new imaging equipment, and a new low oxygen culturing system. The education team at WiCell has improved its 3-day, hands-on, training course by adding feeder-free culturing of both hES and iPS cells (wicell.org). Changes in services provided to SCRMC members by WiCell is an evolving process that will be driven by scientific need and overseen by a UW-Madison appointed Scientific Advisory Board.

WISCBankculturesanddistributesavarietyhumanESandiPScelllines.Theselinesareavailableto SCRMC membersatnocostandcanbeordereddirectlyviawww.wicell.org.Anewcardiomyocyte-specificreporter cell line, produced by the Kamp lab, is now available, Named H9-hTnnTZ-pGZ-D2, this is a modification of the H9 cell line and contains a cardiac-specific troponin T promoter driving GFP expression and Zeocin resistance. This makes it useful for identification (by GFP) and/or selection/enrichment (by Zeocin treatment) of cardiac cells in culture following differentiation.



Campus SCRMC Seminars Move to WID

Starting in 2011, both our regular weekly and our new visiting scientist monthly seminars will move to the new Wisconsin Institutes for Discovery (WID) Contact Sue Gilbert *sggilber@wisc.edu* if you'd like to present your research, nominate a visiting speaker, or get the schedules, including times and locations for these two popular series.

Summer Science Camp



For the fourth year, **Rupa Shevde**, senior scientist and director of education and outreach, led her team of Morgridge, WiCell and SCRMC educators as they introduced many of the state's brightest young science students to a week of stem cell and regenerative medicine lab experiments and presentations.

(*Photos by Conor Lenon*)









Reaching Out

SCRMC staff and members kept busy with many education, outreach and awareness activities this summer and fall. These included:

- Sponsoring a WiCell/SCRMC exhibit at the International Society for Stem Cell Research annual meeting in San Francisco in June, and the World Stem Cell Summit in Detroit in October.
- Presenting hands-on stem cell science activities as part of a free day of public outreach and education at the Detroit Science Museum on October 3, 2010. The event preceded the World Stem Cell Summit in Detroit October 4-6.









- Authoring an update on stem cell and regenerative medicine research, education, funding and economic impact in Wisconsin for the World Stem Cell Report published by the Genetics Policy Institute for the World Stem Cell Summit.
- Highlighting SCRMC activities not only on our host website, but as part of the California Institute for Regenerative Medicine's premiere Stem Cell Awareness Day National Events site.
- Coordinating ongoing statewide community and school outreach programs through SCRMC, WiCell, the Wisconsin Institutes for Discovery/Morgridge Institute for Research, the Wisconsin National Primate Research Center, Genetics-Biotechnology Center and other departments and entities.
- Speaking at a September press conference by Governor Jim Doyle on the critical importance of human embryonic stem cell research to patients, researchers, students and the public. Doyle addressed the news media while flanked by UW-Madison and other state officials, deans, scientists and patient advocates.



(Above photo) From the left, WI State Senator Jon Erpenbach, Dean Rick Moss (directly behind Erpenbach), David Walsh, **Sam Gubbels**, Jody Montgomery and her daughter Maddi, **Derek Hei,** Beth Donley, **Erik Forsberg,** Carl Gulbrandsen, **James Thomson**, Marsha Seltzer, **David Gamm**, Chancellor Biddy Martin, **Su-Chun Zhang**, WI Rep. Kelda Helen Roys, **Qiang Chang**, Governor Jim Doyle, **Tim Kamp**. *(Photo by J. Lenon).*

UW Institute for Clinical and Translational Research
UW ICTR

SCRMC/ICTR 2010
Pilot Grants Awarded and Call for 2011

The SCRMC partnered with the Institute for Clinical and Translation Research (ICTR) for its pilot grant award program. These $50,000 one year, Type 1 pilot grants support basic research, clinical trials, and research where a basic laboratory discovery may lead to the prevention, diagnosis, or treatment of a specific disease. Type 1 funding also supports a wide spectrum of patient-oriented research that embraces innovations in technology and biomedical devices. The program is targeted at new investigators or investigators taking a new direction. The program provides peer review of applications. For 2010, the SCRMC jointly supported two grants that had a focus in stem cells or regenerative medicine. ICTR funded an additional two SCRMC grants based on scientific merit. The proposals funded were:

1) Modeling genetic skin diseases using patient-specific iPS cells (PI, **Joyce Teng,** Co-I's, **Vijay Setaluri**, **Sean Palecek**).
2) Human RPE cell electrophysiology to model eye disease (PI, Bikash Pattnaik**,** Co-I's, De-Ann M. Pillers, **David Gamm**).
3) Generation of induced pluripotent stem cells to study autism (PI, **Anita Bhattacharyya**, Co-I, Leonard Abbeduto).
4) iNs from neurodevelopment and neurodegenerative diseases (PI, **Qiang Chang,** Co-I, **Su-Chun Zhang** and Hrissanthi Ikonomidou).

Congratulations to the awardees for their excellent proposals! Unfortunately, like most funding mechanisms now, not all of the meritorious projects could be funded with a total of 16 SCRMC applications and total applicant pool of approximately 100. However, the program is moving forward again this year with the SCRMC supporting two pilot grants. Letters of intent are due December 1, 2010, see https://ictr.wisc.edu//node/124 for more information.

SCRMC Member Services

The following core services are available to SCRMC members and appear on our website at www.stemcells.wisc.edu/research/.

- Immunology and Pathology Services
- Nonhuman Primate Services
- Cellular and Molecular Imaging Services
- Small Animal Imaging Services
- WiCell Research Institute and WiscBank
- Research Materials and Services
- Training Courses

… and much more!

The Other November Election: Your SCRMC Executive Committee

All SCRMC members contribute and benefit from the center, but we especially receive leadership and guidance from members of the executive committee. Current members are Tim Kamp (Medicine), Erik Forsberg (WiCell Research Institute), Jamie Thomson (Anatomy), Bill Murphy (Biomedical Engineering), Linda Hogle (Medical History and Bioethics), Emery Bresnick (Pharmacology), Derek Hei (Waisman Center), and Judith Kimble (Biochemistry). These faculty members have dedicated precious time to help the SCRMC thrive. We now request nominations by Nov. 15 for two new SCRMC faculty members (see www.stemcells.wisc.edu/faculty/) to succeed Jamie Thomson and Judith Kimble, beginning in January 2011. Self-nominations and consecutive terms are accepted. Please send your nominations to Sue Gilbert sggilber@wisc.edu by Nov. 15. Voting will take place electronically by Nov. 30.

Save the Date—

6th Annual Wisconsin Stem Cell Symposium



April 27, 2011
BioPharmaceutical Technology Center, Madison, WI

Topic: Stem Cell Reprogramming

Confirmed presenters:

Kristi Anseth, Ph.D. (Tisone Professor, Associate Professor of Surgery, HHMI Investigator, Chemical and Biological Engineering, University of Colorado-Boulder, Boulder, CO)
Helen Blau, Ph.D. (Donald E. and Delia B. Baxter Professor & Director, Baxter Laboratory for Stem Cell Biology, Stanford University School of Medicine, Stanford, CA)
Shen Ding, Ph.D. (Professor, Chemistry Department, The Scripps Research Institute, La Jolla, CA)
John Gurdon, Ph.D. (Emeritus Professor & Distinguished Group Leader, The Wellcome Trust/Cancer Research UK Gurdon Research Institute, University of Cambridge, UK)
Juan Carlos Ispisúa Belmonte, Ph.D. (Professor, Gene Expression Center, Salk Institute for Biological Studies, La Jolla, CA)
Stuart Orkin, Ph.D. (Professor, Department of Pediatric Oncology, DFCI; Children's Hospital and Dana Farber Cancer Institute; Howard Hughes Medical Institute; Harvard Stem Cell Institute, Boston, MA)
James Thomson, Ph.D. (Director, Regenerative Biology, Morgridge Research Institute, University of Wisconsin-Madison, Madison, WI)



For a snapshot of SCRMC research news, and Wisconsin and UW-Madison headline makers in the field, visit newsroom.stemcells.wisc.edu/news.

Second Annual SCRMC Faculty Retreat Connects Researchers



For the second year in a row, not only did retreat weather cooperate, with sunny skies drawing groups outside the UW-Madison Arboretum for breaks, but more faculty members also connected through novel "Rapid Fire" presentations to directly share research projects, goals and needs with one another.

A variety of presentations and focus groups, as well as plenty of impromptu collaborative meetings, highlighted a successful Sept. 30 retreat. In the Rapid Fire sessions, faculty and scientific staff were given three minutes to showcase their research, goals and needs, then respond to questions from colleagues. (Lest presenters run over the allotted time, facilitators stood by ready to ring a Bucky cowbell.)



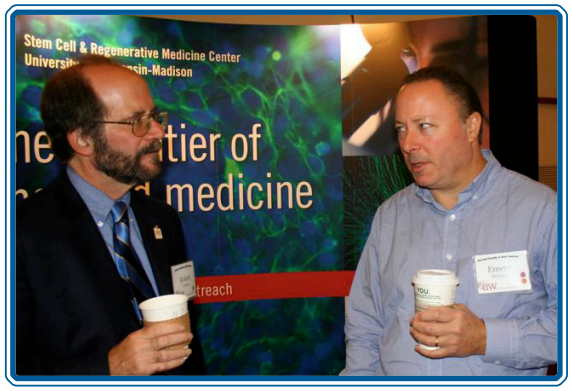
The meeting kicked off with a welcome and update from SCMRC Director **Tim Kamp**, followed by a keynote from John Denu, professor of biomolecular chemistry, who focused on epigenetics and packaging of DNA. Morgridge Insitute for Research Director Sangtae Kim gave the lunch presentation on novel and necessary ideas for moving research from the bench through preclinical work and into clinical applications.

In the afternoon, **Erik Forsberg** and **Tenneille Ludwig** of WiCell shared core services for investigators and addressed potential new services. **John Centanni**, recently hired as SMPH regulatory affairs specialist and previously at Stratatech Corp., followed. Breakout groups then focused on stem cell education and establishment of scientific focus groups.

The education breakout group led by Jayne Squirrell and Anita Bhattacharyya identified exciting new efforts on campus to advance stem cell-related education. The newly forming Department of Cellular and Regenerative Biology is moving forward to establish a Developmental and Regenerative Biology graduate program. A much-needed new graduate level course for Fall of 2011 is in the works, Fundamentals of Stem Cells and Regenerative Biosciences, directed by Emery Bresnick. To help the SCRMC contribute to education in this area on campus and serve as clearinghouse for information on relevant courses and training programs, it was recommended that the SCRMC form an education committee, and this is being actively pursued.



Bill Murphy and **Amish Raval** led the scientific focus groups breakout session. The discussion rapidly identified benefits of having groups that could foster collaboration, exchange key expertise, work on collaborative funding opportunities, and participate in and help organize symposia and educational events. It was recommended that the SCRMC should administratively support establishment and maintenance of such groups. These groups should both be thematic and multifunctional. To move this process forward, the SCRMC will survey members on potential thematic areas in which they believe a focus group would be beneficial. The SCRMC will then generate a list of potential focus groups and poll members on their interest in joining these groups. During the Spring semester of 2011, the SCRMC will facilitate the establishment of groups with needed administrative support and leadership.



Next on the agenda, **Jamey Weichert**, in the Department of Radiology, and Kevin Eliceiri, who directs the LOCI biophotonics instrumentation laboratory, shared a keynote presentation on multidimensional and multimodal imaging approaches for stem cells.

Lisa Wilson, Legal Services, gave the final talk before closing remarks. She updated the group on the recent U.S. district court injunction banning federal funding for hES cell research, and the subsequent appeals court decision to lift the ban pending full appeal. Wilson explained the lengthy and detailed legal processes that will likely be involved in order to resolve this issue.



The SCRMC retreat planning committee, chaired by Bill Murphy, wishes to thanks all guest speakers and participants, our hosts at the Arboretum Visitors Center and Darin Harris from the Office of Strategic Planning for their hard work to plan this retreat. Based on responses from the evaluation, it was a productive day and participants identified important ways for the SCRMC to move forward. A full detailed summary of the retreat is available for those who were unable to make the event. Any SCRMC member who wishes a copy may contact Sue Gilbert sggilber@wisc.edu.





