Welcome to our first newsletter

FROM THE DIRECTORS

Welcome to the first newsletter of the UW Stem Cell & Regenerative Medicine Center. One of the messages that came through loud and clear from our September retreat at the UW Arboretum was that SCRMC communication was not getting the job done. So this biannual newsletter will try to add another tool to foster communication among members of the SCRMC and keep you up to date on the latest developments, resources, and scientific advances. This is our first attempt at a newsletter, and so we welcome your suggestions for improvement in future editions. In addition, we remind you that the most up to date information on all of the features of the SCRMC is at our website, www.stemcells.wisc.edu.

The SCRMC is beginning its third year since being established as a center under the joint auspices of the Graduate School and the School of Medicine and Public Health. We are delighted at the growth of the SCRMC which now includes seventy-eight faculty and staff members representing forty-two departments across campus. The participation in our first retreat at the Arboretum was wonderful with fifty faculty and staff spending there day working together. We came away from that retreat with a number of clear messages and action items which are summarized later in the newsletter.

In this newsletter you will find highlights of faculty research not meant to be all inclusive, but to share some of the late breaking and exciting research on campus. We'll also highlight a

(After the above text, there is a chart indicating the contents of the newsletter. The chart lists articles like: Featured Researcher: Wendy Crone, Save the Date: 5th Stem Cell Symposium, Public Outreach, Spring 2009 Highlights, Current Research Highlights, Elections for SCRMC Executive Committee, Fellowships Available for 2010, First Faculty & Staff Retreat Report, Core Services.)
Wendy Crone’s area of research expertise is in experimental mechanics, with emphasis on problems related to biomaterials and medical devices. Her interests are focused on improving fundamental understanding of mechanical response of materials, improving material behavior through surface modification and nanostructuring, and developing new applications and devices. Crone is an associate professor of engineering physics, with affiliate appointments in biomedical engineering and materials science and engineering.

In addition to ongoing efforts in biomaterial characterization and medical device development, Crone has recently initiated a project on the response of stem cells to a surrounding three-dimensional hydrogel matrix. The objective of this research, performed in collaboration with other UW faculty, is to test the influence of hydrogel material properties and mechanical stimulation on the differentiation of stem cells. It is well known that differentiation of stem cells on a 2D substrate is influenced by the stiffness of the substrate and mechanical loading applied to the substrate. However, prior work on stem cell encapsulation in a 3D hydrogel matrix is limited and the influences of mechanical stiffness and mechanical loading on such a matrix with encapsulated stem cells are open areas of study. Our central hypothesis is that the differentiation of human embryonic stem cells (hESCs) can be controlled by both the mechanical environment of the 3D hydrogel matrix in which they live and the dynamic loading to which they are subjected through that 3D hydrogel matrix.

Crone teaches a number of courses at UW-Madison, including Mechanics of Materials, Advanced Mechanics of Materials I, Fracture Mechanics, Micro- and Nanoscale Mechanics, Introduction to Engineering Research, and Introduction to Engineering Design. She received her B.S. at University of Illinois, her MS at Brown University and her PhD at the University of Minnesota.

To read more about Crone, please see the American Association of University Women’s Jan. 16, 2009 article, “Meet Wendy Crone: Engineering Professor and Mentor”


Recent publications:


featured researcher on campus to introduce in more depth a new faculty member or new researcher in the field.

Providing resources for SCRMC members is a critical part of our mission. You will find a summary of existing core services later in the newsletter. We are delighted that our partnership with the WiCell Research Institute has grown, and WiCell provides a number of useful and high quality services. We are also enthusiastic about a new partnership with the Keck Center for Biological Imaging led by Ron Kalil to provide additional access for confocal and multi-photon imaging. We will continue to support the services that are of most benefit to the membership as we continue to look for ways for supplementing the funding of these services. This year a committee of SCRMC members will formally review these services and make recommendations for moving forward.

The SCRMC fellowship program to support post-doctoral and pre-doctoral trainees was launched last year and not surprisingly we were flooded with more than thirty outstanding candidates for the four positions. Congratulations to those that were selected and see the story inside. Also, this year we will have two more fellowships available, and applications will be due December 10. Please see the website for more details. Additionally, this is the year for renewal of the NIH T32 Stem Cell training grant, so we will work to grow this program and ask for your support for a renewal application going out in May.

Supporting meetings and seminars is another important activity of the SCRMC. The Tuesday noon campus stem cell lab meetings (with pizza) continue to be a popular venue with 40-90 attendees each week. Also get ready for an outstanding 5th Annual Stem Wisconsin Stem Cell Symposium on April 21 at Promega entitled “The Road to Stem Cell Applications: Bioprocessing, Safety, and Preclinical Evaluation.” Derek Hei and Linda Hogle are leading the efforts at organizing this symposium and are putting together an excellent meeting which will include local speakers as well as several prominent outside speakers such as Peter Andrews (University of Sheffield), Don Fink (FDA), Peter Zandstra (University of Toronto).

The SCRMC is also working to synergize with the many exciting if not sometimes turbulent developments on campus. The Wisconsin Institutes for Discovery building is rapidly taking shape and in the WID component we are excited to see the BIONATES group led by Tom Turng advancing new concepts in tissue engineering. The MIR component will also have a strong SCRMC presence with Jamie Thomson directing the Regenerative Biology group. More SCRMC investigators have moved to west campus in the Wisconsin Institute for Medical Research (WIMR) first tower. We also anticipate a strong presence in tower two which may be starting construction soon. Finally, the realignment of the basic science departments in the SMPH has provided a new opportunity for focus on regenerative and developmental sciences that the SCRMC supports. Creation of such a department would help advance the goals of the SCRMC in ways that as a center we are challenged, such as establishing new educational programs. Although some have questioned whether such a new department would end the reason to have the SCRMC, the directors feel such a department would only strengthen the SCRMC given the interdisciplinary nature of this field and ongoing cross campus participation. A more mature example of such an evolution at UW and elsewhere is the comprehensive cancer center model.

Finally, the SCRMC is you, and faculty governance is the way. So elections are this month for the turnover of the executive committee seats. Please participate in the election which will be done electronically at the end of November with nominees coming in now. Also we welcome your comments and suggestions any time. We will continue to shape the SCRMC to best serve its members, and this will undoubtedly change as the rapid advances in the field move us forward.

Tim Kamp and Clive Svendsen
Co-directors
Jordana Lenon, SCRMC university relations specialist, and Marian Piekarczyk, assistant director of lab operations, WiCell Research Institute, shared a combined booth at the 2009 World Stem Cell Summit in Baltimore, Maryland, September 21-23. Tim Kamp, SCRMC co-director, presented two sessions on cardiology and stem cells. Close to 1,200 people attended the summit, learning about a broad range of topics covering stem cell biology, policy, licensing, ethics, advocacy, fundraising, and industry. Additional science tracks addressed biotechnology, nanotechnology and bioengineering, as well as the growing number of diseases and disorders scientists are researching using cell and regenerative medicine approaches. (Photo by S. Carlson)

Rupa Shevde, SCRMC administrator and WiCell senior scientist, runs the raffle with a young helper at the SCRMC/WiCell exploration station April 4 at UW-Madison’s Science Expeditions. The annual events draws more than 1,000 visitors to campus each spring to partake in hands-on science outreach activities. SCRMC/WiCell partners schedule weekly school and community outreach programs throughout the year, at WiCell, on campus and on the road. Please contact rshevde@wicell.org or jlenon@primate.wisc.edu for more information. (Photo by J. Lenon)
Rupa Shevde (front row, second from right, top photo), senior scientist, director of education and outreach, WiCell Research Institute, and her colleagues build on their Madison experience by reaching out to students and teachers in rural areas that may lack science education resources. WiCell sponsors a Summer Science Camp each summer that hosts four students and a teacher from each of five high schools selected in a competition. Participants in the four-day summer camp met with prominent science professors, spoke with young scientists, attended lectures and enjoyed hands-on lab experiences. Students also received information about college and career choices. In the WiCell cytogenetics lab, below, Laura Cominetti (center), Assistant Research Specialist instructs students on how to stain human chromosomes. (Photos by J. Lenon)
FELLOWSHIP WINNERS HELP LAUNCH SPRING SEMESTER

Five individuals have received the new SCRMC Fellowship Competition for graduate students and postdoctoral fellows at UW-Madison.

The honorary graduate fellowship went to Nathaniel Pope from Emery Bresnick’s laboratory, Pharmacology. Graduate fellowship winners are Hongda Li from Qiang Chang’s laboratory, Genetics, and Josh Selekman from Sean Palecek’s laboratory, Chemical and Biochemical Engineering.

The post-doctoral fellowship awardees were Sheeny Lan from William Murphy’s laboratory, Biomedical Engineering, and Fan Wang from Aseem Ansari’s laboratory, Biochemistry.

The awards provide two years of funding for the winners, plus a $10,000 stipend to the laboratory conducting the research. This competition builds on the existing NIH-funded UW-Madison stem cell training grant, now in its fifth year, and support from WiCell Research Institute.

Applicants must either be accepted into a graduate program on campus, or identify an SCRMC faculty member with whom they would like to do post doctoral training. Candidates for the next round of grants may submit on-line applications in November 2009, via http://stemcells.wisc.edu.

Fellowship recipients and their mentors (from left to right): Aseem Ansari, Fang Wan, Sean Palacek, Josh Selekman, Honga Li, Tim Kamp, Clive Svendsen, Qiang Chang, James Pope, and Bill Murphy. (Photo by J. Lenon)
Check out “Stem Cells: The All-Around Athletes” an eight-minute educational video produced by WiCell & the SCRMC with additional funding from the Ira and Ineva Reilly Baldwin Wisconsin Idea Endowment. Available for viewing on the SCRMC and WiCell websites.

SCRMC PARTICIPATES IN 4TH ANNUAL STEM CELL SYMPOSIUM:
CANCER, STEM CELLS AND CANCER STEM CELLS

Coordinating with the BioPharmaceutical Technology Center Institute (BTCI), on April 15, this symposium brought together world leaders in the area of cancer stem cells, and recruitment of tumor precursor cells. The focus was on basic cellular and molecular mechanisms that govern the cell growth potential of tumors, and whether there is a relationship between the long-lived/immortal cells of tumors and the long-lived/immortal cells of somatic tissues.

HIGHLIGHTED ISSUES WERE:

* Breast cancer - is it a stem cell based disease?
* How do somatic stem cells relate to lung tumor development?
* How do these systems compare to the rapidly regenerating lineages such as the hematopoietic lineage?
* What do we need to know about stem cells to understand brain tumors?
* Does this information need to be incorporated into therapeutic strategies?

The event followed in the footsteps of the three previous symposiums: Conserved Mechanisms of Stem Cell Control and Regeneration (2008); Heart & Blood (2007); and Neural Stem Cells (2006). Karin Borgh worked tirelessly with her BTCI team to pull together the fourth annual Stem Cell Symposium, reporting a record number of attendees at close to 300 people. (Photos by J. Lenon)
Exploring hematopoietic (blood-related) stem cell possibilities

Igor Slukvin and Peiman Hematti along with James Thomson are exploring hematopoietic (blood-related) stem cell possibilities. Slukvin has grown different types of blood cells from ES cells and, in 2009, grew blood cells from iPS cells. He and Hematti are researching them as a source for expanded blood products and bone marrow transplants. Bone marrow transplantation is one of the most effective treatments for blood cancers such as leukemia, lymphoma and multiple myeloma; however, there are not enough matched bone marrow donors to successfully treat patients today. In addition, blood stem cells from pluripotent cells may someday be transplanted into patients with sickle cell anemia, hemophilia, and other genetic diseases of the blood. Such transplants could theoretically improve, or even cure these patients. However, graft versus host disease is a major and potentially fatal complication after bone marrow transplantation. Thus, Hematti is also working on mesenchymal stem cells to make such transplants safer. He has developed a novel method to derive mesenchymal stem cells from ES cells and these cells could greatly make ES cell transplantation safer and more effective. Generating platelets, red blood cells and other blood components from ES or iPS stem cells could also help alleviate blood bank shortages. (Photo courtesy I. Slukvin.)


Successful growth of multiple types of retina cells from two types of stem cells

Jason Meyer, David Gamm and an ophthalmology and visual sciences team of researchers at the Waisman Center have successfully grown multiple types of retina cells from two types of stem cells — suggesting a future in which damaged retinas could be repaired by cells grown from the patient’s own skin. Even sooner, 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. The work is an important step forward because it not only confirms that multiple retinal cells can be derived from human iPS cells using the Wisconsin approach, but also shows how similar the process is to normal human retinal development. Su-Chun Zhang, working with James Thomson, was among the first to create neural cells from embryonic stem cells. Zhang was also part of the Gamm lab’s retinal study. Meyer says the retina project began by using embryonic stem cells, but incorporated the iPS cells as they became available.

**Mass spectrometry as a highly versatile diagnostic tool**
Mass spectrometry is the new “can-do” super-machine of stem cell research and other scientific disciplines. Using this highly versatile diagnostic tool, which allows scientists to sift through thousands of different molecules in complex biological soups, Josh Coon, assistant professor of chemistry and biomolecular chemistry, in 2009 uncovered phosphoproteomes, or specially modified proteins present in embryonic stem cells that help give these cells their remarkable property of pluripotency — they can become any cell type in the body.


**Improved stem cell preservation methods**
Growing and maintaining stem cells so they remain robust, uncontaminated and ready to go to work in a variety of applications — from long-term culture to growing elaborate cell and tissue 3-D structures — is also the job of stem cell engineers, who work closely with biologists. Sean Palacek is a chemical and biological engineer who in 2008 developed improved stem cell preservation methods through mechanically straining cells to control culture conditions and inhibit differentiation. He is also interested in developing skin cells from stem cells to develop improved skin substitutes for burn victims and others who need skin grafts.


**hESCs directed to become ventral spinal progenitors and motor neurons**
Su-Chun Zhang at the Waisman Center is researching neural-based stem cells and their potential for treating multiple sclerosis, amyotrophic lateral sclerosis (ALS) and spinal cord injury. Because it is difficult to obtain...
just the right type of neuron to do the job in this disease, Zhang’s team advanced the field in 2008 by discovery of a small molecule that can direct the human embryonic stem cell to become critical therapeutic cell types—such as ventral spinal progenitors and motor neurons.


Directing stem cells into becoming dopaminergic neurons for Parkinson’s disease

Several investigators at the Wisconsin National Primate Research Center and Waisman Center are collaborating on attempts to direct stem cells into becoming dopaminergic neurons to treat Parkinson’s disease. They include James Thomson, Clive Svendsen, Su-Chun Zhang, and Marina Emborg. To explore cell replacement therapies using both human and monkey embryonic stem cell derived dopamine neurons, in 2008 Emborg and her collaborators conducted a pilot study to assess the transplanted cells’ viability and safety in monkeys. Results suggested that the differentiated hES cells provoked an immune response that adversely affected dopaminergic characteristics and survival. To overcome this undesired but not unexpected effect, investigators are going a step further to try and develop personalized medicine approaches using iPS cells. Emborg and Zhang were awarded a grant from the Parkinson's Disease Foundation in 2009 to grow and transplant dopaminergic neurons from rhesus-derived iPS cells into monkey parkinsonian models.

For a snapshot of SCRMC research news, and Wisconsin and UW-Madison headline makers in the field, visit newsroom.stemcells.wisc.edu/news. Please send your highlights or those of your colleagues for consideration in this highlights column.
Fellowships Available for 2010

The SCRMC Fellowship Program is an interdisciplinary pre- and post- doctoral program which 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 and WiCell Research Institute. We are currently applications through January 1, 2010 for review by January 15, 2010.

FIVE WENT TO WHITE HOUSE IN MARCH

From the left, Center members Tim Kamp, Clive Svendsen, James Thomson, Derek Hei, and Alta Charo met with U.S. Rep. Tammy Baldwin, D-Madison (in blue jacket) at the White House March 9. The SCRMC delegation witnessed President Obama signing a stem cell research executive order that lifted the federal funding restrictions on embryonic stem cell research imposed by the Bush Administration. A flurry of news media attention followed, for both the Washington, D.C., attendees as well as surrounding our scientists on campus. We thank our traveling members for all their public information efforts in addition to their sound science. At home, we’d like to especially thank Allison Ebert, Anita Battacharyya, Jon Odorico, Gabby Cezar, Carl Gulbrandsen, Igor Slukvin, Ron Kalil, Erik Forsberg, and Jason Meyer. We’re sorry if we’ve missed anyone, it was a busy day! (White House photo property of Rep. Baldwin Staff, used by permission. More photos in the stemcells.wisc.edu newsroom.)
First Scientific Retreat Welcomes 75 to Arboretum

We thank the 50 faculty and staff members and 25 others who energetically participated in our first SCRMRC scientific retreat Sept. 17, 2009, at the UW Arboretum Visitors Center. Outstanding keynote speakers highlighted the remarkable science including a presentation on “Regeneration, Stem Cells and Planarians as a Model System” by Alejandro Sánchez Alvarado from the University of Utah and on “Human Induced Pluripotent Stem Cells” by Jamie Thomson.

Feedback from four scientific working groups—neuroscience, cardiovascular, skeletal and wound, and regenerative biology—resulted in a host of challenges, tools and priorities identified for SCRMRC directors, staff and members to address in the coming year. Based on this input, center staff plans to work with members on main “action items.” These include: 1) highlight and improve website as a central source of information including expanding the Intranet portal at www.stemcells.wisc.edu/research for members (NetID access); 2) form core services committee to review existing cores and prioritize for future based on needs (core survey) and available/future funding; 3) create interdisciplinary focus groups that will meet quarterly based on the focus groups described above and potentially others; 3) move forward with a seminar series in addition to campus stem cell lab meeting with a given theme each year/semester; and 4) discuss realignment of SMPH basic science departments with campus leaders and committee charged with making recommendations, emphasizing the opportunity for creation of a Department of Regenerative Sciences and how it will provide needed infrastructure and vision for research and education.

The Intranet portal, at stemcells.wisc.edu/research, will help link investigators to needed resources and tools prioritized at the retreat. These include material transfer agreements, antibodies, cell lines, protocols, engineering tools, iPS screening, viral approaches, and training resources. We will continue to listen to our members to develop this portal and our other center services.

Another action item we hope to address, based on the education breakout sessions, is to build stem cell and regenerative medicine education more into the undergraduate curriculum by initiating an undergraduate basic stem cell biology course. In addition, the establishment of more formal graduate education can be advanced by creation of a certificate degree program for stem cells and/or regenerative Medicine under the umbrella of an existing training program. Additionally, for post-doctoral training, a strategy for renewing the T32 training grant needs to be finalized including a new PI to lead the effort and working with the NIH to target the grant to the appropriate institute(s).

Those in attendance at the retreat, in addition to our strong research force, included facilitator Darin Harris of the UW Office of Quality Improvement; invited speakers Michael Falk, Paulanne Chelf and Andy DeTienne from WARF; keynote speaker Alejandro Sánchez Alvarado of the University of Utah, Chancellor Biddy Martin, Dean Robert Golden, Dean Richard Moss, Carl Gulbrandsen (Director of WARF), Barb McCarthy (UWF), Susan Lambert-Smith (SMPH Communications), Terry Devitt (UW Communications), and Heather McFadden (SCRO Committee). Also present were SCRMRC staffers Sue Gilbert & Jordana Lenon; and notetakers Summer Hanson, Quyen Tran, Xiaoqing Zhang, Sarah Crittenden, and Melissa Breunig; A special thank you to Susan Halverson at the Arboretum for welcoming us to this venue.

Sincerely,

The SCRMRC retreat planning committee:
Bill Murphy, Wan-Ju Li, Jason Meyer, Sue Gilbert, Tim Kamp, Rupa Shevde, Su-Chun Zhang, Jordana Lenon, Darin Harris

(Photos by J. Lenon)
SCRMC Services for Members

The complexities and interdisciplinary nature of stem cell and regenerative medicine research necessitate collaboration and access to facilities outside the scope of any one investigator's laboratory. Thus, to facilitate stem cell and regenerative medicine research on campus, shared resources are an essential aspect of the SCRMC. These resources give individual investigators access to state-of-the-art technologies, with appropriate expertise to assist in training, experimental planning and data analysis. Members can apply for access to these services via our website. We hope to significantly subsidize costs associated with these services, but this will depend on use over time and is subject to change.

Stem Cell Services (James Thomson, Director) thomson@primate.wisc.edu 263-3585
This service will provide new tools for efficient maintenance of stem cells and will provide access to cutting edge techniques to enable genetic manipulation of hESCs. For example, such technologies could permit purification of specific cell populations as well as tracking of cells once they are implanted into recipient animals and tissues. This service will also provide SCRMC members with FGF-2 protein where needed for maintenance of hES cells.

Immunology and Pathology Services (William Burlingham, Director) burlingham@surgery.wisc.edu 263-0119
Immune rejection of transplanted allogeneic stem cells or derivatives is a major barrier to bringing such cell-based transplantation to clinics. The Immunology and Pathology Core will provide detailed immunologic testing and immunopathologic evaluation. These steps are essential for developing strategies to facilitate allogeneic transplants. The resources and services will provide a broad assessment of the humoral and cellular immune responses to transplantation of hES cells or their derivatives in a variety of contexts, e.g., across MHC barriers and using varying degrees of immunosuppression.

Nonhuman Primate Services (Joseph Kemnitz, Director) kemnitz@primate.wisc.edu 263-3588
Projects to develop cell replacement therapies may require that researchers implant stem cells into nonhuman primates to test efficacy and assess possible side effects before proceeding to human trials. In this context, nonhuman primates will be made available through the Nonhuman Primate Services core at the Wisconsin National Primate Research Center. Specific services include the provision of appropriate monkeys and primate tissue for projects, specialized animal husbandry, assistance with procedures such as surgeries and clinical assessments of monkeys, and appropriate terminal procedures and preparation of tissues for analysis.

Cellular and Molecular Imaging Services (Clive Svendsen, Director) cnsvendsen@wisc.edu 265-8668
Understanding the ability of stem cells to differentiate in vitro or tracking the fate of transplanted stem cells requires advanced microscopic imaging techniques and analyses. This service will provide access to confocal microscopy imaging and stereology through the Waisman Center Cellular and Molecular Core, as well as assistance with image analysis through discussions with qualified staff.

Small Animal Imaging Services (Jamey Weichert, director) jweichert@uwhealth.org 265-0835
Serial tracking of transplanted stem cells in living animals will provide essential information regarding the fate and localization of the cells and their ability to repair damaged tissue. Service technicians will perform whole animal imaging that will enable tracking of cells with micro CT, PET, MRI and 3D fluorescent and bioluminescent optical imaging. They will use state-of-the-art equipment following transplantation in collaboration with the Department of Radiology and Medical Physics and will assess in vivo physiological effects of transplantation. Moreover advanced image reconstruction capability allowe 3-dimensional mapping of functional optical signals into anatomic frameworks provided my CT or MRI scanning. In addition, the core will provide imaging using one of the world's only small animal combined PET/CT scanner, which can provide functional information for precise anatomical localization studies.

WiCell Research Institute (Erik Forsberg, director) eforsberg@wicell.org 441-8043
WiCell Research Institute is a non-profit organization established in 1999 to advance the science of stem cells at the University of Wisconsin-Madison and worldwide. WiCell hosts the National Stem Cell Bank as well as the WiCell International Stem Cell (WISC) Bank. In addition, WiCell offers pre-qualified core reagents including MEFs, cytogenetic services and training courses. As part of WiCell's mission to support stem cell research at the UW-Madison, SCRMC members may also apply for research support in the form of credit towards WiCell services and qualified reagents as well as WiCell facility use. This service includes Core Reagents (Matrigel, TeSR1, FBS, KOSR, antibodies, growth factors), Cytogenetic Services (karyotyping, FISH, SKY, aCGH, STR), Research Support (research space, financial credit), and Training Courses (culturing pluripotent stem cells, embryoid bodies).