Considerable excitement has been generated over the past decade from the potential therapeutic applications of human embryonic stem cells (hESC), and their recently derived relatives, induced pluripotent stem cells (iPSC), in treating human disease. Embryonic stem cell lines are derived from embryos created by in vitro fertilization clinics, and were in excess of clinical need, so they were donated for scientific research instead of being discarded. Embryonic stem cells have two essential characteristics that make them valuable—they have the ability to divide for an apparently unlimited length of time, and they are derived from the early embryo before lineages differentiate, so they retain the capacity to form all the cell types of the body, a characteristic referred to as “pluripotency”.

Based on studies of hESC, it was possible to identify a number of the proteins responsible for maintaining these unique characteristics of pluripotency and self-renewal. Surprisingly, when scientists introduced a cocktail of these proteins into somatic (fully differentiated) cells, these adult cells began to behave like embryonic stem cells. These cells are called induced pluripotent stem cells (iPSC), and just how similar they are to ESC is currently the object of intense research interest.

Regardless of the source, the great hope is that pluripotent stem cells may someday be capable of replacing cells lost to injury, normal aging or birth defects. They represent a potentially unlimited source of differentiated cells for drug testing, and a novel path for understanding gene function in early human development. The University of Michigan has been a leader in these efforts since the early part of this decade: UM was among the first institutions nationally to sponsor a Stem Cell Research initiative that resulted in the founding of the Center for Stem Cell Biology in 2003, and was one of the very first institutions in the US to receive federal funding to establish a human embryonic stem cell laboratory in 2004. Despite originally being hampered by one of the most restrictive legislative environments in the US, since the passage of Proposition 2 in November 2008 by the voters of the State of Michigan the embryonic stem cell research efforts at the University of Michigan have redoubled.

In light of these changes, the hESC laboratory was recently reorganized and expanded as the A. Alfred Taubman Medical Research Institute Consortium for Stem Cell Therapies. This consortium will derive new embryonic stem cell lines using excess embryos from fertility clinics to aid in the search for disease treatments and cures.
As usual, it is my pleasure to bring you greetings accompanying our third annual newsletter. It has been a busy and exciting year for the Department of Cell and Developmental Biology; we have hired new faculty colleagues and have been joined in our research efforts by numerous new graduate students and postdoctoral fellows. In this newsletter we have highlighted some, but far from all, news from the past year, summarized some of the exciting research going on in our labs, and highlighted some changes and advancements in our teaching efforts.

With the passage of Michigan Proposition 2 last Fall, which eased the restrictions on embryonic stem cell research, it is an exciting time to be working in stem cell research at the University of Michigan. During the year, the Department received gifts from the A. Alfred Taubman Institute as well as multiple Departments and Centers at the University of Michigan, to expand the embryonic stem cell laboratory into the A. Alfred Taubman Medical Research Institute Consortium for Stem Cell Therapies. The launch of this new enterprise, combined with the recent state law changes and President Obama’s actions easing restrictions on federal funding for embryonic stem cell research, will transform embryonic stem cell research at the University of Michigan.

As you all know, the Department has an extremely rich tradition of medical and graduate student teaching excellence (beginning more than 150 years ago in the Department of Anatomy). Our faculty are the major purveyors of didactic lectures and empirical demonstrations in M1 Histology, Embryology, and Neurobiology. We are also responsible for teaching graduate courses in Cell Biology, Principles of Development, Organogenesis and Histology in addition to contributions to courses offered by other departments and programs throughout the University. CDB faculty are actively involved in the continued development of educational resources to provide enhanced learning opportunities to students within and beyond the walls of the institution. As a demonstration of the continuation of the CDB tradition of excellence, one of the Department’s very own (Dr. Matthew Velkey) has been recognized by multiple teaching awards in 2009 (see page 4).

We hope you enjoy this year’s newsletter, with its new design and informative and interesting articles. Finally, please take a look at our recently updated web site at www.med.umich.edu/cdb/ to see what is going on throughout the year.

James Douglas Engel, Ph.D
It is not often that one encounters members of the lay public who possess the vision and conviction to alter the direction of scientific research, but Bob Alpern was precisely that kind of individual. His support of embryonic stem cell research at the University of Michigan, and Marge Alpern’s support of this vision, formed the foundation for continuing our critical research efforts after our initial federal support ran out, and it is not overstating the case to say that without Bob and Marge, this important new avenue of scientific investigation may have passed into oblivion.

Bob’s support of human embryonic stem cell research in our Department was born from equal parts intellectual curiosity and profound dismay with our policy makers that this potentially life saving research should be used as a political football when patients were suffering and dying. The Alpern gift was all the more poignant given that their beloved grandson, Miles Levin, developed a national following on his blog while he described in detail his battle with cancer, which he eventually lost.

Bob and Marge were in the forefront of the fight against the ignorance and fear that threatened to slow research efforts that might prevent future parents and grandparents from suffering the devastating effects of Miles’ disease. Bob and Marge were strong supporters of Michigan Proposition 2 in November 2008, which overturned some of the most oppressive anti-embryonic stem cell legislation in the country.

Bob passed away this past February. He leaves behind his loving wife, Marge, and his children and grandchildren. He will be fondly remembered in the Department as someone who would have made a fabulous graduate student.

A memorial plaque and ginkgo tree will be installed this Fall on main campus in Bob’s memory.

“His support … formed the foundation for continuing our critical research efforts after our initial federal support ran out, … without Bob and Marge, this important new avenue of scientific investigation may have passed into oblivion”
The past several years have indeed been very good for CDB’s histology teaching staff with four of our faculty receiving a total of fifteen teaching awards. In just the past two years alone, Dr. Matt Velkey, the director of medical histology and co-director of the dental and graduate histology courses, was recognized with five such awards:

Dental School D1 Faculty Award, chosen by the dental school class of 2012 on the basis of enthusiasm for teaching and outstanding service to the first year dental students.

American Medical Women’s Association Gender Equity Award, chosen by a vote of the school’s student body to honor those faculty members who promote a gender-fair environment for the education and training of physicians and assure equal opportunities for women and men to study and practice medicine.

Thomas G. Varbedian Award for Excellence in Service to Students, awarded annually by the Medical School Student Council to the medical school alumnus/a, faculty or staff member most dedicated to serving medical students.

Elizabeth Crosby Award for Excellence in Basic Science Teaching, given by the student members of the Galen’s Medical Society to a faculty member for outstanding teaching of medical students in a basic science area.

University of Michigan Provost’s Teaching Innovation Prize, awarded to Matt and Dr. Lloyd Stoolman in the Department of Pathology for their roles in developing a virtual microscopy resource that is now used to teach histology and pathology to dental, medical, and graduate students here and at other institutions.

Matt shares these awards along with Dr. Kate Barald, who has won six D1 faculty awards, Dr. Kent Christensen, a Crosby Award winner, and Dr. Sun-Kee Kim, who has not only received Varbedian and Crosby Awards, but also the 2008 Kaiser Permanente Teaching Award for Pre-clinical Education, which is the most prestigious teaching award given by the Medical School. While these are significant individual achievements, they are more importantly a reflection of the overall excellence of the histology courses which are team taught and, at their core, reliant upon the dedication and effort of all of the faculty and staff involved.

The histology curriculum has shifted dramatically into an online format...
whereby a wealth of resources are now available to our students, and it is this unfettered access in combination with an outstanding faculty presence in lectures and lab sessions that students most cite as their reasons for valuing the courses so highly. None of this would be possible without the support of staff in the Medical School and CDB, and, most importantly, the current histology instructors who actually develop the educational resources and teach in the labs and deliver lectures. Among these are Drs. Steve Ernst, Rex Holland, Michael Hortsch, and Mike Welsh. Past contributors include Drs. Al Beaudoin, Susan Brown, Deb Gumucio, Donna Livant, Don MacCallum, Sue O’Shea, and Pamela Raymond. Finally, several faculty who have recently joined the ranks of the histology staff and will no doubt carry this tradition of excellence forward are Drs. Diane Fingar, Roman Giger, Jiandie Lin, Kentaro Nabeshima, Bill Tsai, Kristen Verhey, and Yukiko Yamashita.

Of course, excellence and innovation in the teaching of histology is nothing new at the University of Michigan. As documented in Horace Davenport’s history of the University of Michigan Medical School, Not Just Any Medical School, histology had its beginnings in 1877 when the University bought fifteen microscopes and first offered a short course in histology to its medical students initially as a supplement to the physiology curriculum. Students in the course had to prepare and stain their own slide sets, but the course and its teachers turned out to be so popular that it had to be offered five times each term. 132 years later, the nature of teaching histology may have changed dramatically, but the tradition of outstanding teaching is clearly alive and well.

“132 years later, the nature of teaching histology may have changed dramatically, but the tradition of outstanding teaching is clearly alive and well.”
Ben Allen
Assistant Professor
P: Otorhinolaryngology

Richard Altschuler
Professor
P: Otorhinolaryngology

Kate Barald
Professor

Scott Barolo
Assistant Professor

Andrew Campbell
Lecturer

William Dauer
Associate Professor, P: Neurology

Marina Di Magliano
Assistant Professor, P: General Surgery

Andrzej Dlugosz
Professor, P: Dermatology

James Douglas Engel
Professor and Chair

Xing Fan
Assistant Professor, P: Neurosurgery

Diane Fingar
Assistant Professor

Philip Gage
Associate Professor, P: Ophthalmology & Visual Science

Roman Giger
Associate Professor

Jun-Lin Guan
Professor, P: Molecular Medicine & Genetics

Deborah Gumucio
Professor

Zhe Han
Assistant Professor, P: Molecular Medicine & Genetics

Peter Hitchcock
Professor, P: Ophthalmology & Visual Science

Michael Hortsch
Associate Professor

Tomonori Hosoya
Research Investigator

Patrick Hu
Assistant Professor, P: Internal Medicine: Hematology/Oncology

Cheng-Yu Lee
Assistant Professor, P: Molecular Medicine & Genetics

Kim-Chew Lim
Research Assistant Professor

Jiandie Lin
Assistant Professor

Ivan Maillard
Assistant Professor, P: Molecular Medicine & Genetics

Sean Morrison
Professor, P: Molecular Medicine & Genetics

Kentaro Nabeshima
Assistant Professor

Sue O’Shea
Professor

Osamu Tanabe
Research Assistant Professor

Bing Ye
Assistant Professor

Yuan Zhu
Assistant Professor, P: Molecular Medicine & Genetics

Alphonse Burdi
Professor Emeritus

Walter Castelli
Professor Emeritus

A. Kent Christensen
Professor Emeritus

Stephen Ernst
Professor Emeritus

Pentti Jokelainen
Professor Emeritus

Sun Kee Kim
Professor Emeritus

Margaret Lomax
Professor Emeritus
P: Otorhinolaryngology
B.S. Cornell University  
Ph.D. University of Wisconsin-Madison  
Postdoctoral Training Harvard University (McMahon).  

Research Focus  
Dr. Allen's research interests broadly lie in understanding the regulation of growth factor and morphogen signaling during embryogenesis. More specifically, the Allen lab uses a combination of mouse genetics, in ovo chick electroporation, cell biology and biochemistry to address fundamental questions regarding the control of the Hedgehog (Hh) signaling pathway in development and disease. Hh proteins represent one of a relatively small number of families of critical signaling molecules that control many developmental processes during embryogenesis. Abnormal Hh signaling is responsible for several of developmental diseases, as well as a number of cancers in adults.

The focus of the Allen lab is to identify and characterize a growing list of cell surface and extracellular proteins that mediate cellular responses to secreted Hh ligands.

As part of this research, the lab is exploring the function of several novel pathway components in multiple Hh-responsive tissues, including neural tube patterning, digit specification, and craniofacial development. The long-term goal of the lab is to uncover and understand novel regulatory mechanisms of Hh signaling that may lead to treatments and therapies for a range of Hh-dependent human developmental diseases and cancers.

Current model of cell surface regulation of the vertebrate Hh signaling pathway  

**Figure 1.** In the absence of Hh, Ptc1 inhibits the activity of Smo. Gas1, Cdo and Boc expression sensitizes cells to low levels of ligand and permits full Hh pathway activation. Bottom panel: Hh binding to Ptc1 results in de-repression of Smo and activation of a signal transduction cascade that culminates in the transcriptional modulation of Hh target genes, including upregulation of Hh antagonists (Ptc1, Ptc2, Hhip1), and downregulation of positive acting Hh pathway components (Gas1, Cda, Boc).

Shh-dependent specification of the ventral neural tube during mouse embryogenesis.  

**Figure 1.** In the developing mouse neural tube, Shh is initially expressed in the notochord (NC) underlying the ventral neural tube; as development progresses, Shh auto-induces a secondary domain of Shh production within the floor plate (FP) of the neural tube at the ventral midline. Several lines of evidence indicate that Shh acts in a concentration dependent manner to specify all ventral cell types of the developing neural tube (PV3, PMN, PV2, PV1, PV0). Importantly, markers exist for these cell types (center panel), allowing for both qualitative and quantitative assessment of alterations in Shh signaling during neural patterning. A representative example of such marker analysis is shown in the right panel. Yellow, FoxA2; purple, Nkx2.2; green, Olig2; blue, Nkx6.1; red, Pax7.
Research Focus

We study regeneration of the injured adult mammalian central nervous system, focusing on growth inhibitory mechanisms following Spinal Cord Injury, Optic Nerve Injury, and Multiple Sclerosis.

We pursue a mouse genetic approach to study mechanisms that contribute to the regenerative failure of severed axons in the injured central nervous system. Following CNS injury, damaged axons do not regenerate spontaneously. Loss of axonal connections leads to permanent neurological deficits. A long standing goal of our research is to understand how neuronal growth and sprouting is regulated in the mammalian nervous system during development, adult neuronal plasticity, and following CNS injury (i.e., spinal cord injury, optic nerve injury, or multiple sclerosis). We use a combination of different techniques, including cell biology, biochemistry, electrophysiology, surgery, and mouse genetics to study the function of different classes of proteins that directly regulate neuronal growth and plasticity.

We focus on members of the Semaphorin family of guidance molecules and their cognate receptors (the neuropilins and Plexins), myelin-associated inhibitors (Nogo, MAG, OMgp) and their receptors, including the Nogo Receptor family members NgR1, NgR2, and NgR3 and the leukocyte immunoglobulin-like receptor PirB. NgR1, NgR2, and PirB have been shown to regulate neuronal responses to myelin the inhibitors Nogo, Myelin-Associated Glycoprotein (MAG), and Oligodendrocyte-Myelin Glycoprotein (OMgp) in vitro. We study the role of these molecules in the intact (non-injured) and experimentally injured central nervous system. We develop antagonists for inhibitors of growth and test their therapeutic efficacy in CNS injury models.

The physiological role of myelin inhibitors and their receptors in the non-injured brain and spinal cord is not well understood. We recently identified NgR1 as an important regulator of activity-dependent synaptic plasticity. Ongoing studies are aimed at understanding the mechanisms of how enhanced neuronal plasticity leads to improved functional outcomes following nervous system injury.

A second line of investigation is focused on mechanisms of axon-glia interaction during nervous system development, adult homeostasis and disease such as Multiple Sclerosis. Myelin-associate glycoprotein (MAG) has axon protective function in vivo, however, the mechanisms of MAG mediated axon protection are poorly understood. We have identified the Nogo receptor family member NgR2 as a high affinity receptor for MAG and we are currently investigating the role of NgR2 in MAG signaling in vivo. The long-term goal of our research is to develop therapeutic strategies to promote nervous system regeneration and repair following injury or disease.
Ivan Maillard
Assistant Professor

M.D. University of Lausanne, Switzerland
Ph.D. Swiss Academy of Medical Sciences
Hematology-Oncology fellowship and post-doctoral training, University of Pennsylvania

Research Focus
Ivan Maillard is a physician-scientist with interests in the regulation of blood-forming stem cell homeostasis, T cell immunology and Notch signaling. The laboratory is using cellular and molecular approaches to study these questions and the mouse as a model system. Our work is supported by the University of Michigan’s Biological Sciences Scholars Program, the Damon Runyon Cancer Research Foundation and the American Society of Hematology.

Beyond this fundamental research, Dr Maillard is also a practicing physician taking care of patients with hematological malignancies. His research has several themes:

1) Investigate the role of Notch signaling in T cell immune responses, particularly in alloimmunity. We have identified Notch signaling as a novel critical regulator of T cell responses in the setting of allogeneic hematopoietic stem cell transplantation (allo-HSCT). After allo-HSCT, donor T cells eliminate cancer cells through their graft-versus-tumor activity, but also damage normal host tissues through graft-versus-host disease (GVHD). Notch-deprived alloreactive T cells can expand normally after transplantation, but fail to differentiate into potent effector T cells, leading to decreased GVHD severity and improved survival. We are investigating the cellular and molecular mechanisms of Notch action in alloreactive T cells and the therapeutic potential of Notch inhibition in alloimmunity.

2) Study the epigenetic regulation of hematopoietic stem cell function by histone methyltransferases, focusing on Trithorax homologues. We have shown that the protein menin (encoded by the tumor suppressor gene Men1) plays an essential role in the regulation of hematopoietic stem cell function in situations of hematopoietic stress. Menin interacts with the Mixed Lineage Leukemia gene product. We are currently investigating the mechanisms of Menin’s effects in the hematopoietic system. In addition, in collaboration with the Camper laboratory (Human Genetics), we are studying a protein called Ash1L that was recently identified as an H3K4 methyltransferase in mammalian cells. We are investigating the molecular effects of Ash1L in hematopoiesis and a possible interaction of Ash1L with MLL and menin.

3) Explore the function of the “shelterin” complex in blood-forming stem cells and the role of the shelterin complex in the hematopoietic system.

"regulation of blood-forming stem cell homeostasis, T cell immunology and Notch signaling"
B.S. University of Michigan
Ph.D. Harvard University
Post-Doctoral Training Harvard Medical School

Research focus

Microtubules are cytoskeletal filaments that provide structural support for cells and also serve as tracks for vesicle transport, form the mitotic spindle for separation of chromosomes during cell division, and comprise the axoneme in cilia and flagella. Defects in these microtubule-based functions are associated with a variety of diseases, including neurodegeneration, cancer, and ciliopathies. Our work is focused on the molecular and cellular mechanisms by which microtubules and associated motor proteins participate in vesicle transport and ciliary function. Motor proteins use the energy of ATP hydrolysis to carry cargoes along microtubule tracks. This is an essential function in all cells but is particular important in polarized cells such as neurons which have a high transport load due to the long distances and choice of direction (axon versus dendrite) that cargoes must be carried. Our work in axonal transport is focused on how kinesin motor proteins bind to their cargoes and become activated for transport. We have shown that kinesin motors are kept in an inactive state by autoinhibitory mechanisms that prevent motility in the absence of cargo. Autoinhibition appears to be a general mechanism for regulating kinesin motor activity and allows kinesin motors to be activated on demand. We are also interested in how directional choices are made by kinesin motors. Our current hypothesis posits that there is a “tubulin code” in which post-translational modifications of tubulin subunits provide directional cues to kinesin motors. This is by analogy to the “histone code” in which post-translational modifications of histone subunits direct transcriptional events along chromatin. We have shown that kinesin-1 motors move preferentially along microtubules marked by two post-translational modifications, acetylation and detyrosination, whereas kinesin-2 and kinesin-3 motors are not selective for modified microtubules. We are testing whether these modifications provide an “axonal signal” that directs Kinesin-1 transport events to axons rather than to dendrites. Our work in cilia is focused on the role of kinesin motors in the assembly, function and disassembly of primary cilia during the G1 phase of the cell cycle. Ciliary transport is driven by two motors of the kinesin-2 family. One of these kinesin-2 motors, the heterotrimeric KIF3A/KIF3B/KAP complex, is involved in generating ciliary structures whereas the other kinesin-2 motor, the homodimeric KIF17 complex, drives the ciliary transport of channels and other signaling molecules. We are currently studying how KIF17 binds cargo and is targeted to primary cilia in mammalian cells. The work in Dr. Verhey’s lab is supported by research grants from the National Institutes of Health and the Human Frontier Science Program Organization.
Research focus

Adult stem cells continuously supply highly differentiated but short-lived cells, such as blood, skin, intestinal epithelium, and sperm cells, throughout life. The daughters of stem cell division have two possible fates: stem cell self-renewal or commitment to differentiation. It is critical to maintain a balance between these cell populations as an excess of stem cell self-renewal can lead to tumorigenesis, whereas an excess of differentiation can deplete the stem cell pool, reducing tissue regenerative capacity. To maintain the balance between stem cells and differentiating cells, many stem cells have the potential to divide asymmetrically so that each division produces one stem cell and one differentiating cell. Although the control of stem cell division is crucial for tissue homeostasis, the mechanisms that regulate asymmetric stem cell division are poorly understood.

Furthermore, it has been hypothesized that declining stem cell function contributes to tissue degeneration during aging, although the mechanism by which this occurs and whether it involves changes in stem cell division is unknown. Our laboratory is investigating the molecular and cellular mechanisms that govern stem cell behavior, in particular, the regulation of asymmetric stem cell division, using Drosophila male germline stem cells (GSCs) as a model system.

Drosophila male germ line stem cells serve as an ideal model system to study stem cell behavior. They reside in the stem cell niche, which specifies stem cell identity by sending signal(s). Stem cells have elaborate cellular mechanisms to ensure the asymmetric outcome of the division, producing one stem cell and one differentiating cell, which is the key to tissue homeostasis. We have discovered the cellular mechanisms by which stem cell divide asymmetrically; one such mechanism is depicted below: The mother centrosome (red and green) is maintained close to the Niche (blue line)-Stem cell (dotted line) interface, while daughter centrosome (red but not green) migrates away from the niche. Such stereotyped behavior of centrosomes prepares the orientation of mitotic spindle in germ line stem cells, so that stem cells always divide perpendicularly to the niche, placing one daughter within and the other outside the niche.

YUKIKO YAMASHITA
Assistant Professor

Hebao Yuan (postdoctoral fellow) studies how centrosome orientation in germ line stem cells (GSCs), key to asymmetric stem cell division, is monitored and ensured by a novel checkpoint mechanism.

Therese Roth (postdoctoral fellow) studies how GSC centrosome orientation is modulated by nutrient conditions, thereby adjusting the cell cycle activity of stem cells.

Jun Cheng (postdoctoral fellow) studies how GSC centrosome orientation is modulated by nutrient conditions, thereby adjusting the cell cycle activity of stem cells.

Martin Kracklauer (postdoctoral fellow) studies how GSCs and CySCs coordinate their divisions.

Mayu Inaba (postdoctoral fellow) studies how CySCs, that accompany and support GSCs, divide asymmetrically.

Swathi Yadlapalli (graduate student) studies chromosome segregation in GSCs.

Ason Chiang (research associate) studies the function of GSK3 kinase in asymmetric GSC division.

Viktoria Salzmann and Ami Tiyaboonchai (research associates) study the asymmetric cytokinesis in GSCs.

B.S. Kyoto University
Ph.D. Kyoto University
Post-Doctoral Training Kyoto University (Takeda)
Post-Doctoral Training Stanford University (Fuller)
Faculty Honors and Research Leadership Roles

The Department’s faculty, students and postdoctoral scholars continue to be honored for their research and scholarly achievements. Listed below are some of the recognitions that have been accrued at the time this newsletter went to press.

Kate Barald is a member of the AAAS Electorate Nominating Committee of the Section on Biological Sciences Editorial Board, Developmental Dynamics, member of the NSF graduate fellowship review panel for the Engineering Directorate, member of the NSF Developmental Neural Systems cluster review panel (IOS) and member of an NIH NINDS K99 study section; ad hoc reviewer for the Wellcome Trust, the National University of Singapore, the Australian and New Zealand MRC, and served as chair of the CDMRP Neurofibromatosis review panel.

Michael Hortsch is the Editor of Frontiers in Bioscience, International Journal of Cell Biology and Advanced Studies in Biology. Also, completed the book The Sticky Synapse - Cell Adhesion Molecules and Their Role in Synapse Formation and Maintenance.

Patrick Hu received a prestigious Sidney Kimmel Foundation for Cancer Research Scholar Award.

Jiandie Lin received the Anthony Linnane Young Investigator Award, Mitochondrial Research.

Ivan Maillard received an Innovation Award from the Damon Runyon Cancer Research Foundation.

Sean Morrison received the 2008 Harland Winfield Mossman Award in Developmental Biology from the American Association of Anatomists.

Kentaro Nabeshima received a March of Dimes Basil O’Conner Scholar Research Award.

K. Sue O’Shea is the Co-Chair for the National Stem Cell Bank - Scientific oversight committee, an ad hoc reviewer for the NIH, NINDS, and a member of the Stem Cells International, Editorial Board Co-director consortium for Stem Cell Therapies.

Billy Tsai is a member of the editorial board for the Journal of Virology.

Kristen Verhey is an ad-hoc reviewer for the National Science Foundation, MCB - Cellular Systems and a member of the NIH Center for Scientific Review, Cell Structure and Function (CSF) Study Section, ad hoc.

Lois Weisman is a member of the NIH CSR Study Panel, CSF and J Cell Biology, Editorial Board and is an ad hoc reviewer for Wellcome Trust Fund, Austrian Science Fund, Israel Science Foundation and Research Grant Council, Hong Kong.

Mike Welsh is a member of the Cellular Biochemistry and Physiology Editorial Board and Oakridge Associated Universities Peer Review Panel.

Yukiko Yamashita received the 2009 Women in Cell Biology Junior Faculty award from the American Society for Cell Biology, the 2008 Searle Scholar Award, and the March of Dimes Basil O’Conner Scholar Award. Is a member of the Current Protocols in Stem Cell Biology Editorial Board.

Bing Ye received a Whitehall Foundation, Inc. award, “Synapse formation of single drosophila somatosensory novelons”.

Scott Barolo is the Organizer of the 2009 Midwest Drosophila Research Conference and member of the NICHD - Development Biology Review Group and American Heart Association Basic Science Subcommittee.

Doug Engel is an Editor of Molecular and Cellular Biology, Chair of the NIH Erythrocyte and Leukocyte Biology Study Section, a consultant for AmGen, Inc., and served as an ad hoc program reviewer for the Medical Research Council (U.K.), the Babraham Institute (U.K.) and RIKEN (Japan).

Deb Gumucio is a member of the Molecular and Cellular Biology Editorial Board and a member of the Developmental Biology Committee at NICHD.
**Thesis Defenses**

Kaleena Bernardi (Tsai Lab)  
"Derlin-1 and the E3 Ubiquitin Ligases Hrd1 and gp78 Facilitate Cholera Toxin Retro-translocation."

Will Brandt (Engel Lab)  
"The role of Gata2 in hematopoietic and vascular development." Dr. Brandt is currently a postdoctoral fellow at Johns Hopkins Medical School.

Chong Chen (Zheng Lab)  
"The role of the Tsc-mTOR pathway on the regulation of the hematopoietic stem cells."

Lisa DeBoer-Emmett (O'Shea Lab)  
"Novel BMP antagonists and neural induction in the mouse."

Amanda Evans-Zacharias (Gage Lab)  
"Lineage-specific functions of the transcription factor Pitx2 in eye development."

Michele Forster (Tsai Lab)  
"Elucidating the Functions of Protein Disulfide Isomerase Family Proteins during Quality Control in the Endoplasmic Reticulum."

Jennetta Hammond (Verhey Lab)  
"Kinesin Regulation: Discovering the Mechanisms that Mediate Autoinhibition, Cargo Complex Formation, and Selective Microtubule Use in Neurons."

Meghna Waghray (Merchant Lab)  
"Cell specific regulation of Sonic Hedgehog in adult stomach: understanding mechanisms leading to gastric atrophy/metaplasia." She is now at Johns Hopkins in a postdoctoral fellowship studying Sonic Hedgehog in pancreatic cancer.

Alisha Yallowitz (Wellik Lab)  
"Hox function in mammalian kidney development."

Will Zacharias (Gumucio Lab)  
"Roles for intestinal hedgehog signaling during adult homeostasis and inflammation." Currently Will is an MSTP student who is finishing his clinical requirements at Michigan.

**Awards**

John Dishinger (Verhey Lab) received a NIH Ruth L. Kirschstein National Research Service Award - Postdoctoral Fellowship.

Michelle Durance (Gumucio Lab) received a Crohn’s and Colitis Foundation of America Fellowship; "Effects of hedgehog signaling in mice on intestinal immune development."

Bilgen Ekim (Fingar Lab) received an American Heart Association Predoctoral Fellowship Award.

Ann Grosse (Gumucio Lab) received a pre-doctoral fellowship award from the Organogenesis Training Grant.

Masayuki Yamamoto, MD/PhD (Engel Lab) Former postdoctoral fellow in the Engel Lab, who discovered the GATA family of transcription factors, recently became Dean of the Medical School and Vice-President for Research at Tohoku University in Sendai, Japan.
The Department continues to actively foster partnerships between its faculty, visiting scholars and UM undergraduate students in providing a range of (often) first research experiences for the students. In the past year, we proudly note that more than 30 of Michigan’s “Brightest and Best” undergrads worked in twelve Department laboratories.

Why is the Department and its already heavily-committed faculty involved in these campus wide undergraduate research initiatives? Here is why: many of our participating faculty recall that their own undergraduate research experiences played pivotal roles in the shaping of their own future teaching and research careers. Also, the research mentoring of our own undergraduate students is another way of “giving back”. The Department sees itself as being one of the key players in the educational mission, not only in the Medical School but in the University as a whole.

In addition to furthering the research missions of our own laboratories, the CDB faculty strive to provide meaningful experiences that allow these students to achieve such things as:

- learning through hands-on work outside of the traditional classroom;
- developing new research skills that may be useful both in their ongoing UM undergraduate education and in their future professional pursuits;
- identifying future academic and career interests in the biomedical sciences;
- developing a working relationship with a faculty mentor.

So, if there is any remaining question about why we should be involved with undergraduate research mentoring, the simplest answer is “Why not?”
In her role as Senior Administrative Specialist in the Center for Organogenesis (CFO), Rebecca Pintar enjoys talking and interacting daily with faculty members in 29 departments of five schools and colleges, Organogenesis Pre and Postdoctoral trainees, and a broad range of administrative staff across campus. It’s all in a day’s work for Becky, a nine-year veteran of the CFO and recipient of the 2009 Professional Staff of the Year Award — an honor befitting an employee her supervisor, Deb Gumucio calls “a jewel” of the school.

And Bec’s job is a complex one - she is directly responsible for, or plays a major role in, the fulfillment of several major CFO initiatives, including the graduate course, “Organogenesis of Complex Tissues,” the Center’s seminar series, website, newsletter, accounting and rebilling, grant writing, planning of the International Symposium on Organogenesis — which typically draws more than 250 attendees — training grant administration, and other complexities of the day-to-day operations of the Center.

Rebecca Pintar Wins Dean’s Professional Staff of the Year Award

Becky also shines during the summer months when things might be slower at the University. It is then that one of her most important roles heats up. While most people are milling about and enjoying the Ann Arbor Art Fairs, Becky is hard at work in another of the CFO’s key initiatives: Bio-Artography, which celebrates microscopic tissue photography as art. She collects images and creates a portfolio of art to serve as an outreach and fundraising tool for the Center at the Art Fairs. She constantly is printing, matting and framing the works of art, sometimes up to 12 hours a day. At other times of the year, Becky is busy planning Bio-Art displays and working with other groups around campus who are also interested in arts and health at Michigan.

Pintar began her U-M career in 1975 as a technical typist in the Department of Dermatology Research. She has also held appointments in the Department of Radiology’s Breast Cancer Detection Center and the Department of Environmental and Industrial Health. Her most recent role before joining the Center for Organogenesis was as executive secretary in the Institute of Gerontology.

After 30 years of service to the U-M, she is lauded with an award and the backing of many in the Center and around the University. “I couldn’t believe it because there are so many people who are just as deserving,” she says of winning the award. “I am honored that my nominators think so highly of me. Hard work and dedication does pay off, and we are all very lucky to be a part of this great institution.”

When she is not serving the Center for Organogenesis, Becky enjoys camping with her husband David and Pug dog, Curly, along with gardening, cooking, and spending time with her 89 year old mother.

Becky thanks Deb Gumucio for being a terrific boss, mentor and friend, along with the many Center faculty members and trainees, and administrative staff in the Department of Cell and Developmental Biology. She also thanks David in particular for his support of her U-M career.
The Microscopy and Image-analysis Laboratory (MIL) has been awarded funds from a number of internal sources to purchase a 2-photon confocal microscope system. This system represents the next level of laser based fluorescent microscopy systems that will allow our researchers to image deeper into tissues, either fixed or live, minimizing damage associated with conventional filter based laser confocal systems.

The system will be fitted to the Leica SPS-X platform, which in itself is a novel advancement in imaging because it utilizes a tunable “white-light laser” that allows researchers to select any wavelength they desire for excitation of their fluorophores. It will be coupled with a 405 nm diode ultraviolet laser and a Picoquant fluorescent lifetime imaging (FLIM) module making this a one-of-a-kind system for shared use on the University of Michigan campus.

With the new confocal system, combined with the ability to image 2-photon excitation, our researchers now have the ability to chromatically select the emission band for the detection channel with patented Leica SP® spectral detection technology. Up to five spectrally-definable channels can be equipped. For each detection channel, the emission bandwidth can be set with nanometer specificity. A 5nm bandwidth is the narrowest possible band gap and 400nm the widest.

With this innovative technology, this new instrument will essentially have a set of freely-definable filtersets. The system will therefore always have the most appropriate filterset to image a dye or combination of dyes.

Installation is expected to be complete late November. Please visit www.milimaging.com, for MIL updates, announcements, and training opportunities.

Advancements in Basic-Science Imaging Technology

Exitation lines can easily be selected to any wavelength with 1 nm accuracy. Tuning via the LCD control panel allows to select excitation light while scanning.

Images courtesy of Leica Microsystems.
Highlights of the new Leica TCS SP5X “White Light Laser” Confocal”

New Wavelengths

Wide Range of Freely Selectable Excitation Lines (online tuning)

A single light source replaces a stack of many separate lasers

Free optimization of excitation line, emission band for increased signal/noise

Choice of up to 8 excitation lines—simultaneously tunable

Excitation unmixing

2-photon imaging for thicker tissue samples

Fluorescence lifetime imaging (FLIM).

“…our researchers now have the ability to chromatically select the emission band for the detection channel…”

Sample illustrating 8 fluorescent signals: Cy2 (491 nm), Latex particles (474 nm), Acridine Orange (484 nm), Cy3 (551 nm), TexasRed (562 nm), Alexa 594, Alexa 633, Cy5 (640 nm)
Thank you so much for your donations! Every little bit helps. Below are some examples of what we have been able to do with your kind donations:

**Graduate Student Education**

In the past, we have solicited gifts to enhance our graduate education program – you have answered our call! The donations we received have given the department an opportunity to award travel grants to students. In addition, it has brought us closer to our goal of recognizing the efforts of one extraordinary Ph.D. student each year! To us, this support is essential as we compete with major research universities around the world for the very best graduate students.

**Stem Cell Research**

Recently, we have received several gifts towards the enhancement of stem cell research. In fact, a recent graduate requested donations to stem cell research in lieu of graduation gifts! We have also received large donations for stem cell research that have enabled us to honor faculty members with research dollars.

"...a recent graduate requested donations to stem cell research in lieu of graduation gifts!"

**Lectureships**

We have two lectureships: The Burton Baker and the Sarah Newman Lectureships allow us to bring in high caliber speakers, with whom our students have the opportunity to meet and discuss their work. In the past, we have had faculty members suggest speakers. This year students and post docs are suggesting and organizing the lectures!

**Professorship**

We are very fortunate to have the Crosby-Kahn Collegiate Endowed Professorship established in Cell and Developmental Biology. Dr. K. Sue O'Shea has the honor of receiving the first ever Crosby-Kahn Endowed Collegiate Professorship in Cell and Developmental Biology.

The full amount of your donation is used for the cause(s) you stipulate or for graduate education (no administrative costs are deducted). Your support is greatly appreciated by the Department and by our most deserving graduate students.

If you would like to support graduate education by making a gift to the Department of Cell and Developmental Biology visit www.giving.umich.edu/give/med-cell, or send a check payable to the University of Michigan to:

Cell and Developmental Biology
3062 BSRB, 109 Zina Pitcher Pl.
Ann Arbor, MI 48109-2200
Mary Jane Showers arrived at the University of Michigan in 1947 to pursue her Master’s in Anatomy. Having completed her nursing and bachelor’s degrees in Chicago, she was in pursuit of advanced studies in anatomy in order to take over the textbook by her teacher Nellie Millard. “The impetus came from the need to have a greater diversity and depth of knowledge,” Dr. Showers reflected. Millard’s educational background was at Michigan, and she was familiar with both the anatomy department and Elizabeth Crosby, making it a natural place to direct Dr. Showers for her studies.

While at Michigan, Showers obtained not only her master’s degree but also her Ph.D. in Anatomy. Dr. Elizabeth Crosby served as her major professor, her thesis director, and a “very fine role model.” They spent a significant amount of time together, operating together on the experimental animals, as required for the doctoral thesis.

The influence of a female mentor in the field was exceptionally important for Dr. Showers. “There was still a prevailing feeling that you were an inferior,” Dr. Showers noted in reflecting on the position of women in science during her time at Michigan.

At the time of Dr. Showers’s graduation from the Ph.D. program at Michigan in 1957, women were still seen as a drag on the market in basic science research. Dr. Crosby knew of an opening in a lab on campus, and attempted to persuade Dr. Showers to take the job since the job market was so tenuous. “I told Elizabeth [Crosby] ‘I’ll work in a dime store before I’ll work as a technician,’” Dr. Showers recalled. Rather than take the lab position at Michigan, Dr. Showers joined the faculty at Our Lady of Cincinnati College. She went on to serve at the professorial level at the University of Kentucky, Hahneman College of Medicine, and the Philadelphia College of Osteopathic Medicine, and as a visiting professor at Rutgers University and Duke University, eventually settling at the University of Cincinnati where she stayed until her retirement in 1994.

The women kept in touch long after Dr. Showers left Michigan. The two communicated through letters and by phone, and Dr. Crosby once visited Cincinnati to see Dr. Showers. “The three things that Dr. Crosby taught me were persistence, quality, and curiosity,” Dr. Showers noted, reflecting on her time with Dr. Crosby.

Today, Dr. Showers honors Dr. Elizabeth Crosby’s legacy through her support of the Crosby-Kahn Professorship. Dr. K. Sue O’Shea is the current Crosby-Kahn Professor of Cell and Developmental Biology. Dr. O’Shea is the Co-Director of the A. Alfred Taubman Medical Research Institute Consortium Stem Cell Therapies, and studies the differentiation of neural stem cells and embryonic stem cells, and the very early development of the vertebrate nervous system. Dr. O’Shea said in recollection of Dr. Crosby, “Dr. Crosby was retired when I was first hired at the University of Michigan, but was actively interested in research and the research faculty. I was invited to join her for tea—unfortunately, she was out of tea bags, but we had an enjoyable cup of hot water!”

Where are they now?

Mary Jane Showers
MAKE A DIFFERENCE

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