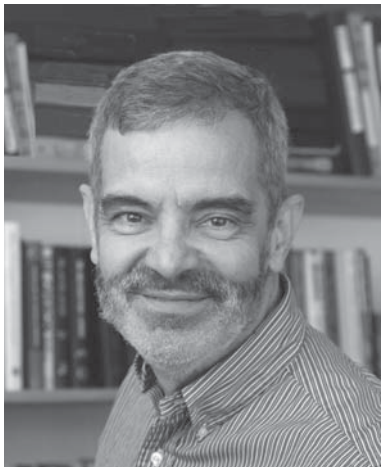
Molecular, Cellular, and Developmental Biology
University of Michigan
Fall 2007

MCDB News

Inside

A New Curriculum for Biology Students

Beginning this fall, introductory biology students will see a new and expanded approach to the subject, as we transition from a single course, to a group of three new courses. "More learning is the goal, rather than more teaching," explains Professor Bob Bender, Associate Chair for Curriculum in MCDB.



Professor Bob Bender
Associate Chair for Curriculum

The new curriculum grew out of the discussions of a joint committee of MCDB and Ecology and Evolutionary Biology faculty members, which was charged with evaluating the previous introductory course, Biology 162. This one semester course unified some key concepts in biology, but lacked depth and breadth. This was supplied by supplementary courses in the Biology major. Now, with more than half-dozen different majors and minors in the life sciences, many of which do not include the supplemental courses that were key parts of the Biology major, the one-semester course could no longer provide a sufficient coverage of biological concepts. The new courses give a more effective experience, Professor Bender says. "Even those students who take only the new introductory courses will have a broad and deep experience of modern biology."

> "More learning is the goal, rather than more teaching."

Although the new two semester format allows for coverage of additional topics, the increase is only about twenty to thirty percent. "What we decided was that we would cover a few more topics, which would use some of the expanded class time; the rest of the time would be devoted to expanded coverage of the topics and to a more interactive style of teaching," says Professor Bender. "There are about as many new vocabulary words learned in a typical one semester intro Biology course as there are in an intro French course. We want to get beyond vocabulary, and get into grasping the concept. That takes time and a variety of educational approaches."

Two of the new courses' topics split along the interest lines of EEB (Biology 171) and MCDB (Biology 172). Realizing that the separation poses a risk of creating an artificial division of biology, the committee decided the lab course (Biology 173) would be fully integrated. Fusing concepts and technologies from both departments, the unified lab course gives an integrated biology experience, similar to how modern science works. "Ecologists who are doing population sampling use DNA technology to do so," says Professor Bender. "People who are doing bioinformatics and genomics are looking are at evolutionary connections."

As a consequence of changes in the format of introductory biology, changes to the rest of the undergraduate curriculum will be introduced in subsequent years. In the fall 2008 we will introduce changes to key mid level courses offered by MCDB, such as genetics, biochemistry and animal physiology. By 2009 the transition will be complete, as changes are incorporated into our capstone 400 level courses.

A Message from the Chair

The greatest challenge the Department of MCDB has faced in its first six years has been dealing with a massive wave of retirements. To maintain faculty size, we had to replace over 40% of our founding members! Helping the thirteen new tenure-track faculty members and two new lecturers we have hired get their teaching and research careers started is exhausting. However, because of the exciting ideas these young colleagues bring to the Department, it is among the most rewarding parts of my job. In 2006-07 both our new and established faculty members had an extremely productive year. The curricular efforts of the Department

Richard Hume

(some of which are described on page one) have been recognized by the LSA Dean's office, which recently announced that MCDB will receive the 2007 Departmental Award for Contributions to the Undergraduate Initiative. On page four you will see a list of new grants received by MCDB faculty members. With federal funds extremely tight, it is a remarkable achievement that 27 of the 29 MCDB labs have at least one active grant, and that the only exceptions are a Professor in phased retirement and an Assistant Professor who just joined the Department and is sure to be funded soon. On pages six and seven you will see some of the recent accomplishments of our students. Looking to the future, our number of undergraduate concentrators has increased over 40% since 2002-03, and the 2007 class of PhD students is near record size, so I am very confident that even greater achievements lie ahead.

Science Spotlight with Pamela Raymond

When Pamela Raymond began as an undergraduate student at the University of Michigan in 1968 the campus was a focal point for political change and student activism, but for her the research going on in the Kraus building was an even more compelling attraction! As an undergraduate student she majored in Zoology and worked in the laboratory of Stephen Easter, now Professor Emeritus of Molecular, Cellular and Developmental Biology. She remained in his laboratory as a graduate student where she began studying neurogenesis. Her doctoral dissertation resulted in a series of papers published in the late 1970s that continue to be cited today, in which she showed that new neurons are added to the goldfish retina throughout adult life. Later work from her group showed that self-renewing, multipotent retinal progenitors are retained in the differentiated retina of adult fish and in response to injury they regenerate neurons that can restore visual function. This evidence demonstrates that adult fish have true retinal stem cells.

Pamela Raymond

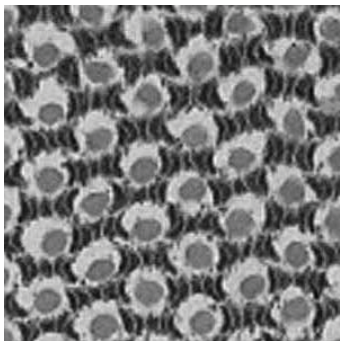
The current focus of research in Professor Raymond's group is to understand the molecular basis of cell-cell interactions that regulate retinal stem cells and that mediate neuronal specificity. Her laboratory now uses zebrafish as a genetic model system to study both embryonic retinal development and growth and regeneration of the neural retina in adults. In a recently completed analysis Raymond's group showed that the stem cell compartments in the fish retina have molecular and cellular characteristics similar to those described for neural stem cell niches in the mammalian brain. Retinal progenitors in the zebrafish also possess a unique combinatorial and regionalized expression of regulatory genes that are involved in specification and differentiation of the embryonic eye and neural retina, including the retinal homeobox genes, *rx1* and *rx2*. Earlier studies from Raymond's group showed that *rx2* plays a fundamental role in the specification of retinal identity in neural progenitors.

Like all parts of the nervous system, the retina includes several types of neurons and supporting glial cells that derive from the same pool of stem cells, and the choice between these two primary fates, neuron versus glia, is mediated in part by the Notch signaling pathway. Raymond and her collaborators showed that when Notch signaling is inactivated either genetically or pharmacologically in zebrafish embryos the major glial cell type in the retina, Müller glia, fails to differentiate, implying that Notch has an instructive role in the choice of

Pamela Raymond continued on page three

Pamela Raymond continued

glial fate. In a paper published in July 2007, her group reported the surprising discovery that Müller glial cells are not irreversibly committed to a glia fate. They found that Müller glia in the differentiated zebrafish retina periodically reenter the cell cycle and function as neuronal progenitors specifically for the rod photoreceptor lineage. Even more significantly, when the zebrafish retina is damaged, Müller glia proliferate extensively and recreate the molecular and cellular characteristics of a retinal stem cell niche. When this happens, the progeny of dividing Müller glia become retinal stem cells with the ability to regenerate retinal neurons and repair the injured retina. What is particularly exciting about this finding is that the human retina also has abundant Müller glial cells that proliferate actively in the injured or diseased eye; however, in mammals including humans, Müller glia fail to reactivate a program of neurogenesis. Fish therefore provide a unique model in which to discover the critical factors that allow differentiated glial cells to produce neuronal progenitors for repair of damaged neural tissues.



The cone mosaic pattern in a zebrafish retina: vertical rows of alternating UV cones (large pale circles) and blue cones (the knots on the bow-tie shapes) are separated by intervening rows of red and green double cones (the loops on the bow-tie shapes).

A second major area of research interest in the Raymond laboratory is to uncover the developmental mechanisms that pattern the array of cone photoreceptors in the zebrafish retina. Unlike the human retina, in which the cones are packed into a small area called the fovea, in fish the planar density of cones is approximately constant across the entire retina. Moreover, the cones are laid out in a precise mosaic array according to their spectral type, in that the neighbor relationships between individual red and green and blue and ultraviolet cones are invariant. We know virtually nothing about the molecular control of cone photoreceptor determination — the choice of whether to be a red, green, blue or ultraviolet cone — and how this precise mosaic pattern is achieved during development. To get at this question Raymond and her group are using forward genetic screens in zebrafish to identify mechanisms that pattern the cone mosaic. She notes that in many invertebrate animal models, choice of cell fate is determined in the context of single cells each with a specific identity, but the cone mosaic array in the fish retina is a unique example in vertebrate development of cell fate determination and patterning of differentiated tissue at the level of individual cells.

Science Spotlight with Steven Clark

Stem cells are not limited to debates on embryonic research, they are a critical part of development in both plants and animals. The unique properties of stem cells that allow them to specialize as a large number of different cell types – for example as neurons, skin cells or muscles in humans – is what allows them to carry out such important functions in normal development.

Lindsey Gish, Chunghee Lee, and Steven Clark

In adult animals, stem cells appear to be more limited in their normal potential than stem cells in embryos. In contrast, adult stem cells in plants are as active and flexible as embryonic stem cells. Because plants continuously form new organs and tissues as adults, they need a population of flexible stem cells to draw upon for new organs such as leaves, branches, and flowers.

At the tip of every growing branch or root is a group of stem cells that act similar to their counterparts in animals. However, plants are masters of stem cell control, with the ability to form new stem cells as required. Every time you trim back your bushes, you remove stem cells from the branch tips, but you also activate new populations of stem cells elsewhere in the plants, giving rise to new branches that will need to be trimmed again next month.When the stem cells divide, one daughter cell remains a stem cell, while the other daughter differentiates, forming new organs and tissues. In both plants and animals, these stem cells divide very slowly, requiring a specific environment, or stem cell niche, to be able to remain stem cells.

Steven Clark continued on page five

New Grants

Akaaboune, Mohammed Post-synaptic Rapsyn Dynamics at the Neuromuscular Junction of Living Animals, *NSF*

Chapman, Matt Assembly of Curli Fibers of Escherichia Coli, *NIH*

Clark, Steven CLE Domain Function and Processing Across Plants and Nematodes, *USDA*

Clark, Steven Receptor-Mediated Signaling Regulating Stem Cell Fate, *NIH*

Csankovszki, Gyorgyi The Dosage Compensation Machinery of C. elegans, *NIH*

Denver, Robert Leptin Physiology throughout the Life Cycle of the Frog, *NSF*

Duan, Cunming Engineering Microenvironments for Control of Embryonic Development, *Keck Foundation*

Jakob, Ursula Oxidative Thiol Modifications and Aging, *NIH*

Klionsky, Daniel The Trek Toward Active Learning: From High School to the University, *HHMI*

Kumar, Anuj Organelle DB / Organelle View: A Community Resource of Protein Localization and Function, *NSF*

Kumar, Anuj Integrated Large-Scale Analysis of Filamentous Invasive Growth in Yeast, *American Cancer Society*

Kumar, Anuj was named Research Scholar for the American Cancer Society.

Kuwada, John Role of Transient Receptor Potential Channel TRPM7 for Neural Circuit Function, *NSF*

Olsen, Laura Understanding Peroxisomal Protein Networks using Proteomics, Subcellular Localization of Fluorescent Protein Fusions, and Reverse Genetics, *NSF*

Pichersky, Eran GEPR: Building and Operating a Chemical Factory: Glandular Trichomes of Solanum Species, *NSF*

Pichersky, Eran Biosynthesis of the naturally synthesized insecticides methylketones in tomato glands, *USDA*

Pichersky, Eran Structural, Functional, and Evolutionary Basis for the Utilization of a Quinone Methide-Like Mechanism in the Biosynthesis of Plant Specialized Metabolites, *NSF*

Schiefelbein, John Interdisciplinary Training and Curriculum for Undergraduates in Biological and Mathematical Sciences (UBM) at the University of Michigan, *NSF*

Schiefelbein, John Arabidopsis 2010: Constructing and Analyzing a Model Gene Regulatory Network, *NSF*

Wang, Yanzhuang Assembly and Function of the Golgi Stacks during the Cell Cycle, *Pardee Foundation*

Yocum, Charles The Function of PsbO, the Photosystem II Manganese-Stabilizing Protein, *NSF*

The Michigan Difference

Funding priorities for MCDB and detailed descriptions are available at:

www.mcdb.lsa.umich.edu/gifts.php

For change of address, or if you do not wish to receive future MCDB publications, please email: MCDB.alumni@umich.edu

Faculty Honors

Steven Clark was promoted to Professor.

Ursula Jakob was promoted to Associate Professor with tenure.

Daniel Klionsky was appointed Alexander G. Ruthven Professor of Life Sciences.

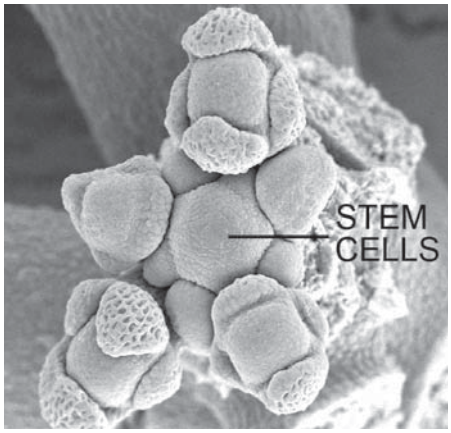
Laura Olsen was named Editorial Board member for *Autophagy* journal 2007-2010.

Pamela Raymond was appointed the Stephen Easter Collegiate Professor of MCDB. She also was Distinguished Lecturer at the Cole Eye Institute, Cleveland Clinic.

Steven Clark continued

Steven Clark's lab has spent over a decade investigating how these cells are regulated. "We are interested in what controls the maintenance of these cells, how the correct daughter cell differentiates, and what signals provide the positional queues that are the driving force for this process," says Clark. Most of the research in the Clark lab uses Arabidopsis, a Brassica species closely related to cauliflower, canola, and broccoli. "We can grow 50,000 Arabidopsis plants at one time, and with the genome completely sequenced, we have many tools to speed our research."

Stem cells undergo what are called asymmetric cell divisions, in which the two daughter cells acquire different, or asymmetric, fates. According to Clark, "The asymmetric division of stem cells is the key to understanding how they are controlled. Without this asymmetry, their unique ability to both self-renew and give off new cells for differentiation would be lost." Research in the Clark lab is now focused on how this asymmetry is established, what signals drive it, and how those signals are detected by the stem cells.



Stem cells of the plant Arabidopsis (center) are the source of new organs, such as the flower primordia forming around the periphery.

Research from a number of labs has shown that the pathways studied by the Clark lab in Arabidopsis have similar counterparts across flowering plants, from rice to corn to tomatoes. Other interesting studies have shown that one major difference between wild plant species and their cultivated cousins is that the agricultural versions have more stem cells. "Domestication has selected for larger stem cell populations to provide faster organ formation and larger fruits," according to Clark. "One of the goals of our research is to eventually provide the tools to optimize stem cell control so that organ formation, fruit size and seed production can be best matched to growing conditions that can vary across different regions and different years."

The Clark lab is also interested in an ongoing comparison between plant and animal stem cells. Clark adds, "Plant stem cells are so easy to identify and manipulate that perhaps we can learn how to make animal stem cells match the flexibility of plant stem cells by understanding the machinery underlying their great adaptability. Fortunately, we have highly talented undergraduates, graduate students and postdoctoral fellows all working together on these challenging questions."

Welcome New Faculty

Assistant Professor **Erik Nielsen** has joined us from the Donald Danforth Plant Science Center and from the Biology Department at Washington University, St. Louis where he was an Assistant Member and Adjunct Assistant Professor respectively. Dr. Nielsen is a plant cell biologist whose research focuses on understanding the cellular machinery involved in proper deposition of plant cell wall components.

On January 1st, 2008, Assistant Professor **Catherine Collins** will join the department from Washington University, St. Louis. After receiving her PhD from University of California, San Francisco in 2000, Dr. Collins served as a postdoctoral fellow at University of California, Berkeley and at Washington University. Her research focuses on the structural plasticity of neurons.

Assistant Professor **Stefan Walter** will join the department January 1st, 2008, from the Technical University of Munich in Munich, Germany. Dr. Walter served as a research associate at the Howard Hughes Medical Institute at Yale University with Professor Arthur L. Horwich. His research involves the molecular chaperone Hsp104 from yeast, prion proteins in yeast, and the development of enzyme-based biosenors.

Post-Doctoral Fellows
Where Are They Now?

Ronald Bonnett, Assistant Professor in the Biological Sciences Department at the University of Tulsa, Oklahoma. *Mentor – Bob Denver*

Pratik Jagtap, Post-Doctoral position with Phil Andrews in the Biochemistry Department, University of Michigan Medical School. *Mentor – Janine Maddock*

Choong Je Ma, Senior Research Scientist at the Korea Institute of Oriental Medicine, South Korea. *Mentor – Eran Pichersky*

Jason Meyer, Assistant Professor at Colgate College, Hamilton, NY. *Mentor – Pamela Raymond*

Louis St. Amant, Assistant Professor in the Pathologie et Biologie Cellulaire department at Université de Montréal, in Montreal, Canada. *Mentor – John Kuwada*

Goro Taguchi, Lecturer at Shinshu University, Japan. *Mentor – Eran Pichersky*

Ryoichi Tanaka, Kagoshima University, Japan. *Mentor – Amy Chang*

Marina Varbanova, Researcher at Michigan State University. *Mentor – Eran Pichersky*

Guodong Wang, Researcher at the Noble Foundation in Ardmore, Oklahoma. *Mentor – Eran Pichersky*

PhD Degrees Granted

Peter Schlueter (Duan) "In vivo functions of Insulin-like Growth Factor signaling during zebrafish development."

Jiandong Liu (Bodmer / Cadigan) "The Anterior-Posterior Specification and Positioning of the Cardiac Progenitor Cells in Drosophila."

Li Qian (Bodmer / Cadigan) "Genetic Control of Cardiac Morphogenesis and Function in Drosophila Melanogastor."

Jun Ni (Clark) "Evidence for Functional Conservation, Sufficiency and Proteolytic Processing of the CLAVATA3 CLE Domain."

Yue Yang (Pichersky) "Synthesis and hydrolysis of methylated plant hormones."

Hao Wang (Li) "Characterization of two mutants identified in activation tagging reveal some new aspects of BR signaling."

Zhenyan Yan (Li) "Regulation of a GSK3 like kinase in Arabidopsis steroid hormone signaling pathway."

Hua Jin (Li) "Suppressor screening of a mutated brassinosteroid receptor reveals ER quality control system in Arabidopsis."

Ju Huang (Klionsky) "Mechanism of the vacular targeting pathways in yeast Saccharomyces cerevisiae."

Yang Zhao (Duan) "Insulin-like growth factor binding protein 5 (IGFBP5): a protein of two destinations."

Andrew Hegle (Wilson) "Voltage-dependent regulation of intracellular signaling by Ether α go-go K+."

Yan Liu (Cadigan) "Genetic and Molecular Characterization of ISWI Family Chromatin Remodelers in Wingless Signaling."

Meng Yao (Denver) "Mechanisms of Corticotropin-Releasing Factor (CRF) Gene Regulation in the Frog Xenopus laevis."

2007 Undergraduate Honors Recipients

Highest Honors

CMB

Derek T. Peters, Transcriptional Regulation of Novel Modulators of Insulin-like Signaling in C. elegans.

David B. Zhen, The Role of Osteoclastogenesis in Neuroblastoma Mediated Bone Metastasis: Implications of IGF-I and IGR-IR on RANKL, RANK, and OPG.

High Honors

CMB

Bryan A. McGuffie, CsgB Mediated Amyloid Nucleation and Expression of the Curlin Subunits CsgA and CsgB.

Jee Shim, Mapping of SIP1Transcription Activation and CID-independent Repression Domains.

Jeffrey J. Tosoianm, A Humanized Mouse Model for Study of Prostate Cancer Treatment.

Lauren E. Wooley, The Role of Regulatory B Lymphocytes in the Context of Rheumatoid Arthritis.

Biology

David A McNamara, The Effect of Host Genetic Background on the Immune Response to C. neoformans 52D Infection.

Janelle E. O'Brien, Genetics of Autosomal Regions that Interact with the X Chromosome in a House Mouse Hybrid Zone.

High Honors continued

Alex A. Smith, Exploring the Origins of Nodulation: An Examination of the GRAS Family Transcription Factor nsp2 across the Legumes.

Honors

CMB

Meng Du, Characterization of ATG1: An Autophagy-related Protein in Arabidopsis thaliana.

Amrita M. George, The Effect of BMP4 Inhibition on Primordial Germ Cell Development in the Mouse Embryo.

Mary-Margaret T. Kober, The Interaction of Polycationic Polymers with Supported Lipid Bilayers.

Brandon M. Wojcik, Investigation of the Expression, Localization, and Function of sHSP15 in Arabidopsis thaliana.

Nan Xiang, Regulation of MYPT Phosphorylation via GLUT4 Glucose Transporter Activity.

Michelle J. Yang, Adaptation of RNA Interference Techniques to Examine Transcription Factor Functions in the Chick Spinal Cord.

Biology

Christina W. Li, High Copy Suppressors of the Ribosome-Associated GTPase BipA.

Microbiology

Efrem S. Lim, Factors Contributing to Mouse Adenovirus Type 1 Pathogenesis.

Neuroscience

Daniel Marcovici, Effects of Prenatal Androgen Exposure on Estrogen Receptor in the Medial Preoptic Area of Prepubertal Rams.

Stephanie A. Jimenez, Intra-amygdala Pathways for the Expression of Learned Fear.

Rebecca Runge, Sex Difference ER-α Immunoreactivity in the Striatum of Rats.