



MCDB News

MOLECULAR, CELLULAR, AND DEVELOPMENTAL BIOLOGY AT THE UNIVERSITY OF MICHIGAN

A MESSAGE FROM THE CHAIR

On July 1 of this year, the Chair of MCDB changed hands when Rich Hume stepped down after five years of dedicated and tireless efforts on behalf of the department. We all owe him a heartfelt ‘thank you’ for all his many contributions to building MCDB into the strong and vibrant department it is today. I am relatively new to the MCDB faculty, having only joined the department three years ago, in July 2005. However, my academic roots are firmly planted here – I hold three degrees from the UM Department of Zoology (B.S., M.S., Ph.D.), and during the 25 years I spent as a member of the faculty in the UM Medical School, I always felt a very special connection to Biology in the Kraus building. I am grateful

for the opportunity to serve as Chair, and I am eager to work with all of you to further strengthen MCDB so that it will flourish.

During the upcoming year, we are looking forward to an external review of the department, which is scheduled for November 2008. This will be the first review of MCDB since its inception, and we are delighted that the College has identified an advisory committee of truly outstanding scientists and educators from among the most prestigious academic institutions in the country. Their advice and counsel will be invaluable in helping us to shape the future of MCDB and to convey to the College and the University the critical importance of the unique research and educational missions of this department.



Pamela Raymond

for the opportunity to serve as Chair, and I am eager to work with all of you to further strengthen MCDB so that it will flourish.

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In this issue, as always, we are highlighting the accomplishments and changes of the past year. In particular, I want to bring your attention to our outstanding group of graduate students and postdoctoral trainees, some of whom are featured on the cover and elsewhere in this issue. They are the real heart of the scientific enterprise in MCDB! In recognition of their exceptional work, Sonia Bardy and Nicola Harrison-Lowe have received prestigious national awards, Annie Hiniker received the Rackham Distinguished Dissertation Award, and Rackham Predoctoral Fellowships have been awarded to Congcong He and Xuan Wang. You may be aware that President Coleman this year established a matching challenge of \$1 for every \$2 contributed in gifts and pledges for graduate student support, which will be placed in an endowment to provide financial assistance for the future training of graduate students. More information about this exciting opportunity is included in this issue. 

PRESTIGIOUS POSTDOCTORAL AND GRADUATE STUDENT AWARDS

Annie Hiniker, former Ph.D.



student and Bardwell lab member, was awarded the Rackham Distinguished Dissertation Award.

The award recognizes exceptional and unusually interesting work produced by doctoral students in the last phase of their graduate work.



Dr. Sonia Bardy, a postdoctoral fellow in the Maddock’s lab, has been awarded a prestigious NIH Pathways to Independence award.

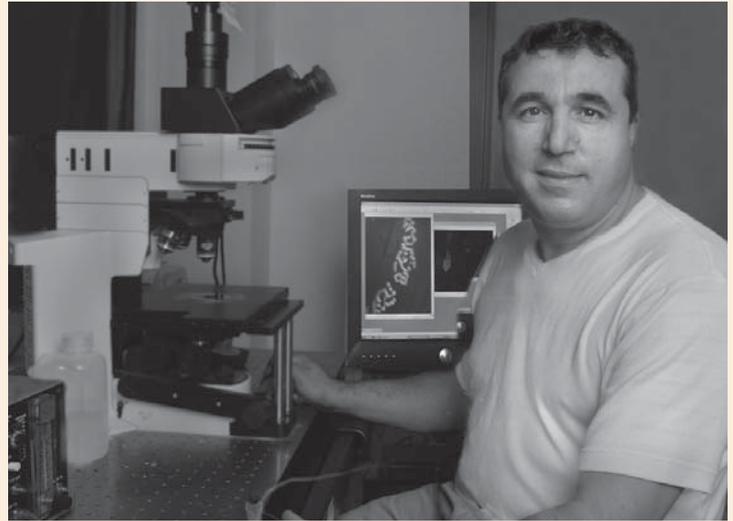


Nicola Harrison-Lowe, a member of the Olsen lab, received the American Society of Plant Biology -Pioneer Hi-Bred

International Award from the American Society of Plant Biology (national chapter).

SCIENCE SPOTLIGHT WITH MOHAMMED AKAABOUNE

The goal of the research program in my laboratory is to improve our understanding of the cellular and molecular mechanisms underlying synapse formation, maintenance, and aging *in vivo*. In particular, we are interested in investigating how key components of the synapse (acetylcholine receptors (AChR), acetylcholinesterase (AChE) and scaffolding proteins) are maintained and regulated in developing, mature, and aged synapses. We are exploring these questions in the simplest and the best understood of all synapses in the vertebrate nervous system, the synapse made between motor axons and the skeletal muscle fiber, the neuromuscular junction. Our strategy incorporates state-of-the-art imaging to directly visualize changes in the neuromuscular junction by viewing the same synapse over days, months, and even years. Additionally, we are using molecular tools to investigate the mechanisms underlying these changes.



Mohammed Akaaboune

“[W]e feel that our research...will help us define new approaches that might be used to develop effective therapies for devastating neuromuscular diseases.”

In central nervous synapses, direct study of the regulation of synaptic components is technically difficult due to the inaccessibility and small size of most synapses. In our studies we use an easily accessed muscle in the necks of mice (sternomastoid muscle) where all the nerve-muscle connections are bundled together and synapses are large in size. In normal muscle fibers, the AChRs are highly concentrated on the muscle cell membrane where they



Mouse neuromuscular junction

are held in clusters between the nerve and the muscle through a network of scaffold proteins to assure a high safety factor for synaptic transmission which is crucial for triggering an electrical impulse that makes the muscle contract.

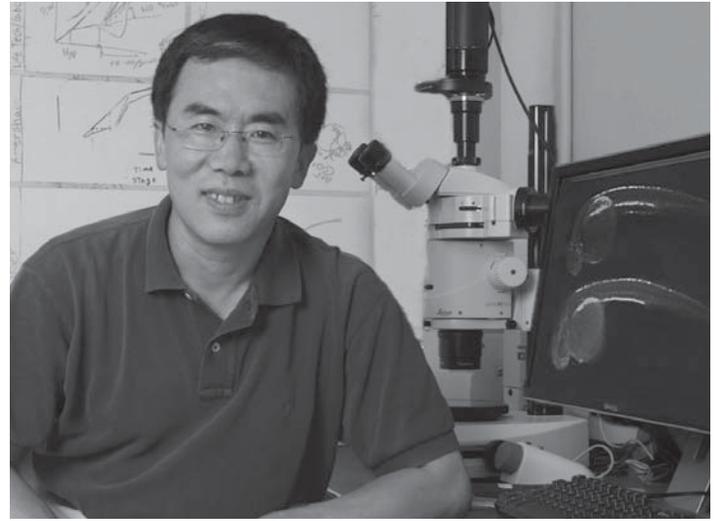
Over the past several years, we have developed and used imaging tools to directly study alterations in the number of AChRs and their associated proteins at individual neuromuscular junctions in living mice. We have found that AChRs are surprisingly dynamic and are able to disperse and re-aggregate from positions within a synapse in response to alterations in synaptic activity. This indicates that

muscle fibers have a mechanism to rapidly gain or lose receptors. More recently, we devised a novel labeling method that allows us to get a closer look at receptors and their activity. We found that when electrical impulses reach nerve endings and stimulate the muscle, a significant number of receptors, instead of being degraded in the interior of the cell, are recycled back to the membrane. These findings have changed our view about the turnover of receptors at the synapse. We are now using animal models where postsynaptic scaffold proteins are missing to better understand the molecular mechanisms of receptor stability.

Given the importance of neurotransmitter receptor turnover in synaptic plasticity, we feel that our research at the neuromuscular junction may impact how we think about plasticity at less accessible synapses in the central nervous system and will help us define new approaches that might be used to develop effective therapies for devastating neuromuscular diseases. 

SCIENCE SPOTLIGHT WITH CUNMING DUAN

One need not be a developmental biologist or a cell biologist to marvel at the tightly controlled process whereby human beings and animals grow. Growth of an animal or an organ is determined by the rate of cell proliferation, differentiation, migration, and programmed cell death. As a graduate student at the University of Tokyo, Cunming Duan became fascinated with growth regulation. To understand how a single cell grows to be a full size organism is the long-term goal of his research interest.

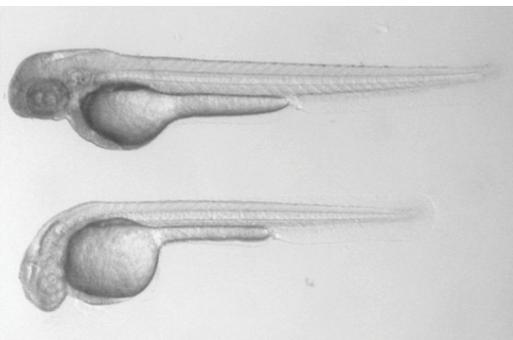


Cunming Duan

“Knowledge gained...also furthered our understanding of human growth physiology.”

Duan's group studies how a family of peptide hormones called insulin-like growth factors (IGFs) regulates cell, tissue, and organismal growth. Six specific IGF binding proteins have been identified. These IGF binding proteins bind IGF with high affinities and are placed in a central regulatory position between IGFs and their cell surface receptors. The Duan lab has been investigating the physiological roles of these IGF binding proteins and the underlying cellular and molecular mechanisms using zebrafish embryos and cultured mammalian cells. The accessibility and rapid development make zebrafish well suited for investigating the mechanisms by which IGFs, IGF-IR, and IGFBPs act to regulate cell proliferation, differentiation, and apoptosis in early life stages. Taking advantage of the free-living and transparent zebrafish embryos, the spatial and temporal expression patterns of IGF ligands, receptors, and IGF binding proteins have been mapped and their functions elucidated. Knowledge gained from these genetic studies in zebrafish has not only provided novel insight into how each of the IGF binding proteins acts *in vivo* to control tissue growth in fish, but also furthered our understanding of human growth physiology.

Animals exhibit reduced growth and developmental rate to cope with adverse environmental conditions. In zebrafish embryos, for example, reduced oxygen availability (hypoxia) causes



Zebrafish

significant developmental delay and growth retardation. This phenomenon is documented in a wide range of animals for many decades but the underlying molecular mechanisms are poorly understood. Recent studies from the Duan lab have provided new evidence suggesting that one of the IGF binding proteins (i.e., IGFBP-1) is strongly induced by hypoxia and the up-regulation of IGFBP-1 plays a key role in coordinating embryonic growth and developmental speed in response to hypoxia. IGFBP-1 acts by binding to and inhibiting the activities of IGFs. In addition to hypoxia, the IGFBP-1 gene is also highly responsive to food deprivation, malnutrition, stress, and chronic diseases in a wide variety of animal species ranging from fish to humans. The induction of IGFBP-1 expression by hypoxia and other catabolic conditions may be an evolutionally conserved physiological mechanism to restrict IGF-stimulated growth and developmental processes under adverse conditions.

A related interest in the Duan lab is to decode the complexity of chemical environments that guide embryo growth and development. Duan's group is a part of an interdisciplinary team who are trying to invent, build, and test new microsystems that will allow developmental and cell biologists to access and control the chemical messages underlying developmental programs of a vertebrate embryo. If successful, these tools will radically change the way cell culture and embryology experiments are performed, and will lead to biological and medical research technologies that better capture *in vitro* the complexity of the *in vivo* cellular environment. 

FACULTY NEWS

Mohammed Akaaboune was promoted to Associate Professor with tenure. He also was the mini-symposium chair and speaker at the Society for Neuroscience meeting.

Kenneth Balazovich was an invited Speaker and participant at the University of Michigan Stem Cell Forum Student Society for Stem Cell Research and Students for Life on March 15th, 2007.

Robert Bender gave the opening talk at IMAGE meeting (Integrating Metabolism and Genomics) in Montreal. The meeting was sponsored by the American Society for Microbiology.

Kenneth Cadigan was the lead Speaker in the Development Section at the Midwest Drosophila Meeting in Atherton, Illinois on October 5th-6th, 2007.

Matt Chapman was the Associate Editor for the Journal of Alzheimer's Disease.

Cathy Collins was awarded the James L. O'Leary Prize at the Department of Neurology, Washington University.

Cunning Duan was promoted to Professor. He was also the plenary lecture speaker at the International Symposium on Comparative Environmental Physiology, Biochemistry, and Toxicology – Diversity in a Changing Environment, October 7-12, 2007, in Hanzhou, Zhejiang, China.

Jon Demb was the keynote speaker for the European Retina Meeting in Frankfurt in October 2007.

Robert Denver was chair for the Society for Integrative and Comparative Biology, Division of Comparative Endocrinology.

Ursula Jakob was featured in the University of Michigan article "U-M scientists developing tool to probe role of oxidative stress in aging, disease," on February 15th 2008.

Daniel Klionsky was the plenary speaker at the FEBS2007 Conference in Vienna, Austria.

Anuj Kumar was named "Top" Rising PI, Genome Technology Magazine in 2007.

Jianming Li was invited to talk at the Regulation of Brassinosteroid Signaling on Oct 9, 2007, 2nd International Symposium on Plant Growth Substances: Intracellular

Hormonal Signaling and Applying in Agriculture, Kiev, Ukraine.

Erik Nielsen was the invited speaker to the Department of Molecular Biology, University of Wyoming, Laramie, WY in March 2008. His talk was "A Role for Phosphoinositides in Polar Secretion During Root Hair Development."

Laura Olsen was the organizer of the American Society of Plant Biologists Workshop on Lab Leadership in Chicago, IL, in July 2007.

Eran Pichersky chaired the Gordon Research Conference, on Floral and Vegetative Volatiles, Les Diablerets, Switzerland, October 2007.

John Schiefelbein gave an invited symposium talk at the International Meeting on Plant Signaling in Seoul, South Korea.

Tzvi Tzfira was editor on the Editorial Board on Plant Signaling and Behavior.

Haoxing Xu was honored in the Biological Sciences Scholars Program, University of Michigan, 2007.

IN MEMORIUM

Dr. Helen Gay, age 89, died peacefully on April 16, 2008. She received her Bachelor of Arts degree from Mt. Holyoke College in 1940, her Master's degree from Mills College in 1942, and her Ph.D. from the University of Pennsylvania in 1955. Her professional career as the first woman cyto geneticist spanned from 1942 to 1983 and included research and teaching in various institutions. She was Professor of Zoology and Biology at the University of Michigan.

COLLEGIATE PROFESSORSHIP INAUGURAL LECTURE

Professor Eran Pichersky will be presenting his Collegiate Professorship Inaugural Lecture on Wednesday, November 19th, for his appointment to the Michael M. Martin Collegiate Professorship in Molecular, Cellular and Developmental Biology.

WELCOME NEW FACULTY



Assistant Professor **Lyle Simmons** joined the department September 1st, 2008. Lyle comes to us from the Department of Biology at Massachusetts Institute of Technology, where Lyle has been a NIH postdoctoral fellow with Professors Graham Walker and Alan Grossman. Lyle's research investigates the cellular responses to DNA damage in the bacterium *Bacillus subtilis*.

The Michigan Difference

THE PRESIDENT'S CHALLENGE

This year, gifts and pledges up to \$1 million will be matched by UM President Mary Sue Coleman at the rate \$1 for every \$2 contributed for graduate student support. The University match is placed into an endowment, so that your giving can generate valuable graduate student aid far into the future. Pledges must be made by December 31, 2008 to ensure a match and can be paid over a five year period (by Dec. 31, 2012). More information is available at www.giving.umich.edu/where/presidents_challenge.htm. To give to the President's Challenge, please designate your gift to the President's Challenge for MCDB Grad Support. You may also make your gift online at www.giving.umich.edu.

Funding priorities for MCDB and detailed descriptions are available at: www.mcdb.lsa.umich.edu/gifts.php.

PFIZER EQUIPMENT SAVINGS

Recently donated supplies and equipment from Pfizer resulted in an estimated savings of \$150,000 for the department! Supplies that could not be used were given to other departments.

STAFF NEWS

The LSA Spotlight Committee has selected our Animal Care Team as the LSA Staff Spotlight group winner for Winter 2008. Congratulations to **Kathy Gimson, Julie Stewlow, Jim Donner,** and **Mike Amburgy!**

Gregg Sobocinski joined the department as Imaging Specialist / Microscopist in August 2007.

Sarah Cathey joined the department as Administrative Office Assistant in September 2007.

Mark Farrugia joined the department as Laboratory Course Technician in January 2008.

Kim Mark joined the department as Grants and Contracts Accountant in July 2008.

Alex Lannigan joined the department as Laboratory Course Technician in August 2008.

NEW GRANTS

Akaaboune, Mohammed Postsynaptic Rapsyn Dynamics at the Neuromuscular Junction of Living Animals, *NSF*

Chapman, Matt A New Amyloidogenesis Paradigm, *UM Alzheimer's Disease Research Center*

Chapman, Matt Assembly of Gurli Fibers by *Escherichia coli*, *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 REU: Rachel Diehl, *NSF*

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

Bardy, Sonia (Maddock, Janine) Spatial Organization of Chemotaxis Systems in *Pseudomonas aeruginosa*, *NIH*

Nielsen, Erik The Role of RabA4b in Polarized Secretion of Cell Wall Components in Arabidopsis Root Hair Cells, *Department of Energy*

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

Wang, Yanzhuang Structural and Functional Defect of the Golgi Apparatus in Alzheimers' Disease, *UM Alzheimer's Disease Research Center*

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

Wang, Yanzhuang Golgi Structure and Function, *UM Rackham*

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

POSTDOCTORAL FELLOWS WHERE ARE THEY NOW?

W. Ted Allison, Assistant Professor, Department of Biological Sciences, University of Alberta, Canada.



Mentor – Pamela Raymond

Jennifer Kennell, Assistant Professor at Vassar College, Poughkeepsie, New York.



Mentor – Kenneth Cadigan

Michele Barnhart, Lead Scientist at Novozyme in Davis, California.



Mentor – Matthew Chapman

Lars Leichert, Assistant Professor at the University of Bochum, Bochum, North Rhine-Westphalia, Germany.



Mentor – Ursula Jakob

Tim Blauwkamp, Postdoctoral position, Stanford University, Roel Nusse's lab.



Mentor – Gyorgyi Csankovszki

Zheping Huang, Department of Pharmacology and Toxicology, University of Arizona.



Mentor – Yanzhuang Wang



PH.D. DEGREES GRANTED

Daniel Marble (G. Wilson) “Activity dependent regulation of Ether L go-go K⁺ channels.”

Jin-Hee Chang (Cadigan) “Transcriptional regulation of the Wnt signaling pathway.”

Sean Friday (Hume) “Electrophysiological characterization of channel function, pH potentiation, and zinc modulation of the ATP-gated rat P2X2 receptor through site-directed mutagenesis of the extracellular acidic residues and heterologous expression in *Xenopus* oocytes.”

Zhiping Xie (Klionsky) “Dissection of Autophagosome Formation.”

Hessun Cheong (Klionsky) “Mechanistic role of Atg1 complexes for Autophagy-related process in yeast.”

Jun Ma (Kumar) “The application of functional genomics in yeast signaling networks and genome studies.”



Congcong He

RACKHAM PREDOCTORAL FELLOWSHIPS AWARDED

Graduate students **Congcong He**, a member of the Klionsky lab, and **Xuan Wang**, a member of the Chapman Lab, were awarded Rackham predoctoral fellowships.



Xuan Wang

IMAGING AREA

The Imaging Labs microscope core consists of several microscopes available to all MCDB researchers. In addition to our recently acquired digital transmission electron microscope, we have two confocal microscopes and epifluorescent scopes in upright, inverted, and stereo configurations. Gregg Sobocinski is in charge of all things microscope, including training, maintaining, and sharing nearly two decades of academic and industry research experience.

2008 UNDERGRADUATE HONORS RECIPIENTS

High Honors

CMB

David R. Blair, A type II myosin ATPase inhibitor reduces contraction-stimulated glucose transport in rat skeletal muscle.

Alicia M. Giordimaina, Etiology of hearing deficits in congenitally hypothyroid *Prop1^{df}* mice.

Shawn M. Sprague, The Zebrafish *ennui* gene encodes for low density lipoprotein receptor-like protein 4 (Lrp-4) and is essential for normal clustering of acetylcholine receptors in the developing neuromuscular junction.

Biology

Matthew B. Davis, Seven new species of the Malagasy feather mite genus *Vanginyssus* Mironov, 2001 (Astigmata: Pteronyssidae) provide support for monophyly of their hosts, the vangas (Passeriformes: Vangidae).

Microbiology

Alaina S. Ritter, Does chronic atmospheric nitrogen deposition alter the composition of microbial communities in soil?

Honors

CMB

Heather R. Bowman, Trigeminal motor nucleus acetylcholine release in anesthetized Wistar rat is increased by morphine and not blocked by naloxone.

John D. Cramer, Analysis of the molecular mechanisms underlying *Pitx2*-mediated migration in the developing hypothalamus.

Owen A. Darr, Characterization of a cyclin-independent mutant of human CDK2.

Mudit Gupta, Development of imaging strategy for chemokine receptor CXCR4 signaling.

Hu, Lily, Wnt regulation of retinal stem cell in developing zebrafish retina.

Hana M. Russo, The role of PSGL-1 and P-selectin in obesity.

Kerri A. Serecky, Exploration and manipulation of β -Catenin and the Wnt signaling pathway in the mouse adrenal gland.

Biology

Andrea J. Magurie, Distribution of leaf shape variability in a tropical forest.

Microbiology

William P. Shield, The role of ribosome-associated complex proteins Ssz1 and Zuo1 in flock house virus RNA.

Plant Biology

Kamali N. Sripathi, Comparison of urea- and calcium chloride-washed preparations of spinach photosystem II.

Neuroscience

Sara Foley, γ -aminobutyric Acid (GABA) System, Alcoholism, and Personality: Haplotype analysis of GABRA2.

Deepak Mangla, Transient Transfection Analysis of PKA Gene Regulation of Neural Differentiation.

Michael Mooney, Exploring the treatment of epilepsy through intrahippocampal GABA modulation with an HSV-vector expressing GAD67.

Alison Tisack, Autogenous Schwann Cell Migration in Peripheral Nerve Allografts Treated with Anti-CD40L Monoclonal Antibody.

Terrence Yang, KCl-induced depolarization facilitates differentiation of P19 embryonic carcinoma cells into neurons.