

Integrative Biology & Pharmacology Newsletter



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Chair, IBP

Dr. John Hancock

Vice Chair, IBP

Dr. Roger O'Neil

Director of Management Services

Monica Gardner

The IBP Newsletter ~ *An Introduction*

Welcome to the inaugural edition of the IBP Newsletter. Each quarter, we plan to include a variety of informative and interesting articles on the people and the activities of Integrative Biology and Pharmacology. Among the articles we hope to include are the following:

- An article from Dr. Hancock or his designee to include general updates about significant events and activities as well as enrollment and research funding trends;
- Student achievements and activities, including awards, honors, publications and successful doctoral defenses;
- Faculty and staff achievements and milestones, including research awards, publications, honors and website developments / updates.
- A facilities article providing updates on renovations;
- Research Corner, written by Senior Contracts and Grants Specialist Deborah Brougher will offer information on the department's sponsored research activities as well as news critical to proposal

submissions;

- A Calendar of Events will be included to provide information on the recent and upcoming activities of the department. Hea Jin, IBP's newest Administrative Assistant, will coordinate this effort.

In the future, we look as well to shining a spotlight on any or all of the following:

- a prominent alumnus or alumna and his/her contributions to the field;
- new employees (faculty, students and staff);
- educational activities within the department; and
- Our labs—what they do, what they are working on, goals, achievements, etc.

We welcome articles of interest shining the spotlight on your research, your lab or one of your students (current or former). The next publication is scheduled for March, 2012, so if you have an idea or a contribution you would like to make to the newsletter, please contact Anne Dybala at Anne.L.Dybala@uth.tmc.edu.

~Anne Dybala



2011 CRB Program Retreat in Camp Allen, Texas

DEPARTMENTAL NEWS & EVENTS

2011 Medical School Research Retreat

Recently, the 2011 Medical School Research Retreat took place and a number of IBP faculty were speakers. The speakers for the New Investigator series included:

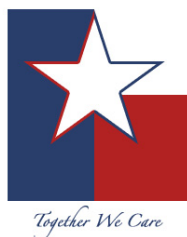
- Ghislain Breton, Ph.D., Assistant Professor who spoke on "Dissecting Circadian Clock Cis-Regulatory Networks in Zebra Fish";
- Shane Cunha, Ph.D., Assistant Professor, who spoke on "Defects in Ankyrin-Based Membrane Protein Targeting Underlie Atrial Fibrillation"; and
- Jeffrey Chang, Ph.D., Assistant Professor, speaking on "Signaling Networks in Cancer"

Rebecca Berdeaux, Ph.D., Assistant Professor represented the department as a symposium speaker and her topic was "Hidden Functions of CREB in Skeletal Muscle Adaptation"



State Employees Charitable Campaign

State Employee Charitable Campaign



The State Employees Charitable Campaign (SECC) had a successful run this fall led by Trish McFarland, IBP's Education Coordinator. The campaign makes it easy for state employees to donate to the charities of their choice, with full confidence that the charities are bona

fide. One or more organizations can be chosen for the employee to support. Contributions may be made in lump-sum, one-time payments or by payroll deduction, as long as at least \$2 a pay period is contributed. If payroll deduction is chosen, it begins in January and follows the calendar year.

Trish accepted the tasks of coordinating two bake sales and a raffle as well as keeping faculty and staff apprised as to the contributions of the department for the SECC.

The raffle winners were:

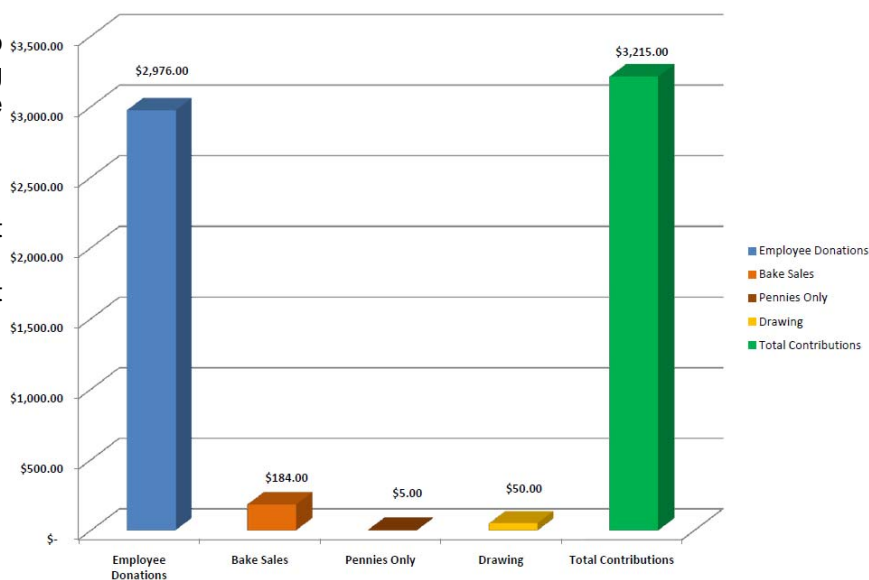
- Sandy Cegielski--Texas Roadhouse gift certificate, a \$30 value
- Lisa Byrd--Natural Science Museum gift certificate with four passes, a \$100 value
- Anne Dybala--Alley Theater gift certificate, an \$80 value
- Mike Zhu--Goode company gift certificate, a \$25 value

- Norman Weisbrodt--Goode company gift certificate, a \$25 value
- Ghislain Breton--Natural Science Museum gift certificate with four passes, a \$100 value
- Riad Efendi--Gringos gift certificate a \$25 value
- Erika Cassimere--hand made hot pads donated by Trish McFarland— invaluable!

Thanks to all the IBP employees who contributed to the bake sales!

~Anne Dybala & Trish McFarland

2011 IBP SECC



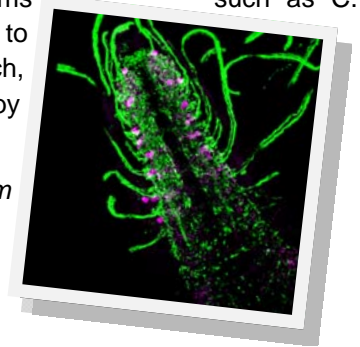
Neurobiology of Model Organisms Journal Club



Kartik Venkatachalam, PhD
Assistant Professor

The field of neuroscience is at a very exciting juncture. Many labs around the world are studying the neurobiology of model organisms with the goal of elucidating the principles of neural function. Studies range from molecular function of individual proteins to network architecture and dynamics of the whole brain. The purpose of the "Neurobiology of Model Organisms" journal club is to highlight the most recent and exciting research being performed in order to understand the function of the nervous system using a variety of model organisms such as *C. elegans*, *Drosophila* and mice. The purpose of this journal club is to educate students, post-docs and faculty about cutting-edge research, and facilitate the development of new ideas that may be utilized by individuals interested in neuroscience at UTHSC.

~Kartik Venkatachalam



Cytodynamic Imaging Facility Opens

The UTHSC Cytodynamic Imaging Facility is a state-of-the-art microscopy facility, which directly supports the Department of Integrative Biology and Pharmacology. The facility is also available for use by scientists within UTHealth and the Texas Medical Center.

We currently have a Nikon A1 CLSM and a Zeiss 510 Meta CLSM as our main work horses, with a BD Pathway BioImager for high content imaging, live cell imaging and assay development. We also feature an Olympus TIRF system and a Nikon based microscope with a Lambert FLIM module. We have several image analysis computers available; with offline versions of each instrument's operating software, Metamorph, Autoquant, Corel Draw, Adobe Creative Suite 4 and MatLab.

The staff of the imaging facility provides initial training on using the microscopes as well as assistance with image analysis and experimental design. Potential users must meet with the facility staff to discuss research requirements. To schedule a consultation or training session contact the facility manager.

Users will be trained on their instrument of choice. Users may require several training periods before they are allowed to operate the instruments independently.

Guidelines for instrument usage that will maintain quality of the instruments and allow access for numerous users will be adhered to or facility privileges may be revoked.

Preliminary screening of fluorescence staining should be done on conventional fluorescence microscopes prior to use of the microscopes.

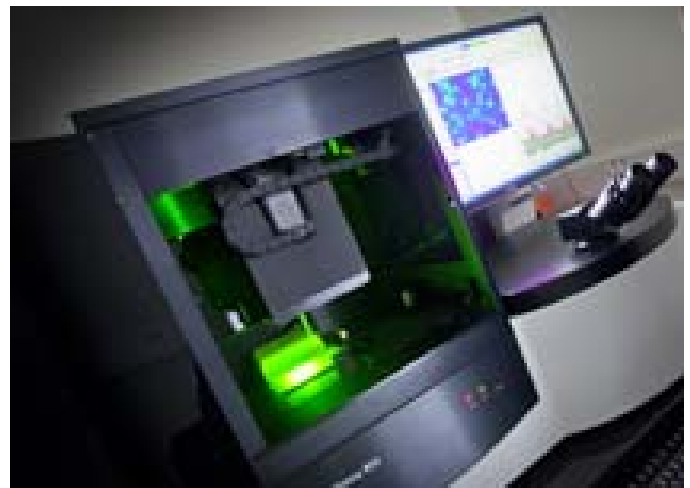
Users are expected to be familiar with basic immunostaining, fixation techniques and slide preparation, as well as the fundamental principles of fluorescence microscopy.

Interactions that involve more than basic instruction on how to operate the microscopes should lead to a collaborative work arrangement and co-authorship of papers, by mutual agreement of all parties.

Citation/Publication Policy: Please acknowledge the IBP Cytodynamic Imaging Facility in all publications and presentations supported with the use of the facility.

IBP Cytodynamic Imaging Facility booking system launches

This booking system allows a user to register a profile, schedule training, schedule equipment time, and provide billing information.



FACULTY SPOTLIGHT

Rebecca Berdeaux Receives Two NIH Awards



Rebecca Berdeaux, Ph.D.
Assistant Professor

Dr. Rebecca Berdeaux was awarded two NIH grants in July of this year. Dr. Berdeaux and her team study how cells respond to environmental cues and changing physiologic conditions by altering the complement of genes expressed in order to adapt or return to a normal state. An organism's DNA encodes many genes, not all of which are turned on, or expressed,

at any given time. Understanding how genes are regulated can shed light onto normal adaptive mechanisms that go awry in disease or can help identify new ways to treat disease. Two new five-year grants from the NIH will allow the Berdeaux Lab the chance to study gene regulation in two different clinically relevant settings: type 2 diabetes and muscular dystrophy.

Since starting in IBP, the Berdeaux Lab has been intensely focused on understanding the regulation and actions of an enzyme called salt inducible kinase (SIK1), which is known to normally act as a brake on new glucose synthesis in the liver. In normal mammals, blood glucose concentration is maintained within a very small range. After every meal, glucose released into the blood stream is rapidly absorbed by muscle, fat and liver for use as fuel or storage. Between meals, blood glucose is kept constant in part by synthesis of new glucose in the liver. Patients with type 2 diabetes have elevated blood sugar due to both reduced glucose uptake by the muscle and fat as well as uncontrolled synthesis of new glucose. An understanding of how this process becomes misregulated could lead to identification of new therapeutic approaches to treat type 2 diabetic patients.

During fasting, the gene encoding SIK1 is turned on in the liver, and the protein acts just after a meal to turn off new glucose production. However, little is known about what happens to the SIK1 enzyme after a meal and why

the enzyme no longer seems to work in mice with type 2 diabetes. One clue came from observations in the Berdeaux lab that the SIK1 enzyme is very unstable. At the end of fasting, SIK1 has only a short time to inhibit glucose output before it is degraded in liver cells. Berdeaux identified a new possible regulator of SIK1 that may be responsible for this rapid degradation. In the R01 project funded by the National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), Dr. Berdeaux' team will explore how SIK1 is degraded and how the dynamics of SIK1 activity might be altered in mice with type 2 diabetes. They will use non-invasive small animal imaging equipment in the IBP Cytodynamic Imaging Facility to study how high fat diet and SIK1 deletion affect glucose control in mouse strains that they developed since coming to IBP. New insights into this pathway may identify new therapeutic strategies for maintenance of blood glucose in diabetic patients.

SIK1 is not only an important regulatory enzyme in liver. In skeletal muscle, SIK1 also exerts crucial functions, though the molecular details differ. During postdoctoral work, Dr. Berdeaux found that SIK1 is crucial for muscle fiber survival in mice. In muscle cells, SIK1 indirectly activates expression of muscle specific genes important for maintenance of muscle structure in adult mice. Because the same muscle-specific genes are important for embryonic muscle development, Dr. Berdeaux hypothesized that SIK1 may be important for differentiation of muscle stem cells into mature, contractile muscle fibers. Indeed, her team found that removal of SIK1 had stark consequences on the survival and differentiation of muscle progenitor cells. They also identified SIK1 as a gene turned on during regeneration of skeletal muscle, a process that requires activation and differentiation of muscle stem cells. Based on these pilot studies, the National Institute of Arthritis and Musculoskeletal and Skin Diseases (NIAMS) awarded funding to the Berdeaux Lab to study the dynamics of SIK1 activity in myogenic differentiation and to test muscle survival and regeneration in mice lacking SIK1. Although it is currently not known whether human mutations in *SIK1* are associated with muscle disease, therapeutic agents that activate SIK1 may promote regeneration in patients with different types of muscular dystrophy.

The federal funding will allow the Berdeaux Lab to nearly triple in size. In addition to the dedicated research assistants Randi Stewart and Christopher Robb, three new postdoctoral fellows are slated to join the lab by the beginning of 2012. Dr. Jingqi Fu, an expert in transcriptional regulation in metabolic tissues, has already

begun his postdoctoral work on SIK1 regulation in liver. Two other fellows with expertise in biochemistry, physiology and metabolism will soon join. Tutorial rotation and full-time training positions are still available for Ph.D. students in the GSBS Cell and Regulatory Program.

~Rebecca Berdeaux

Oleh Pochynyuk Receives Carl W. Gottschalk Research Scholar Award



Oleh Pochynyuk, Ph.D.
Assistant Professor

Dr. Pochynyuk was recently awarded a Carl W. Gottschalk Research Scholar grant from the American Society of Nephrology titled "Purinergic control of mechano-sensitivity in the distal nephron". Epithelial cells in the in the distal part of renal nephron are usually exposed to a variety of mechanical stresses, including

increases in tubular flow and osmotic pressure gradients. Cells respond to these environmental changes by adjusting the electrolyte and water transport. Inability of the distal nephron cells to properly respond to changes in flow/tubular composition is clearly linked to a number of disease states associated with changes in the circulating plasma volume and electrolyte imbalance. These include hypertension, congestive heart failure, hyponatremia etc. In addition, improper mechano-sensitivity in this part of renal nephron has been implicated in cysts formation and development of the polycystic kidney disease in humans. It has been suggested that paracrine release of ATP can mediate cellular responses to mechanical stimuli. Using the unique comprehensive experimental design combining Ca^{2+} -imaging and electrophysiology in the native split-opened murine distal nephrons, immunohistochemistry, genetic animal models with targeted deletion of P2Y2 receptors, Cx30 hemichannels, and TRPV4 ion channel channels; Dr. Pochynyuk's lab developed experimental evidence that locally released ATP during mechanical stimulation of native distal nephrons is essential for the activation of mechano-sensitive Ca^{2+} permeable TRPV4 channels, which, in turn, is critical for sustained cellular responses to mechanical stimuli. These findings have been recently

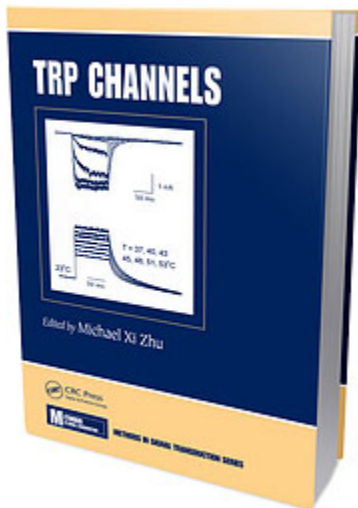
published in the *PLoS One* Journal. Overall, Dr. Pochynyuk's studies will help us to identify new pharmacological targets to control mechano-sensitivity of the renal nephron in order to manage multiple kidney disorders, including polycystic kidney disease.

Dr. Pochynyuk received his PhD degree in Bogomoletz Institute of Physiology, National Academy of Sciences, Kiev, Ukraine in 2003. After completion of his PhD program, Dr. Pochynyuk was a postdoctoral fellow and then a research assistant professor at the University of Texas Health Science Center at San Antonio, in Prof. J.D. Stockand's laboratory from 2004 to 2010. He next joined the Department of Integrative Biology and Pharmacology, University of Texas Health Science Center at Houston as an assistant professor in June 2010. Dr. Pochynyuk is an author of more than 35 publications in numerous peer-reviewed journals. He received young investigator research recognition awards from the Renal and Cell & Molecular Sections of the American Physiological Society. In addition to the support from the American Society of Nephrology, Dr. Pochynyuk's research program is also currently funded by the American Heart Association.

Carl W. Gottschalk Research Scholar Grant

The purpose of the Carl W. Gottschalk Research Scholar Grant is to provide funding for young faculty to foster evolution to an independent research career by providing transition funding toward successful application for an RO1 grant.

~Oleh Pochynyuk



TRP Channels

A book edited by **Michael X. Zhu, Ph.D.**, was published by CRC press in April 2011. The book entitled **TRP Channels** is a part of the *Methods in Signal Transduction Series* by the CRC Press Taylor & Francis Group. **TRP Channels** contains 21 chapters (460 pages) that cover the major techniques used and main findings in various areas of TRP channel research. It is aimed to provide a comprehensive overview and practical approaches to investigators working in this active and exciting research field. Contributors of the book chapters include investigators from both academia and industry. **Roger G. O'Neil, Ph.D.**, and **Hongzhen Hu, Ph.D.**, of the Department of Integrative Biology & Pharmacology also contributed to two chapters in the book.

GRADUATE STUDENT AWARDS & ACTIVITIES

Priyanka Parekh, Cameron Brand, Harrison Hocker, Jennifer Dulin



Third-year medical student **Priyanka Parekh** is one of 50 recipients of the **2011 Alpha Omega Alpha Carolyn L. Kuckein Student Research Fellowship**.

The fellowship provides \$5,000 for 8 to 10 weeks, 30 hours or more per week, for clinical investigation, basic laboratory research, epidemiology, or social science/health services research. Only one student from each U.S. medical school may be nominated for the annual fellowship.

Parekh will use the fellowship to expand upon the research she began last summer when working in **Dr. Edgar Walters'** lab in the Department of Integrative Biology and Pharmacology.

[Read more information in Scoop](#), the Medical School's electronic newsletter.



Cameron Brand was the recipient of a Pharmacological Sciences Training Program fellowship with the Keck Center for Quantitative Biomedical Sciences which is part of the Gulf Coast Consortia. The head of the training program is Dr. Tom Caskey at the IMM. Cameron's pre-doctoral traineeship under the mentorship of Drs.

Carmen Dessauer and Claudio Cavasotto will focus on finding new isoform specific inhibitors of adenylyl cyclase. Precise inhibition of individual isoforms could produce therapeutic benefit for several diseases. One such example is the involvement of type 5 adenylyl cyclase activity in chronic heart failure. Finding novel inhibitors will be explored by computer-simulated docking of small molecule ligands to the catalytic structure of adenylyl cyclase. This will be followed by high throughput screening of compounds that bind to the catalytic domains of adenylyl cyclase, and subsequent characterization of the inhibitor capabilities of promising small molecules.

His project title is: ***Isoform Specific Disruption of AC 5/6 cAMP Production by Small Molecule Inhibitors***

~Cameron Brand



Harrison Hocker, a third year student in the Ph.D. program, was recently awarded a fellowship from the Keck Center for Quantitative Biomedical Sciences of the Gulf Coast Consortia for training in pharmacological sciences, which is managed by Dr. Thomas Caskey. The work entitled, "Development of

Allosteric Ras Inhibitors" will be supervised by Drs. John F Hancock and Alemayehu A. Gorfe. The training grant funds research that has the potential to directly lead to the discovery of new and novel drugs.

Ras proteins are enzymes that control cell growth and development. They are found mutated in approximately 15% of all human tumors and in up to 90% of specific tumor types. However, decades of research by both academia and industry have failed to yield drugs to treat these diseases. Some of the key reasons for the lack of effective drugs to block Ras signaling are: the presence of many other enzymes sharing the same active site architecture with Ras so that anti-Ras drugs also attack other enzymes and become toxic; the difficulty for a drug to compete against the high number of other molecules in the cell that tightly bind to Ras; the ability of Ras to interact with many different partners so that blocking the activity of one partner is of limited value; and the toxicity of drugs that disrupt the functionally required membrane binding of Ras. Thus, an alternative strategy to block Ras function is an urgent imperative.

Harrison's work places an emphasis on using in-silico methods to find an allosteric inhibitor for Ras. The in-silico approach utilizes the concept of fragment optimized growth (FOG) of drug cores to build new drug-like molecules from very basic chemical structures. The advantage of the FOG method is that one can focus on specific chemical structures that have the greatest potential to bind to a site of interest, and then to generate additional compounds based on these core structures. Additionally, a relaxed complex scheme (RCS) will be used to account for protein dynamics by including multiple non-crystallographic structures of Ras into the drug screening process. This allows for targeting allosteric sites that are not always captured in the available crystal structures. The study also aims to validate the predicted drugs by cell-based assays that will monitor their ability to inhibit selected Ras-mediated signaling pathways. The research benefits from a wide ranging experience of Dr Gorfe in computational methods and Dr Hancock in experimental cell biology, as well as in Harrison's several

years of experience in computational structure-based drug discovery and previous training in bioengineering. Successful conclusion of the work will break new ground in cancer therapy by developing the first inhibitor of oncogenic Ras proteins.

~Harrison Hocker



Jennifer Dulin is a third year GSBS student in the Neuroscience Program who is near completion of her PhD work in Dr. Grill's laboratory in the Dept. of Integrative Biology and Pharmacology. She is a recent recipient of the prestigious Dean's Research Award for her graduate research project entitled, "Targeting P-glycoprotein-mediated drug resistance

to improve therapeutic treatment of spinal cord injury.

Jennifer's thesis work is focused on developing a greater understanding of the pathological mechanisms that contribute to the destructive and permanent outcomes that follow trauma to the spinal cord. Despite years of effort, there remains no effective, FDA-approved, treatment that will preserve or restore function in human beings following spinal cord injury (SCI). Jennifer has identified an important change in the spinal vascular environment elicited by SCI that may have profound implications in the development of effective treatment strategies. Interestingly, the crux of her studies is based on results reported in the cancer research/treatment field. It has been long known that several forms of cancer will develop a resistance to one or more chemotherapeutic agents. This in turn reduces the effectiveness of the chemotherapeutic agent in reducing or destroying the cancer. One of the key elements in the development of chemotherapeutic resistance is the enhanced expression of classes of membrane-bound anti-porter systems; the role of which is to prevent the passage of systemically-present substances from the blood stream into the tumor. One such anti-porter is the P-glycoprotein; known to interact with a wide range of endogenous and exogenous substrates including a wide range of chemotherapeutic agents. P-glycoprotein (Pgp) expression and activity can be elevated by inflammatory conditions. Jennifer asked whether such inflammatory conditions might similarly drive Pgp expression following SCI. In her initial set of experiments, Jennifer found that Pgp expression did undergo a substantial increase in expression early using a rat model of SCI. This increase in Pgp was not restricted to the early phase of injury, but instead could be detected as far out as nine months post-SCI. These results have great clinical significance as many of Pgp's substrates are

Graduate Student Awards & Activities~ *Continued*

known therapeutics that have been tested and failed in human clinical trials for SCI. In fact, one such substrate, the FDA-approved drug Riluzole, is currently undergoing Phase I trials for the acute treatment of SCI in humans. Jennifer's studies have uncovered additional, clinically-important findings: 1) that the spinal bioavailability of systemically-delivered Riluzole decreases after SCI, and 2) that the targeting of multiple pro-inflammatory pathways both reduces SCI-induced Pgp expression and increases

Riluzole bioavailability. Her thesis work may lead to the development of novel combinatorial therapies in which the efficacies of a wide range of therapeutics; for spinal cord injury as well as many other disease processes; may be enhanced by the pharmacological suppression of Pgp. Her work was recently described in the October issue of the *Paraplegia Newsletter*, a publication of the Paralyzed Veterans of America.

~Ray Grill

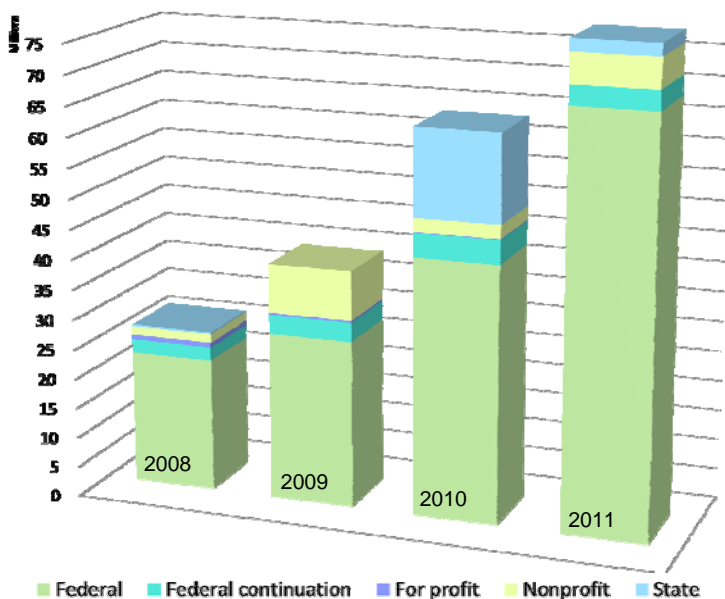
RESEARCH CORNER

New Facilities & Administrative Rate (*Indirect Costs*)

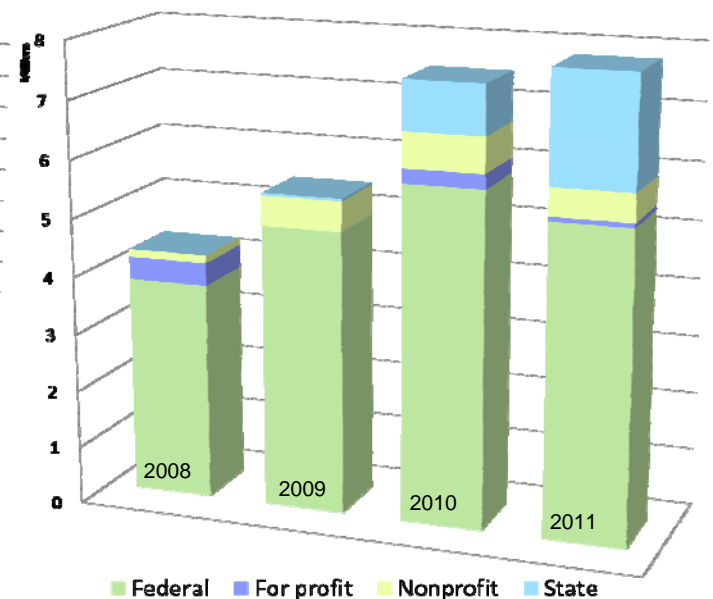
Effective 09/01/11, the Facilities and Administrative Rate (indirect costs) has increased from 50% to 52% of Modified Total Direct Costs. Modified Total Direct Costs, consisting of all salaries and wages, benefits, materials, supplies, services, travel and subgrants and subcontracts up to the first \$25,000 of each subgrant or subcontract (regardless of the period covered by the subgrant or subcontract). Modified total direct costs shall exclude equipment (any cost greater than \$5,000), capital expenditures, charges for patient care, student tuition remission, rental costs of off-site facilities, scholarships, and fellowships as well as the portion of each subgrant and subcontract in excess of \$25,000.

~Deborah Brougher

Proposals Submitted FY2008-FY2011



Awards Received FY2008-FY2011



Proposals submitted by the Department of Integrative Biology & Pharmacology increased from \$31.6 million in 2008 to \$88.8 million in 2011. Awards have also been steadily on the rise. In 2008, \$4.2 million in awards were made to the department, and by 2011, those awards had increased to just under \$8 million.

CALENDAR OF EVENTS

IBP Seminar Series~ *Directed by Drs. Rebecca Berdeaux and Catherine Denicourt*



November 7, 2011

Qingyun Jim Liu, Ph.D.
UTHSCH-IMM

“Regulation of cancer cell motility and mitosis by the RhoA activating protein Net1”

Host- Dr. Yi-Ping Li



November 21, 2011

Denis Guttridge, Ph.D.
Ohio State University

“Deciphering NF- κ B Signaling Functions in Skeletal Muscle Differentiation and Disease”

Host-Dr. Yi-Ping Li



November 14, 2011

Jianming Xu, Ph.D.
Baylor College of Medicine

“SRC-1 & Twist, the Evildoers in Breast Cancer Metastasis”

Host-Dr. Guangwei Du



November 28, 2011

Jun-Ming Zhang, M.D.
University of Cincinnati

“Activity-dependency of pathological pain”

Host- Dr. Terry Walters

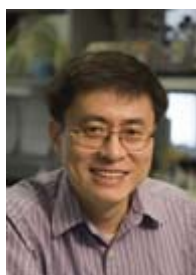


December 9, 2011

Eran Andrecheck, Ph.D.
Michigan State University

“Modeling Breast Cancer in the Mouse: Genetic Tests of Genomic Predictions”
**Seminar in MSB 2.103*

Host-Dr. Jeffrey Chang



December 12, 2011

Xinzhong Dong, Ph.D.
Johns Hopkins University School of Medicine

“Molecular and genetic analysis of pain and itch sensation”

Host-Dr. Hongzhen Hu.



December 19, 2011

Fred Pereira, Ph.D.
Baylor College of Medicine

“Tuning Cholesterol for Hearing Sensitivity”



January 9, 2012

Bill Mitch, M.D.
Baylor College of Medicine

Title to be announced

Host-Dr. Yi-Ping Li



January 23, 2012

Gregg Roman, Ph.D.
University of Houston

Title to be announced

Host-Dr. Kartik Venkatachalam



January 30, 2012

Armen Akopian, Ph.D.
UTHSC San Antonio
“Interaction of TRPV1 and TRPA1 in control of inflammatory hyperalgesia/pain”

Host-Dr. Hongzhen Hu

NOTE

Seminars are held on Mondays at 4:00 PM in MSB 2.135, unless otherwise noted. For information and questions, please contact Hea Jin at Hea.Y.Jin@uth.tmc.edu or 713-500-7514.