# Biochemistry and Molecular Biology NOTES

Volume 22, No. 2 July, 2010

## Welcome!

Dr. Amber Mosley will be joining us in August as a new assistant professor. Amber's area of study is the analysis of protein-protein interaction networks and post-translational modifications that regulate RNA Polymerase II transcription using protein mass spectrometry and genomics. She received her Ph.D. in Biochemistry in 2004 from the University of Kentucky College of Medicine. She was a Postdoctoral Fellow from 2004-2010 at the Stowers Institute for Medical Research. Amber's office will be in room MS1021H, and her lab will be in room MS1017G. She'll be moving in on August 1st.

**Update: TRAVEL REIMBURSEMENT DEADLINE POLICY**

Beginning September 1, 2010, employee and non-employee travelers will have 60 days from the return date of their trip in which to submit travel reimbursement claims. Reimbursements submitted after this 60 day period will be subject to income tax assessment. Reimbursement claims submitted after 120 days from the return date of the trip will not be reimbursed. Indiana University Foundation funds may ***not*** be used for the reimbursement after this time period. These deadlines are required by the IRS, and will be strictly observed.


The Protein Analysis Research Center (educational research component of Monarch Life Sciences) has returned to the IU School of Medicine. The lab is located in MS0005. Dr. Mu Wang is the Primary Investigator of the lab, and Dr. Jin-Sam (Teddy) You is the senior research scientist.

## Wedding Bells

On May 30th, Graduate student **Reddy Palam** married his fiancé Sree Latha. Congratulations to the bride and groom!

On June 5th, **Jamie Schroeder**, Administrative Accounts Coordinator, was married to her fiancé Ryan Mayfield. Many Congratulations!

# Congratulations!

- In IUSM Faculty Elections, **Anna Depaoli-Roach** was elected to the Awards Committee, and **Clark Wells** was elected to the IUPUI Faculty Council.

- **Maureen Harrington** was selected to receive the 2010 Trustee's Teaching Award for her sustained dedication and outstanding practice of the art and science of teaching.

- **Tom Hurley** has been awarded a Chancellors Professorship. Congratulations to Tom on this well deserved recognition!

- **Howard Edenberg** was recognized at IU's Founder's Day Celebration, where he received the rank of Distinguished Professor. The rank of distinguished professor honors outstanding scholarship, artistic or literary distinction, or other achievements that have won signficant recognition by peers.

- **Howard Edenberg** also received the 2010 Prestigious External Award Recognition (PEAR) award. This award was in honor of being named an Indiana University Distinguished Professor and he also received the Research Society of Alcoholism's Distinguished Research Award. The PEAR award was presented at the Chancellor's Academic Honors Convocation on Friday, April 16, 2010. Congratulations!

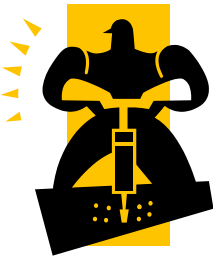
- **Katie Pawelczak**, graduate student in the lab of John Turchi, was recently awarded a travel award for the 11th International Workshop on Radiation Damage to DNA, where she presented her research in a talk.

- In the recently held Sigma Xi Research Competition, the department had several winners. **Vinnie Tagliabracchi**, of Peter Roach's lab, was awarded 1st place (the *Raymond Paradise Award*) in the 2004-05 graduate student group. In that same group, **Sulo Baskaran**, of Tom Hurley's lab, received an Honorable Mention. In the 2007 graduate student group, **Bill Ranahan**, of Clark Wells lab, received 1st place (the *David M. Gibson Award*). In the same student group, **Rachel Mullen**, of the lab of Simon Rhodes, received third place honors, and **Erica Daniels** of Debbie Thurmond's lab received an Honorable Mention. Finally, in the 2008-09 Student Group, **Karl Staser**, of Wade Clapp's lab, received 2nd place honors. Congratulations to all of our winners and participants in this prestigious competition!

- On May 6th, the IU Simon Cancer Center held its annual Cancer Research Day, with entrants from a variety of schools across campus. In the Basic Science category, the first place award was given to **Bill Ranahan** of Clark Wells lab for his poster "The Role of AMOT in Breast Cancer Progression". Second place in this category was awarded to **Justin Babcock** of Lawrence Quilliam's lab for his poster "Targeting mTOR-Induced Endoplasmic Reticulum Stress: A Rational Treatment for Sporadic AML/LAM?" Congratulations to both students!

- **Harikrishna Nakshatri** was one of four IU researchers named to the inaugural 62 member Susan G. Komen for the Cure's new Scientific Advisory Council.

## Construction Update



If you are interested in getting an idea of the projected end result of all of the construction on/around campus, you can check out this link... **www.masterplan.iupui.edu**.

## Centralized postdoc job database created

Postdoc positions can now be posted in a centralized, searchable database. This will enhance the recruitment of quality postdocs and the ease of managing positions. Please visit the online Postdoctoral Job Posting System on the faculty section of the postdoctoral affairs website, **www.postdoc.medicine.iu.edu**. First-time users will need to create an account. After that, simply log in to manage job postings. Through this system:

- Departments can post, remove, monitor, and repost their own postings including the deadline
- Job descriptions are saved, so they can easily be duplicated for future recruitment needs

Also, through this system, prospective postdocs are able to:

- Access all postdoc opportunities at IUSM in a centralized database
- Search positions by keyword as well as P.I. name

If you have any questions, please contact Jennifer Williams at jlw25@iupui.edu.

## Birth Announcements

**Anurada Landeru**, and her husband Ageshbabu welcomed their first child, a son named Kushal on February 23rd. Anu is a research technician in the lab of Quyen Hoang.

**Ross Cocklin** and his wife Carrie had their third child—a daughter named Elizabeth Reese, born on March 15th. Elizabeth has an older sister Claire and older brother Alex. Ross was a graduate student in the lab of Mark Goebl, and is now a Postdoc in the lab of Craig Pikaard in Bloomington.

**Sarah Delaplane** and her husband Brad had their first child—a daughter named Alma Elizabeth, born on April 9th. Everyone doing fine. Sarah is a research technician in the lab of Millie Georgiadis.

**Jun Wang** and her husband WenJun Zhang had their second child, a boy named Terry. Terry was born on April 15th. Terry has one older sister, Lindsey. Jun is a research analyst in Howard Edenberg's lab.

**Derrick Johnson** and his wife Melissa had a baby boy on April 16th. His name is Dylan Ethan, and everyone is doing well. Derrick is a graduate student in Andy Hudmon's lab.

**Brian Teske** and his wife Melissa had a baby boy - Jackson Jeffrey - on May 17th. Brian is a graduate student in Ron Wek's lab.

**Tolanda Larry**, gave birth to a baby girl on June 18th. Her name is Kaily, and mom and daughter are both doing fine. Tolanda is an hourly lab assistant in the lab of Mark Goebl.


Our condolences to Andy Hudmon on the passing of his mother Billie Hudmon. She passed on January 18th, in Opelika, Alabama.

# Discovery of enzyme activation process could lead to new heart attack treatment

Researchers at the Indiana University and Stanford University schools of medicine have determined how a "chemical chaperone" does its job in the body, which could lead to a new class of drugs to help reduce the muscle damage caused by heart attacks.

Such drugs would work by restoring the activity of a mutated enzyme, rather than taking the more common approach of blocking the actions of a disease-related protein.

The team, led by **Thomas Hurley**, associate chair and professor of biochemistry and molecular biology at IU, and Daria Mochly-Rosen, professor of chemical and systems biology at Stanford, report in the journal *Nature Structural Biology* published online Jan. 10 that the compound, called Alda-1, acts much like a shim to prop up a mutated form of a key enzyme, restoring the enzyme's function.

The enzyme, called ALDH2, plays an important role in metabolizing alcohol and other toxins, including those created by a lack of oxygen in the wake of a heart attack. It also is involved in the metabolism of nitroglycerin, which is used to prevent chest pain (angina) caused by restricted blood flow and oxygen to the heart.

However some people, including about 40 percent of people of East Asian descent, carry a mutated form of the ALDH2 enzyme that does not carry out its intended functions well. People with the mutated form of the enzyme are at increased risk of cardiovascular damage.

The IU and Stanford team reported in 2008 in the journal *Science* that in laboratory tests Alda-1 bypassed the body's usual signaling system and activated the ALDH2 enzyme directly, reducing damage to heart muscle tissue. That finding raised the possibility of new treatments for heart attacks, methods to protect hearts during open heart surgery, organ transplants, stroke and other situations in which blood flow is interrupted.

Their current paper describes how Alda-1 activates the ALDH2 enzyme in a process that Hurley likens to a woodworking procedure in which Alda-1 attaches to the ALDH2 enzyme at a crucial spot and acts like a shim or wedge to prop it up.

"Because of the mutation in the gene, parts of the protein structure become loose and floppy. Alda-1 reactivates the enzyme by propping up those parts of the structure so they regain normal function," said Hurley, director of the Center for Structural Biology on the Indiana University-Purdue University Indianapolis campus.

Determining how the Alda-1 compound works will enable the researchers to begin working on alternative compounds that hold more promise as potential drugs. One primary improvement needed is the ability to give the drug orally, rather than by injection, Hurley said.

"Based on the information from these studies, we're now ready to sit down with medicinal chemists and start designing new analogues by applying our understanding of what we need to leave alone and what we can modify to improve the properties of Alda-1," he said.

He predicted that alternative compounds could be available for testing by mid-2010.

The research was supported by grants from the National Institute of Alcohol Abuse and Alcoholism at the National Institutes of Health.

# School of Medicine Research Team Discovers TB Disease Mechanism and Molecule to Block It

Indiana University School of Medicine researchers have identified a mechanism used by the tuberculosis bacterium to evade the body's immune system and have identified a compound that blocks the bacterium's ability to survive in the host, which could lead to new drugs to treat tuberculosis.

**Zhong-Yin Zhang**, Ph.D., the Robert A. Harris Professor and chairman of the Department of Biochemistry and Molecular Biology, and his colleagues revealed the biochemical processes that TB bacteria employ to subvert macrophages – key infection-fighting cells – in this week's (Feb. 18, 2010) online early edition of the Proceedings of the National Academy of Sciences. They also described a compound they have synthesized – I-A09 – that blocked the TB bacterium's activity in laboratory tests.

About one-third of the world's population is infected with TB, a contagious disease that causes nearly 2 million deaths annually, according to the Centers for Disease Control and Prevention. Although medicines to treat TB are available, they must be taken for at least six months to fully eliminate all TB bacteria from the body. People who do not follow the lengthy treatment regimen can become sick and infectious with a more virulent form of the disease that is resistant to standard medicines.

The compound synthesized by the IU group is a proof of concept that a small molecule drug targeted against an essential virulent factor of the TB bacterium can be an effective strategy, Zhang said. If it can be developed into an approved drug, the result could significantly shorten treatment times for TB, he said.

The focus of the research was TB actions inside macrophages, which are infection fighting cells in the body's immune system. Macrophage cells' tools include the production of special proteins called cytokines to attack foreign invaders. Infected macrophages can also initiate a self-destruction mechanism called apoptosis, which signals other immune system cells to mount a defense against the infection.

TB bacteria are able to disable the macrophage defenses by secreting virulent factors into the host. The IU team found that the actions of a particular virulent factor – a protein phosphatase enzyme called mPTPB – blocked both the production of the infection-fighting cytokines, and the macrophage's self-destruct system.

Using combinatorial chemical synthesis and high-throughput screening, the researchers developed the I-A09 compound, which successfully blocked the action of mPTPB. Tests involving live TB bacteria were conducted at the Institute of Tuberculosis Research, University of Illinois at Chicago. Currently, compound I-A09 is being evaluated in a TB animal model at the Johns Hopkins University School of Public Health. More potent forms of the I-A09 compound are being pursued by the IU team for possible future clinical testing, Dr. Zhang said.

The research was supported by grants from the National Institutes of Health.

# Science without borders: Research Frontiers Trailblazer Awards Announced

The inaugural winners of the Research Frontiers Trailblazers Award were announced at the second annual IUPUI Research Day which took place this Spring. Two of the three faculty awardees were from the IU School of Medicine, and also affiliated with the Department of Biochemistry and Molecular Biology.

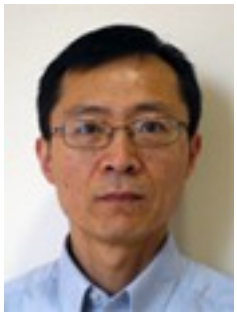
**Dr. Irina Petrache** and **Dr. Debbie Thurmond** are great examples of faculty who are bridging the gap between basic and translational science. Dr. Petrache, Associate Professor of Medicine and Biochemistry & Molecular Biology is making remarkable strides in the area of treatment therapies for those suffering with emphysema. Dr. Thurmond, Associate Professor of Pediatrics, Biochemistry & Molecular Biology, and of Cellular & Integrative Physiology, is making significant advancements in the fields of diabetes and cell biology.

According to the April 20th edition of the E-newsletter *Research Enterprise*, the honor is awarded to "outstanding Associate Professors within the first three years of promotion or appointment who show great promise and are becoming nationally and internationally known for their accomplishments in advancing the frontiers of knowledge".

# Grant Awards

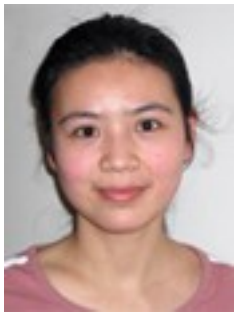
| PI | Project Title | Award Dates | Agency |
|---|---|---|---|
| Howard Edenberg | Collaborative Study on the Genetics of Alcoholism (COGA) | 9/1/09 - 8/31/10 | Res Fdn St Univ NY |
| Quyen Hoang | Specific inhibition of nucleation of alpha-synuclein aggregation as a therapeutic strategy | 12/29/09 - 12/30/10 | Michael J. Fox Foundation |
| Daniela E Matei | Targeting the transglutaminase-fibronectin interaction in ovarian cancer | 1/1/10 - 12/31/10 | American Cancer Society |
| Gerry Oxford and Joyce Hurley | Role of TRP Channels in Environmental Irritant-Induced Headache | 04/01/10 – 03/31/14 | NIH 1R01ES017430-01A1 |
| Hyun-Suk Lim | Direct inhibitors of K-ras as a novel targeted cancer therapy | Starts 4/1/10 | BRG |
| Irina Petrache | Molecular mechanism of alveolar injury caused by cigarette smoke | 4/1/10 - 3/31/11 | NIH-NIDA |
| Clark Wells | Role of Amot in Promoting Breast Cancer | Starts 4/1/10 | BRG |
| Mike Vasko and Andy Hudmon | An intracellular signaling switch for maintaining peripheral sensitization | 4/15/10-03/31/14 | NIH/NINDS R01 NS 069915 |
| Debbie Thurmond | Regulation of Glucose Homeostasis by Munc18 Protein | 4/15/10 - 3/31/11 | NIH-NIDDK |
| Edward McKee | Metabolism and toxicity of nucleoside reverse transcriptase inhibitors in non-replicating tissues | 4/20/10 - 3/31/11 | Walther Cancer Fdn |
| Howard Edenberg | Equipment Grant, Applied Biosystem SOLiD 3 System | 05/20/10 – 05/19/11 | NIH 1S10RR02805 |
| Claire Walczak | Acquisition of a DeltaVision OMX Super Resolution Imaging System | 5/13/10 - 5/12/11 | NIH-NCRR |
| Peter Roach | Glycogen Metabolism and its Regulation | 06/01/10 – 05/31/15 | NIH Merit 4R37DK027221-32 |
| Charlie Dong | The Role of Foxo Transcription Factors in Metabolic Regulation | 07/01/10 – 06/30/11 | Ralph W. and Grace M. Showalter Research Trust Fund |
| Andy Hudmon | Preventing Excitotoxic Neuronal Death via Inhibtion of Ca2+/Calmodulin-Dependent Protein Kinase II | 07/01/10 – 06/30/11 | Ralph W. and Grace M. Showalter Research Trust Fund |
| Mike Kalwat | Regulation on SNARE-mediated Biphasic Insulin Secretion by F-actin | 07/01/10 – 06/30/12 | fellowship from American Heart |
| Suk-Hee Lee | Molecular Analysis of the SET-Transposase in DNA Repair | 07/01/10 – 06/30/11 | RSFG |
| Dorothy Lo | | 07/01/10 – 06/30/11 | DeVault Fellowship through Microbiology |
| Samy Meroueh | Computational Design of Small Molecule Inhibitors of Ral GTPases to Block Tumor Invasion and Metastasis | 07/01/10 – 06/30/11 | RSFG |
| Ron Wek | Translation and Stress Regulatory Pathways in Health and Disease | 07/01/10 – 06/30/11 | Ralph W. and Grace M. Showalter Research Trust Fund |
| Clark Wells | Role of Amot in Breat Cancer Progression | 07/01/10 – 06/30/11 | RSFG |
| Zhong-Yin Zhang | Small Molecule Inhibitors for the Oncogenic Protein Tyrosine Phosphatase SHP2 | 07/01/10 – 05/31/15 | NIH 1R01CA152194-01 |

# New Faces in the Biochemistry Department

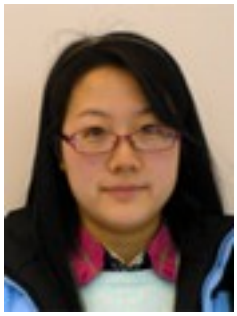


Weihua Shen,
Visiting Asst. Research Professor, Zhang Lab

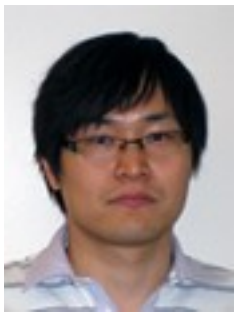
Jin-Sam (Teddy) You,
Visiting Assoc. Research Professor, PARC



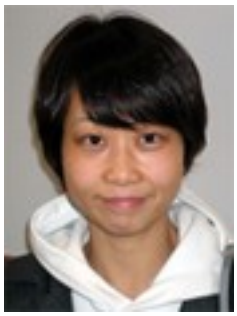
Wei Wang,
Postdoctoral Fellow,
Hoang Lab



Wantong Yao,
Visiting Research Assoc.
Lu Lab



Kyung-Chang Seo,
Postdoctoral Fellow,
Lim Lab



JingLing Liao,
Postdoctoral Fellow,
Hoang Lab

Hai Yuan,
Postdoctoral Fellow,
Ye Lab

Kerry Bemis,
Biostatistician,
PARC

Seok-Min (David) Hong,
Visiting Research Assoc.,
PARC

Guihong Qi,
Visiting Research Assoc.,
PARC

Yasmeen Rahimi,
Graduate Student,
Harris Lab

Thomas Baird,
Graduate Student
Wek Lab

Derrick Johnson,
Graduate Student,
Hudmon lab

Candace Myers,
Hourly Lab Assistant,
T. Hurley Lab

Victor Dominguez,
Summer Student,
Roach Lab

Cassie Xu,
Summer Student,
Ye Lab

Not pictured: Christopher Contreras, Graduate Student, Roach Lab; Brandon Downing, Combined Degree Student, Ingram Lab; Punitee Garyali, Graduate Student, Roach Lab.