

Alumni return to Ann Arbor for the Pharmacology and Experimental Therapeutics Career Day

INSIDE THIS ISSUE

- 1 Pharmacology and
Experimental
Therapeutics Career Day
- 2 New Faculty Research
 - 2 Michael Holinstat
 - 3 Paul Jenkins
- 4 Pharmacological
Sciences and Bio-Related
Chemistry Symposium
- 5 42nd Annual
Pharmacology Research
Colloquium
- 6 Pharmacology in Ethiopia
- 7 News
- 9 Milestones



Career Day Speakers and Organizers

Left to right: RaShonda Flint (Baghdoyan Lab, 2010), Emily Jutkiewicz (Woods Lab, 2004), Paul Jenkins (Martens Lab, 2010), Erin Booth (Lucchesi Lab, 2006), Anwar Dunbar (Osawa Lab, 2005), Kelly Cameron (Osawa Lab, 2012), Toby Freedman (Keynote Speaker), Ezra Lowe (Osawa Lab, 2004), Elizabeth Peckham (Traynor Lab, 2005), Adam Kuszak (Sunahara Lab, 2009)

On June 2, 2015, the department hosted its annual Pharmacology and Experimental Therapeutics Career Day. The event was designed to expose the department's current students to the multiple career options following their Doctoral or Master's degree training. The Department invited some of its alumni to discuss their careers and share their experiences. The keynote speaker was Dr. Toby Freedman, President of Synapsis Search, a life sciences business and R&D recruiting services. Dr. Freedman is author of the book "*Career Opportunities in Biotechnology and Drug Development*".

The event was organized by Drs. Emily Jutkiewicz, Paul Jenkins and Lori Isom.

More on this event has been posted by Anwar Dunbar (Osawa Lab 2005). See <http://www.examiner.com/article/the-university-of-michigan-s-2015-pharmacology-career-day>

Holinstat Lab

*By Michael Holinstat
Associate Professor*



Back row:
Devon Pope, Meral
Ebrahim, Reheman
Adili, Katrin Niisuke,

Front row:
Ben Tourdot, Jen
Yeung, Mike Holinstat

The Holinstat lab focuses on understanding the complex signaling mechanisms that regulate hemostasis and thrombosis. Work in the lab concerns four primary areas of platelet research spanning a basic science and drug discovery program to clinical and translational projects including a clinical trial focused on platelet function in type 2 diabetes mellitus and a clinical study of racial disparity in thrombotic risk. This work is fully funded by four National Institutes of Health grants (NIH R01 grants), support from the American Heart Association (AHA), and the Parenteral Drug Association Foundation (PDAF), and has resulted in 4 patents being filed. Additionally, the early findings in the lab have been recognized by several national and international research associations. In 2012, Dr. Holinstat was awarded the Kenneth M. Brinkhous Young Investigator Prize in Thrombosis from The American Heart Association for his discovery of a novel approach to inhibition of platelet function and development of small molecule inhibitors for the prevention of thrombosis. In 2013, Dr. Holinstat was awarded the Young Investigator Award in Structure/Function at the International meeting for Bioactive Lipids in Cancer, Inflammation, and Related Diseases for identifying a novel bioactive metabolite which functions to prevent platelet activation and has the clinical potential to prevent myocardial infarction and stroke in patients at high risk for thrombosis.

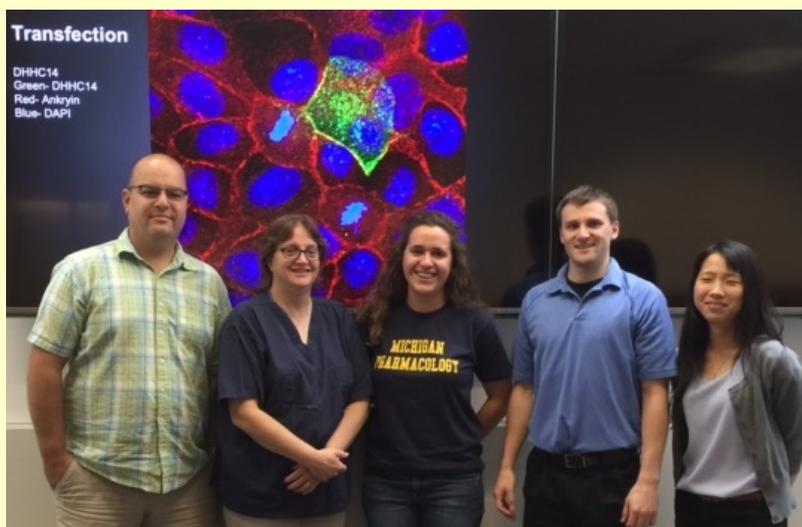
Another area of interest in the lab is to identify inherent racial differences in platelet function between blacks and whites. This clinical project investigates some of the underlying genetic and pharmacogenomic differences in blacks and whites that predispose some people to a higher risk for thrombosis and stroke while sparing others. Through this effort we will be able to determine for the first time how to differentially treat patients based on their genetic/racial background. This area of research, often termed “precision medicine” has the potential to shift our mode of treatment from disease to patient by understanding that not all treatments will equally benefit every patient who presents with a thrombotic event. More importantly prevention of thrombotic events may differ based on genetic or racial background.

Platelet activation is regulated by the enzyme 12-lipoxygenase (12-LOX). Similar to COX-1, 12-LOX oxidizes free fatty acids to form bioactive metabolites (eicosanoids). The lab has recently shown that the 12-LOX eicosanoids derived from arachidonic acid in the platelet are pro-thrombotic and has developed the first selective inhibitor against human 12-LOX activity. This new class of inhibitors prevents agonist-mediated platelet activation and clot formation in human platelets. Subsequently, a new bioactive lipid was also identified, 12-HETrE, as a potent inhibitor of platelet function. Ongoing studies are focused on identifying the underlying mechanisms by which 12-HETrE protects against platelet activation, clot formation, and stroke. This work has been extended to investigate if altering the fatty acid content of the platelet may allow for formation of 12-LOX metabolites which would protect type 2 diabetics from suffering a thrombotic event. This is an important area in diabetes research as 65% of deaths in type 2 diabetics are due to thrombosis and stroke.

Overall, these studies will help to identify novel signaling regulators in the platelet and determine new approaches for the prevention of occlusive thrombus formation leading to myocardial infarction and stroke.

Jenkins Lab

By Paul Jenkins
Assistant Professor



Left to right:

Paul Jenkins, Kathy Ignatoski, Katie Hahm, Andrew Nelson, Bing Zheng

The Jenkins Lab is working towards understanding of the molecular underpinnings of complex neuropsychiatric disorders, such as bipolar disorder and schizophrenia. Ankyrin-G (product of the ANK3 gene) has been implicated in a growing number of genetic screens for neuropsychiatric disorders, and is responsible for the formation of the axon initial segment (AIS) and nodes of Ranvier. Importantly, the AIS and its associated ion channels have been implicated in several important human diseases, including epilepsy, cognitive dysfunction, and bipolar disorder. Moreover, human patients that are predicted to completely lack the giant 480 kDa isoform of ankyrin-G, exhibit intellectual disability (IQ<50), severe behavioral problems, and ADHD. Elucidating the mechanisms by which ANK3 mutations cause disease is critical for the development of novel therapeutic strategies.

Despite the discovery of a giant (480 kDa) splice variant of ankyrin-G more than 20 years ago, very little is known about its function. Recently, I demonstrated that genetic deletion of the exon responsible for coding giant ankyrin-G in mice, causes complete loss of the AIS and 80% reduction in nodes of Ranvier. These mice exhibited a profound loss of GABAergic synapses on the soma and AIS of cortical and hippocampal pyramidal neurons. Ankyrin-G, through its giant exon-encoded sequence, interacts directly with the GABA receptor associated protein (GABARAP) to stabilize extrasynaptic GABA receptors allowing the generation of GABAergic interneuron synapses. Through access to the Heinz C. Prechter Bipolar Research Fund, a longitudinal study of 1,200 bipolar patients and controls at the University of Michigan, we will be evaluating exome and whole genome sequencing data from bipolar patients and relatives to identify ANK3 mutations that affect structure and function of ankyrin-G. Then, using induced pluripotent stem cells (iPSCs) from these patients, we will examine effects of ANK3 mutations on neuronal cell biology and organization. Furthermore, we will be developing mouse models to evaluate the significance of genetic alterations in ANK3 in disrupting the proper formation of neuronal circuitry and behavior. Overall, we hope to identify the genetic causes of ankyrin-G dysfunction that underlie neuropsychiatric diseases and discover novel therapeutic targets for treatment of these disorders.

Another area of focus of the Lab is elucidating the mechanisms of membrane organization in polarized cells. Epithelial cells are the most highly represented cell type in the human body and lie at the interface between the body and the outside environment, where they play critical roles in ion homeostasis, absorption and excretion, and protection from microbial invasion. Ankyrin-G and its binding partner β III-spectrin localize to the lateral membrane of columnar epithelial cells, where loss of either protein impairs cell height and lateral membrane formation. Recent work identified the lateral membrane-localized palmitoyltransferases as the mediators of palmitoylation of ankyrin-G. My lab is interested in the mechanisms of protein targeting to the lateral membrane and how palmitoyltransferases, Ankyrin-G, and Spectrin work together as a team to promote lateral membrane biogenesis.

The 35th Pharmacological Sciences and Bio-Related Chemistry Symposium

was held on Friday April 3rd in the A. Alfred Taubman Biomedical Sciences Research Building. This symposium is unique in that it is fully organized and run by students from the Departments of Pharmacology, Medicinal Chemistry, Pharmaceutical Sciences and Biochemistry who are members of the NIH funded Interdepartmental Training (Program) in the Pharmacological Sciences. The keynote speaker was Dr. Robert Lefkowitz, M.D., James B. Duke Professor of Medicine and Professor of Biochemistry and Chemistry at Duke University, HHMI Investigator and winner of the 2012 Nobel Prize in Chemistry. Dr. Lefkowitz spoke on his life's work deciphering the mechanisms of action of seven transmembrane receptors, with a glimpse of current and future work. The symposium also traditionally features an expert on research ethics, this year's speaker being Dr. Edward Goldman, J.D., Adjunct Assistant Professor of Health Management and Policy and Associate Professor in the Department of Obstetrics and Gynecology at the University of Michigan.



Dr. Lefkowitz with the student organizers and Drs. Paul Hollenberg and Ron Woodard

Dr. Robert Lefkowitz delivering his lecture "Seven Transmembrane Receptors"



Dr. Edward Goldman delivering the ethics lecture, "Research on Human Subjects: How Much Can I Get Away With?"



Dr. Lefkowitz discussing pharmacology with a group of students during lunch

The 42nd Annual Pharmacology Research Colloquium was hosted on Friday June 12th by the University of Toledo (UT) Dept. of Physiology and Pharmacology. The Pharmacology Colloquium brings together graduate students and faculty from the “pharmacology” departments of the Michigan State University, the University of Michigan, Wayne State University, and the University of Toledo for a day-long scientific program. The colloquia were initiated 43 years ago by Dr. Benedict Lucchesi (UM) and by Dr. Theodore M. Brody (MSU), primarily to provide a forum for doctoral students to present their research in both oral and poster presentations and an opportunity for all participants to exchange ideas.

Participants at this year’s meeting were welcomed by Dr. Howard Rosenberg, Interim Chair of the Dept. of Physiology and Pharmacology at the UT College of Medicine and Life Sciences and Dr. William Messer, Vice President for Research at UT. The keynote lecture was presented by Dr. Tim Wiltshire, Director of the Center for Pharmacogenomics and Individualized Therapy at the University of North Carolina, Chapel Hill.

There were 139 registrants from the 4 schools including over 90 students, both graduate and undergraduate as well as 45 faculty members. The program included 13 oral presentations and 40 poster presentations. Two University of Michigan graduate students took home first prize for Best Oral presentation and best poster presentation.

Dr. Wiltshire delivering his keynote lecture, “Pharmacogenomics, Great Promise but Poor Implementation”



Colleen Carpenter (left, Gnegy Lab) receiving the best oral presentation award and Kathryn Livingston (Traynor Lab) winner of the best poster award at the 42nd Annual Pharmacology Colloquium. Colleen and Kathryn are pictured receiving their awards from Dr. Andrew Beavis (University of Toledo)

EM-PACE: A Crash Course in Chalk-Talks and International Communication

*By Larisa Kruger
Graduate Student - Isom Lab*

In a late evening in early May, my co-teachers and I were gathered around our plastic table and chairs with only our laptops and flashlights for light. Peter and Brittany were debating which biochemical pathways were most critical for their students' later studies and should thus be included in tomorrow's lecture. Meanwhile, I constructed in-class questions in hopes of getting students to overcome their hesitancy to talk during class. The power had been out for hours so Peter's laptop had died, but we were determined to finish the lectures for the following day. The following day, we lost power three times during class and had to keep switching to 'chalk-talks.' But our students asked questions during class, despite their usual hesitancy. Afterward, they all seemed excited about the upcoming weeks and several of them thanked us for the lecture. This apparently unusual set of circumstances was typical of our time teaching 52 first-year medical students in Ethiopia.

Our Ethiopian teaching experience was part of the EM-PACE (Ethiopia-Michigan Platform for Advancing Collaborative Engagement). Graduate education is growing rapidly within Ethiopia, faster than the country can manage. Brittany Clawson (MCDB), Peter Chockley (Immunology) and I spent 4 weeks in Ethiopia to establish relationships, teach courses, and create networks within Adama Hospital Medical College. These efforts will serve as launching points for further collaborative development within the EM-PACE program.

We co-taught the Biochemistry, Physiology, and Pharmacology courses for the first-year medical students. Although we were working off a general syllabus, we were responsible for selecting textbooks and reading materials and developing the course content, including lectures, quizzes, tests, and reading materials. The students were eager to learn but less willing to interact during class, so we had to work hard to integrate active learning techniques into the course. The payoff for all of this work was huge - our students told us many times they loved being in class and really enjoyed all the activities. For some of them it was very different than the style of teaching they are used to receiving in their country.

Outside of the teaching experience, we also had the chance to participate in some fun cultural experiences. Ethiopian eating is typically 'family-style' but everyone eats with their hands - scooping food up with the injera (fermented bread made out of teff flour). One meal they brought us a plate of raw beef (some of us ate it cooked!!). More commonly we enjoyed shiro (chickpea stew) or more usual dishes such as pizza and stir-fry. We also got to see the traditional dancing (Eskesta or 'dancing shoulders') and a comedian playing the masenqo (a lute).



My favorite moment on the trip was on one of our last days, we told our students we were leaving and they all wanted photos with us. I don't think I've had so many photos taken at one time since my wedding! We also had a student that wrote us a letter thanking us for teaching him and how he learned how to be punctual for our classes. It was really rewarding to hear all the positive feedback from students that our hard work had helped them learn.

If any faculty, students or alumni are interested in being involved in EM-PACE can contact Professor John Williams jawillms@umich.edu to be added to the mailing list for future updates on the program.



Larisa Kruger with EM_PACE students and Peter Chockley (Immunology Graduate Program, UM)

News

Faculty News

Dr. Ron Holz received the 2015 Sir Bernard Katz Award for Excellence in Research in Exocytosis and Endocytosis presented by the Exocytosis and Endocytosis Subgroup of the Biophysical Society. Ron joins a list of 10 previous awardees including 3 Nobel Prize winners and 8 members of the National Academy of Sciences.

Dr. Mark Cohen (together with Dr. Anna Schwendeman, Medicinal Chemistry) won Michigan's first Biomedical Innovation "Shark Tank" for a new drug for the treatment of adrenal cancer. The Shark Tank event was co-sponsored by UM-MTRAC (Michigan Translational Research and Commercialization program) and the Michigan Economic Development Corporation and hosted by Mike Finney, Special Advisor to Governor Rick Snyder. The winner was decided by a group of biomedical investment experts.

Dr. Roger Sunahara has accepted a position as Professor of Pharmacology at the University of California, San Diego. Roger joined our department as an Assistant Professor in 2001. We wish Roger all the best in his new position.



John Tesmer, Roger Sunahara, Jorge Iniguez, and Paul Hollenberg at Roger's leaving party

Alumni News

Ryan Frieler (Mortensen Lab, 2014) received an honorable mention for the ProQuest Distinguished Dissertation Award for his PhD thesis entitled "Protection from Stroke through Immunomodulatory Mechanisms." Ryan is continuing his research in Dr. Mortensen's lab on macrophage phenotypes and mineralocorticoid receptors in cardiovascular disease.

Jessica O'Konek (Shewach Lab, 2008) is the recipient of the 2015 Food Allergy Research & Education (FARE) New Investigator Award. Jessica is a Research Investigator at the U-M Nanotechnology Institute for Medicine and Biological Sciences.

Jennifer Lamberts (Traynor Lab, 2013) was recently appointed to the National Postdoctoral Association Board of Directors as co-chair elect of the Meetings Committee. Jenny is currently Assistant Professor of Pharmacology, Ferris State University and a Visiting Scientist at the Van Andel Institute.

Postdoc News

Chad Frasier (Isom Lab) received a MICHR \$100,000 Postdoctoral Translational Scholars Program Career Development Award.

Jyoti Malhotra (Isom Lab) has been promoted to Senior Principal Scientist, Translational Biology, Mitobridge, Inc., Boston MA.

Matt Merrins (Satin Lab) is now a tenure track Assistant Professor of Endocrinology and Metabolism at the University of Wisconsin, Madison, with a joint appointment in Biomolecular Chemistry.

Gustavo Patino, (Isom Lab) has accepted a position as an Assistant Professor of Neuroscience at Oakland University William Beaumont School of Medicine.

Benjamin Tourdot (Holinstat Lab) received postdoctoral fellowships from both the American Heart Association (AHA) and an F32 NRSA from the NIH (NHLBI) for his work on pharmacogenomics in racial disparity in thrombotic risk.

Eileen Vesely (Satin Lab) has accepted a position as an Assistant Professor at DeSales University in Pennsylvania.

Pete Vollbrecht, (Ferrario Lab) is heading to Hope College in Holland, MI as a visiting Assistant Professor in the Biology Department.

Student News



Nicole Michmerhuizen (Brenner/Carey Labs) received a prestigious National Science Foundation (NSF) Graduate Research Fellowship. The NSF Graduate Research Fellowship Program recognizes and supports outstanding graduate students in NSF-supported science, technology, engineering, and mathematics disciplines who are pursuing research-based Master's and doctoral degrees at accredited United States institutions.



Jennifer Yeung (Holinstat Lab) has been awarded predoctoral fellowships from both the American Heart Association and an F31 NRSA from the NIH (NHLBI) for her work on 12-lipoxygenase regulation of Heparin-Induced Thrombocytopenia and Thrombosis (HITT).



Nayiri Kaissarian (Shayman Lab) received a University of Michigan - Israel Partnership Research Training Fellowship.

Colleen Carpenter (Gnegy Lab) received the 2015 “EDGE” award from the Endowment for Basic Sciences. Colleen’s research on tamoxifen analogues as potential treatments for amphetamine abuse was featured in a blog at the 2015 EB meeting (see <https://everydaybiochemistry.wordpress.com/2015/04/03/new-tamoxifen-analog-reduces-amphetamine-neurochemical-and-behavioral-effects/>).

Colleen Carpenter (Gnegy Lab) won the best oral presentation award and Kathryn Livingston (Traynor Lab) won the best poster award at the 42nd Annual Pharmacology Colloquium on June 12, 2015 at the University of Toledo (see page 5).

Larisa Kruger (Isom Lab) traveled to Ethiopia to teach medical students as part of the Ethiopia-Michigan Platform for Advancing Collaborative Engagement (EMPACE) (see Larisa’s article on page 4).

Recent Grants

The Interdepartmental Training Grant in the Pharmacological Sciences was competitively renewed in May for an additional 5 years of funding. The grant award includes funds to support 10 pre-doctoral trainees per year and includes participating mentors from Pharmacology, Medicinal Chemistry, Pharmaceutical Sciences and Biochemistry. Co-directors of the training grant are Paul Hollenberg and George Garcia (Medicinal Chemistry).

Les Satin's R01 (NIDDK) on islet metabolic oscillations was recently renewed for another 5 years, and he is also a co-Investigator with Dr. Peter Butler of UCLA on a R01 to study the role of human islet amyloid polypeptide in type 2 diabetes.

Dr. Satin also received funding from the Massey Research foundation to support new work on the effect of traumatic brain injury on synaptic transmission in cortical pyramidal neurons, and from UM “FastForward” (part of the U-M Medical School’s Strategic Research Initiative) for studies on ER Ca dysfunction and ER stress in Protein Folding Diseases.

John Traynor received a new R01 grant from NIDA for 5 years to study allosteric modulators of the opioid receptors.

Milestones



Eileen Ferguson (Student Services Associate) will be retiring on August 31 after 43 years at the University including more than 28 years of service to the Pharmacology department. Happy retirement Eileen - we will miss you.

Dr. Adam Lauver (Research Assistant Professor) and his wife have a new baby boy, Van Arthur Lauver, born on June 22nd.

Kiran (Satin Lab) and Geetha Vadrevu are new parents of a healthy baby boy, Vyas Vadrevu, born on May 21st.

Dr. Rheaclare Fraser (Gnegy Lab, 2013) was married to Mr. Keith Spears at the Turtle Back Zoo in West Orange, New Jersey on May 10th.

For Daily News Updates

check our webpage:

<http://www.pharmacology.med.umich.edu/Pharmacology/Home.html>**And don't forget to "friend or like us" on Facebook**<https://www.facebook.com/pages/Michigan-Pharmacology/193058470712533>

If you have news or views you would like to share with alumni, faculty, students and staff, please send information to John Traynor:

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