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ECP Gazette

The Newsletter of the Department of Experimental & Clinical Pharmacology

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Dear Friends,

The record-breaking snowfalls of February may have slowed our travels around campus, but progress on our academic year goals presses on! We have spent the fall semester digging in to our research, teaching, and administrative projects, and the dedication of our faculty, staff, and students is bearing fruit.

In October, ECP put in a notable showing among poster and travel award winners at the annual meeting of the American College of Clinical Pharmacy in Seattle, Washington. Our Faculty, post-docs, professional and graduate students, all returned from the conference with fresh honors.

We look forward to spring and its challenges with excitement. This year, we are planning a retreat that will enjoy the benefit of external review of the ECP department to help us focus and refine our plan for the coming years, with a special eye towards departmental priorities for hiring and support for our research initiatives.

We will be seeking a new colleague to join us in these endeavors. This individual will replace Diane Blumenfeld. We very much appreciated Diane’s contributions to ECP and wish her the best as she pursues new opportunities in the dental school. We will also begin seeing less of William Oetting and John Rotschafer on campus, as both have began to enjoy their phased retirements. Though we will miss their experience and daily contributions, we wish them well during the next few years of their phase. In the meantime, we look forward to building on the teaching and research foundations these valued members of ECP have help to lay down in their combined 54 years of service.

Please read on for details on these and other items of interest in the department, and join me in wishing faculty, staff, and students smooth sailing as we close out the academic year.

Sincerely,

Robert J. Straka, Pharm.D.
Department Head
When faced with a cancer diagnosis, a patient’s and his or her care team’s primary concern is to confront and eliminate the imminent threat the cancer poses to the patient’s life and health. However, for many cancer survivors, cancer remission is not necessarily the end of health challenges related to the disease. Cancer treatment frequently causes long-term, sometimes silent, damage to critical organs and systems that can result in chronic diseases and reduce quality of life or life expectancy for cancer survivors.

Assistant Professor Beshay Zordoky would like to help cancer survivors move on from illness, rather than from one illness to the next.

Dr. Zordoky received his degree in pharmacy, with honors, from Ain Shams University in Cairo, Egypt, where he also went on to earn his master’s degree in clinical pharmacy. While conducting his graduate studies, he worked as a teaching assistant and assistant lecturer in Ain Shams’ clinical pharmacy department, teaching several classes on topics ranging from pharmacokinetics to clinical pharmacy. It was at Ain Shams during his undergraduate years that Dr. Zordoky first became interested in studying or teaching at the University of Minnesota, drawing inspiration from many of his professors who had studied at the U of M and returned to Egypt to teach.

Dr. Zordoky’s excellence in research and teaching at Ain Shams earned him a scholarship to pursue graduate studies in Canada, where he enrolled in the Ph.D. program in the Pharmaceutical Sciences Department, University of Alberta. There, he completed his doctoral degree in Pharmaceutical Sciences—Drug Metabolism in 2012 with a dissertation on the role of cytochrome P450 enzymes in the pathogenesis of cardiac hypertrophy and doxorubicin-induced cardiotoxicity. In addition to pursuing his research career, Dr. Zordoky passed the Pharmacy Examining Board of Canada (PEBC) qualifying exam and became a registered clinical pharmacist with the Alberta College of Pharmacists, Canada.

While pursuing his bench side research projects, Dr. Zordoky was dealing with a large number of patients who were cancer survivors. Of this period, he says, “It was my delight when patients mentioned cancer as a ‘past medical history’. However, I also noticed that these cancer survivors usually suffered from several health problems, including cardiovascular diseases. One of these patients was taking four different medications for hypertension in very high doses to control her blood pressure. Thinking of these patients, I decided to apply my basic research knowledge to find appropriate therapies that can prevent or even cure cancer treatment-related cardiovascular adverse effects.”

After completing his Ph.D. program, he joined the Cardiovascular Research Centre, Department of Pediatrics, University of Alberta, as a Postdoctoral Clinician Fellow funded by the Canadian Institutes of Health Research and Alberta Innovates – Health Solutions. In his postdoctoral role, he continued his study of cardiovascular damage caused by chemotherapy and how the natural polyphenolic
compound, resveratrol, can prevent it. He also worked as an instructor at the Faculty of Pharmacy University of Alberta, where he taught pharmacy students the drug metabolism lectures in the “Principles of Drug Action and Disposition” course.

In July, 2015, Dr. Zordoky joined the faculty of ECP with the goal that his research program may help to prevent or even reverse the cardiovascular toxicities of cancer treatment. He is currently interested in studying delayed cancer treatment-induced cardiotoxicity (e.g. anthracycline-induced cardiotoxicity) in animal models for childhood cancer survivors.

So far, Dr. Zordoky has focused on identifying the molecular mechanisms of juvenile doxorubicin-induced cardiotoxicity and sex-related differences of doxorubicin-induced cardiotoxicity. Of particular interest are his findings that show exposure of juvenile mice to low doses of doxorubicin caused subclinical cardiotoxicity that did not immediately reduce the cardiac function of juvenile mice, but made the mice more vulnerable to the detrimental effects of a “second-hit” such as angiotensin II-induced hypertension or psychosocial stress. In his most current research, he is leading a collaborative research team to bridge together cardiovascular and cancer research. Their objective is to identify novel cardioprotective therapies that won’t interfere with the therapeutic benefits of cancer treatment.

Going forward, Dr. Zordoky hopes to identify biomarkers that can predict those survivors who are going to develop cardiovascular complications and discover effective therapies to protect them from such complications. Since childhood cancer survivors show signs of premature aging, one novel therapeutic intervention is the use of anti-aging medications (senotherapeutics) to reverse the toxicity of cancer treatment. If proven successful in preclinical studies, Dr. Zordoky believes this novel approach can prevent and even reverse cancer treatment-induced toxicities of different organs and systems in childhood cancer survivors.

**Current Studies:**

- **Masonic Cancer Center, University of Minnesota – Zordoky (PI, Masonic Cancer Center Women’s Health Scholar)**
  01/01/2018 – 12/31/2019
  Title: Molecular Mechanisms of Sexual Dimorphism in Delayed Doxorubicin-induced Cardiomyopathy

- **American Cancer Society - Institutional Research Grant, Zordoky (PI)**
  12/01/2018 – 11/30/2019
  Title: Psychosocial Stress Unmasks Juvenile Doxorubicin-Induced Latent Cardiotoxicity

- **Rally Foundation for Childhood Cancer Research – Zordoky (PI)**
  07/01/2018 – 06/30/2019
  Title: Role of Galectin-3 Signaling in Juvenile Doxorubicin-induced Cardiotoxicity (Renewal)
The College of Pharmacy had a strong showing at the 2018 American College of Clinical Pharmacy (ACCP) Global Meeting in October, with particularly impressive representation from ECP students, faculty, fellows and undergraduate research scholars. The team of Jeannine Conway, Parker Johnson, Chris Conley and Christopher Olsen earned third place in the ACCP Foundation's Trivia Challenge.

Seenae Eum won the Best Resident/ Fellow Poster Award and the CNS PRN Travel Award for her presentation on "Catechol-O-Methyltransferase (COMT) and Treatment Response to Meditation and Group Therapy in Veterans with PTSD."

Kerui Peng (PD4), was a poster presentation finalist and won a travel award in the Pharmacokinetics/Pharmacodynamics/Pharmacogenetics (PK/PD/PGx) PRN for her work as a Melendy scholar in the lab of Robert Straka in 2016.
Alumni Spotlight: Ahmed Hamed Salem, Ph.D. ’10

Where are you now and how long have you been there?
I work at Abbvie in North Chicago, IL. I have been working with Abbott and its spin-off Abbvie for 9 years. My title is Director, Clinical Pharmacology and Pharmacometrics.

Have you had any recent promotions or major field changes since you began your career?
While working at Abbvie, I have been promoted 5 times. I started as a Senior Scientist I in 2010, then was promoted to Senior Scientist II in 2012, Associate Principal Scientist in 2014, Associate Director later in 2014, Director in 2016 and finally I was promoted in November 2018 to the “higher grade” Director. In 2017, I became an adjunct Associate Professor at ECP.

What would you say is your primary role in your current position?
I currently lead the clinical pharmacology, biopharmaceutics and early clinical development strategy in the oncology therapeutic area. I design clinical trials and analyze and interpret their data. I make recommendations for regulatory pathways to make the drugs approved by health authorities and hence available to patients.

Since graduating from ECP’s grad program, what would you say are your most significant professional accomplishments? What particular achievement are you most proud of?
The achievement I’m most proud of is developing venetoclax (Venclexta ®) which is a first-in-class selective BCL-2 inhibitor. I worked on this drug when it was still in the preclinical stage to project the doses we should use in humans. I also worked on its clinical development and, finally, regulatory submissions. Venetoclax has breakthrough designations by the FDA in multiple indications. It received several approvals for treatments of certain hematologic malignancies and I’m still working with the team to evaluate venetoclax in other malignancies. It is very rewarding to listen to patients and see the remarkable impact this drug made in their life.

Other professional achievements include contributing to several regulatory submissions and approvals in the HIV and hormone areas, becoming a fellow of the American College of Clinical Pharmacology in 2017, publishing over 130 publications, having two accepted patents and receiving the AAPS high impact article award.

Reflecting back on your experiences as an ECP Graduate Student, what are your fondest memories from that time?
My best memories from ECP days are the “aha moments,” which were countless. It is a great feeling when you understand a certain scientific concept, and you like what you understood and you realize this is what you want to do for the rest of your life.

I still remember the first pharmacometrics article that I read as part of the “Readings” class in my first semester at ECP. It was so much fun to understand its methodology with the help of a 3rd year student (Thanks Manisha Lamba). The advanced PK course offered at my time by Drs. Sawchuk, Emquist, and Zimmerman was full of aha moments.

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In research, I still remember an aha moment when I figured out how to use the D-Optimality feature in ADAPT to optimize the concentrations in pharmacodynamic experiments instead of its more standard use to optimize sampling times for pharmacokinetic assessments. This project later became the first article to list me as a first and corresponding author.

**What advice can you give to current and/or prospective students in ECP?**

Take as many courses as you could. This is your best chance to learn and develop your understanding of clinical pharmacology concepts. If you are considering a career in industry, you may want to explore internship opportunities after your 2nd or 3rd year. It will help you decide if this is what you would like to do when you graduate. It will also make you a stronger candidate when you apply for jobs in the industry.

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*My best memories from ECP days are the ‘aha’ moments...*
**Grants**

Lisa Coles is part of two teams that received R01 grants from the NIH: “The role of beta-catenin in the pathophysiology of infantile spasms” (NINDS), and “A longitudinal study evaluating three RDOC constructs in adolescents with non-suicidal self-injury” (NIMH).

Beshay Zordoky received a $30,000 American Cancer Society Institutional Research Grant for his project, “Psychosocial Stress Unmasks Juvenile Doxorubicin-Induced Latent Cardiotoxicity.”

**Recognition**

James Cloyd received a faculty recognition award from the Pharmacy Alumni Society and was elected to the National Institute of Neurological Disorders and Stroke (NINDS) NeuroNEXT Data and Safety Monitoring Board.

Jeannine Conway was named PharmD Teacher of the Class by the PharmD class of 2018.

Betsy Hirsch received a 2017 Young Investigator Award from the Society of Infectious Diseases Pharmacists in recognition of past research accomplishments and to acknowledge her promise as a researcher in the broad area of infectious diseases. Dr. Hirsch was also selected by the class of 2020 as the Teacher of the Semester for Fall, 2018.

Pamala Jacobson received the Sara Evans Faculty Woman Scholar/Leader Award from the University of Minnesota Women’s Center, Office for Equity and Diversity and was honored at their Celebrating Changemakers Awards event on October 11, 2018.

Ramaiah Muthyala received the India Association of Minnesota (IAM) 2019 Lifetime Achievement Award in recognition of his outstanding work on awareness and policy advocacy for rare diseases for the Asian Indian community.

Mark Kirstein and ECP Adjunct Professor Ahmed Salem spoke in a symposium at the American College of Clinical Pharmacology’s annual meeting in September, along with Nam Atiqr (Atiq) Rahman, Division Director, Food and Drug Administration and Hao Xiong, Director, Clinical Pharmacology, AbbVie.

**Media**


Swayam Prabha was the featured research profile in the October issue of the MOCA Messenger, the monthly newsletter of the Minnesota Ovarian Cancer Alliance (MOCA), for her project, “Glycoengineered Mesenchymal Stem Cells for Combination Chemo and Immunotherapy of Ovarian Cancer.”
Abeer Alharbi completed her M.S. and moved on to Oxford University to begin work on her Ph.D.

Angela Jeong was runner-up in the College of Pharmacy’s inaugural 3-minute thesis competition.

Sarah Kim and Irene Vuu received Rare Disease Day research awards for their respective projects, “A Review of Immune Tolerizing Regimens for In Vivo Gene Therapy,” and “Intramuscular versus Intravenous Allopregnanolone Pharmacokinetics and Safety in Dogs for Early Treatment of Status Epilepticus.”

Abhishek Sathe celebrated his engagement to fiancée Ketaki Katdare on December 23, 2018 in Mumbai, India. Ms. Katdare is currently pursuing her Ph.D. in Neuroscience at Vanderbilt University in Nashville, Tennessee.

Abhishek Sathe also received a Junior Investigator Travel Award from the Parkinson Study Group to present his poster, “A Comprehensive Evaluation of Ursodeoxycholic acid Pharmacokinetics, Biological Target Engagement and Mechanism(s) of Action in People with Parkinson’s Disease (PWP’s)” at their Annual Meeting and Symposium in April.

Natalie Schmitz successfully defended her thesis in September and has taken a position as Assistant Professor at the University of Wisconsin - Madison.

Irene Vuu received an American Foundation for Pharmaceutical Education Pre-Doctoral Fellowship.

Jay Wen received an American College of Clinical Pharmacy (ACCP) Cardiology PRN travel award at the ACCP’s 2018 Global Conference.
Diane Blumenfeld has moved on from ECP to a new opportunity in the dental school.

Seenae Eum (post-doc in the lab of Dr. Jeffrey Bishop) won the Best Resident/Fellow Poster Award and the CNS PRN Travel Award for her presentation on “Catechol-O-Methyltransferase (COMT) and Treatment Response to Meditation and Group Therapy in Veterans with PTSD” at the American College of Clinical Pharmacy’s 2018 Global Conference. Dr. Eum went on to complete her post-doc on December 31.

Buddhadev Layek received a travel award from the American Association of Pharmaceutical Scientists.

Kerui Peng (PD4) received a Pharmacokinetics/Pharmacodynamics/Pharmacogenetics (PK/PD/PGx) travel award at the ACCP’s 2018 Global Conference.

Lusi Zhang (PD2 Melendy student, Bishop lab) received an award from the College of Psychiatric and Neurologic Pharmacists Foundation for her research project on patients on long-term antipsychotic treatment.

THANK YOU to all our attendees of the ECP Alumni Reception at the 2018 meeting of the American College of Pharmacometrics (ACoP). We look forward to seeing you again next year (and to getting a better group photo). Cheers!