

Pharmacology & Toxicology Update

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Boonshoft
School of Medicine
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Department of Pharmacology
and Toxicology

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CHAIR'S CORNER



The Department of Pharmacology and Toxicology has started a newsletter to keep our alumni and the Boonshoft School of Medicine and Wright State University apprised of the happenings in the department. This is the second newsletter—the first was in the fall of 2015. The newsletter will be issued three times per year, and can be found online: medicine.wright.edu/pharmacology-and-toxicology

Each issue will also contain a "Spotlight" section that highlights a faculty colleague or a program. To get on the departmental mailing list to receive an electronic version, or to provide suggestions as to content, please contact Catherine Winslow

at catherine.winslow@wright.edu.

FACULTY NEWS

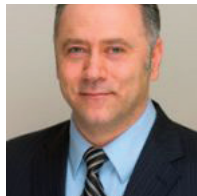
Dr. Yong-jie Xu recruited to department



Yong-jie Xu, Ph.D.

It is with great pleasure that we announce that Yong-jie Xu, M.D., Ph.D., has been recruited as an assistant professor of pharmacology and toxicology. Dr. Xu's laboratory is interested in understanding the molecular mechanism of the replication checkpoint, a complex signaling pathway that is activated when DNA replication is perturbed. Dr. Xu comes to us from the WSU Department of Biochemistry and Molecular Biology. Also of note, the National Institutes of Health has awarded Xu a five-year R01 grant worth \$1.295 million to study the signaling mechanism of the DNA replication checkpoint.

Dr. Simman promoted to full professor



Richard Simman, M.D.

We are pleased to announce that Dr. Richard Simman, M.D., has been promoted to full professor, becoming official July 1, 2016. Congratulations to Dr. Simman!

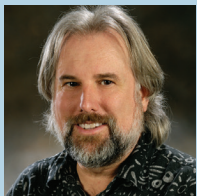
Terry Oroszi represents USA at UN workshop on terrorism

In February, Terry Oroszi, M.S. was invited to attend United Nations Conference on Human Rights of Victims of Terrorism, held at the UN Headquarters in New York. She represents all of us quite well!



FACULTY SPOTLIGHT

Each issue of the departmental newsletter will “spotlight” an individual faculty member or program in the department. For our second newsletter, we are taking the opportunity to spotlight David R. Cool, Ph.D., professor of pharmacology and toxicology.



Dr. Cool was born and raised in Jackson, Ohio, the oldest of three brothers. His father, Story, was an agent for the Detroit, Toledo & Ironton

Railroad and his mother, Trevena, a homemaker and church secretary. Dr. Cool recalls that he was always interested in science. After graduating from Jackson High School, he did a short stint at Ohio University, followed by working as an engineer on the DT&I Railroad out of Springfield, Ohio. After being laid off from the railroad, Dr. Cool took the opportunity to return to college and graduated with a B.S. in biology here at WSU in 1985. His senior undergraduate project involved electron microscopy with Dr. Jim Amon and was a major turning point that propelled him into a career in research. He then received his M.S. in biology here at WSU with Dr.

Barbara Hull in 1988. His master’s thesis work entailed the replacement of heat-damaged mouse skin with a skin equivalent. Dr. Cool then left the Buckeye State to pursue his Ph.D. in biochemistry and molecular biology at the Medical College of Georgia, in Augusta, where he worked on regulation of the plasma membrane serotonin transporter in human placenta. After receiving his doctorate, he completed a postdoctoral fellowship at the NIH from 1991-97 with Dr. Peng Loh in NICHD. He studied the intracellular trafficking of prohormones and the regulation of secretory pathways in neuroblastoma cells and pituitary. Dr. Cool returned to Ohio and was the first recruit of then new pharmacology and toxicology chair Dr. Mariana Morris. Dr. Cool quickly became successful, garnering first a large American Heart Association grant on the trafficking of vasopressin. Large NIH grants followed in succession on diabetes insipidus and then the neurodegenerative and inflammatory effects of the nerve agent sarin. He also is on multiple extramural grants, playing a key role in measuring various agents. Part of the reason for Dr. Cool’s success has been his ability to develop new analytical techniques and his penchant for collaboration. Since

1997, Dr. Cool has directed the departmental Proteomics Core, which contains mass spectrometry and other analytical and imaging systems (see medicine.wright.edu/pharmacology-and-toxicology/proteome-analysis-laboratory for details).

Dr. Cool clearly enjoys the science and that “everything is always changing.” He also finds tremendous satisfaction in teaching the next generation, and working on projects with students. One of his primary inspirations has been his father, who “had a can do anything attitude in life—never giving up and always working.” The son continues these traits but in the context of obtaining new knowledge and training pharmacologists.

When not conducting experiments or classes, Professor Cool enjoys time with his family, wife Martha (who works two floors below in the animal facility) and 21-year-old daughter India. He enjoys music, and is an accomplished musician on both the piano and guitar.

For Professor Cool, our colleague who is the resource in the department for measuring, we are very pleased to highlight you and your efforts!

DEPARTMENT UPDATES

New best-selling book on terrorism from department



It is with great pride we announce that the new book, *Weapons of Mass Psychological Destruction and the People Who Use Them*, coedited by Dr. Larry James and Terry Oroszi, was released. This popular book has been described as, “A must-read for every concerned citizen, this absorbing book goes inside the mind of the psychological terrorist to look at what motivates him to act and to choose the weapon he does.” This book featured contributions from many WSU colleagues.

We are looking forward to the planned two more books from our colleagues!

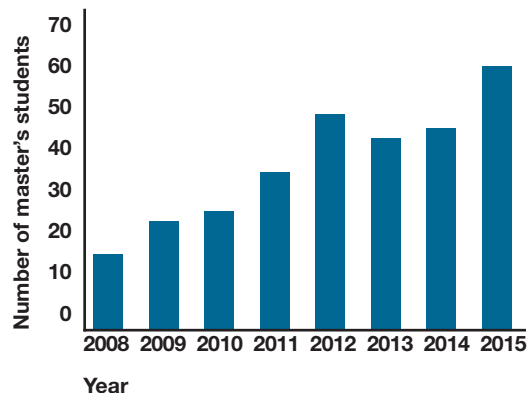
New laboratory space for the department in Biological Sciences II

The department has been allocated approximately 2,000 square feet of laboratory and office space in the Biological Sciences II building. Drs. Travers and Xu’s laboratories will be housed there. Please visit the east wing of the Pharmacology and Toxicology Department.

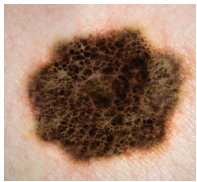
Record numbers of Pharmacology and Toxicology master’s students enrolled

The numbers of master’s students in the department has continued to grow, and in 2015 reached historic numbers. Kudos to the faculty for their expert teaching, and of course to Terry Oroszi for her leadership as well as Catherine Winslow and Wenfeng Zhang for their help.

Pharmacology and Toxicology master’s students enrollment



Pharmacology Translational Unit begins first clinical trial



One of the goals of the department is to foster translational studies to facilitate the process where discoveries at the laboratory bench can be brought to the clinic. The new Pharmacology Translational Unit (PTU) is set up to conduct pharmaceutical clinical trials. We are pleased to announce that we are recruiting subjects for our first clinical trial, the MAVIS melanoma vaccine study. Dr. Jeffrey Travers and noted Wright State University cancer surgeon Dr. James Ouellette are the investigators for this study. With more than 30 sites nationwide, the objective of this double-blinded placebo-controlled Phase III study is to test the efficacy of a melanoma adjuvant vaccine on patients with medium-thickness malignant melanomas, who have no evidence of metastatic disease. Please see clinicaltrials.gov/ct2/show/NCT01546571 for details. For more information, please contact PTU director Faye Hager at 937.245.7500.

Earl H. Morris Symposium features Karolinska Institute Scientist

Internationally known researcher Anita Aperia, M.D., Ph.D., was the keynote speaker at the Boonshoft School of Medicine Department of Pharmacology and Toxicology Earl H. Morris Endowed Lectureship on Thursday, Oct. 22. Dr. Peter Lauf was the host.

Dr. Aperia, professor of pediatrics at the Karolinska Institute in Stockholm, Sweden, is known for her research on the energy efficiency of the body and its individual cells. Her pediatric cell and molecular biology lab is focused on understanding the many aspects of Na/K ATPase, which is known as the ion pump that maintains the electrochemical gradient across the plasma membrane. This enzyme has a central role in all mammalian cells and consumes more than 30 percent of all energy in the body.

Dr. Aperia's research group has made several pioneering contributions to the understanding of the specific function of neuronal Na/K ATPase. She is studying the functional consequences of disease mutations, using a variety of imaging and modeling approaches. The Na/K ATPase signal has been shown to play a major role in the protection against apoptosis, or programmed cell death, in fetal malnourishment, infections with Shiga toxin-producing *E. coli* and chronic kidney disease.

SCHOLARLY ACTIVITY

GRANTS

Congratulations to **Dr. Ji Bihl** who received the Scientist Development Award (American Heart Association). Her grant, "Role of ACE2 over-expressing endothelial progenitor cells in cerebral hemorrhage." is for \$308,000 total, 2016-2019. The major goal of this project is to determine the preventive and therapeutic role of ACE2 over-expressing endothelial progenitor cells (ACE2-EPCs) in hemorrhagic stroke animal model and determine the underlying mechanisms.

Congratulations to **Dr. Yong-jie Xu** who was awarded a five-year \$1.295 million to study "Signaling mechanism of the DNA replication checkpoint." grant from The National Institutes of Health.

PUBLICATIONS

Bihl J, Rapp C, **Chen Y**, Travers **JB** (2016) "UVB generates microvesicle particle release in part due to platelet-activating factor signaling," *Photochem Photobiol.* Feb 15. doi: 10.1111/php.12577.

Wang J, **Chen Y**, Yang Y, Xiao X, Chen S, Zhang C, Jacobs B, Zhao B, **Bihl J**, Chen Y (2016) "Endothelial progenitor cells and neural progenitor cells synergistically protect cerebral endothelial cells from hypoxia/reoxygenation-induced Injury via Activating the PI3K/Akt pathway," *Mol Brain*, 9(1):12.

Bihl J, Zhang C, Zhao Y, Xiao X, Ma X, **Chen Y**, Chen S, Zhao B, Chen Y (2015) "Angiotensin-(1-7) counteracts the effects of ang II on vascular smooth muscle cells, vascular remodeling and hemorrhagic stroke: role of NFkB inflammation pathway," *Vascul Pharmacol*, 73: 115-23.

Chen Y, Xiao Y, Lin Z, Xiao, X, He C, **Bihl J**, Zhao B, Ma X, Chen Y (2015) "The role of circulating platelets microparticles and platelet parameters in acute ischemic stroke patients," *J Stroke Cerebrovasc Dis*, 24 (10): 2313-20.

Xiao X, Ma X, Miao H, Zhang C, Wang J, Liu L, Chen S, Zeng R, **Chen Y**, **Bihl J** (2015) "Angiotensin-(1-7) counteracts angiotensin II-induced dysfunction and apoptosis in cerebral endothelial cells via modulating Nox2/ROS and PI3K/NO pathways," *Experimental Cell Research*, 336: 58-65.

KUDOS

Dr. Courtney Sulentic received the Ohio Valley Society of Toxicology Distinguished Service Award for her dedication in helping to host and organize numerous annual meetings and to connect our K-12 outreach efforts with those of the national Society of Toxicology. Dr. Sulentic was past president of the Ohio Valley Society of Toxicology.

Dr. Courtney Sulentic was elected to the Society of Toxicology Awards Committee.

Dr. Mauricio Di Fulvio's research was showcased as best images in endocrinology and his image is on the cover of *Journal of Endocrinology* January 2016. This is the third time our colleague's work has been so featured. With this success, who needs to be "on the cover of the *Rolling Stone*?"

Dr. Ji Bihl not only was awarded a very prestigious American Heart Association grant, she gave birth to a daughter, Talia. She was born on February 3, 2016, at 5:38 a.m., weighing 5 pounds 13 ounces and measuring 20 inches. Mother and baby are doing well.



Dr. Courtney Sulentic's master's student **Nicole Pastingel** was awarded the Dermal Tox Specialty Section Battelle Student Award for her project entitled "The Effect of Silver Nanoparticles on Human Integument Post Thermal Injury." She will receive a check for \$2,500 and a plaque.





"Regulated phosphorylation of the K-Cl cotransporter KCC3 is a molecular switch of intracellular, potassium content, and cell volume homeostasis." Norma C. Adragna, Nagendra Babu Ravilla, **Peter K. Lauf**, Gulnaz Begum, Arjun Khanna, Dandan Sun, and Kristopher T. Kahle. *Frontiers in Cellular Neurosciences*, 9: doi 10.3389/fncel.00255- June 2015

"K⁺-Cl⁻ cotransporters, cell volume homeostasis and neurological disease." Kristopher T. Kahle^{1,2#}, Arjun R. Khanna, Seth L. Alper, Norma C. Adragna, **Peter K. Lauf**, Dandan Sun, and Eric Delpire. *Frontiers in Cellular Neurosciences*, 2015, TRMOME

Y. J. Xu (2016) "Inner nuclear membrane protein Lem2 facilitates Rad3-mediated checkpoint signaling under replication stress induced by nucleotide depletion in fission yeast." *Cell Signal*. 28:235-245 PMID: 26746798"

"The AhR and NF- κ B/Rel proteins mediate the inhibitory effect of 2,3,7,8-tetrachlorodibenzo-p-dioxin on the 3' immunoglobulin heavy chain regulatory region" Richard L. Salisbury and **Courtney E. W. Sulentic**

"Functional and molecular evidence for expression of the renin angiotensin system and ADAM17-mediated ACE2 shedding in COS7 cells." **Grobe N**, Di Fulvio M, Kashkari N, Chodavarapu H, Somineni HK, Singh R, Elased KM. *Am J Physiol Cell Physiol*. 2015 May 1;308(9):C767-77. doi: 10.1152/ajp-cell.00247.2014. PMID: 25740155

"Loss of prollyl carboxypeptidase in two-kidney, one-clip goldblatt hypertensive mice." **Grobe N**, Leiva O, Morris M, Elased KM. *PLoS One*. 2015 Feb 23;10(2):e0117899. doi: 10.1371/journal.pone.0117899. PMID: 25706121.

PRESENTATIONS

Drs. Peter Lauf and Norma Adragna were invited speakers at the Puerto Rico Physiological Society 6th Annual Meeting at the University of Puerto Rico Medical Sciences Campus San Juan, PR, on February 12, 2016. Dr. Lauf's presentation was "Role of Bcl-2 Proteins and the Na/K Pump ATPase in the Cell's Fate." Dr. Adragna's presentation was "Oxidative Stress Modulation of K-Cl Co-transporters."

POSTERS & ORAL PRESENTATIONS

Elased KM & Grobe N. MALDI-TOF mass spectrometric analysis of enzyme activity of the renin angiotensin system facilitates the discovery of new biomarkers for chronic kidney disease (CKD). Dubai International Pharmaceuticals & Technologies Conference, Dubai, UAE, March 8-10, 2015. Sponsor(s): Council High Blood Pressure Res, Council Kidney Cardiovascular Disease and Inter-American Society of Hypertension. *Hypertension* 62: 208P, 2015.

Alawi L, Emberesh S, **Elased KM**. Effect of rosiglitazone on renal neprilysin activity and protein expression in db/db diabetic mice. Scientific Sessions of High Blood Pressure Research, Washington, D.C., September 16-20, 2015. Sponsor(s): Dubai Health Authority and several international pharmaceutical societies (ASHP, EUFEBIS, SHPA, ISPE, ESOP, SPS, IATDMCT, CPhA).

Dr. Elased attended and voted in the United States Pharmacopeial (USP) Convention delegate meeting for development of the 2015 resolutions. The Council of the Convention put out its official Call for Resolutions. At that time, it also provided details on the process for submitting a resolution proposal, the review process, and the timeline for delivery of resolutions to the convention, Washington, D.C., April 25, 2015.

Dr. Xu's first Ph.D. student Amanpreet Singh has successfully defended his thesis and is doing his postdoc work at the University of Albany, New York.

Dr. Simman's student, Walid Mari, M.D., received the Symposium on Advanced Wound Care Certificate of Achievement for his work, Correlation between wound healing rate and circulating microvesicles collected from stage III and IV pressure wounds fluid treated with NPWT alone vs. NPWT and oasis ultra.

Dr. Elased's service on grant review committees and study sessions: NIH/NIDDK: Special Emphasis Panel/Scientific Review Group, Biomarkers for Diabetes, Kidney Diseases and Urology (R01)-PAR -13-228. American Heart Association (AHA): Peer reviewer of the National AHA Cardiac Biology Study Section grants applications for Spring 2015. Feb. 2, 2015. American Heart Association (AHA): Reviewer of the abstracts for the Annual AHA Council on Hypertension Meeting in Washington, D.C., September 16-19, 2015.

Dr. Chen reviewed grants for the NASA Hero Head-down bed rest panel.

Mari, M. MD, Younes, S., **Simman, R., Oroszi, T., Alsabri, Chen, Y., Cool, D.R.**, (2016). Correlation between wound healing rate and circulating microvesicles collected from stage III and IV pressure wounds fluid treated with NPWT alone vs. NPWT and oasis ultra. Society of Thoracic Surgeons, STS 52nd Annual Meeting.

Scott, R. P., Gallimore, J., Burke, B., Benton, N., Carabello, H., Davidson, M., Ingmundson, P., McCoy, S., Graham, C., **Oroszi, T., Dominguez, M.**, (2015). The VA Virtual Medical Center: Implementing a vision for a virtual health care campus for our veterans, in Interservice/Industry Training, Simulation, and Education Conference (ITSEC).

Mari, M. MD, Younes, S., Alsabri, S.G., Shaban, A., **Simman, R., Chen, Y., Cool, D.R., Oroszi, T.**, (2015). Correlation between wound healing rate and circulating microvesicles collected from stage III and IV pressure wounds fluid treated with NPWT alone vs. NPWT and oasis ultra. The Amputation Prevention Symposium, Chicago, IL.

Oroszi, T. (2015). Traditional faculty meeting style is not conducive to group decision making. Midwest Academy of Management Conference. (Manuscript)

Oroszi, T. (2015). Egos at the table, a study of meeting behaviors. Midwest Academy of Management Conference. (Manuscript)