

# Pharmacology & Toxicology

VOL 6, ISSUE 1

WINTER 2019



Boonshoft  
School of Medicine  
WRIGHT STATE UNIVERSITY

Department of Pharmacology  
and Toxicology

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## CHAIR'S CORNER



The Department of Pharmacology and Toxicology newsletter is designed to keep our alumni, and the Boonshoft School of Medicine, and Wright State University apprised of the happenings in the department.

The newsletter can be found on the departmental website: <http://medicine.wright.edu/pharmacology-and-toxicology>

Each issue contains a "Spotlight" section that highlights a faculty member, colleague, or program. In this issue, we will be highlighting Dr. Francisco Javier Alvarez-Leefmans, professor in the department. To join the departmental mailing list to receive an electronic version, or to provide suggestions for content, please contact Ms. Catherine Winslow, assistant to the chair, at [catherine.winslow@wright.edu](mailto:catherine.winslow@wright.edu).

## DEPARTMENT UPDATES

### Drs. Oroszi and Ellis Publish New Terrorism Book



Assistant Professor and Director of the Pharmacology & Toxicology Masters and CBRN Programs Terry L. Oroszi, Ed.D., and Adjunct Faculty David H. Ellis, Ph.D., have published an exciting new book, *The American Terrorist: Everything You Need to Know to be a Subject Matter Expert* (2019; Greylander Press, LLC). Dr. Oroszi has been lecturing in this important area at multiple venues both locally and in Washington, D.C. Please be sure to attend a lecture and book signing on April 25, from 6-8 p.m., at the

Dayton Club, 40 N. Main St., Dayton, Ohio 45423.

***Congratulations to these two, who are truly subject matter experts!***

### Dr. Michael Kemp Garners First NIH Grant



We are pleased to announce that Dr. Michael Kemp, research assistant professor, has been awarded his first five-year R01 grant (2/1/2019 to 1/31/2024) from the National Institutes of Health. The title of his grant is: "DNA damage response kinase signaling in non-replicating human cells and tissues." These exciting studies build upon his expertise in DNA damage and his very clinically relevant ideas that could protect non-cancerous tissues from agents such as chemotherapy.

***We suspect more grants will be coming from this gifted colleague!***

## DEPARTMENT UPDATES

### Dr. Alvarez-Leefmans is awarded Wright State Medical Student Educator Award

Dr. Alvarez-Leefmans has been awarded the inaugural Wright State Medical Student Educator Award for 2019. He was given the honor for his many contributions to medical student education. For more details regarding Professor Alvarez-Leefmans, please see the Spotlight Section of this newsletter.

### Professor Alvarez-Leefmans will be a tough act to follow for future awardees!

### Dr. Ulas Sunar awarded first small pilot grant under new departmental program



The department has a novel small pilot grant program designed to promote basic science-translational studies involving the Pharmacology Translational Unit (PTU). These grants cover

\$10,000-\$20,000 direct costs for one year. The funds are designed to encourage clinicians and scientists at Wright State University to use the PTU. The goal is to fund projects that will take advantage of the

clinical expertise of the PTU and the research interests of the WSU investigator. The human studies could involve obtaining blood and urine samples, or taking skin biopsies, etc., from normal subjects or those with various disease states. Interventional studies may also be proposed. We are pleased to announce that Ulas Sunar, Ph.D., associate professor of engineering at Wright State University, was awarded the first pilot grant to test a novel spectral device on human skin. Congratulations to Dr. Sunar.

If you have a potential project and are interested in applying for a pilot grant, please send a one-page letter outlining a translational research idea to Dr. Jeffrey Travers ([jeffrey.travers@wright.edu](mailto:jeffrey.travers@wright.edu)) and a meeting will be scheduled to discuss the proposal. We expect to fund one to two proposals per year. Contact Dr. Travers with questions.

### New personnel and new studies begin in the Pharmacology Translational Unit

One of the goals of the department is to foster translational studies to facilitate the process through which discoveries at the laboratory bench can be brought to the

clinic. Moreover, the Pharmacology Translational Unit (PTU) located in the Wright State Physicians Health Center next to our campus is set up to conduct both translational research studies as well as pharmaceutical clinical trials. We are pleased to announce that Hannah Hayes, RN, has been recruited to the PTU. The unit also has several new studies that opened in the winter. Three are psoriasis studies testing a device with an IL-23 inhibitor and a Phosphodiesterase-4 inhibitor in both adults and children. There also is one new study in adult atopic dermatitis testing a histamine receptor inhibitor. New studies involving prurigo nodularis and hidradenitis suppurativa will be starting soon. If you have questions or desire more details, please contact PTU Director Elizabeth Cates at 937.245.7500.

## KUDOS



**Dr. Yanfang Chen**, who is serving on the Research Grant Committee for the American Diabetes Association.

### How sweet of Professor Chen!

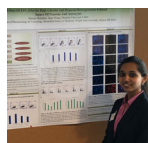


**Dr. Jeffrey B. Travers**, whose VA Merit Grant, "Validation of Mesoscopic Imaging to Predict Cutaneous Carcinogenesis and its Therapeutic Response," received a 0.7% score!

### Sounds like a project that will be funded!

**Drs. Peter Lauf and Norma Adragna**, who just published a research article entitled, "Kinetic studies of K-Cl transport in cultured rat vascular smooth muscle cells," in the American Journal of Cell Physiology (316: C1; 2019).

### Congrats on your sustained scholarship!



**Manasi Halurkar**, Master's student of Dr. Ji Bihl, was awarded a first place prize for her poster. Mili Bhakavia, Immunology Master's student of Dr. Courtney Sulentic, was awarded second place for her poster at the OVSOT meeting in November 2018.

### Top students from our top faculty!

**Dr. Courtney Sulentic**, who was elected vice president of the Women in Toxicology Special Interest Group for the Society of Toxicology.

### What a special honor!



**Dr. Jinju Wang**, postdoctoral fellow with **Dr. Bihl** and former Ph.D. student of **Dr. Chen**, who gave a superb departmental seminar on her work with exosomes and exercise.



**PTU staff and Dr. David Morris celebrate Dr. Travers receiving a bright red Swingline stapler for his birthday!**

Each issue of the departmental newsletter spotlights an individual faculty member or program in the department. For this issue, we are taking the opportunity to spotlight Francisco Javier Alvarez-Leefmans, M.D., Ph.D., professor of pharmacology and toxicology.



Dr. Alvarez-Leefmans was born in Caracas, Venezuela, the sixth of seven children of Francisco Javier and Elizabeth Alvarez-Leefmans. His father (and namesake) was originally from Mexico, of Spanish descent, and completed his graduate education in Philadelphia. His father obtained a law degree from Temple University and two bachelor's degrees from Saint Joseph's College, one in chemistry and the other in philosophy and English literature. Francisco Javier senior began working at Wyeth Pharmaceuticals in Philadelphia and went to Venezuela to develop a branch of the company in Caracas.

"Two crucial things happened to my father during that time: he became president of Wyeth Pharmaceuticals in Venezuela, where he built the company from scratch, and he married Elizabeth, my mother, also born in Venezuela, of Dutch ancestry," Dr. Alvarez-Leefmans said. "My mother was not only a homemaker but also a highly intelligent and successful entrepreneur. I feel very fortunate I had parents like them."

"Reflecting back on my early childhood, I think my passion for science began while listening to my father teach chemistry to my older brothers. He was a natural teacher, explaining difficult concepts in simple ways. As for my love of music, I probably developed it while in my mother's womb. Music was and is for me, a constant miracle," Dr. Alvarez-Leefmans said. "I believe I was 7 or 8 years old when my parents gave me a microscope kit with a set of slides as a Christmas present. I became fascinated with the microcosm, examining diatoms, volvox, pollen, spores and other tiny creatures. Ever since, microscopes and microscopy have been a central part of my life."

A couple years later, Dr. Alvarez-Leefmans recounts, his father gave him a Gilbert chemistry set and showed him how to change water into wine. The transformation occurred while his father pronounced some magic words. Then, magic became science when his father explained that phenolphthalein was the substance that changed color depending on the pH of the solution. "I think this is the root of my fascination with fluorescent indicator dyes used to measure intracellular ions in living cells," Dr. Alvarez-Leefmans said.

At age 10, Dr. Alvarez-Leefmans moved to Mexico City, where his father retired. Three years later, his father died. A close friend of his father, Dr. Humberto Fernandez-Morán became one of his significant mentors. Fernandez-Morán was an outstanding Venezuelan scientist who invented the diamond scalpel, used to this day for ultra-thin sectioning of electron microscopy samples. Due to political reasons, he was forced to leave Venezuela in 1958, and became the A.N. Pritzker Professor of Biophysics at University of Chicago. While in Chicago, he conducted electron microscopy and electron diffraction studies of rock samples of the Moon collected by the Apollo 11 astronauts.

Dr. Alvarez-Leefmans describes that he maintained constant correspondence with Fernandez-Morán during this time (1970), which was crucial in defining the path he would take in his academic development. "I will be eternally grateful to Dr. Fernandez-Morán for the time and devotion he spent in replying to every single letter I sent as a young medical student trying to find a path to follow as a research scientist," Dr. Alvarez-Leefmans said.

After obtaining his medical degree, *summa cum laude*, from the Faculty of Medicine at the National University of Mexico in 1973, Dr. Alvarez-Leefmans received a competitive scholarship from the British Council to pursue postgraduate studies at University College London, where he received his Ph.D. in Physiology in 1977. Dr. Alvarez-Leefmans describes an amazing academic environment, with teachers of the stature of Professors Andrew Huxley (Nobel Laureate, 1963), J.Z. Young, P. Fatt, S. Zeki, P.D. Wall and John O'Keefe (Nobel Laureate, 2014). He continued as a postdoctoral fellow for another three years at University College London, working at the Biophysics Department with professors Ricardo Miledi and the Nobel Laureate Sir Bernard Katz. "I have always been impressed by the creativity, scientific rigor, generosity and humility of Professors Katz and Miledi," he said.

Alvarez-Leefmans did a second postdoc-

toral fellowship at Cambridge University (1979-1980) with Drs. Timothy Rink and Roger Y. Tsien, pioneering the development of calcium (Ca<sup>2+</sup>) sensitive microelectrodes for measuring intracellular Ca<sup>2+</sup> in single cells. At that time, Tsien was also developing fluorescent dyes for measuring intracellular Ca<sup>2+</sup> and other intracellular ions.

"Roger was fun and genius. I consider him a Mozart of cell biology. He turned fantasies into realities. He played and got excited with science with the freshness of a kid," Dr. Alvarez-Leefmans said. Years later, in 2008, he was awarded the Nobel Prize in Chemistry for his development of green fluorescent protein. In 1981, Dr. Alvarez-Leefmans secured a faculty position at the Center of Research and Advanced Studies at the National Polytechnic Institute in Mexico City, where he quickly became a full professor. There he pioneered the development of ion-sensitive microelectrodes to measure intracellular Mg<sup>2+</sup>, to study its regulation in excitable cells. Then, between 1984 and 1985, using chloride (Cl<sup>-</sup>) selective microelectrodes, he discovered the sodium-potassium-chloride cotransporter in the vertebrate nervous system (NKCC1), specifically in sensory neurons.

In these neurons, NKCC1 generates an outward Cl<sup>-</sup> gradient pivotal in the gating and processing of nociceptive and other sensory information entering the spinal cord. Dr. Alvarez-Leefmans first reported these findings in 1986, at the 30th meeting of the Biophysical Society in San Francisco. In the same year, sponsored by the Mellon Foundation, Dr. Alvarez-Leefmans did a sabbatical at University of California at Berkeley, working again with Roger Y. Tsien, this time probing caged Ca<sup>2+</sup> compounds. In 1987, as a member of the International Program Committee for the IBRO Second World Congress of Neuroscience in Budapest, Hungary, Dr. Alvarez-Leefmans organized a workshop on Cl<sup>-</sup> regulation in neurons. This became the seed of the first of four books, *Chloride Channels and Carriers in Nerve, Muscle and Glial Cells*, published in 1990.

In 1991, Dr. Alvarez-Leefmans joined the Department of Physiology and Biophysics at the University of Texas Medical Branch at Galveston as adjunct professor, a position he held until 1998. During those years, he developed a method for measuring water volume changes in single cells using live-cell imaging fluorescent microscopy of cells loaded with the dye calcein. In Galveston, he was awarded numerous National Institutes of Health grants to fund his research for nearly two decades.

In 1997, Dr. Alvarez-Leefmans received

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a prestigious Guggenheim Fellowship to continue his research on Cl<sup>-</sup> transport proteins and cell volume control in neurons. In 1998, Dr. Peter Lauf recruited him as adjunct professor to Wright State University in the Department of Physiology and Biophysics. In 2003, he joined the Department of Pharmacology and Toxicology, continuing his highly impactful studies on water and ion transport in sensory neurons and epithelial cells. His latest research focuses on NKCC1 function in choroid plexus epithelium, where he and his team have provided important insights into the role of this transport protein in cerebrospinal fluid ion regulation and secretion. Given the clinical impact of his research for treatment of idiopathic intracranial hypertension and hydrocephalus, Dr. Alvarez-Leefmans was awarded a recent grant from the Dayton Children's Hospital Foundation. Part of this

groundbreaking research was recently published in the American Journal of Physiology-Cell Physiology.

In addition to his research, Dr. Alvarez-Leefmans enjoys teaching and being around students. He finds it highly satisfying when the students around him flourish. Dr. Alvarez-Leefmans takes considerable time and effort in his teaching and mentoring, encouraging students to develop critical thinking skills. Because of this, he is being honored with the Wright State Medical Student Educator Award for 2019.

When not pondering the mysteries of ion and water transport, Dr. Alvarez-Leefmans enjoys spending time with family and friends, listening to music, and reading. He enjoys traveling the world, exploring medical and art history, and current geopolitical affairs.

For Dr. Alvarez-Leefmans, our very accomplished colleague, we are very pleased to highlight you and your efforts!