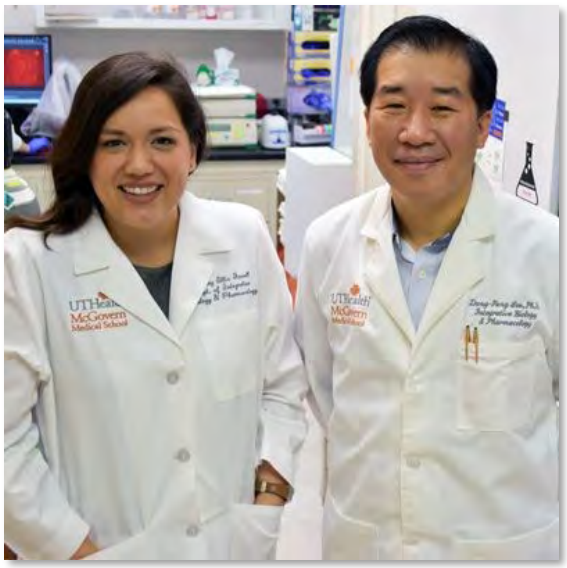
Integrative Biology & Pharmacology Newsletter

UT System's new student regent is working to reduce childhood cancer deaths

Rob Cahill, Office of Public Affairs



The war against cancer is personal for the Houston graduate student appointed to The University of Texas System Board of Regents by Texas Gov. Greg Abbott.

Brittany Jewell, whose one-year term as a member of the UT System Board of Regents runs through May 31, 2019, is conducting cancer research at The University of Texas MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences.

"Everyone knows someone who has been affected by cancer," said Jewell of Houston. "Since beginning my graduate studies, I have been able to focus my long-standing interest in oncology to make a difference for children affected by this debilitating disease."

Bone cancer or osteosarcoma is the third leading cause of cancer-related deaths in children in the United States.

Working in the laboratory of Dung-Fang Lee, Ph.D., at McGovern Medical School at UTHealth, Jewell is researching a rare genetic disorder that predisposes children to bone cancer. It is called Rothmund-Thomson Syndrome.

"Brittany has the qualities of a good researcher," said Lee, a bone cancer researcher and an assistant professor of integrative biology and pharmacology at McGovern Medical School. "She is very determined."

In particular, Jewell is using reprogrammed stem cells to develop a bone cancer model that she will use to study bone cancer formation. Formally called induced pluripotent stem cells, the cells are derived from human skin cells. Ultimately, researchers could use findings from these studies to test promising treatments for osteosarcoma.

A graduate of Baylor University and Clear Lake High School, Jewell is also exploring the role of a genetic alteration in a gene, called RECQL4, that contributes to Rothmund-Thomson Syndrome.

Jewell plans to graduate in May of 2020 with a doctoral degree in biochemistry and cell biology from the MD Anderson UTHealth Graduate School. "Students such as Brittany contribute a lot to medical research. They have new ideas and a fresh perspective," Lee said.

In 2005, the 79th Texas Legislature authorized the Texas governor to appoint one student regent to the Board of Regents for the UT System. Students must be in good standing and be recommended by their respective institution's president.

"It's important for students to have a voice on the UT System Board of Regents. My focus this year is on student wellness, with a particular interest in mental health," Jewell said. "I plan to use this year as regent to learn the wellness needs of students across the UT System and work with other student leaders to achieve greater accessibility and awareness of available resources."

Charged with representing the 200,000 plus students at the UT System's 14 institutions, Jewell plans to visit with as many students as possible during her term.

"Brittany is a very personable student and will do a good job as a student regent," said Lee, who is a member of the faculty of the MD Anderson UTHealth Graduate School and a 2008 graduate. The school has trained more than 2,600 biomedical scientists.

"I am thankful for the opportunity to serve on the UT System Board of Regents, and moreover for the opportunity to continue my research toward a meaningful discovery for those children with cancer," Jewell said.

IN THIS ISSUE

Faculty Spotlight

Soy lecithin NSAID combo drug protects against cancer with fewer side effects, UTHealth reports

Rob Cahill, Office of Public Affairs

HOUSTON – (May 25, 2018) – When scientists at The University of Texas Health Science Center at Houston (UTHealth) applied a chemical found in soybeans to a non-steroidal anti-inflammatory drug (NSAID), they increased its anticancer properties and reduced its side effects. Findings of the preclinical study of phosphatidylcholine, also called lecithin, appear in the journal Oncology Letters.

"The results support the potential use of NSAIDs associated with phosphatidylcholine for the prevention and treatment of colorectal cancer," said Lenard Lichtenberger, Ph.D., the study's lead investigator and a professor of integrative biology and pharmacology at McGovern Medical School at UTHealth.

The NSAID indomethacin associated with phosphatidylcholine was studied in a head-to-head comparison with three other NSAIDs (one of them aspirin). According to the results, the combination provided superior colorectal cancer protection with less gastrointestinal bleeding. The study was conducted in a mouse model and in laboratory experiments.

Colorectal cancer is the third leading cause of cancer-related death in the United States and is expected to claim 50,630 lives this year.

NSAIDs work by decreasing the production of substances that promote inflammation, pain and fever. They are used to prevent heart disease and reduce arthritis pain. NSAIDs, notably aspirin, also guard against colorectal cancer.

"Many cancers are inflammation based," he said. "The anti-inflammatory drugs also have the potential use for cancer therapy."

However, when taken on a daily basis for months to years, NSAIDs can cause problems, Lichtenberger said. "The intestinal injury is worse than the stomach ulcers, for non-aspirin NSAIDs like indomethacin," he said.

"This is our latest preclinical study on the use of phosphatidylcholine to mitigate the side effects of using NSAIDs and protect against a number of cancers," he said.

Lichtenberger's coauthors from UTHealth included Tri Phan, Dexing Fang, Ph.D., and Elizabeth Dial, Ph.D.

The study, titled "Chemoprevention with phosphatidylcholine non-steroidal anti-inflammatory drugs in vivo and in vitro," was supported by National Institutes of Health grants (R03 CA171613 and R41CA171408).

Lichtenberger is on the faculty of McGovern Medical School and The University of Texas MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences.

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Department News

UTHealth opens Texas' first Nikon Center of Excellence to offer researchers advanced imaging technology

Kendrick D. Callis, Office of Public Affairs

The Center for Advanced Microscopy, one of the UTHealth Research Service Centers, held an open house April 25 to unveil its new Nikon Center of Excellence (COE). The new center features two new super-resolution Nikon microscopes and upgraded confocal microscopes that will provide researchers from UTHealth and other Texas Medical Center institutions access to the latest optical systems to advance their research and exposure in the field. This is the first Nikon Center of Excellence established in the state of Texas.

"We've seen a steady increase in National Institutes of Health (NIH) funded research by our faculty," said Michael Blackburn, Ph.D., executive vice president and chief academic officer at UTHealth. "Access to these high-end research microscopes will allow UTHealth researchers to be more competitive for NIH and other external grants as well as improve the quality of our data, science and publications, which is the currency of the research industry. This new center is a logical investment in our faculty and students."

The new microscopes are:

Nikon A1Rsi HD confocal + n-STORM super-resolution microscope, which combines ultra-high speeds, enhanced sensitivity and the ability for localization fluorescent imaging with a spatial resolution of 20nm, and

Nikon n-SIM Structured Illumination super-resolution microscope, which gives a two-fold enhancement in resolution while maintaining the ability to image dynamic events in live samples in 2D, 3D and TIRF modes.

"Light microscopy is fundamental to biological and biomedical research," said Kandice R. Levental, Ph.D., director of Center for Advanced Microscopy. "Super-resolution microscopy approaches enhance the spatial resolution of light microscopy by an order of magnitude, providing insights that were unattainable with any available techniques until now. Having access to these systems in-house will allow UTHealth researchers to 'see' things that have never been seen before and answer questions that previously could not be addressed."

A Nikon Center of Excellence is a partnership and exchange of knowledge with selected research centers around the world that invest in Nikon advanced imaging instruments to provide young researchers access to the latest optical systems. In addition to providing access to state-of-the-art Nikon microscopy and imaging equipment, the center will offer training courses on basic and advanced light microscopy techniques and introduce the latest innovations in light microscopy and imaging.

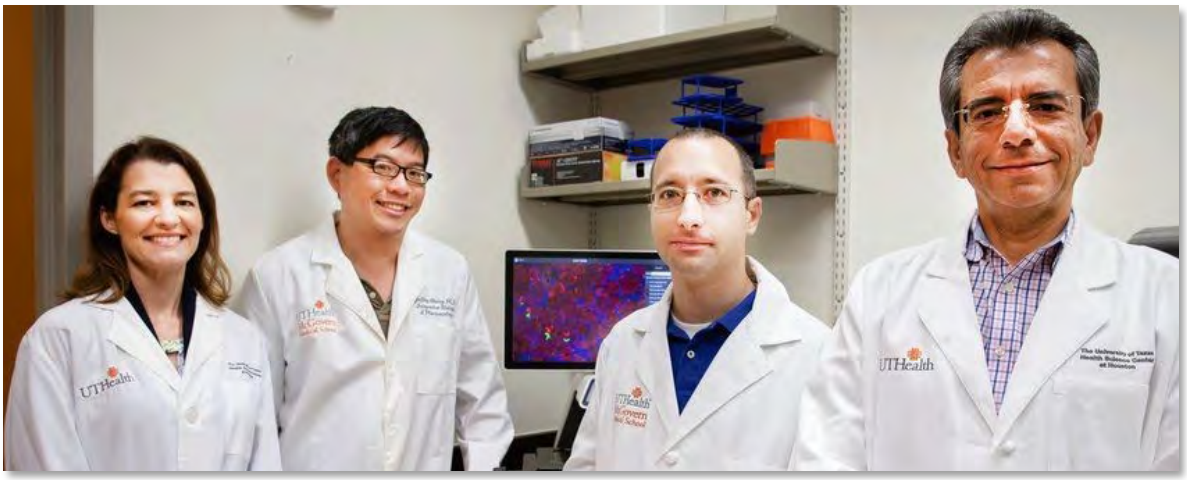
The center is a fee-based facility that provides equipment that academic and commercial entities in the Texas Medical Center can pay by the hour to use.

For more information about the Nikon Center of Excellence, contact Kandice Levental, Ph.D., at Kandice.R.Levental@uth.tmc.edu or 713-500-5566.

Department News

Berdeaux awarded $1.9 million by NIH to research muscle regeneration

Rob Cahill, Office of Public Affairs



As people age, their muscle regeneration capacity declines because they can no longer generate enough muscle stem cells to replace damaged tissue. To offset that, a scientist UTHealth is working to enhance the body's ability to repair damaged skeletal muscle.

The research is supported with a $1.9 million grant from the National Institute of Arthritis and Musculoskeletal and Skin Diseases of the National Institutes of Health (NIH).

Increasing the number of stem cells could enhance growth of new muscle, believes the study's principal investigator, Rebecca Berdeaux, PhD, associate professor in the Department of Integrative Biology and Pharmacology with McGovern Medical School at UTHealth.

"Muscle stem cells are normally dormant until an injury occurs. We're researching the molecular mechanisms that boost the cells' ability to multiply," Berdeaux said.

One of three types of muscle, skeletal muscles control your every movement and utilize much of the energy from your diet. Sports, aging, and genetics can contribute to skeletal muscle injury. During aging, loss of muscle reduces quality of life.

Berdeaux's team is using a mouse model of muscle injury to outline the chain of events that occur when muscle stem cells are activated as the tissue heals. Her research centers around a switch, programmed to be on and off, that triggers muscle stem cell multiplication during the muscle regeneration process (cAMP-responsive transcription factor CREB).

"It is known that the CREB transcription factor plays a critical role in muscle stem cell proliferation during the regeneration process. However, less is known about how CREB and its partner proteins control the accurate timing of muscle stem cell division after an injury," Berdeaux said. "We want to learn more about the molecular pathways that drive muscle stem cell division, and ultimately muscle regeneration."

The researchers believe that identification of the signaling pathways and genes that stimulate muscle stem cell proliferation could reveal new ways to help maintain muscle health and function during aging.

"We are fortunate to have a fantastic team of scientists from UTHealth collaborating on this project," Berdeaux said.

Collaborators include Radbod Darabi, MD, PhD, assistant professor with the Center for Stem Cell and Regenerative Medicine at the Brown Foundation Institute of Molecular Medicine for the Prevention of Human Diseases at UTHealth, Jeffrey T. Chang, PhD, associate professor in the Department of Integrative Biology and Pharmacology and Cancer Prevention and Research Institute of Texas Scholar, and Dmitry Akhmedov, PhD, a research scientist in the Department of Integrative Biology and Pharmacology.

Darabi specializes in the isolation and analysis of muscle stem cells while Chang is a leader in genomics and transcription factor function.

The five-year study is titled "Promotion of satellite cell proliferation by cAMP signaling."

Berdeaux, Chang, and Darabi are on the faculty of MD Anderson Cancer Center UTHealth Graduate School of Biomedical Sciences.

The NIH award number is R01AR072368.

Department News

Levental part of research group awarded $1 million HFSP grant

Tracey Barnett, Office of Public Affairs

MD Anderson UTHealth Graduate School faculty member Ilya Levental, PhD, and researchers from Ohio, Finland, and Germany, were awarded a three-year grant worth over $1 million from the Human Frontier Science Program to research the regulation of membrane receptor function in the brain by lipid composition and dietary inputs.

Levental is an associate professor in the Department of Integrative Biology and Pharmacology at McGovern Medical School at UTHealth. He joined the graduate school faculty in 2012, and is affiliated with the Program in Biochemistry and Cell Biology.

The joint project involves research from Levental, Ilpo Vattulainen, PhD, from the University of Helsinki; Mikael Simons, MD, from the German Center for Neurodegenerative Diseases in Munich; and Adam W. Smith, PhD, from the University of Akron in Ohio. Together, these researchers are investigating how membrane receptors in the brain are regulated by their surrounding lipid composition, and how these lipid compositions are in turn influenced by diet. The multidisciplinary team includes experts in biophysics and biochemistry, lipidomics, and neuroscience, as well as scientific computing, taking a comprehensive approach to solve the long-standing riddle of how dietary factors affect neuronal signal transduction.

From epidemiological studies, it is clear that dietary factors contribute to nearly all health and wellness outcomes. However, the mechanisms underlying many of these effects are still poorly understood. It is also clear that neural cells have unique membrane lipid compositions that are functionally important, evidenced by wholesale brain lipid alterations in many neurological disorders.

Levental and his team will explore the mechanistic links between brain lipid compositions, their diet-induced alterations, and neurological disorders. These links have been previously unexplored because no single lab can couple lipidomic analyses of living tissue with biophysical, molecular, cellular, and organismal analysis of the phenotypes resulting from membrane disturbances. This synergy will be enabled by the Human Frontier Science Program grant to test the paradigm-changing idea that lipid composition affects receptor function in the brain, and that modulation of that composition by dietary inputs can have robust pathological or beneficial effects.

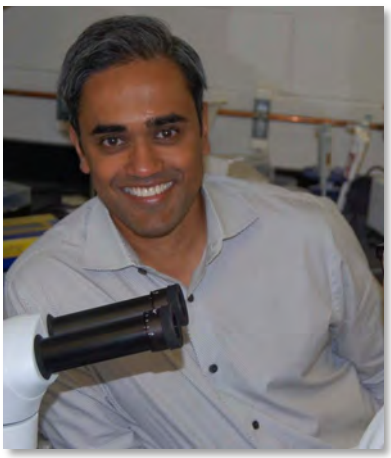
"Our lab has recently realized that the membranes that enclose our cells are remarkably susceptible to dietary lipid inputs," Levental said. "Diet-induced changes to membranes can guide stem cells to differentiate or cancer cells to die. But we do not yet understand how these processes work. This grant will allow us to take a major step in this project by linking dietary fats, cell membranes, and neuronal function from the molecular to the organismal level."

Ashabari Mukherjee Receives Award

Ashabari Mukherjee recently received a Ruth L. Kirschstein Predoctoral Individual National Research Service Award (F31), which will fully fund her thesis project for the next three years. She is currently a third year Ph.D. student in the lab of Dr. Jeff Frost lab, where she focuses on understanding mechanisms underlying breast cancer metastasis. Ms. Mukherjee's project is specifically focused on understanding how Src and JNK, two non-receptor tyrosine kinases, regulate localization and activity of the RhoA GEF Net1A to promote breast cancer cell motility and metastasis.

Department News

Dr. Venkatachalam receives new grant!



Dr. Venkatachalam was recently awarded an NIH R21 titled, "Modulation of mitochondrial proliferation and function in Drosophila neurons. The overarching goal of the grant is to further the understanding of evolutionarily conserved mechanisms that modulate mitochondrial proliferation and energy metabolism. Although significant progress has been made in understanding the consequences of mitochondrial dysfunction and characterizing emergent disease, it remains unclear whether manipulation of overall mitochondrial proliferation to alter mitochondrial number and/or mass would impact on disease phenotypes. This conceptual gap exists largely due to the genetic redundancy, relative intractability, and functional complexity associated with regulation of mitochondrial proliferation and function in mammals. To mitigate these limitations, mitochondria are often studied in Drosophila, which are genetically tractable organisms characterized by extensive conservation with mammals in terms of mitochondrial biology. However, transcriptional networks that regulate mitochondrial proliferation and function are unknown in Drosophila. A master transcriptional regulator of mitochondrial proliferation in Drosophila has been identified that is both necessary and sufficient to determine mitochondrial mass. This creates a position to finally delineate the relationship between mitochondrial proliferation and function. In this grant, Dr. Venkatachalam and his lab will test the hypothesis that the transcription factor we have identified modulates mitochondrial function in addition to mitochondrial mass. Successful completion of this aim could present unprecedented opportunities for en masse modulation of mitochondrial function in Drosophila models of human diseases. The lab will also examine the interrelationship between AMPK, a known regulator of mitochondrial biogenesis and metabolism, with the identified regulatory network. These studies could reveal previously unrecognized, fundamental mechanisms by which AMPK regulates mitochondrial function. Finally, the lab will test whether the signaling network and the human homologs of the identified transcription factor regulate mitochondrial biogenesis and/or function in the human cell. Taken together, their experimental strategies are designed to reveal novel conceptual insights into the regulation of mitochondrial proliferation and function. The multidisciplinary and systems-based approach will enable a deeper understanding of the pathophysiology of mitochondrial diseases. Dr. Venkatachalam hopes that upon completion of these studies, his lab and other biomedical researchers can leverage the insights gleaned to inform innovative avenues for therapeutic intervention for treating human diseases involving mitochondrial dysfunction.

Dr. Rosenfeld receives award!

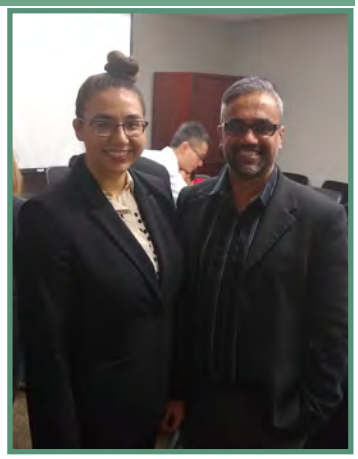
Dr. Rosenfeld received the Pat Finnerty Lifetime Achievement Award. This award is bestowed upon an individual member who has demonstrated a sustained involvement in and commitment to the advancement of the International Association of Medical Science Educators (IAMSE) through their many types of service to the organization at the highest levels of performance. The special nature of this award makes it one for which a member may not apply, but rather, it represents the highest level of recognition that the organization, through selection by its Board of Directors, can provide to a most worthy individual whose work on behalf of IAMSE has shown a consistent history of distinguished accomplishments.

Dr. Rosenfeld was presented his award on June 8th at the opening ceremony of the 23rd Annual IAMSE Meeting, Roanoke, VA.

Department News

IBP Retreat—South Shore Harbour 2019

Student Awards & Activities



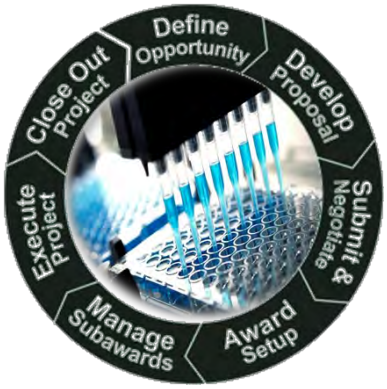
Congratulations to the following students for successfully defending!

Tanya Baldwin
Adviser: Dr. Carmen Dessauer
Samantha Berkey
Adviser: Dr. Carmen Dessauer
Kristen Clemons
Adviser: Dr. Kartik Venkatachalam

Kelsey Maxwell
Adviser: Dr. John Hancock
Max Odem
Adviser: Dr. Terry Walters
Lingxiao Tan
Adviser: Dr. John Hancock

Barbara Diaz-Rohrer was the recipient of a 2018 John J. Kopchick Fellow for her research project titled "Molecular Mechanisms of Microdomain-dependent Protein Trafficking".

Brittany Jewell was the recipient of a 2019 Charlene Kopchick Fellow. Her research project is titled "Cellular Mechanisms Associated with Osteosarcomagenesis in Rothmund-Thomson Syndrome".



Proposals & Awards

Data provided by Deborah Brougher, Supervisor, Grants and Contracts Specialist

Thirty proposals were submitted by the Department of Integrative Biology & Pharmacology in the third and fourth quarter of Fiscal Year 2018 by Drs. Berdeaux, Breton, Cheng, Cunha, Denicourt, Dessauer, Du, Frost, Gorfe, Kim, Lee, Levental, Li, Lichtenberger, Pochynyuk, Venkatachalam, Walters, Wong, and Zhu.

Thirty Four proposals were awarded during these quarters. Faculty receiving awards include Drs. Chang, Cheng, Dessauer, Frost, Gorfe, Hancock, Lee, Levental, Li, Lichtenberger, Pochynyuk, Venkatachalam, Walters, and Zhu.

Proposals Submitted FY2018 3rd QTR		
	# Submitted	Amount
Federal	14	$16,729,540.00
Private	0	$0.00
State	0	$0.00
Total	**14**	**$16,729,540.00**

Awards Received FY2018 3rd QTR		
	# Received	Amount
Federal	7	$1,858,758.00
Private	1	$10,332.00
State	2	$835,720.00
Total	**10**	**$2,704,810.00**

Proposals Submitted FY2018 4th QTR		
	# Submitted	Amount
Federal	13	$12,879,099.00
Private	2	$234,245.00
State	1	$897,483.00
Total	**16**	**$14,010,827.00**

Awards Received FY2018 4th QTR		
	# Received	Amount
Federal	17	$3,150,196.00
Private	5	$455,844.00
State	2	$143,895.00
Total	**24**	**$3,749,935.00**

New Awards

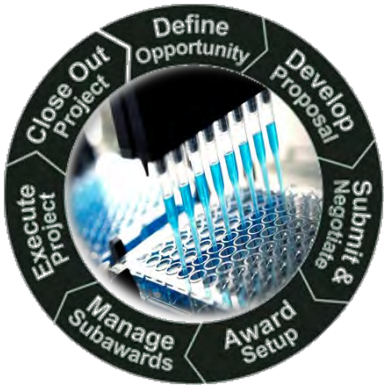
New Awards received during the third and fourth quarter of Fiscal Year 2018 include:

Dr. Dessauer. Craig Neilson. *Mechanisms of Opioid Resistance After Spinal Cord Injury.*

Dr. Hancock . NIH. *Decoding the structures and lipid binding specificity of small GTPase membrane anchors.*

Dr. Frost—Mukherjee Fellowship. NIH. *Elucidating the Role of Src and JNK signaling in Net1A-depedent Breast Cancer.*

Dr. Venkatachalam. NIH. *Modulation of mitochondrial proliferation and function in Drosphila neurons.*



Proposals & Awards

Data provided by Deborah Brougher, Supervisor, Grants and Contracts Specialist

Ninety Three proposals were submitted by the Department of Integrative Biology & Pharmacology during the first three quarters of Fiscal Year 2019.

Twenty Eight proposals were awarded during this time. Faculty receiving new awards include Drs. Berdeaux, Chang, Denicourt, Dessauer, Du, Frost, Hancock, Lee, Levental, Li, Lichtenberger, Loose, Pochynyuk, Tomilin, Walters, Wong, and Zhu.

Proposals Submitted FY2019 1st QTR		
	# Submitted	Amount
Federal	31	$28,013,527.00
Private	4	$3,565,000.00
State	0	$0.00
Total	**35**	**$31,578,527.00**

Awards Received FY2019 1st QTR		
	# Received	Amount
Federal	7	$945,144.00
Private	1	$110,298.00
State	0	$0.00
Total	**8**	**$1,055,442.00**

Proposals Submitted FY2019 2nd QTR		
	# Submitted	Amount
Federal	17	$22,039,746.00
Private	7	$1,735,000.00
State	0	$0.00
Total	**24**	**$23,774,746.00**

Awards Received FY2019 2nd QTR		
	# Received	Amount
Federal	6	$1,550,777.00
Private	1	$115,000.00
State	1	$300,000.00
Total	**8**	**$1,965,777.00**

Proposals Submitted FY2019 3rd QTR		
	# Submitted	Amount
Federal	25	$25,508,878.00
Private	5	$1,254,991.00
State	4	$3,334,529.00
Total	**34**	**$30,098,398.00**

Awards Received FY2019 3rd QTR		
	# Received	Amount
Federal	9	$1,930,633.00
Private	2	$177,000.00
State	1	$500,000.00
Total	**12**	**$2,607,633.00**

New Awards

New Awards received during the first three quarters of Fiscal Year 2019 include:

Dr. Berdeaux. NIH. *Promotion of Satellite Cell Proliferation by cAMP Signaling.*
Dr. Denicourt. NIH. *Mechanisms of Aberrant Ribosomal RNA (RRNA) Methylation and Altered MRNA Translation in Cancers.*
Dr. Du. AHA. *2019 Transformational project Award.*
Dr. Pochynyuk. NIH. *Regulation of K+ Balance by Distal Nephron TRPV4 Channel.*
Dr. Tomilin. AHA. *Importance of collecting duct CIC-Kb/2 channel for urinary electrolyte excretion.*
Dr. Walters—Lopez Fellowship. NIH. *Mechanisms in nociceptors driving ongoing activity and ongoing pain.*
Dr. Walters and Dr. Zhu. NIH. *Mechanisms in Primary Nociceptors that Drive Ongoing Activity and Ongoing Pain.*
Dr. Wong. NIH. *Regulation of Apolipoprotein Secretion by TTHY1 and Tweety in Glial Cells.*

Publications

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Publications

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