UTHealth awarded $3.5 million to develop treatments for extremely lethal cancers

Robert Cahill, UTHealth Media Relations

HOUSTON – (Jan. 15, 2015) – Scientists at The University of Texas Health Science Center at Houston (UTHealth) have been awarded $3,481,666 by the State of Texas to develop innovative treatments for several of the most lethal types of cancer including pancreatic, colon and lung.

The research, which is funded through the Cancer Prevention & Research Institute of Texas, is focused on a molecular mechanism that is associated with approximately 400,000 new cases of cancer in the United States annually, according to the National Institutes of Cancer.

Researchers received 3-year grants designed to bridge the gap between promising new discoveries achieved in the research laboratory and commercial development.

Cancer is characterized by uncontrolled cell growth and can be caused by breakdowns in the cell signaling cascades. Signals are controlled by molecular switches and their failure can trigger cell growth and division. One of those switches is a protein called K-Ras and its mutated versions are found in about 20 percent of human tumors, researchers report.

Scientists in the UTHealth Medical School are using their two grants to identify new compounds that may ultimately be used to treat these cancers as well as to gauge the effectiveness of a promising compound.

“K-Ras is mutated in more than 90 percent of pancreatic cancers, 50 percent of colon cancers and approximately 25 percent of non-small cell lung cancers,” said John Hancock, MB, BChir, Ph.D., ScD., chairman of the Department of Integrative Biology and Pharmacology at the UTHealth Medical School.

“The discovery of drugs to inhibit K-Ras is of vital importance if we are to successfully treat this group of cancers. However, no anti K-Ras drugs have yet to be developed,” said Hancock, holder of the John S. Dunn Distinguished University Chair in Physiology and Medicine and executive director of the Brown Foundation Institute of Molecular Medicine for the Prevention of Human Diseases at the UTHealth Medical School.

The co-principal investigators of a $1,969,826 grant – Alex Gorfe, Ph.D., and John Putkey, Ph.D. – are using computer simulations to screen millions of compounds, followed by biophysical and cell biological studies of thousands of predicted hits. Their goal is to develop novel therapeutic strategies to inhibit the activity of K-Ras mutations.
“We have decided to attack this elusive foe by assembling a team of experts from diverse fields and adopting a strategy that integrates theoretical biophysics, computational simulations, and high-end nuclear magnetic resonance as well as other biophysical and biological approaches,” said Gorfe, associate professor in the Department of Integrative Biology and Pharmacology at the UTHealth Medical School.

Putkey, a professor in the Department of Biochemistry and Molecular Biology at the UTHealth Medical School, said, “I would hope at the end of this project we would have several promising lead compounds that could be developed into drugs that inhibit the biological activity of mutated K-Ras.”

Whereas Gorfe and Putkey are working to identify new and novel K-Ras inhibitors, Hancock is improving the effectiveness of a promising anti K-Ras medication called fendiline. It is an obsolete antianginal agent used in Europe in the 1980s.

“The purpose of this project is to improve the K-Ras inhibitor function of fendiline by modifying the molecule and synthesizing new chemical derivatives,” Hancock said. “These studies will lead to the identification of more potent anti K-Ras drugs that are ready for evaluation in patients with pancreatic cancer.”

Hancock plans to test enhanced versions of fendiline in a mouse model of pancreatic cancer. Hancock’s grant is for $1,511,840.

Hancock, Gorfe and Putkey are on the faculty of The University of Texas Graduate School of Biomedical Sciences at Houston.

“The work will advance laboratory discoveries to clinically and commercially viable outcomes, which will break new grounds in cancer therapy with profound benefit to millions suffering from the many diverse K Ras-related carcinomas,” Gorfe said.

Congratulations to Dr. Alemayehu (Alex) Gorfe, who has been promoted to Associate Professor with tenure!
Dr. Lichtenberger Receives Multiple Grants

Lenard Lichtenberger, Ph.D.

Lenard Lichtenberger, has been awarded a 2-year grant from the Army to study the effects of phosphatidylcholine (PC) - associated nonsteroidal anti-inflammatory drugs (NSAIDs) to attenuate pain and promote healing after burn injury. The family of PC-NSAIDs, was originally developed in his lab to reduce gastrointestinal ulceration and bleeding associated with orally –consumed NSAIDs, which is now being developed and commercialized by PLx Pharma, LLC, a company which Dr. Lichtenberger co-founded 12 years ago. His lab also reported that the PC-NSAIDs in addition to their reduced GI toxicity, also possessed prominent effectiveness to reduce inflammation, pain and fever, which will be further evaluated in the new Army grant in the treatment of thermal injury.

Dr. Lichtenberger is also the recipient of two small developmental grants from MD Anderson Cancer Center (MDACC) to study the effects of Aspirin –PC to protect against two contrasting cancers, based upon compelling clinical data from other research centers that aspirin consumption reduces cancer incidence and prolongs survival rates of individuals from 9 different cancers. Aspirin -PC, which is the lead drug of PLx Pharma was approved January 2013 by the FDA under the name PL2200aspirin. Based upon its reduced GI toxicity and preliminary evidence of effectiveness in preventing and/or treating animal models of ovarian and colorectal cancer Dr. Lichtenberger will be working with his colleagues at MDACC (Dr. Anil Sood, is his co-investigator on a Developmental ovarian SPORE grant; and Drs. Jennifer Davis, Scott Kopetz and Ernest Hawk are his co-investigators on a subproject of a Moon Shot grant from MDACC to prevent Colorectal cancer) on these two related studies. Both of these developmental grants will provide much needed resources to determine if PL2200aspirin may have equivalent or superior anti-cancer activity, which if successful may lead to clinical studies in the near future.

Tour de Pink

Dr. Shane Cunha

For the last 3 years, members of the IBP department have participated in the Tour de Pink, an annual bike ride to raise funds for breast cancer awareness and treatment for medically underserved women in the greater Houston area. Routes for the bike ride range in distances from 12 to 100 miles. Each rider commits to raising $125, which is the average cost of a mammogram. This year was the 10th anniversary of the ride that is based in Prairie View, Texas. The UT Health cycling team consisted of Shane Cunha, Dick Clark, Tanya Baldwin, Dhananjay Thakur, and Agi Schonbrunn (plus 2 of Agi’s family). Our team raised $1190 and for a third year in a row Dr. Clark was the top fundraiser. Tanya Baldwin, a second year graduate student in Carmen Dessauer’s lab, receives an honorable mention for second place in fundraising and completing the 100 mile route for her inaugural ride. We thank all the members of the IBP department who have donated to the cause. We welcome riders of all skill and look forward to representing UT Health in the 2015 ride.
It may be time to go back to the drawing board when it comes to explaining the cause of the chronic pain experienced by many of the nearly 300,000 people with a spinal cord injury in the United States.

While it is widely held the pain emanates from injured nerve cells (neurons) in the spinal cord, research at UTHouston suggests uninjured sensory (injury-detecting) neurons in other parts of the body also contribute to the pain. This research has promising implications for developing new treatments for chronic pain.

Investigators tested their theory in a rat model of spinal cord injury and there was a reduction in chronic pain when the scientists selectively blocked the activity of peripheral injury-detecting neurons distant from the injury. Findings appeared in The Journal of Neuroscience.

“The earlier assumption was that the pain came from electrical activity generated at the injury site in the spinal cord,” said Edgar Walters, PhD, senior author and professor in the Department of Integrative Biology and Pharmacology at the UTHouston Medical School. “However after spinal cord injury, peripheral sensory neurons in many parts of the body act as if they sense the injury, and they appear to remain permanently activated -- continually driving pain.”

This new information on the molecular mechanisms involved in chronic pain transmission could aid efforts to develop new treatments for the chronic pain tied to spinal cord injury and possibly other poorly treated chronic pain conditions like chemotherapy-induced pain.

“Many people don’t realize how serious chronic pain is,” said Walters, noting that 40 to 50 percent of people with spinal cord injury experience chronic pain. One in three Americans can expect to suffer from some form of chronic pain, often associated with traumatic injury or diseases such as diabetes or arthritis. “We have good treatments for acute pain but not for truly chronic pain,” said Walters, who is the Ray A. and Robert L. Kroc Faculty Fellow and Fondren Chair in Cellular Signaling at UTHouston.

The molecular mechanisms in question involve protein channels in membranes that relay electrical impulses only in injury-detecting neurons. In the preclinical study, researchers blocked the synthesis of these channels, preventing the electrical activity of the peripheral injury-detecting neurons.

“We hope these unexpected results will encourage pharmaceutical companies in their efforts to identify new drugs to target these channels that are essential for this type of chronic pain,” Walters said.

UTHouston Department of Integrative Biology and Pharmacology co-authors include assistant professor and lead author Qing Yang, MD, Zizhen Wu, PhD, Julia K. Hadden, postdoctoral fellow Yan Zuo, PhD, postdoctoral fellow Robyn Crook, PhD; graduate student Max Odem, and associate professor Jeffrey Frost, PhD.

Walters and Frost are on the faculty of The University of Texas Graduate School of Biomedical Sciences at Houston. Odem is a student at the graduate school, a joint venture of UTHouston and The University of Texas MD Anderson Cancer Center.

The study titled “Persistent Pain After Spinal Cord Injury is Maintained by Primary Afferent Activity” received support from the United States Department of Defense, Mission Connect/TIRR Foundation and Craig H. Neilsen Foundation.
Dr. Qing Yang Receives an Award from the Department of Defense
Qing Yang, Ph.D.

Dr. Qing Yang recently receives Investigator-Initiated Research Award of the spinal cord injury research program (SCIRP) from Department of Defense (DoD) entitled "Neuroprotective Effect of Targeting KCNQ/Kv7 Channels for Spinal Cord Injury" to support her research work on spinal cord injury. The SCIRP was established by Congress in 2009 to support research into regenerating/repairing damaged spinal cords and improving rehabilitation therapies. The SCIRP focuses its funding on innovative projects that have the potential to make a significant impact on improving the function, wellness, and overall quality of life for military service members as well as their caregivers, families, and the American public.

Traumatic injury to the spinal cord results in permanent motor impairment, sensory dysfunction, and often chronic pain. In most cases, traumatic injury fails to completely sever the spinal cord. Recent studies reported that preservation of even a small fraction of the neuronal fibers passing through injured area of spinal cord could enable significant recovery of motor and sensory function. Unfortunately, many of the fibers that survive the initial injury later degenerate and die. Much of this later loss of neurons and fibers is driven by intense, long-lasting excitation of neurons in the injured area. Reducing this excessive excitation may protect neurons from degeneration and promote the survival of spinal tissue needed to preserve and restore function. In this DoD funded Investigator-Initiated Research Award, a specific drug to open KCNQ/Kv7/M channels which are abundantly expressed in many neurons and neural fibers including spinal cord and dorsal root ganglion is used to neutralize the hyperexcitability of spinal neurons and axons that receive intense excitation during the acute phase of SCI, thus protecting neurons from degeneration and preserve neurological function that would be lost otherwise during the chronic stage.

ALS Walk for a Cure
Raymond Grill, Ph.D.

Dear friends and colleagues,
I want to thank all of you who supported me in the ALS Association’s Walk for a Cure held in October. With your help, I was able to raise over $5000.00 that will go to fund ALS research and provide support for families caring for those living with ALS. I wish to extend special thanks to Alissa Poteete, formerly from my lab but now working across the street at Baylor, who created the festive garb that I wore for this year’s walk. It is my goal to double our donation target for next year. I may be contacting many of you for suggestions as to appropriate “walk wear” for next year’s extravaganza! Again, please accept my heartfelt gratitude for your generosity. I have chosen this particular charity because a dear friend of mine recently lost her daughter, at the age of 14, to ALS. Your generous support will hopefully bring us yet closer to a day when this horrible disease will become only a bad memory.

Best Wishes,
Ray
Max Odem and Alexis Bavencoffe Win Poster Competition

Max Odem and Alexis Bavencoffe from Terry Walters and Carmen Dessauer’s labs presented their recent findings during the poster session of the TIRR Foundation Mission Connect 2014 Annual Scientific Symposium last December 5th. This is a symposium dedicated to research focusing on spinal cord and traumatic brain injuries (SCI and TBI). Max was awarded the “best overall SCI poster” and Alexis the “first place prize for SCI” for postdocs. This was their first time attending this symposium. In addition, Alexis also received the second place prize for UTHealth postdocs at the 21st Annual Neuroscience Poster Session at the Neuroscience Research Foundation symposium, December 6th.

New Members of the Team

Abdallah Sayyed Ahmad
Research Scientist
Dr. Gorfe

Upasana Banerjee
Postdoctoral Fellow
Dr. Cheng

Hui Ding
Visiting Scientist
Dr. Li

Janani Subramaniam
Research Assistant
Dr. Cunha

Vaidehi Thanawala
Postdoctoral Fellow
Dr. Schonbrunn

Victor Tomilin
Postdoctoral Fellow
Dr. Pochynyuk

Xubo Lin
Postdoctoral Fellow
Dr. Gorfe

Chunrong Qu
Visiting Student
Dr. Zhu

Xianfeng Shen
Visiting Scientist
Dr. Zhu

Arzu Ulu
Postdoctoral Fellow
Dr. Frost

Jingshu Wang
Visiting Student
Dr. Du


Cameron Brand Recognized by the Dean!

Dean Giuseppe Colasurdo and the Medical School Graduate Student Education Committee held the 2014 Dean’s Research Award Ceremony and reception to honor students for their outstanding research and academic accomplishments. Cameron Brand mentored by Carmen Dessauer, Ph.D., was honored during this reception. Congratulations to Cameron and all his hard work!

Max Odem Wins Poster Competition.

Max Odem, a second year graduate student who joined Dr. Edgar Walters’ lab in the spring of 2014, has recently won awards in two poster competitions and a travel award. He was the first place winner ($500) in the poster competition held at the Neuroscience Program's annual retreat in Galveston, TX. Remarkably, Max was the first pre-candidacy student ever to win first place in this competition. He then received a second place award ($300) at the Graduate Student Education Committee poster session at the annual Medical School research retreat. Max will be presenting a poster at Society for Neuroscience in Washington DC in November. The Neuroscience Graduate Program has offered Max a travel award ($200) for his trip. Max is investigating unexpected mechanistic links between chronic pain and anxiety in a rat model of spinal cord injury.

Courtney Olsen Receives Fellowship.

Courtney Olsen received a TL1 fellowship through the Center for Clinical and Translational Sciences for her project: The Role of SHANK Proteins in Somatostatin Receptor Signaling. The fellowship is open to PhD predoctoral students in the 6 UTHealth schools who are pursuing a clinical or translational research project. The fellowship provides additional training in translational science through a monthly seminar series, coursework, and clinical experiences. The aim of Courtney's project is to elucidate novel signaling mechanisms of the Somatostatin receptor with the hope of improving our understanding of the function of clinically used somatostatin analogs.

Congratulations!

Congratulations to Nabila Boukelmoune for successfully defending her thesis on December 10, 2014.

Congratulations to Kelsey Maxwell, Randi Stewart, and Ryan Fortune on passing their candidacy exams!

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Proposals & Awards
Catrina Stevens & Deborah Brougher

Twenty proposals were submitted by the Department of Integrative Biology & Pharmacology in the first quarter of Fiscal Year 2015 by Drs. Breton, Chang, Cunha, Denicourt, Du, Hancock, Levental, Li, Lichtenberger, Loose, Pochynyuk, Schonbrunn, Walters, Yang, and Zhu. Nine proposals were awarded this quarter. Faculty receiving awards include Drs. Cheng, Lichtenberger, Schonbrunn, Walters, and Yang. The success rate for awards is approximately 45% so far this year.

~Data provided by Deborah Brougher, Sr. Grants and Contracts Specialist

<table>
<thead>
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<th>Proposals Submitted FY2015 1st QTR</th>
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<td># Submitted</td>
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<th>Awards Received FY2015 1st QTR</th>
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New Awards
Awards received during the first quarter of Fiscal Year 2015 include:

Cheng, Xiaodong. UTMB. Novel Pharmacological Probes Targeting Exchange Proteins Activated by cAMP (EPAC).

Cheng, Xiaodong. UTMB.

Lichtenberger, Lenard. UT MD Anderson Cancer Center. Evaluation of the chemopreventive activity of Aspirin-PC, using in vitro and in vivo models of colorectal cancer (CRC).


Walters, Edgar. DOD. Novel Target for Ameliorating Pain and Other Problems after SCI: Spontaneous Activity in Nociceptors.

Walters, Edgar. Feinstein. Contributions of Inflammatory Mediators in Chronic SCI.

Yang, Qing. USAMR. Neuroprotective Effects of Targeting KCNQ/Kv7 Channels after Spinal Cord Injury.
December 1, 2014
Hugo Bellen, D.V.M., Ph.D.
Molecular and Human Genetics
Baylor College of Medicine
Title of Talk: “The demise of neurons”
Host: Kartik Venkatachalam, Ph.D.

December 8, 2014
Janos Peti-Peterdi, M.D., Ph.D.
Physiology, Biophysics and Medicine
University of Southern California
Title of Talk: “Renal physiology provides clues for new approach to nephron regeneration”
Host: Oleh Pochynyuk, Ph.D.

December 15, 2014
Sarah Veatch, Ph.D.
Department of Biophysics
University of Michigan
Title of Talk: “Phases and fluctuations in biological membranes: functional roles and misregulation by general anesthetics”
Host: Ilya Levental, Ph.D.

January 5, 2015
Robert Dantzer, D.V.M., Ph.D.
Symptom Research, Division of Internal Medicine
MD Anderson Cancer Center
Title of Talk: “Is there a role for inflammation in depression?”
Host: Edgar T. Walters

January 12, 2015
Catherine Collins, Ph.D.
Molecular, Cellular, and Developmental Biology
University of Michigan
Title of Talk: “Axonal regeneration and degeneration after injury”
Host: Kartik Venkatachalam

January 26, 2015
Stephen Russ Price, Ph.D.
Department of Nephrology
Emory University School of Medicine
Title of Talk: “Skeletal muscle atrophy and chronic diseases: Post-translational regulation by microRNAs”
Host: Yi-Ping Li, Ph.D.

February 2, 2015
Kirill Martemyanov, Ph.D.
Molecular Signaling Section
Scripps Research Institute, Florida
Title of Talk: "Molecular control of G protein mediated neurotransmission"
Host: Carmen Dessauer, Ph.D.

February 9, 2015
Anthony Means, Ph.D.
Molecular & Cellular Biology
Baylor College of Medicine
Title of Talk: “CaMKK2 as an Integral Mediator of Inflammation and Cancer”
Host: Agnes Schonbrunn, Ph.D.

February 23, 2015
Jurgen Wess, Ph.D.
Molecular Signaling Section
National Institutes of Health
Title of Talk: “Cell Type-Specific Modulation of GPCR Signaling Pathways: Potential Implications for the Treatment of Diabetes and Obesity”

March 2, 2015
Fernanda Laezza, M.D., Ph.D.
Pharmacology and Toxicology
University of Texas Medical Branch
Title of Talk: TBA
Host: Alemayehu Gorfe Abebe, Ph.D.

Seminars are held on Mondays at 4:00 PM in MSB 2.135, unless otherwise noted. For information and questions, please contact Catrina Stevens at catrina.m.stevens@uth.tmc.edu or 713-500-7536.
<table>
<thead>
<tr>
<th>Date</th>
<th>Speaker</th>
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<th>Title of Talk</th>
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<tr>
<td>March 9, 2015</td>
<td>Karl-Dimiter Bissig, M.D., Ph.D.</td>
<td>Molecular and Cellular Biology</td>
<td>TBD</td>
<td>Rebecca Berdeaux, Ph.D.</td>
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<td>March 16, 2015</td>
<td>Swathi Arur, Ph.D.</td>
<td>Department of Genetics</td>
<td>TBD</td>
<td>Kartik Venkatachalam, Ph.D.</td>
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<td>March 23, 2015</td>
<td>Alan Daugherty, Ph.D., D.SC.</td>
<td>Medicine and Physiology</td>
<td>TBD</td>
<td>Cell and Regulatory Biology Graduate Students</td>
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<td>April 6, 2014</td>
<td>George Holz, Ph.D.</td>
<td>Medicine and Pharmacology</td>
<td>TBD</td>
<td>Xiaodong Cheng, Ph.D.</td>
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<td>April 13, 2015</td>
<td>George Rodney, Ph.D.</td>
<td>Molecular Physiology &amp; Biophysics</td>
<td>TBD</td>
<td>Rebecca Berdeaux, Ph.D.</td>
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<td>April 20, 2015</td>
<td>Melinda Sheffield-Moore, Ph.D.</td>
<td>Neuroscience and Cell Biology</td>
<td>TBD</td>
<td>Yi-Ping Li, Ph.D.</td>
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<td>May 4, 2015</td>
<td>Agnes Schonbrunn, Ph.D.</td>
<td>Integrative Biology and Pharmacology</td>
<td>“Exploiting mechanistic insights into somatostatin action to develop better drugs for neuroendocrine tumors”</td>
<td>Yi-Ping Li, Ph.D.</td>
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<td>May 11, 2015</td>
<td>Zheng (Jake) Chen, Ph.D.</td>
<td>Biochemistry &amp; Molecular Biology</td>
<td>TBD</td>
<td>Yi-Ping Li, Ph.D.</td>
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<td>May 18, 2015</td>
<td>Damian W. Young, Ph.D.</td>
<td>Center for Drug Discovery</td>
<td>TBD</td>
<td>Xiaodong Cheng, Ph.D.</td>
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Welcome Baby Elise!

Elizabeth Marjory Justice

Born
August 22, 2014
at 3:04pm

7 pounds, 8 ounces

To proud parents
Rebecca Berdeaux & Nicholas Justice

Just Married

Randi Stewart
&
Ryan Fitzgibbon
Were married on
November 29, 2014
In San Antonio, TX
IBP Calendar of Events

**Administrative Staff Meetings, 3:00-4:00 PM, MSB 4.136**
January 21, February 18, March 18, April 15, May 20

**CRB Meetings, 12-1 PM, Room 4.100**
January 8; February 5; March 5; April 2; May 7

**Faculty Coffee/Tea, 10-11 AM, MSB 4.100**
January 7, 14, 21; February 4, 11, 18, 25; March 4, 11, 18, 25; April 1, 8, 15, 22, 29

**STG Seminar, 4-5 PM, MSB 4.100**
January 7, 21; February 4, 18; March 4 18; April 1, 15, 29; May 6, 13, 27

**Dates to Remember:**

- **December 24-January 2:** Winter Holiday—December 24-26 & January 1—The University will be closed for Official Business; December 28-31 & January 2 are skeleton crew holidays
- **December 25:** Christmas Day—The University will be closed for Official Business
- **December 31:** New Year’s Eve—The University will be closed for Official Business
- **January 1:** New Year’s Day—The University will be closed for Official Business
- **January 19:** Martin Luther King Day—The University will be closed for Official Business
- **February 2:** Groundhog Day
- **February 14:** Valentine’s Day
- **February 16:** President’s Day—The University will be closed for Official Business
- **March 8:** Daylight Savings Time—Turn your clocks forward one hour!
- **March 17:** St. Patrick’s Day
- **April 1:** April Fool’s Day
- **April 7-8:** CRB Retreat, Camp Allen, Navasota, TX
- **April 22:** Earth Day
- **May 25:** Memorial Day—The University will be closed for Official Business