

Integrative Biology & Pharmacology Newsletter

Scientists discover a cancer homing system

Rob Cahill, UTHealth Media Relations

The discovery of an intracellular homing system that guides a cancer-causing protein called K-Ras could help in the fight against some of the world's deadliest cancers, report scientists from The University of Texas Health Science Center at Houston (UTHealth).

The research appears in the journal *Cell*.

Cancer-causing mutations in the K-Ras protein are found in approximately 20 percent of human tumors including cancers of the lungs, pancreas and colon. These three types are responsible for nearly 250,000 deaths in the United States annually. Currently, no effective treatments directly inhibit K-Ras, which works as a molecular switch that normally helps the body replace cells as they die off. Mutations in K-Ras lock the switch in the on-position, leading to uncontrolled cell growth and cancer.

In order to work, K-Ras must bind to the plasma membrane of the cell. "We've known for 25 years that the membrane anchor located at one end of K-Ras is positively charged. Since the plasma membrane is negatively charged, we all believed that K-Ras anchoring was simply a matter of opposite charges attracting each other. Amazingly what we have now discovered is that the K-Ras anchor actually operates as a highly sophisticated ZIP code that seeks out very specific lipids on the plasma membrane," said John F. Hancock, M.B., B.Chir., Ph.D., Sc.D., the study's senior author and chair of integrative biology and pharmacology at McGovern Medical School at UTHealth.

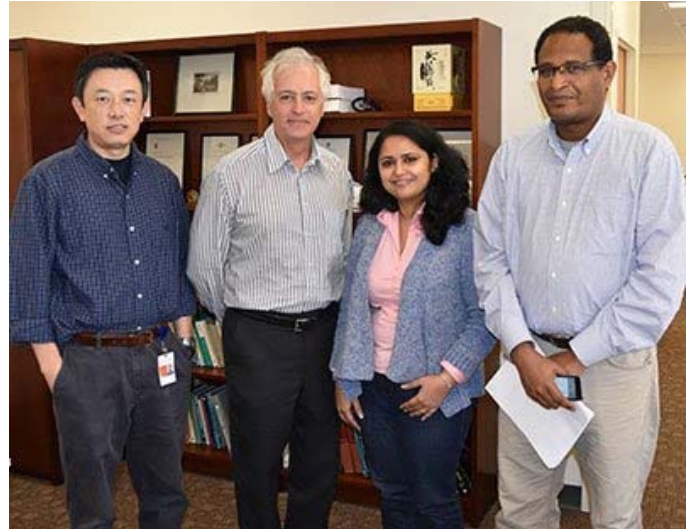
"If we mess with the sequence of the ZIP code, we misdirect K-Ras to the wrong lipids on the plasma membrane, just like mail being sent to the wrong city or state if the ZIP code is misspelled. Importantly, when K-Ras is misdirected in this way, its ability to function is severely compromised," said Yong Zhou, Ph.D., the study's lead author and assistant professor of integrative biology and pharmacology at McGovern Medical School.

"This paper gives us a new perspective on how we see the K-Ras protein," said Alemayehu Gorfe, Ph.D., the paper's co-senior author and associate professor of integrative biology and pharmacology at McGovern Medical School. "At this point, the discovery is still basic science, but it allows us to think about K-Ras in a totally different way and opens up new strategies for designing anti-K-Ras drugs."

Deciphering the K-Ras "ZIP code" and figuring out exactly how it works required the combined expertise of Hancock and Gorfe's teams using high-resolution electron microscopy and sophisticated computer simulations. Their McGovern Medical School collaborators included Priyanka Prakash, Ph.D., Hong Liang, M.D., and Kwang-Jin Cho, Ph.D.

The study, titled "Lipid-sorting specificity encoded in K-Ras membrane anchor regulates signaling output," was supported by the Cancer Prevention & Research Institute of Texas (RP130059), National Institutes of Health (R01GM100078, K99-CA188593), Texas Advanced Computing Center and Extreme Science and Engineering Discovery Environment (MCB150054).

Hancock and Gorfe are on the faculty of The University of Texas Graduate School of Biomedical Sciences at Houston, which is a partnership of UTHealth and The University of Texas MD Anderson Cancer Center. Hancock is the vice dean of research and the John S. Dunn Distinguished University Chair in Physiology and Medicine at McGovern Medical School.



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MYKOLA MAMENKO LANDS A FACULTY POSITION OUTSIDE HOUSTON

Oleh Pochynyuk



Congratulations to Dr. Mykola Mamenko for accepting a tenure-track Assistant Professor position in the Department of Physiology Medical College of Georgia, Augusta University starting from April 10th 2017. During his postdoctoral time (2010-2016) in our Department, Mykola demonstrated a stellar performance producing 26 publications (13 as first author) in a variety of highly-ranked journals, including Hypertension, J. Biol. Chemistry, J. American Soc. Nephrology, Kidney International, American Journal of

Physiology to name a few. He received numerous awards by the American Physiological Society Renal Section Research Recognition (2017), and Postdoctoral Excellence in Research Award (2015), The Society of Experimental Biology and Medicine Young Investigator Award (2015), The University of Texas Medical School Dean's Excellence in Research Award (2015) as well as several travel awards to attend National Meetings. His talents and potential multiplied by hardworking led to development of his own independent scientific project unraveling a role of the store-operated Ca²⁺ entry in controlling water-electrolyte transport in the renal tubule and how its deficiency result in systemic pathology. Dr. Mamenko was successful to receive a postdoctoral fellowship (2014-2015) and subsequently a scientist development grant (2015-2019) from the American Heart Association.

While feeling sad about his departure, I am sure that Mykola will continue to excel in this new capacity as a leader of independent research team in the Medical College of Georgia, Augusta University. During his last month with us, please stop by and say few warm farewell words to him.

The **IBP Newsletter** is published quarterly by the department and distributed to faculty, staff and students. An electronic copy is available on the IBP website at <http://ibp.med.uth.tmc.edu/>

Chair, IBP

Dr. John Hancock

Vice Chair, IBP

Dr. Agnes Schonbrunn

Director of Management Operations

Monica Gardner

Editor

Catrina Stevens

Please contact any of our dedicated staff for whatever assistance you may require:

Catrina Stevens

Senior Administrative Coordinator

Catrina.M.Stevens@uth.tmc.edu

713.500.7536

Cordelia Conley

Administrative Manager

Cordelia.P.Conley@uth.tmc.edu

713.500.7459

Deborah Brougher

Sr. Contracts & Grants Specialist

Deborah.Brougher@uth.tmc.edu

713.500.6322

Lisa Byrd

Senior Administrative Coordinator

Lisa.Byrd@uth.tmc.edu

713.500.7508

Monica Gardner

Director, Management Operations

Monica.Gardner@uth.tmc.edu

713.500.7516

Sandy Cegielski

Senior Administrative Coordinator

Sandy.Cegielski@uth.tmc.edu

713.500.7514

Trish McFarland

Coordinator II, Educational Programs

Patricia.McFarland@uth.tmc.edu

713.500.5470

New Members of the Team



Guojie Li

Research Technician

Dr. Yang

Photo
Not
Available

Mo Liu

Postdoctoral Fellow

Dr. Lee

Student & Postdoc Awards & Activities

CONGRATULATIONS!



Dr. Amit Gupta has been awarded a one-year postdoctoral appointment in the CPRIT-funded Computational Cancer Biology Training Program. This fellowship has been awarded to Dr. Gupta to pursue his research on the "Identification of potential K-Ras inhibitors by computer aided drug design and experiments."

IBP Star Awards

Each year, UTHealth celebrates employee leadership and longevity at the STAR Awards. Congratulations to this year's STAR Awards recipients!

Lenard Lichtenberger 40 years

Dina Montufar-Solis 30 years

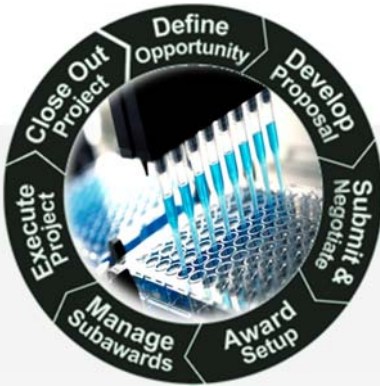
Shawn Brisbay 25 years

Lisa Byrd 15 years

Wei Chen 10 years

Xiaoping Ma 10 years

Yan Zuo 5 years



Proposals & Awards

Twenty Seven proposals were submitted by the Department of Integrative Biology & Pharmacology in the second quarter of Fiscal Year 2017 by Drs. Berdeaux, Breton, Chang, Cheng, Denicourt, Du, Frost, Lee, Levental, Li YP, Li Y, Lichtenberger, Pochynyuk, Srivastava, Venkatachalam, Walters, and Zhu.

Eight proposals were awarded this quarter. Faculty receiving awards include Drs. Du, Frost, Gorfe, Hancock, Lee, Loose, Venkatachalam, and Zhu.

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

Proposals Submitted FY2017 2nd QTR		
	# Submitted	Amount
Federal	16	\$18,302,996.00
Private	8	\$1,310,388.00
State	3	\$599,997.00
Total	27	\$20,213,381.00

Awards Received FY2017 2nd QTR		
	# Received	Amount
Federal	6	\$1,529,273.00
Private	0	\$0.00
State	2	\$1,204,972.00
Total	8	\$2,734,245.00

- Akhmedov D, Mendoza-Rodriguez MG, Rajendran K, Rossi M, Wess J, Berdeaux R. [Gs-DREADD knock-in mice for tissue-specific, temporal stimulation of cAMP signaling](#). Mol Cell Biol. 2017 Feb 6. pii: MCB.00584-16. doi: 10.1128/MCB.00584-16. [Epub ahead of print].
- Boyle G, Richter K., Priest HD, Traver D, Mockler TC, Chang JT, Kay SA and Breton G. [Comparative vertebrate diurnal/circadian transcriptomes PLoS One](#). PLoS One. 2017 Jan 11;12(1):e0169923. doi: 10.1371/journal.pone.0169923. eCollection 2017.
- Breton G, Kay SA, Pruneda-Paz JL. [Identification of Arabidopsis Transcriptional Regulators by Yeast One-Hybrid Screens Using a Transcription Factor ORFeome](#). Methods Mol Biol. 2016;1398:107-18. doi: 10.1007/978-1-4939-3356-3_10.
- Cai M, He J, Xiong J, Tay LWR, Wang Z, Rog C, Wang J, Xie Y, Wang G, Banno Y, Li F, Zhu M, Du G. [Phospholipase D1-regulated autophagy supplies free fatty acids to counter nutrient stress in cancer cells](#). Cell Death Dis. 2016 Nov 3;7(11):e2448. doi: 10.1038/cddis.2016.355.
- Ganesan L, Shieh P, Bertozzi CR, Levental I. [Click-Chemistry Based High Throughput Screening Platform for Modulators of Ras Palmitoylation](#). Sci Rep. 2017 Jan 23;7:41147. doi: 10.1038/srep41147.
- Jaber N, Mohd-Naim N, Wang Z, DeLeon JL, Kim S, Zhong H, Sheshadri B, Dou Z, Edinger AL, Du G, Braga VMM, and Zong WX. [Class III PI 3-kinase Vps34 regulates Rab7 and late endocytic trafficking through recruitment of the GTPase activating protein Armus](#). J Cell Sci. 2016 Dec 1;129(23):4424-4435. Epub 2016 Oct 28.
- Jiang Y, Sverdlov MS, Toth PT, Huang L, Du G, Liu Y, Natarajan V, Minshall RD. [Phosphatidic acid produced by RalA-activated PLD2 stimulates caveolae-mediated endocytosis and trafficking in endothelial cells](#). J Biol Chem. 2016 Sep 23;291(39):20729-38. doi: 10.1074/jbc.M116.752485. Epub 2016 Aug 10.
- Li Y, Hu H, Tian J, Zhu MX, and O'Neil RG. [Dynamic coupling between TRPV4 and Ca-activated SK1/3 and IK1 K channels plays a critical role in regulating the K secretory BK channel in collecting duct cells](#). Am J Physiol Renal Physiol. 2017 Mar 8;ajprenal.00037.2017. doi: 10.1152/ajprenal.00037.2017. [Epub ahead of print].
- Lichtenberger LM, Fang D, Bick RJ, Poindexter BJ, Phan T, Bergeron AL, Pradhan S, Dial EJ, Vijayan KV. [Unlocking Aspirin's Chemopreventive Activity: Role of Irreversibly Inhibiting Platelet Cyclooxygenase-1](#). Cancer Prev Res (Phila). 2017 Feb;10(2):142-152. doi: 10.1158/1940-6207.CAPR-16-0241. Epub 2016 Dec 20.
- Lichtenberger LM, Phan T, Fang D, Edler S, Philip J, Li-Geng T, Dial EJ. [Bioavailability of aspirin in rats comparing the drug's uptake into gastrointestinal tissue and vascular and lymphatic systems: implications on aspirin's chemopreventive action](#). J Physiol Pharmacol. 2016 Oct;67(5):635-642.
- Tay LWR, Wang Z, Du G. Phosphatidic acid regulation of PIPKI. Methods Enzymol. 2017;583:359-374.
- Walters ET. [How is chronic pain related to sympathetic dysfunction and autonomic dysreflexia following spinal cord injury?](#) Auton Neurosci. 2017 Jan 27. pii: S1566-0702(17)30014-0. doi: 10.1016/j.autneu.2017.01.006. [Epub ahead of print].
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- Wu Z, Li L, Xie F, Du J, Zuo Y, Frost JA, Carlton SM, Walters ET, Yang Q. [Activation of KCNQ Channels Suppresses Spontaneous Activity in Dorsal Root Ganglion Neurons and Reduces Chronic Pain after Spinal Cord Injury](#). J Neurotrauma. 2017 Mar 15;34(6):1260-1270. doi: 10.1089/neu.2016.4789. Epub 2017 Feb 27.
- Zhou Y, Prakash P, Liang H, Cho KJ, Gorfe AA, Hancock JF. [Lipid-Sorting Specificity Encoded in K-Ras Membrane Anchor Regulates Signal Output](#). Cell. 2017 Jan 12;168(1-2):239-251.e16. doi: 10.1016/j.cell.2016.11.059. Epub 2016 Dec 29.

IBP Seminar Series

~Directed by Drs. Ghislain Breton and Ilya Levental



March 6, 2017

Mikhail Kolonin, Ph.D.

Center for Metabolic and Degenerative Diseases
University of Texas Health Science Center

Title of Talk: "lineages, function, dysfunction, and targeting of adipose cells"

Host: Dr. Yi-Ping Li



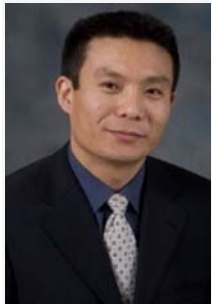
April 10, 2017

Eric Taylor, Ph.D.

Biochemistry
University of Iowa

Title of Talk: "Adaptive Reprogramming of Skeletal Muscle Mitochondrial Metabolism and Integrative Mechanisms of Leanness"

Host: Dr. Rebecca Berdeaux



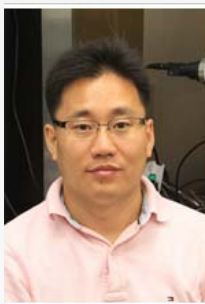
March 13, 2017

Shuxing Zhang, Ph.D.

Experimental Therapeutics
MD Anderson Cancer Center

Title of Talk: "Targeting Ubiquitination for Cancer Therapy"

Host: Dr. Alemayehu Gorfe



April 17, 2017

Yu Shin Kim, Ph.D.

Neuroscience & Cell Biology
UTMB

Title of Talk: "Imaging Pain in vivo"

Host: Dr. Edgar T. Walters



March 20, 2017

David Sheikh-Hamad, M.D.

Medicine-Nephrology
Baylor College of Medicine

Title of Talk: "Mitochondrial pathways for kidney protection"

Host: Dr. Oleh Pochynyuk



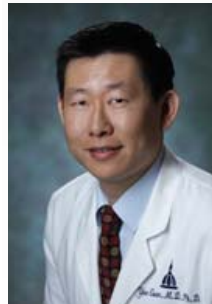
May 1, 2017

Robert Chapkin, M.D.

Integrative Nutrition & Complex Diseases
Texas A&M

Title of Talk: "Emerging role of chemoprotective agents in the dynamic shaping of plasma membrane organization"

Host: Dr. Ilya Levental



March 27, 2017

Yun Guan, M.D., Ph.D.

Anesthesiology and Critical Care Medicine
John Hopkins University

Title of Talk: "A Primary Sensory Neuron-Specific Target for Inhibiting Chronic Pain and Improving Morphine Analgesia"

Host: Dr. Qing Yang



May 15, 2017

Seung-Hee Yoo, Ph.D.

Biochemistry & Molecular Biology
McGovern Medical School

Title of Talk: "Period2 3'-UTR and microRNA-24 negatively regulate PERIOD2 protein accumulation and clock oscillatory amplitude"

Host: Dr. Ghislain Breton



April 6, 2017

Robert Gereau, Ph.D.

Anesthesiology and Neuroscience
Washington University in St. Louis

Title of Talk: "Translational pain research: targeting sensitization"

Host: Dr. Edgar T. Walters

NOTE

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.

IBP Calendar of Events

Administrative Staff Meetings, 2:30-3:30 PM, MSB 4.136

April 6, May 4, June 1, July 6, August 3, September 7



CRB Meetings, 12-1 PM, Room 4.100

April 6, May 4, June 1, July 6, August 3, September 7



Faculty Coffee/Tea, 10-11 AM, MSB 4.100

March 1, 8, 15, 22, 29
April 5, 12, 19, 26
May 3, 10, 17, 24, 31
June 7, 14, 21, 28
July 5, 12, 19, 26
August 2, 9, 16, 23, 30
September 6, 13, 20, 27



Dates to Remember:

March 17: St. Patrick's Day

March 20: First Day of Spring

April 1: April Fools Day

April 14: Good Friday

April 16: Easter

April 22: Earth Day

May 4-5: CRB Retreat

May 14: Mother's Day

May 29: Memorial Day-*The University will be closed for Official Business*

June 18: Father's Day

June 21: First Day of Summer

July 4: Independence Day-*The University will be closed for Official Business*