2015 Ion Channel Symposium at Zhejiang University

Date: Wednesday, June 24th, 2015
Venue: Room 205, Administration Building
Agenda:

Time	Title	Speaker	Unit
8:30-8:45	Welcome speech	Jianhong Luo	Vice president of ZJU
8:45-9:35	Calcium, Calmodulin, and Potassium Chanels	Rick Aldrich	UT Austin
9:35-10:25	AMPA Receptors: Synaptic Physiology, Role in the Circuitry of Epilepsy, and Clinical Translation	Mike Rogawski	UC Davis
	Coffee break		
10:35-11:05	The principle of cooperative gating in a calcium-gated potassium channel	Sheng Ye	Zhejiang University
11:05-11:25	Mechanisms for the Regulation of HCN Channels by the Accessory Subunit TRIP8b	John Bankston	University of Washington
11:25-11:45	Temple-Baraitser Syndrome and Kv10.1 channel	Linlin Ma	University of Queensland
11:45-12:05	Providing human model of cardiac arrhythmia using iPSCs	Ping Liang	Zhejiang University
	Lunch break		
13:30-14:20	Gating mechanisms in cyclic nucleotide-regulated ion channels	Bill Zagotta	University of Washington
14:20-15:10	Structural mechanism underlying capsaicin binding and activation of TRPV1 ion channel	Jie Zheng	UC Davis
	Coffee break		
15:20-16:10	Structure and gating mechanism of thermosensitive TRPV1 channels	Kenton Swartz	NIH
16:10-16:30	Differential patterns of ligands binding to human Transient receptor potential melastatin2 (TRPM2) channel	Wei Yang	Zhejiang University
16:30-16:50	Gating-Transition States of MscL Determined by The TM1-TM2 Interactions	Yuezhou Li	Zhejiang University
16:50-17:10	A pain-inducing centipede toxin targets the heat activation machinery of nociceptor TRPV1	Shilong Yang	Kunming Institute of Zoology, CAS
	Dinner		
20:00-21:00	The Legend of Romance show		

2015 Ion Channel Symposium at Zhejiang University

Date: Thursday, June 25th, 2015
Venue: Room 205, Administration Building
Agenda:

Time	Title	Speaker	Unit
8:00-8:50	SUMO emerges from the nucleus to control membrane excitability	Steve Goldstein	Brandeis University
8:50-9:40	Identification of novel agonists and positive allosteric modulators of alpha 7 nAChR channel for therapeutic potential of neuropsychiatric disorders	KeWei Wang	Peking University
Coffee break			
9:50-10:40	KATP channels and metabolically-induced resistance to epileptic seizures	Gary Yellen	Harvard University
10:40-11:30	Tipping the Balance of Neural Networks through RyR Dysfunction	Isaac Pessah	UC Davis
11:30-11:50	RIM1a, a postsynaptic organizer for NMDA receptor recycling	Shuang Qiu	Zhejiang University
Lunch time			

Prof. Richard W. Aldrich

Chair of he University of Texas at Austin
Investigator, HHMI/1990-2006
A member of the National Academy of Sciences

Richard Aldrich graduated with high distinction from the University of Arizona in 1975 with a Bachelor of Sciences degree in Biological Sciences. He received his Ph.D. in Neuroscience from Stanford University in 1980, after which he did postdoctoral work at Yale University in Physiology. He joined the faculty at Yale in the Section of Molecular Neurobiology before returning to Stanford in 1985 as a faculty member in the Department of Neurobiology and subsequently the Department of Molecular and Cellular Physiology, where he served as department chair from 2001-2004. Dr. Aldrich was a member of the Howard Hughes Medical Institute from 1990 until moving to The University of Texas in 2006, where he is Professor and Chair of the Section of Neurobiology in the School of Biological Sciences and the Karl Folkers Chair II in Interdisciplinary Biomedical Research. He has served on the council and as president of the Society of General Physiologists, and is a Fellow and president (2011-2012) of the Biophysical Society.

Selective Publications:

1. Pyott, S.J., Meredith, A.L., Fodor, A.F., Vazquez, A.E., Yamoah, E.N. and Aldrich, R. W. (2007) Cochlear Function in Mice Lacking the BK channel alpha, beta1, or beta4 subunits. **Journal of Biological Chemistry** 282:3313-3324.
2. Misonou, H., Menegola, M., Buchwalder, L., Park, E.W., Meredith, A., Rhodes, K.J., Aldrich, R.W., and Trimmer, J.S. Immunolocalization of the Ca2+-activated K Channel Slo1 in Axons and Nerve Terminals of Mammalian Brain and Cultured Neurons. **Journal of Comparative Neurology** 496:289-302, 2006.
3. Meredith, A.L., Wiler, S.W, Miller, B.H., Takahashi, J.S., Fodor, A.A. Ruby N. F., and Aldrich, R.W. (2006) BK calcium-activated potassium channels regulate circadian behavioral rhythms and pacemaker output **Nature Neuroscience** 9:1042-1049.
4. Werner, M. E., Knorn, A., Meredith A. L., Aldrich, R. W. and Nelson, M. T. (2006) Frequency encoding of cholinergic- and purinergic-mediated signaling to mouse urinary bladder smooth muscle: Modulation by BK channels. **American Journal of Physiology: Regulatory, Integrative and Comparative Physiology** 292:616-624 .
5. Filosa, J. A., Bonev, A. D., Straub, S. V., Meredith, A. L,. Aldrich, R. W. and Nelson, M. T. (2006) Local potassium signaling couples neuronal activity to vasodilation in the brain. **Nature Neuroscience** 9:1397-1403.
6. Sack, J. and Aldrich, R.W. Binding of a gating modifier toxin induces intersubunit cooperativity early in the Shaker K channels activation pathway. **Journal of General Physiology** 128:119-132, 2006.

7. Piskorowski, R.A., and Aldrich, R.W. Relationship between pore occupancy and gating in BK potassium channels. **Journal of General Physiology** 127:557-576, 2006.
8. Wilkins, C.M., and Aldrich, R.W. State independent block of BK channels by an intracellular quaternary ammonium. **Journal of General Physiology** 128:347-364, 2006.
9. Li, Weiyan and Aldrich R.W State dependent block of BK channels by synthesized Shaker ball peptides. **Journal of General Physiology** 128:423-441, 2006.
10. Fodor, A. and Aldrich, R.W. (2006) Statistical limits to the identification of ion channel domains by sequence similarity. **Journal of General Physiology** 127:755-766.
11. Thorneloe, K.S., Meredith, A.L., Aldrich, R.W. and Nelson, M.T. (2005) Urodynamic properties and neurotransmitter dependence of urinary bladder contractility in the BK channel deletion model of overactive bladder. **American Journal of Physiology, Renal Physiology** 289:604-610.
12. Werner, M.E., Zvara, P., Meredith, A.L., Aldrich, R.W., and Nelson M.T. (2005) Erectile dysfunction in mice lacking the large conductance calcium-activated potassium (BK) channel **Journal of Physiology** 567:545-556.
13. Brenner, R., Chen, Q.H., Vilaythong, A., Toney, G.N., Noebels, J.L., and Aldrich, R.W. BK channel beta4 subunit reduces dentate gyrus excitability and protects against temporal lobe seizures. **Nature Neuroscience** 8:1752-1759, 2005.
14. Wei, A. D., Gutman, G. A., Aldrich, R., Chandy, K. G., Grissmer, S. and Wulff, H. (2005) International Union of Pharmacology. LII. Nomenclature and Molecular Relationships of Calcium-Activated Potassium Channels. **Pharmacol Rev** 57:463-472.
15. Pyott, S.J., Glowatski, E., Trimmer, J.S. and Aldrich Extrasynaptic Localization of Inactivating Calcium-Activated Channels in Mouse Inner Hair Cells. **Journal of Neuroscience.** 24:9469-9474, 2004.

Prof. William N. Zagotta

Department of Physiology & Biophysics
University of Washington
Investigtor, HHMI/1993-2011

MOLECULAR MECHANISMS OF ION CHANNEL FUNCTION：

Ion channel proteins are the fundamental molecular elements for the control of membrane excitability and signaling in the nervous system. In response to one or more of a variety of stimuli, including neurotransmitters, voltage, and internal second messengers, ion channels open and allow the passage of certain selected ions across the cell membrane. In this way, channels can transduce these stimuli into changes in membrane potential and/or intracellular levels of calcium, the signals most used by the nervous system. The properties of each ion channel are highly specialized for its particular function. To this end, our long term goal is to determine the molecular mechanisms of the opening and closing conformational changes in ion channels. We have focused on a family of channels that is regulated by the direct binding of cyclic nucleotides, cAMP and cGMP. These channels play a fundamental role in the initial generation of an electrical signal in sensory receptors such as photoreceptors and olfactory receptors, and in the control of the pacemaker activity in cardiac and neuronal cells. To study the mechanism of gating by cyclic nucleotides, we employ a variety of approaches including electrophysiology, site-directed mutagenesis, protein chemistry, site-specific fluorescent labeling, and X-ray crystallography. By the combination of these approaches we believe we will be able to gain new insights into the molecular mechanisms for channel function.

Selective Publications:

1. Structural Mechanism for the Regulation of HCN Ion Channels by the Accessory Protein TRIP8b. DeBerg HA, Bankston JR, Rosenbaum JC, Brzovic PS, Zagotta WN, Stoll S. **Structure.** 2015 Apr 7; 23(4):734-44.
2. Double electron-electron resonance reveals cAMP-induced conformational change in HCN channels. Puljung MC, DeBerg HA, Zagotta WN, Stoll S. **PNAS** 2014 Jul 8; 111(27):9816-21.
3. Crystal structure of the plant dual-affinity nitrate transporter NRT1.1.. Sun J, Bankston JR, Payandeh J, Hinds TR, Zagotta WN, Zheng N. **Nature.** 2014 Mar 6; 507(7490):73-7.
4. Flavonoid regulation of HCN2 channels. Carlson AE, Rosenbaum JC, Brelidze TI, Klevit RE, Zagotta WN. **J Biol Chem.** 2013 Nov 15; 288(46):33136-45.
5. The structural mechanism of KCNH-channel regulation by the eag domain. Haitin Y, Carlson AE, Zagotta WN. **Nature.** 2013 Sep 19; 501(7467):444-8.
6. Structure of the C-terminal region of an ERG channel and functional implications.

Brelidze TI, Gianulis EC, DiMaio F, Trudeau MC, Zagotta WN. **Proc Natl Acad Sci U S A**. 2013 Jul 9; 110(28):11648-53.

7. Structure and stoichiometry of an accessory subunit TRIP8b interaction with hyperpolarization-activated cyclic nucleotide-gated channels. Bankston JR, Camp SS, DiMaio F, Lewis AS, Chetkovich DM, Zagotta WN. **Proc Natl Acad Sci U S A.** 2012 May 15; 109(20):7899-904.
8. Structure of the carboxy-terminal region of a KCNH channel. Brelidze TI, Carlson AE, Sankaran B, Zagotta WN. **Nature.** 2012 Jan 9; 481(7382):530-3.
9. Fluorescence applications in molecular neurobiology. Taraska JW, Zagotta WN. **Neuron.** 2010 Apr 29; 66(2):170-89.
10. Mapping the structure and conformational movements of proteins with transition metal ion FRET. Taraska JW, Puljung MC, Olivier NB, Flynn GE, Zagotta WN. **Nat Methods.** 2009 Jul; 6(7):532-7.
11. Structural dynamics in the gating ring of cyclic nucleotide-gated ion channels. Taraska JW, Zagotta WN. **Nat Struct Mol Biol.** 2007 Sep; 14(9):854-60.
12. Stoichiometry and assembly of olfactory cyclic nucleotide-gated channels. Zheng J, Zagotta WN. **Neuron.** 2004 May 13; 42(3):411-21.
13. Rod cyclic nucleotide-gated channels have a stoichiometry of three CNGA1 subunits and one CNGB1 subunit. Zheng J, Trudeau MC, Zagotta WN. **Neuron.** 2002 Dec 5; 36(5):891-6.
14. Rotational movement during cyclic nucleotide-gated channel opening. Johnson JP Jr, Zagotta WN. **Nature.** 2001 Aug 30; 412(6850):917-21.
15. Interdomain interactions underlying activation of cyclic nucleotide-gated channels. Varnum MD, Zagotta WN. **Science.** 1997 Oct 3; 278(5335):110-3.

Prof. Gary I. Yellen

Harvard University
HHMI, Investigator / 1986–1992

A major research focus of our lab was inspired by a remarkably effective but poorly understood therapy for epilepsy: the ketogenic diet. Used mainly for the many patients with drug-resistant epilepsy, this high fat, very low carbohydrate diet produces a dramatic reduction or elimination in seizures for most patients. We are investigating the possible role of metabolically-sensitive K+ channels (KATP channels) in the mechanism of the diet, and learning about their basic role in neuronal firing. We have discovered that certain fuel molecules that appear in the blood of people on the ketogenic diet – ketone bodies – can produce opening of KATP channels in various central neurons, which slows action potential firing and may contribute to the anticonvulsant mechanism.

How does ketone body metabolism lead to KATP channel opening? Our main hypothesis is that ketone bodies, or other metabolic manipulations, lead to a shift from glycolytic metabolism to other mechanisms of ATP production, and that glycolytic ATP production is particularly effective in preventing KATP channels from opening. To investigate this hypothesis and other questions in cellular metabolism, we are developing a series of fluorescent biosensors. Our first such sensor lets us visualize the local ratio of ATP:ADP in living cells. We are targeting this sensor to different cellular locations (plasma membrane, cytoplasm, mitochondria) to learn how energy production and consumption varies locally within neurons and other cells.

We also study the “moving parts” of functional ion channel proteins using single channel biophysics and directed mutagenesis. One strategy we use is to introduce individual cysteine residues into the channel protein; these cysteines serve as targets for chemical modification and for metal binding. Our ability to modify the introduced cysteines in different conformational states gives specific information about the functional motions of the protein. These methods are now being applied to elucidate the unusual gating of pacemaker channels, which are important generators of rhythmic electrical behavior in the heart and brain.

Selective Publications:

1. Shestov AA, Liu X, Ser Z, Cluntun AA, Hung YP, Huang L, Kim D, Le A, Yellen G, Albeck JG, Locasale JW. Quantitative determinants of aerobic glycolysis identify flux through the enzyme GAPDH as a limiting step. **Elife**. 2014 Jul 9:e03342.
2. Tantama M, Martínez-François JR, Mongeon R, Yellen G. Imaging energy status in live cells with a fluorescent biosensor of the intracellular ATP-to-ADP ratio. **Nat Commun.** 2013;4:2550.

3. Tantama M, Hung YP, Yellen G. Optogenetic reporters: Fluorescent protein-based genetically encoded indicators of signaling and metabolism in the brain. **Prog Brain Res.** 2012;196:235-63.
4. Giménez-Cassina A, Martínez-François JR, Fisher JK, Szlyk B, Polak K, Wiwczar J, Tanner GR, Lutas A, Yellen G*, Danial NN*. BAD-Dependent Regulation of Fuel Metabolism and KATP Channel Activity Confers Resistance to Epileptic Seizures. **Neuron** 2012 May 24;74(4):719-730.
5. Hung YP, Albeck JG, Tantama M, Yellen G. Imaging Cytosolic NADH-NAD+ Redox State with a Genetically Encoded Fluorescent Biosensor. **Cell Metab.** 2011 Oct 5;14(4):545-54.
6. Tantama M, Hung YP, Yellen G. Imaging intracellular pH in live cells with a genetically encoded red fluorescent protein sensor. **J Am Chem Soc.** 2011 Jul 6;133(26):10034-7.
7. Berg J, Hung YP, Yellen G. A genetically encoded fluorescent reporter of ATP:ADP ratio. **Nat Methods.** 2009 Feb;6(2):161-6. Epub 2009 Jan 4.
8. Webster SM, Del Camino D, Dekker JP, Yellen G. Intracellular gate opening in Shaker K+ channels defined by high-affinity metal bridges. **Nature.** 2004 Apr 22;428(6985):864-8.
9. Shin KS, Maertens C, Proenza C, Rothberg BS, Yellen G. Inactivation in HCN channels results from reclosure of the activation gate: desensitization to voltage. Neuron. 2004 Mar 4;41(5):737-44.
10. Yellen G. The voltage-gated potassium channels and their relatives. **Nature.** 2002 Sep 5;419(6902):35-42.
11. del Camino D, Holmgren M, Liu Y, Yellen G. Blocker protection in the pore of a voltage-gated K+ channel and its structural implications. **Nature.** 2000 Jan 20;403(6767):321-5.
12. Holmgren M, Shin KS, Yellen G. The activation gate of a voltage-gated K+ channel can be trapped in the open state by an intersubunit metal bridge. **Neuron.** 1998 Sep;21(3):617-21.
13. Smith PL, Baukrowitz T, Yellen G. The inward rectification mechanism of the HERG cardiac potassium channel. **Nature.** 1996 Feb 29;379(6568):833-6.
14. Yellen G, Jurman ME, Abramson T, MacKinnon R. Mutations affecting internal TEA blockade identify the probable pore-forming region of a K+ channel. **Science.** 1991 Feb 22;251(4996):939-42.
15. MacKinnon R, Yellen G. Mutations affecting TEA blockade and ion permeation in voltage-activated K+ channels. **Science.** 1990 Oct 12;250(4978):276-9.

Prof. Steve A. N. Goldstein

Provost of Brandeis University

Dr. Goldstein earned B.A. and M.A. degrees in biochemistry in 1978, graduating Phi Beta Kappa. Dr. Goldstein holds an M.D. and Ph.D. in immunology from Harvard University and is an accomplished scientist and scholar. From 1993 to 2004, Dr. Goldstein was on the faculty at the Yale University School of Medicine and founded the Section of Developmental Biology and Biophysics. In 2004, he moved to the University of Chicago to become Chair of the Department of Pediatrics and Physician-in-Chief at Comer Children's Hospital. While at Chicago he founded the Institute for Molecular Pediatric Sciences and cofounded the Institute for Translational Medicine. He is a fellow of the American Academy of Pediatrics and in 2001 received the E. Mead Johnson Award for pediatric research. From 2002 to 2007, he was editor-in-chief of the Quarterly Review of Biophysics.

Research in the Goldstein lab is directed towards understanding how ion channels operate in health and illness. These integral membrane proteins catalyze the selective transfer of ions across membranes and, like enzymes, show exquisite specificity and tight regulation. As a class, ion channels orchestrate the electrical activity that allows operation of the heart, nervous system and skeletal muscles--even the signals in T cells require ion channels. Less sensational but equally important, ion channels mediate cellular fluid and electrolyte homeostasis. Remarkably, fundamental questions remain to be answered. How do ion channels open and close? What is their architecture? How do mutations produce cardiac arrhythmia, hypertension, seizures, or deafness? How do drugs act to produce beneficial outcomes (~20% of our current pharmacopeia targets ion channels) or to yield undesirable side effects? Our laboratory uses macroscopic and single molecule electrophysiology and spectroscopy, molecular genetics, high-throughput and structural methods to pursue five research directions:
(1) Accessory Subunits—discovery, roles in health and disease, and structural basis for function; (2) The K2Ps—discovery of a family of potassium channels that produce background currents; (3) SUMO—a pathway is discovered to control the activity of ion channels at the cell surface; (4) Development of new genetic and high throughput methods for ion channels; (5) Mechanism, diagnosis and treatment for ion channel disease.

Selective Publications:

1. Plant LD, Xiong D, Dai H, Goldstein SA. "Individual IKs channels at the surface of mammalian cells contain two KCNE1 accessory subunits." **PNAS** 8; 111(14):

(2014)
2. Ruscic, K.J., Miceli, F., Villalba-Galea, C.A., Dai, H., Mishina, Y., Bezanilla, F. and Goldstein, Steve A. N. "IKs channels open slowly because KCNE1 accessory subunits slow the movement of S4 voltage sensors in KCNQ1 pore-forming subunits." **PNAS** 10. 1073 (2013).
3. Takacs, Z., Toups, M., Kollewe, A., Johnson, E., Cuello, L.G., Driessens, G., Biancalana, M., Koide, A., Ponte, C.G., Perozo, E., Gajewski, T.F., Suarez-Kurtz, G., Koide, S., and Goldstein, Steve A. N. "A designer ligand specific for Kv1.3 channels from a scorpion neurotoxin-based library." **PNAS** 106. 1 (2009): 22211-6.
4. Thomas, D., Plant, L.D., Wilkens, C.M., McCrossan, Z.A. and Goldstein, Steve A. N. "Alternative translation initiation in rat brain yields K2P2.1 potassium channels permeable to sodium." **Neuron** 58. 1 (2008): 859-870.
5. Plant, L.D., P.N. Bowers, Q. Liu, T. Morgan, T. Zhang, M.W. State, W. Chen, R.A. Kittles and Goldstein, Steve A. N.. "A common cardiac sodium channel variant associated with sudden infant death in African Americans, SCN5A S1103Y." **J. Clin Invest** 116. 1 (2006): 430-435.
6. Rajan, S,L., Plant, M.L. Rabin, M.H. Butler, and Goldstein, Steve A. N.. "Sumoylation silences the plasma membrane leak K+ channel K2P1." **Cell** 121. 1 (2005): 37-47.
7. Chen, H., Kim, L.A., Rajan, S., Xu, S and Goldstein, Steve A. N. "Charybdotoxin binding in the IKs pore demonstrates two MinK subunits in each channel complex." **Neuron** 40. 1 (2003): 15-23.
8. O'Kelly, I., Butler, M.H., Zilberberg, N. and Goldstein, Steve A. N. "Forward Transport: 14-3-3 binding overcomes dibasic retention in endoplasmic reticulum by dibasic signals." **Cell** 111. 1 (2002): 577-588.
9. Abbott, G. W., Butler, M. H., Bendahhou, S., Dalakas, M. C., Ptacek, L. J., and Goldstein, Steve A. N. "MiRP2 forms potassium channels in skeletal muscle with Kv3.4 and is associated with periodic paralysis." **Cell** 104. 1 (2001): 217-231.
10. Bockenhauer, D., Zilberberg, N. and Goldstein, Steve A. N. "Reversible conversion of a hippocampal potassium leak into a voltage-dependent channel by phosphorylation." **Nature Neurosci** 4. 1 (2001): 486-491.
11. Abbott, G. W., Sesti, F., Splawski, I., Buck, M., Lehmann, M. H., Timothy, K. W., Keating, M. T. and Goldstein, Steve A. N.. "MiRP1 forms IKr potassium channels with HERG and is associated with cardiac arrhythmia." **Cell** 97. 1 (1999): 175-186.
12. Ketchum, K. A., W. J. Joiner, A. J. Sellers, L. K. Kaczmarek and Goldstein, Steve A. N.. "A new family of outwardly rectifying potassium channel proteins with two pore domains in tandem." **Nature** 376. 1 (1995): 690-5.

Dr. Kenton J. Swartz

Senior Investigator
Molecular Physiology and Biophysics Section
NINDS

Dr. Swartz received his B.S. degree in Chemistry and Biology in 1986 from Eastern Mennonite College. In 1992 he received his Ph.D. in Neurobiology from Harvard University where he worked with Bruce Bean studying the regulation of voltage-gated calcium channels by G-proteins and protein kinases. He did postdoctoral training with Roderick MacKinnon at Harvard Medical School, where he began isolating and studying toxins that interact with voltage-activated potassium channels. Dr. Swartz joined NINDS as an Investigator in 1997 and was promoted to Senior Investigator in 2003. His laboratory is using biochemical, molecular biological and biophysical techniques to investigate the structure of voltage-activated ion channels and to explore the molecular mechanics by which these channels gate.

Research Topics

Voltage-gated ion channels are expressed in many cells types and are important for an array of physiological processes, including the generation and processing of electrical signals in the nervous system, regulation of heart contraction and secretion of hormones. The role of these channels in electrical signaling is particularly important because they open and close in response to changes in membrane voltage. For example, action potentials result from the orchestrated action of voltage-gated sodium and potassium channels, and voltage-gated calcium channels convert electrical to chemical signals in the process of excitation-secretion coupling. The three main classes of voltage-gated ion channels belong to a common family of membrane proteins constructed from two types of domains: a central pore domain where the conduction pathways for potassium, sodium or calcium ions reside, and four surrounding voltage-sensing domains. A major focus of the lab is to explore the structure of the voltage-sensing domains in voltage-gated potassium (Kv) channels and to define how and where the voltage-sensors interact with the gate region of the pore domain. A complementary aim is to study protein toxins that interact with voltage-gated ion channels. Our work with a class of toxins that we refer to as gating modifier toxins has begun to reveal new mechanisms by which channel-interacting proteins modify activity and to shed light on several fundamental questions concerning the process of voltage-sensing. Since many drugs affecting the nervous system derive their efficacy by modulating the gating of voltage-gated channels, we continue to search for new molecules that interact with these channels and to study the molecular basis for their actions.

Selective Publications:

1. Alabi, A.A., Bahamonde, M.I., Jung, H.J., Kim, J.I., and Swartz, K.J. (2007) Portability of paddle motif function and pharmacology in voltage sensors. **Nature,** 450, 370-375.
2. Krepkiy, D., Mihailescu, M., Freites, J.A., Schow, E., Worcester, D.L., Gawrisch, K., Tobias, D., White, S.H., and Swartz, K.J. (2009) Structure and hydration of membranes embedded with voltage-sensing domains. **Nature,** 462, 473-479.
3. Bosmans, F., Martin-Eauclaire, M.F. and Swartz, K.J. (2008) Deconstructing voltage sensor function and pharmacology in sodium channels. **Nature,** 456, 202-208.
4. Phillips, L.R., Milescu, M., Li-Smerin, Y., Mindell, J., Kim, J.I. and Swartz, K.J. (2005)Voltage-sensor activation with a tarantula toxin as cargo **Nature,** 436, 857-860.
5. Li, M., Chang, T-H., Silberberg, S.D. and Swartz, K.J. (2008) Gating the pore of P2X receptor channels. **Nature Neuroscience,** 11, 883-887.
6. Li, M, Kawate, T, Silberberg, S and Swartz, KJ (2010) Pore-opening mechanism in trimeric P2X receptor channels. **Nature Communications,** 1, 44.
7. Kalia, J. and Swartz, K.J. (2013) The design principle of paddle motifs in voltage sensors. **Nature Struct Mol Biol,** 20, 534-5.
8. Lee, S, Milescu, M, Jung, HH, Lee, JY, Bae, CH, Lee, CW, Kim, HH, Swartz, KJ and Kim, JI (2010) Solution structure of GxTX-1E, a high-affinity tarantula toxin interacting with voltage senors in Kv2.1 potassium channels. **Biochemistry,** 49, 5134-42.
9. Heymann, G., Dai, J., Li, M., Silberberg, S.D., Zhou, H-X. and Swartz, K.J. (2013) Inter- and intrasubunit interactions between transmembrane helices in the open state of P2X receptor channels. **PNAS.**
10. Li, M., Silberberg, S.D. and Swartz, K.J. (2013) Subtype-specific control of P2X receptor channel signaling by ATP and magnesium. **PNAS,** 110, E3455-63.
11. Krepkiy, D., Gawrisch, K. and Swartz K.J. (2012) Structural interactions between lipids, water and S1-S4 voltage-sensing domains. **J Mol Biol**, 423, 632-647.
12. Toombes, E.S. and Swartz, K.J. (2014) Divining the design principles of voltage sensors. **J Gen Physiol.**
13. Milescu, M., Lee, H.W., Bae, C., Kim, J.I. and Swartz, K.J. (2013) Opening the Shaker Kv channel with hanatoxin. **J Gen Physiol**, 141, 203-16.
14. Kalia, J. and Swartz, K.J. (2013) Common principles of voltage-dependent gating in Hv and Kv channels. **Neuron,** 77, 214-16.
15. Swartz KJ (2013) The scorpion toxin and the potassium channel. **eLife,** May 21;2:e00873.

Prof. Isaac Pessah

Ph.D. Univ. Maryland
Associate Dean for Research and Graduate Education
Deputy Director, Center for Children's Environmental Health and Disease Prevention
School of Veterinary Medicine

Dr. Pessah is a leading international expert on calcium signaling in brain and muscle cells and ryanodine receptor research.
Professor Isaac Pessah earned B.S. degrees in Cornell University in 1977.and holds an M.S. and Ph.D. in Toxicology from University Maryland and is an accomplished scientist and scholar. 2012 NIH Honor Isaac Pessah has accepted the invitation of the NIH Center for Scientific Review to serve in the Neurotoxicology and Alcohol Study Section from July 2012 through June 2016. Members are selected for the quality of their research accomplishments, publications in scientific journals, and other significant scientific activities, achievements and honors. Pessah's participation is important in assuring the quality of the NIH peer review process. Membership in this group is both an honor and a major commitment of professional time and energy resulting in a unique opportunity to contribute to the national biomedical research effort.

Research Topics

Dr. Pessah is a toxicologist with research interest in the area of molecular and cellular mechanisms regulating signaling in excitable cells. His current research focuses on the structure, function, and pharmacology of the ryanodine-sensitive calcium channels (RyRs) found in sarcoplasmic and endoplasmic reticulum of muscle cells and neurons. His laboratory is actively studying how dysfunction of RyR complexes contribute to genetic diseases and how genetic alteration of RyRs and environmental factors interact to influence neurodevelopment by utilizing cellular, biochemical and molecular investigations of calcium-signaling pathways. Dr. Pessah has developed a strong, collaborative and interdisciplinary research program with colleagues across the university, as well as nationally and internationally. He is director of The Center for Children's Environmental Health and Disease Prevention, and a member of the MIND Institute.

Selective Publications:

1. Niknam Y, Feng W, Cherednichenko G, Dong Y, Joshi SN, Vyas SM, Lehmler HJ, Pessah IN: Structure-activity relationship of selected meta- and para-hydroxylated non-dioxin like polychlorinated biphenyls: from single RyR1 channels to muscle dysfunction. **Toxicol Sci** 2013, 136:500-513.
2. Girirajan S, Johnson RL, Tassone F, Balciuniene J, Katiyar N, Fox K, Baker C,

Srikanth A, Yeoh KH, Khoo SJ, et al: Global increases in both common and rare copy number load associated with autism. **Hum Mol Genet** 2013, 22:2870-2880.

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Selective Publications:

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Research in his lab is toward the Ion channels are membrane proteins that facilitate ion flux into or out of the cell or its organelles. They play critical roles in fundamental cellular functions such as neuronal signaling, muscle contraction, secretion, and fertilization. The long term goal of my research is to understand the molecular mechanisms underlying the opening and closing of the ion permeation pathway in channels, and how this process is controlled by various physical and chemical stimuli. Malfunctions of the ion channel activation process caused by genetic and pathological factors are the basis for numerous human diseases including long QT syndrome, cystic fibrosis, epilepsy, schizophrenia and deficiency in learning and memory. Research in my lab focuses on the heat activation of thermoTRP channels, which serve as biosensors for ambient temperature as well as noxious (painful) stimuli. We use multidisciplinary approaches to investigate the structural basis, functional properties, and regulation of the highly temperature-dependent activation process.

Selective Publications:

1. Yang, F., X. Xiao, W. Cheng, W. Yang, P. Yu, Z. Song, V. Yarov-Yarovoy, J. Zheng (2015), Structural mechanism underlying capsaicin binding and activation of nociceptive TRPV1 ion channel, **Nature Chemical Biology,** (in press).
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