Biophysical Society

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Biophysical Society Announces New and Notable Symposium Speakers

Rockville, MD— The Biophysical Society has announced the speakers for the New and Notable Symposium at the Society's 56th Annual Meeting in San Diego, California. The New and Notable Symposium highlights the latest and most exciting discoveries in biophysics. Speakers are nominated by the Society's membership and selected by the Program Committee. Over 250 nominations were received this year. The session will take place on Sunday, February 26, 2012, 10:45 AM–12:45 PM in Ballroom 20D of the San Diego Convention Center.

In putting the session together, William Zagotta and Sharona Gordon, both of the University of Washington and Co-Chairs of the Symposium and the Program Committee, noted, "We are excited by the diverse new work that will be presented at this year's New and Notable Symposium. From single-molecule studies through male fertility, the seven presentations will show off the breadth of fields represented by the Biophysical Society and the rigor of the biophysical approach. We are particularly proud to feature a number of junior investigators."

New and Notable Symposium Speakers and Information:

SINGLE-BASE PAIR UNWINDING AND ASYNCHRONOUS RNA RELEASE BY THE HEPATITIS C VIRUS NS3 HELICASE
Wei Cheng, University of Michigan
Nonhexameric helicases use adenosine triphosphate (ATP) to unzip base pairs in double-stranded nucleic acids (dsNAs). Studies have suggested that these helicases unzip dsNAs in single–base pair increments, consuming one ATP molecule per base pair, but direct evidence for this mechanism is lacking. Dr. Cheng and his colleagues used optical tweezers to follow the unwinding of double-stranded RNA by the hepatitis C virus NS3 helicase. Single–base pair steps by NS3 were observed, along with nascent nucleotide release that was asynchronous with base pair opening. Asynchronous release of nascent nucleotides rationalizes various observations of its dsNA unwinding and may be used to coordinate the translocation speed of NS3 along the RNA during viral replication.

PIEZOS ARE PORE-FORMING SUBUNITS OF MECHANICALLY ACTIVATED CHANNELS
Bertrand Coste, The Scripps Research Institute
Mechanotransduction plays a crucial role in physiology. Biological processes including sensing touch and sound waves require yet unidentified cation channels that detect pressure. Mouse piezo1 (mpiezo1) and mpiezo2 induce mechanically activated cationic currents in cells; however, it is unknown if piezos are pore-forming ion channels or modulate ion channels. Dr. Coste and his colleagues show that Drosophila piezo (dpiezo) also induces mechanically activated currents in cells, but through channels with remarkably distinct pore properties including sensitivity to the pore blocker ruthenium red and single channel conductances. mpiezo1 assembles as a ~1.2 million-Dalton tetramer, with no evidence of

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other proteins in this complex. Finally, purified mpiezo1 reconstituted into asymmetric lipid bilayers and liposomes forms ruthenium red-sensitive ion channels. These data demonstrate that piezos are an evolutionarily conserved ion channel family involved in mechanotransduction.

THE CRYSTAL STRUCTURE OF A CONCENTRATIVE NUCLEOSIDE TRANSPORTER
Seok-Yong Lee, Duke University

Concentrative nucleoside transporters are integral membrane proteins that are responsible for the selective uptake of nucleosides and nucleoside-derived anticancer and antiviral drugs into cells using the energy of ion gradients. The structural basis for selective ion-coupled nucleoside transport is unknown. Dr. Lee and his colleagues recently determined the crystal structure of a concentrative nucleoside transporter from Vibrio cholerae in complex with uridine at 2.4 A resolution. Combined with their functional data the structure reveals the overall architecture of this class of transporter for the first time, unravels the molecular determinants for nucleoside and ion binding, and provides a framework for understanding the mechanism of nucleoside and nucleoside-derived anticancer and antiviral drug transport across cell membranes.

REGULATION OF SPERM ION CHANNELS BY FEMALE HORMONE PROGESTERONE AS A DETERMINANT OF MALE FERTILITY
Polina Lishko, University of California, Berkeley
Dr. Lishko is combining human genetics with physiological studies and will present new data about functioning of sperm ion channels in healthy individuals and patient with sperm ion channel defect. Sperm ability to reach and fertilize the egg is under tight control of sperm ion channels. They regulate sperm maturation in the female reproductive tract and trigger key physiological responses required for successful fertilization such as hyperactivated motility, chemotaxis, and the acrosome reaction. A pH-regulated, calcium-selective ion channel CatSper, and potassium channel KSper (Slo3) are core regulators of sperm tail calcium entry and potassium efflux respectively, and play role in regulation of sperm hyperactivated motility and the acrosome reaction. With the development of the sperm patch-clamp technique, CatSper and KSper have been confirmed as the primary sperm ion channels. Moreover, human CatSper serves as a non-genomic progesterone receptor and is the first calcium ion channel which is opened by picomolar concentrations of progesterone. In addition, the voltage-gated proton channel Hv1 has been identified in human sperm tail. Mutations and deletions in sperm-specific ion channels affect male fertility in both mice and humans without affecting other physiological functions. The uniqueness of sperm ion channels makes them ideal pharmaceutical targets for contraception.

SUBNANOMETER STRUCTURE OF THE ACTIN/MYOSIN/TROPOMYOSIN COMPLEX
Stefan Raunser, Max Plank Institute of Molecular Physiology, Germany
Dr. Raunser’s cryo-EM structure of the actin-tropomyosin-myosin complex provides novel insights into the interaction between actin, myosin and tropomyosin. The pseudo-atomic model of the complex obtained from fitting crystal structures into the map defines the large actin-myosin-tropomyosin interface and the molecular interactions between the proteins in detail. It indicates that the N-terminus of actin is involved in this interaction. The data of Dr. Raunser and his colleagues suggest that tropomyosin is stabilized by electrostatic teractions with myosin and likely slides rather than rolls on F-actin when moving from the blocked to the myosin-bound state. These are all novel, important and exiting findings that would be for sure of high interest for a broad audience.

MASS SPECTROMETRY OF INTACT MEMBRANE COMPLEXES

Carol Robinson, University of Oxford, United Kingdom

The electrospray of intact proteins was first described in 1989. Some two decades later, and after many intact soluble complexes have been transmitted into the gas phase, it has finally become possible to “fly” an intact membrane embedded motor. Given the very high concentrations of detergent necessary to maintain solubility of these complexes such an observation had seemed unattainable. In this lecture Dr. Robinson will outline the developments that have made this possible and show how studying intact rotary ATPases in the gas phase is shedding new light on the importance of lipid binding for their regulation and control. She will also highlight very recent advances in which have been able to address the role of lipids in stabising mechansosensitve channels and in assessing lipid-mediated drug binding in multidrug efflux pumps.

A DUAL EFFECT OF THE BIOACTIVE LIPID LPA ON TRPV1 ACTIVATION

Tamara Rosenbaum, National Autonomous University of Mexico

For the last two decades there has been growing evidence that the bioactive phospholipid, lysophosphatidic acid (LPA), whose levels are increased upon tissue injury, activates primary nociceptors resulting in neuropathic pain. The TRPV1 ion channel is expressed in primary afferent nociceptors and is activated by physical and chemical stimuli. Dr. Rosenbaum and her colleagues have shown that LPA produces acute pain-like behaviors in normal mice, which are substantially reduced in Trpv1 null- mice. Their data also demonstrate that LPA activates TRPV1 through a novel mechanism that is independent of G protein-coupled receptors, contrary to what has been widely shown for other ion channels, by directly interacting with the C-terminus of the channel. Dr. Rosenbaum and her colleagues conclude that TRPV1 is a direct molecular target of the pain-producing molecule LPA and this constitutes the first example of LPA binding directly to an ion channel to acutely regulate its function. Moreover, their unpublished data also demonstrate that LPA can modulate singlechannel properties of the TRPV1 by increasing its conductance, constituting the first example of a lipid modulating TRPV1 unitary conductance.