Biophysical Society

Biophysical Society 60th Meeting, Feb. 27 - March 2, 2016, Los Angeles

Demystifying Mechanotransduction Ion Channels

A group of researchers in China has discovered how mysterious mechanosensitive channels, a family of Piezo proteins, respond to mechanical force and, consequently, conduct ions for biological functions

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WASHINGTON, D.C., February 25, 2016 -- As blood flows through our vessels, the cells that constitute these vessels responds to the shear stress of blood flow to ensure normal circulation. This process of converting a mechanical force into a biological function is known as "mechanotransduction."

But a bit of mystery has enshrouded the type of specialized mechanotransducers—force sensors—underlying the process and how they're able to sense a force and, subsequently, transduce to downstream biological functions.

During the Biophysical Society's 60th Annual Meeting, being held in Los Angeles, Calif., Feb. 27-March 2, 2016, Bailong Xiao, an associate professor at Tsinghua University's School of Pharmaceutical Sciences, in Beijing, China, will share a big discovery made while exploring how newly identified mechanotransducers function at the molecular level.

"Mechanosensitive channels represent a class of ion channels that respond to mechanical force stimulation and allow ions to enter or exit cells," explained Xiao. "They are suspected of serving as key

mechanotransducers for mechanotransduction, but the molecular identities of mechanosensitive cation channels in mammals were unknown until the identification of the evolutionarily conserved Piezo family of proteins—including Piezo1 and Piezo2—by Dr. Ardem Patatpoutian's lab at the Scripps Research Institute in 2010."

Since then, it's been shown that Piezo proteins play critical roles in various mechanotransduction processes. "Piezo1, for example, plays a key role in sensing blood-flow-associated shear stress and, consequently, controlling vascular development and function," he said. "In humans, mutations of Piezo1 or Piezo2 genes have been linked to genetic diseases."

Piezo proteins are complex transmembrane proteins that don't possess notable sequence homology with any known class of ion channels. "These features make it difficult to study their structure-function relationship using traditional site-directed mutagenesis approaches," Xiao elaborated. "While working in Patatpoutian's lab as a postdoctoral fellow, we previously demonstrated that Piezo1 proteins form a novel class of ion channels." This work was published in the journal Nature in 2012, and Xiao was co-first author.

But fundamental questions remained unanswered, among them: How do these proteins three-dimensionally organize into mechanosensitive channels? How do they conduct ions and respond to force stimulation?

After setting up his own lab at Tsinghua University in Beijing, Xiao began tackling these questions.

In a paper the group published in Nature in 2015, along with collaborators at the university, they reported resolving the cryo-electron microscopy (cryo-EM) structure of the full-length mouse Piezo1.

Now in a paper published online in Neuron on Feb. 25, 2016, the group reports "functionally identifying bona-fide ion-conducting pore and mechanotransduction components," Xiao said. "Our findings demonstrate that Piezo1 proteins consist of distinct and separate modules responsible for ion conduction, mechanical force sensing and transduction to coordinately fulfill their function as sophisticated mechanosensitive channels."

This is consistent with the structural organization of these functional modules into a unique three-bladed, propeller-shaped architecture of Piezo1, according to Xiao. "Our studies significantly advance our mechanistic understanding of how this evolutionarily conserved and physiologically important class of mechanosensitive channels respond to mechanical force and, consequently, conduct ions for biological functions," he added.

In terms of applications, his group's studies "help us understand the specialized force sensors such as Piezo1 ion channels that play critical roles in vascular development and blood cell function, which might enable us to design novel therapeutics in the future to treat diseases caused by abnormal functions of these mechanotransducers," Xiao said.

Next, Xiao and his group are planning more mechanistic studies to gain a better understanding of the mechanosensitive channels and to identify ways to manipulate their functions. "In the long run, we hope to develop novel therapeutics by targeting these mechanosensors," he said.

Presentation #1722, "Structural and functional characterizations of the mechanosensitive piezo channel," is authored by Bailong Xiao. It will be at 9:45 a.m. PT on Tuesday, March 1, 2016 in Room 515B of the Los Angeles Convention Center. ABSTRACT: http://tinyurl.com/jdl83lw

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MORE MEETING INFORMATION

ABOUT THE MEETING

Each year, the Biophysical Society Annual Meeting brings together more than 6,500 researchers working in the multidisciplinary fields representing biophysics. With more than 3,600 poster presentations, over 200 exhibits, and more than 20 symposia, the BPS Annual Meeting is the largest meeting of biophysicists in the world. Despite its size, the meeting retains its small-meeting flavor through its subgroup symposia, platform sessions, social activities and committee programs. The 60th Annual Meeting will be held at the Los Angeles Convention Center.

PRESS REGISTRATION

The Biophysical Society invites professional journalists, freelance science writers and public information officers to attend its Annual Meeting free of charge. For press registration, contact Ellen Weiss <EWeiss@biophysics.org> or the media line at the American Institute of Physics at <media@aip.org> or 301-209-3090.

NEWS RELEASES

Embargoed press releases describing in detail some of the breakthroughs to be discussed at the meeting are available on Eurekalert, Newswise and Alpha Galileo or by contacting the media line at the American Institute of Physics at <media@aip.org> or 301-209-3090.

QUICK LINKS

Main Meeting Page: http://tinyurl.com/hewekyj
Symposia: http://tinyurl.com/h7lnk4p
Itinerary planner: http://tinyurl.com/hslnx3p

ABOUT THE SOCIETY

The Biophysical Society, founded in 1958, is a professional, scientific Society established to encourage development and dissemination of knowledge in biophysics. The Society promotes growth in this expanding field through its annual meeting, monthly journal, and committee and outreach activities. Its 9,000 members are located throughout the U.S. and the world, where they teach and conduct research in colleges, universities, laboratories, government agencies, and industry. For more information on the Society, or the 2016 Annual Meeting, visit http://www.biophysics.org

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