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EDITORIAL

An international gathering of physiologists in Valparaiso, Chile

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The June issue of the *Journal of General Physiology* is a collection of peer-reviewed articles contributed by participants of the very special Society of General Physiologists (SGP) 73rd Annual Symposium, which was hosted jointly with the Society of Latin American Biophysicists (SOBLA). This unique joint meeting took place in Valparaiso, Chile, on September 4–7, 2019, marking the first time that the SGP Annual Symposium was held outside of its traditional location of Woods Hole, MA. Organizers from Chile (Ramon Latorre) and the US (Jorge Contreras, Miguel Holmgren, and Brad Rothberg) worked to bring together more than 150 scientists and trainees to discuss cutting-edge research on ion channel physiology and to foster novel interdisciplinary collaborations. The success of this meeting reflects and strengthens the long-standing relationship between SGP and SOBLA.

This issue features four original articles. Zhang, 2020 describe a remarkable advance in visualization of cellular transmembrane proton fluxes. This technique was developed by the Kobertz laboratory (University of Massachusetts Medical School) in an international collaboration with the research groups of Castro and Brauchi (Millennium Nucleus of Ion Channel-Associated Diseases [MiNiCAD], Universidad Austral de Chile). The technique exploits the chemistry of the glycocalyx, a matrix of carbohydrates tethered to the extracellular portions of membrane proteins, which is common to most eukaryotic cells and some bacteria. Zhang et al.'s approach involves derivatizing the lectin wheat germ agluttinin (WGA) with a pH-sensitive rhodamine (Zhang, 2020). Because WGA binds very tightly to the glycocalyx, it is ideal for the uniform deployment of the fluorescent pH-sensor over the entire cell surface. By imaging changes in rhodamine fluorescence, the authors were able to detect pericellular proton accumulation and depletion in several cell types. By derivatizing WGA with other fluorescent ion sensors, this method could be useful for visualization and measurement of a range of pericellular ion fluxes in many cells and tissues.

The contribution from Suárez-Delgado, 2020 analyzes mechanisms underlying slow inactivation in mammalian $K_V1.2$ channels. Whereas slow inactivation has been studied in detail in the *Drosophila Shaker* channel, $K_V1.2$ is the only *Shaker*-like K_V channel whose structure has been solved at atomic detail, and the functional details of slow inactivation in $K_V1.2$ channels is not well characterized. In this study from the Islas and Rosenbaum laboratories (Universidad Nacional Autónoma de México), the investigators found that wild type $K_V1.2$ channels undergo slow (C-type) inactivation with slower kinetics than *Shaker*, whereas mutations in $K_V1.2$ at amino acid positions W366 and V381, analogous to W434 and T449 in *Shaker*, could strongly modulate the rate of $K_V1.2$ C-type inactivation. These new results facilitate interpretations of the structural basis for slow inactivation in mammalian $K_V1.2$ channels.

Two offerings in this issue present studies on control of gating in large conductance Ca^{2+}-activated K^+ channels (BK channels). BK channel activation is critical for smooth-muscle relaxation in bladder and cerebral resistance arteries, as well as for controlling action-potential duration in some neurons. Not surprisingly, defects in BK channel gating are implicated in human diseases, including epilepsy, cancer, diabetes, asthma, and hypertension. Expansion of our understanding of BK channel pharmacology, as well as its interaction with endogenous signaling proteins, will be important to development of treatments for disease. In this issue, Rockman, 2020, from Temple University School of Medicine, present an analysis of the molecular action of the smooth muscle relaxant NS11021 on BK channels. By analyzing channel gating kinetics over a wide range of $[Ca^{2+}]$ and membrane voltages, these authors identified the central pore domain of the channel as the primary locus for the drug's major effects (see also Cui, 2020). Kshatri, 2020

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examine modulation of BK channel gating by the RNA-binding protein FMRP, whose deletion (or loss-of-function) results in fragile X syndrome. The authors, from the Giraldez laboratory (University of La Laguna), show that FMRP coexpression has an activating effect on BK channels. Based on quantitative analysis of BK channel gating, the authors hypothesize that FMRP activates the channels through driving the pore domain toward the open state and driving the channel's voltage-sensing domains toward the activated state. The authors further show, by super-resolution microscopy, that FMRP form complexes with BK channels. These results support the idea that FMRP may regulate neuronal excitability at least partially through interactions with BK channels. Together these studies represent advances toward our understanding of BK gating mechanisms and how gating defects may be mitigated in treatment of disease.

The work presented in this special issue is representative of the spirit of international collaboration within the ion channel field, and it celebrates a memorable gathering of scientists in an effort to support a trusted global scientific community.

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