Paul F. Cranefield Award to Matthew Trudeau

The late Paul F. Cranefield, MD, PhD, was the editor of *The Journal of General Physiology* from 1966 to 1995. During this time, he worked tirelessly to advance the mission of the Journal: to promote and publish original research of the highest quality that elucidates basic biological, chemical, or physical mechanisms of broad physiological significance, and provides insight into fundamental mechanisms that govern biological function at all levels.

When Dr. Cranefield stepped down as editor, the Council of the Society of General Physiologists created the Paul F. Cranefield Award to recognize his enduring contributions to the Journal and the Society, and to carry on his vision of excellence. The award was to be given to an early career, independent investigator who in the preceding year published an article of exceptional quality in the Journal. The Council also decided that the criteria for selecting the awardee should be so stringent that the award might not be given every year.

In 2014, the Council selected Matthew C. Trudeau of the University of Maryland for the Cranefield Award. Dr. Trudeau received his PhD in 1998 from the University of Wisconsin. His thesis work, with Dr. Gail A. Robertson, focused on the voltage-gated human ether-á-go-go–related gene (hERG) potassium channel and related channels, including the role of hERG in acquired and inherited cardiac arrhythmia (Trudeau et al., 1995; Furutani et al., 1999) and mechanisms of hERG channel inactivation and closing (deactivation) (Herzberg et al., 1998; Wang et al., 1998). As a postdoctoral fellow, with Dr. William N. Zagotta at the University of Washington, Dr. Trudeau studied retinal rod cyclic nucleotide–gated (CNG) channels, including their role in an inherited form of vision loss (Trudeau and Zagotta, 2002a), their unusual 3:1 subunit stoichiometry (Zheng et al., 2002), and their modulation by Ca^{2+}-calmodulin (Trudeau and Zagotta, 2002b, 2004). These studies involved a combination of protein chemistry, electrophysiology, and advanced fluorescence imaging methods that Dr. Trudeau would later apply to hERG in his own laboratory. Dr. Trudeau was appointed assistant professor of physiology at the University of Maryland, Baltimore in 2004, and promoted to associate professor in 2012.

Dr. Trudeau was given the Cranefield Award for a paper (Gianulis et al., 2013) that investigated the unusually slow deactivation kinetics of hERG channels, a property critical for delayed entry of potassium and membrane repolarization during the cardiac action potential. The first author of the paper, Elena Gianulis, PhD, was awarded the Graduate Student Cranefield Award for her contribution. The paper addressed a controversy regarding the molecular mechanism by which the N-terminal eag domain of hERG regulates deactivation (see Commentary by Zheng, 2013). The authors used patch-clamp recording and spectral FRET analysis to determine which regions of hERG interact with the eag domain to regulate deactivation in functional channels at the plasma membrane. They found that, in channels lacking the C-terminal cyclic nucleotide–binding homology domain (CNBHD), both regulation of gating by a recombinant eag domain and its association with the channel were disrupted. Additional functional and FRET analysis supported the conclusions that CNBHD and eag domains interact directly to regulate deactivation, and that the interaction is between subunits rather than within the same subunit. A recent x-ray structure of an eag domain interacting with the CNBHD from mouse eag channels confirms that the interaction is highly conserved and is important, as cardiac arrhythmia– and cancer-associated mutations are found at the domain–domain interface (Haitin et al., 2013).

The work for which Dr. Trudeau received the Cranefield Award comprises only a fraction of his research on the molecular physiology of channels in the hERG family (K_v10-K_v12). For instance, the Trudeau laboratory has also previously investigated N- and C-terminal determinants of deactivation gating (Gustina and Trudeau, 2009, 2011), including determinants of deactivation within the CNBHD (Brelidze et al., 2013), and shown that the eag domain partially regulates channel inactivation (Gianulis and Trudeau, 2011; Trudeau et al., 2011; Gustina and

Trudeau, 2013). Overall, Dr. Trudeau's research clearly exemplifies in its quality, rigor, and insight into fundamental mechanisms the ideal of the Cranefield Award.

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