UC DAVIS HEALTH | SCHOOL OF MEDICINE

Department of
Physiology and Membrane Biology

Distinguished Lecture Series in Physiology

Ana Isabel Fernandez-Marino, Ph.D.

Post-Doctoral Fellow
National Institutes of Health-National Institute of Neurological Diseases and Stroke

"Electromechanical coupling and slow inactivation in Kv channels"

Disease-causing mutations have been invaluable tools for understanding fundamental ion channel gating mechanisms. Voltage-activated potassium (Kv) channels are membrane proteins that play crucial roles in neural communication, cardiac excitability, muscle contraction, and hormone secretion. These channels contain voltage-sensing domains that activate in response to changes in membrane voltage to open and close the ion permeation pathway within the pore domain. In the first part of my talk, I will describe my efforts to understand the mechanism of electromechanical coupling between the voltage-sensing domains and the pore domain in the model Shaker Kv channel. In the second part of my talk, I will focus on my recent work on the Kv2.1 channel, a particularly fascinating delayed-rectifier Kv channel that is widely expressed in the mammalian brain and where mutations in humans cause epileptic encephalopathy. I will describe a cryo-EM structure of Kv2.1 that we have solved, highlighting several unique features and the location of epileptic encephalopathy mutations. I will focus on one mutation within an intracellular region implicated in electromechanical coupling that render the channel non-conducting by promoting slow inactivation. Unlike slow inactivation in other Kv channels resulting from a conformational change in the ion selectivity filter within the external pore, slow inactivation in Kv2.1 involves electromechanical coupling and reclose of the internal pore. I will end by describing my plans to investigate unexplored mechanisms of Kv2.1 channels, including the development of modulatory nanobodies.

Wednesday, November 9, 2022
In-Person & Zoom
12 p.m.

November
9

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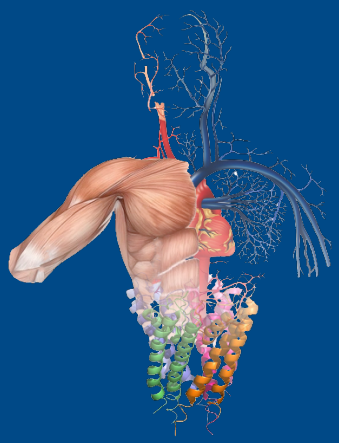

Host: Jorge Contreras
jecontrer@ucdavis.edu