POSTDOC APPRECIATION WEEK 2021: RESEARCH SPOTLIGHT

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Field of Study
Physiology & Biophysics

What impact do you want your research to have?
As a postdoc in the laboratory of Dr. Peter Larsson in the Department of Physiology and Biophysics at the University of Miami, my long-term research goal is to understand the molecular mechanisms underlying mutations that cause cardiac arrhythmias and epilepsy, which can lead to sudden death. Hyperpolarization-activated cyclic nucleotide-gated (HCN) channels are essential for the rhythmic activity of pacemaker cells in the heart and brain. Hundreds of mutations in the HCN channel have been identified in patients with cardiac arrhythmias and epilepsy. However, how these mutations induce diseases is unclear for many of them. Our study aims to determine whether some of these mutations cause life-threatening cardiac arrhythmia and epilepsy by altering the voltage sensor-to-pore coupling in HCN channels. We believe our research will shed new light on the development of better antiarrhythmic and anti-epileptic drugs.

What inspired you to pursue your area of research?
Cardiac arrhythmia and epilepsy affect millions of Americans, leading to one of the most cases of sudden death in adults annually. These conditions can be due to the dysfunction of ion channels. This is the inspiration for me to work on the function of ion channels. Ion channels in the cell membrane play a critical role in cellular function and excitation. The basic function of an ion channel can be distilled into: 'The hole opens. Ions go through. The hole closes.' Dysfunction of ion channels (HCN channels) as a result of mutations leads to diseases such as cardiac arrhythmia and epilepsy. I have been working on understanding the structure and function of HCN channels, which is a critical step to find treatments for diseases associated with ion channels.

What is most exciting about your research?
I have been working on the contributions of voltage-gated ion channels to health and diseases. Such information helps to facilitate the design of future antiarrhythmic and neuropathological treatments, which would benefit millions of Americans. Secondly, HCN channels belong to the family of voltage-gated K+ (Kv) channels. However, why HCN channels are activated by hyperpolarization whereas Kv channels are activated by depolarization is not clear. This big open question has been a hot topic for decades. Understanding how HCN channels sense voltage and gate is critical to find better treatments for HCN channelopathies.

What makes your research unique?
My research aims to elucidate the mechanisms by which mutations in HCN channels cause cardiac arrhythmia and epilepsy by affecting the coupling between the voltage-sensing domain (VSD) and the pore domain (PD). As far as we are concerned, how these disease-associated mutations change the VSD-PD coupling has not been examined yet. Furthermore, we have recently presented a new gating mechanism that in HCN channels, the voltage sensor moves in two steps in response to hyperpolarizations and that the second voltage sensor step correlates with gate opening. This finding would excite many scientists in the field of ion channels.

What are your plans after finishing your postdoc at the University?
I am planning to conduct independent research in the field of ion channels at an academic institution. I would love to have my own lab and keep working on the ion channels. In addition to conducting research, I intend to teach courses in physiology and biophysics at the graduate and undergraduate levels at an academic institution. I love teaching and mentoring. Mentoring and inspiring young minds are equally as important as the research itself as new generations of scientists are coming forth.

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