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Lecture Series

DR. MARK YEAGER PRESENTS:

Electrostatic and Steric Mechanisms for Gap Junction Channel Gating during Tissue Injury

Wednesday, January 19, 2022 @ 3:30 PM

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MEETING ID: 995 2174 5474
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ABOUT THE LECTURE

Gap junction channels (GJCs) are ubiquitous in tissues and play a critical role in normal and pathophysiology by mediating intercellular exchange of nutrients, metabolites, ions and signaling molecules. For instance, in the heart, GJCs mediate action potential propagation between cells and thereby maintain the normal heartbeat, but they also play a role in arrhythmias causing sudden death. GJCs are formed by the end-to-end docking of hemichannels in the plasma membranes of adjacent cells to form intercellular molecular conduits. We have used electron cryomicroscopy (cryo-EM), X-ray crystallography and molecular modeling to understand the molecular basis for regulation of GJCs during tissue injury, which is accompanied by elevated $Ca2^{+}$ and acidic pH. Our results on electrostatic regulation overturn a 30-year paradigm how GJCs are gated by calcium. Our results on pH regulation demonstrate how conformational changes in the protein subunits result in occlusion of the channel by a "ball and chain" mechanism. Such insights are essential for the pursuit of GJCs as therapeutic targets.

ABOUT THE SPEAKER

Dr. Mark Yeager is a physician-scientist with training in chemistry, biochemistry, biophysics, internal medicine and cardiology at Carnegie-Mellon University, Yale and Stanford. His basic research uses electron cryomicroscopy (cryo-EM), X-ray crystallography and molecular modeling to explore the structure and function of macromolecular complexes. One basic research program is focused on membrane channels, receptors and transporters, exemplified by gap junction membrane channels. A second research initiative in virology is focused on the structure and assembly of HIV-1. His translational research is focused on the use of a preclinical porcine model of myocardial infarction to identify small molecule therapeutics to abrogate the long term development of heart failure. **Distinguished physician-scientist takes the helm of Frost Institute**

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