Qiu-Xing Jiang, J Proteomics Bioinform 2017, 10:8(Suppl)
DOI: 10.4172/0974-276X-C1-0100

Qiu-Xing Jiang
University of Florida, USA

Structural basis for the lipid-dependent gating of a Kv channel

Human cell membranes are made of both phospholipids and nonphospholipids. The nonphospholipids, such as cholesterol, have no phosphate groups in their headgroup regions and are quite abundant in cell membranes. Mainly due to technical difficulties, quantitative study of possible effects of nonphospholipids on voltage-gated ion channels has been very challenging. Our prior studies have achieved three major developments: 1. a working hypothesis of lipid-dependent gating based on nonphospholipids stabilizing the voltage sensor domain of the KvAP channel in the resting (down) conformation, 2. a novel bead-supported unilamellar membrane system and a new method to stabilize the KvAP channel in the resting state and 3. chemically functionalized carbon films for cryoEM imaging of low abundance complexes by high-affinity selection or of small macromolecular complexes (100-200 kDa) by keeping vitrified ice thinner than usual. The general idea for lipid dependent gating is that the annular lipids around a Kv channel change their arrangements in accompany with the conformational changes of the voltage-sensor domains. Our technical development made it feasible to study the CHOL-dependent gating effects on Kv channels. We studied the CHOL-dependent gating effects on Kv channels in bSUMs. Because almost all known lipid metabolic defects result from dysregulated homeostasis of nonphospholipids, our studies in animal models carrying CHOL metabolic defects will provide the first test of lipid-dependent gating in an *in vivo* physiological setting. Secondly, we apply our ChemiC method to cryoEM study of the 120 kDa KvAP in both an inactivated and a peptide-stabilized down state. The peptides selected from the nonphospholipid-stabilized down state have been showed to recognize the voltage sensors in the right conformation and keep the channels in the right conformation. Our results will reveal the structural basis for the nonphospholipid-induced conformational changes in Kv channels, and unveil connections to the lipid-metabolic defects in humans.

Biography

Qiu-Xing Jiang obtained his PhD in 2002 from the Department of Cellular and Molecular Physiology at Yale University School of Medicine, where he started his work in cryo-electron microscopy in 1999 with Dr. Fred Sigworthis. He is currently heading the Laboratory of Molecular Biophysics and Cell Physiology in Department of Microbiology and Cell Science in the Institute of Food and Agricultural Sciences at University of Florida and he is serving part-time (20%) as the Faculty Director of Electron Microscopy at the Institute of Cross-disciplinary Biotechnology Research at UF. After a short Postdoctoral training at Yale, he finished his Postdoctoral training in structural biology with Dr. Roderick Mackinnon in 2007 before taking an Assistant Professorship position at UT Southwestern Medical Center at Dallas, Texas. He is the recipient of the NIH EUREKA award in 2009, the AHA National Innovative Award in 2012, and the Junior Faculty travel award from GRC Molecular and Cell Biology of Lipids in 2011.

qxjiang@ufl.edu