

CryoEM Current Practices Webinar

Heat-dependent opening of TRPV1 in the presence of capsaicin



Dohoon Kwon, Ph.D.

Postdoctoral Fellow, Lee Laboratory
Duke University

12PM EDT / 9AM PDT Thursday, March 31st, 2022

Transient receptor potential vanilloid member 1 (TRPV1) is a Ca²⁺-permeable cation channel that serves as the primary heat and capsaicin sensor in humans. In published work, we determined the structures of apo and capsaicin-bound full-length rat TRPV1 reconstituted into lipid nanodiscs over a range of temperatures using cryo-EM. This has allowed us to visualize the noxious heat-induced opening of TRPV1 in the presence of capsaicin. Heat-dependent TRPV1 opening comprises stepwise conformational transitions. Global conformational changes across multiple subdomains of TRPV1 are followed by the rearrangement of the outer pore, leading to gate opening. Solvent-accessible surface area analyses and functional studies suggest that a subset of residues form an interaction network directly involved in heat sensing. Our study provides a glimpse of the molecular principles underlying noxious physical and chemical stimuli sensing by TRPV1, which can be extended to other thermal sensing ion channels. In this talk, I will also discuss how to prepare the grids at high-temperature conditions and the recent results we have obtained at various temperatures.

All are welcome to attend. Registration is at no-cost, but sign-up is required:
https://us02web.zoom.us/webinar/register/WN_SqMBOoMYSF--R360pu4ZSw

This webinar series is jointly hosted by the NIH Transformative High Resolution CryoEM Program Service Centers: the National Center for CryoEM Access and Training (NCCAT), the Pacific Northwest Center for CryoEM (PNCC), and the Stanford-SLAC CryoEM Center (S2C2) who provide no-cost access to cryoEM instrumentation and training. In this monthly series, we will highlight cryoEM methods and use the Q&A session after the seminar to stimulate discussion of best practices and interesting challenges that will be helpful to researchers new to the field. Representatives from all three service centers will also be on hand to answer questions about the CryoEM resources available to biomedical researchers and how to access them.