CryoEM Current Practices Webinar

Structural Mechanisms of TRPM7 Activation and Inhibition Revealed by Cryo-EM

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Transient receptor potential (TRP) channels are polymodal molecular sensors involved in numerous physiological processes and implicated in various human diseases. Among the melastatin subfamily of TRP channels, TRPM7 stands out as a master regulator of the organismal balance of divalent cations, and it is linked to neuronal and cardiovascular disorders, tumor progression, and also emerged as a new drug target. By utilizing cryo-EM, functional analysis, and molecular dynamics simulations, we have uncovered two distinct structural mechanisms of TRPM7 activation: one driven by a gain-of-function mutation and the other by the agonist naltriben. These mechanisms exhibit different conformational dynamics and domain involvement. Additionally, we have identified a binding site for highly potent and selective inhibitors, demonstrating that they function by stabilizing the closed state of TRPM7. These discovered structural mechanisms lay the foundation for understanding the molecular basis of TRPM7 channelopathies and for drug development.

All are welcome to attend. Registration is at no-cost, but sign-up is required:
https://us02web.zoom.us/webinar/register/WN_KOH6glx4TS-fggTHWg5C6g

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.