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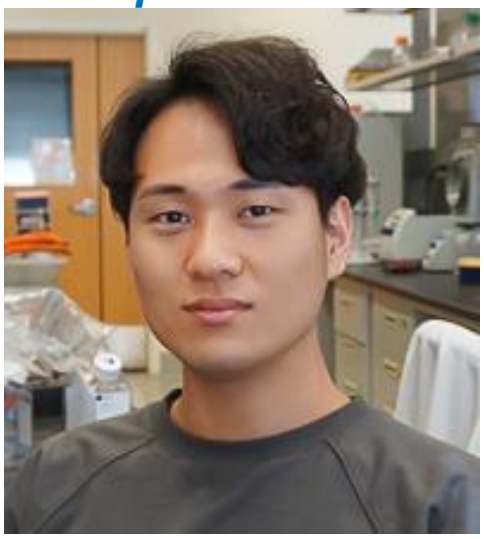
# CryoEM Current Practices Webinar

## *Structure of the mechanosensory TMC-1 complex from C. elegans*

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The sense of hearing and balance begins with the mechanosensory transduction (MT) channel, which converts mechanical stimuli into electrochemical signals, and which is typically localized within hair cells of the mammalian inner ear. Despite decades of effort focused on discovering the molecular architecture and mechanism of the MT channel complex, the structure of the complex has remained unresolved. Here we report the single-particle cryo-EM structure of the native TMC-1 complex isolated from C. elegans. The overall architecture of the complex adopts 2-fold-rotation symmetry, in which TMC-1 forms a domain-swapped dimeric structure through its C-terminal transmembrane helix. The auxiliary subunit TMIE, present in two copies, resides on the periphery of the complex, close to the pore-forming transmembrane helices of TMC-1, and participating in lipid-mediated interactions throughout the interface with TMC-1. CALM-1, an orthologue of vertebrate Ca2+ binding protein CIB2, binds to the cytosolic face of TMC-1 via highly conserved residues. The entire complex structure resembles the shape of an 'accordion', whereby the single transmembrane helixes of TMIE function as the accordion handles. From thorough particle classification, we identified a subset of TMC-1 complexes bound with ARRD-6, an arrestin-like protein, via interactions with the CALM-1 subunit. Together with molecular dynamics simulations, we visualize the membrane-embedded TMC-1 complex and propose structure-based gating mechanisms for the MT channel.


All are welcome to attend. Registration is at no-cost, but sign-up is required:
https://us02web.zoom.us/webinar/register/WN_IP913PM0RXaSQB-SUrUlsg

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.