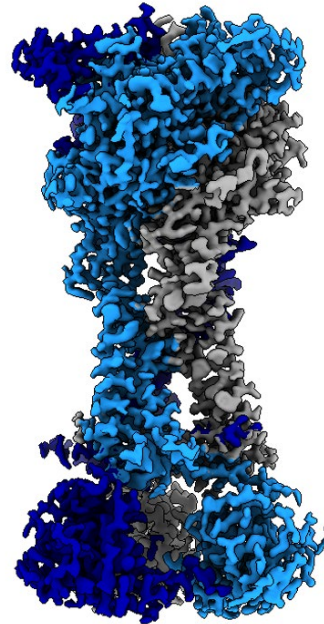




CryoEM Current Practices Webinar

Small-Molecule Modulation of the P2X7 Receptor Revealed by Cryo-EM



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12PM EDT / 9AM PDT Thursday, March 27, 2025

P2X receptors are trimeric ATP-gated ion channels that play roles in numerous physiological and pathophysiological processes from asthma to hearing loss. Acting as a novel node of inflammation, the P2X7 receptor subtype is a prominent pharmaceutical target for atherosclerosis, neurodegeneration, and cancer. However, the molecular pharmacology of P2X7 activation and antagonism is not fully defined. Our data of the P2X7 receptor in apo, agonist-, and antagonist-bound states reveals numerous insights into its pharmacology. With our ligand-bound structures, we can define the molecular determinants of high-affinity agonism as well identify three distinct classes of P2X7 allosteric antagonists. Apo closed state structures reveal how a partially hydrated Na⁺ ion interacts with the channel pore and identifies how key differences in the classical allosteric pockets between rat, mouse, and human P2X7 receptors affects ortholog-specific pharmacology. Altogether, our structures illuminate the molecular determinants of P2X7 receptor function which can be leveraged to design small-molecule modulators with clinical significance.

All are welcome to attend. Registration is at no-cost, but sign-up is required:
https://us02web.zoom.us/webinar/register/WN_L9VVNBq8SCGF5hdXMyV3_g

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.