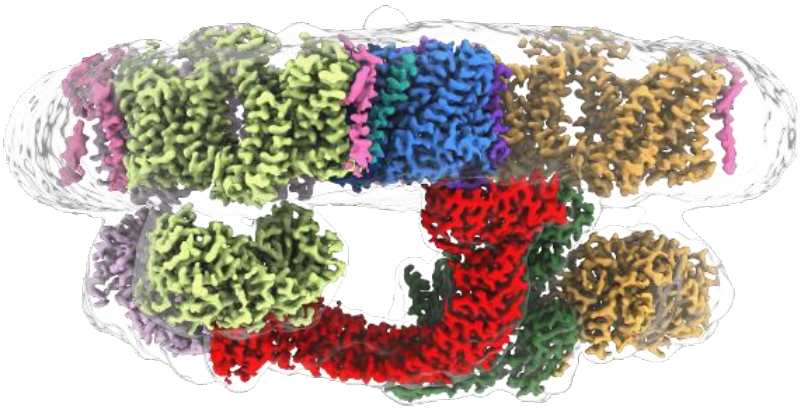
CryoEM Current Practices Webinar

Architecture of the human erythrocyte ankyrin-1 complex



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The ankyrin-1 complex tethers the spectrin-actin cytoskeleton to the red blood cell (RBC) membrane, and acts as a metabolic hub, connecting membrane proteins that are involved in gas exchange, pH control, and regulation of cellular volume and deformability. Mutations in components of the complex lead to inherited defects in erythrocyte shape and stability, such as hereditary spherocytosis. Ankyrins are also broadly expressed adaptors functioning as master-organizers of membrane-associated protein complexes in neurons and other cell types. However, the precise composition of the ankyrin-1 complex, and the structural basis for membrane association and recruitment of target membrane proteins remains unknown in any context. We solve the single particle cryo-EM structures of the human ankyrin-1 complex, which includes the Rhesus polypeptides RhCE & RhAG, ankyrin 1, protein 4.2 and three copies of the dimeric band 3 anion exchanger bound to glycophorin A, assembled into a 1.2 MDa supercomplex. Additional complexes carrying one aquaporin-1 (AQP1) tetramer are also identified. The structure of membrane-bound ankyrin shows that the first five repeats adopt an unexpected T-shaped configuration whereby the inner groove is oriented parallel to the membrane, facilitating recognition of integral membrane binding partners such as RhCE and AQP1. Both the inner groove and the convex outer surface of ankyrin participate in specific interactions with protein 4.2 and band 3. Together, our results uncover the molecular details of ankyrin-1 association with the erythrocyte membrane, and illustrate the mechanism of ankyrin-mediated membrane protein clustering.

All are welcome to attend. Registration is at no-cost, but sign-up is required:
https://us02web.zoom.us/webinar/register/WN_TP7B-my6QcCR7VbYPjqiKg

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.