

CryoEM Current Practices Webinar

The structure and mechanism of LARGE1 matriglycan polymerase



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LARGE1 is a bifunctional glycosyltransferase that polymerizes matriglycan – a linear polysaccharide of alternating xylose and glucuronic acid – on dystroglycan. Mutations in LARGE1 which decrease matriglycan can cause muscular dystrophies that are sometimes accompanied by intellectual disability. Matriglycan acts as a receptor for Old-World Arenaviruses, such as Lassa fever virus. The cryo-EM reconstruction of LARGE1dTM shows that the active sites on each protomer face opposite directions. Consequently, matriglycan is likely polymerized by alternating activities between the xylose transferase site on one protomer and the glucuronate transferase site on the other on the same face of the LARGE1 dimer. We show that LARGE1 processively polymerizes matriglycan by comparing the product of wild-type LARGE1dTM with a combination of active site mutants, which force the distributive polymerization of matriglycan. Elucidating the structure of LARGE1 and the mechanism of matriglycan polymerization is the first step towards informing the design of therapeutics to manage matriglycan-deficient neuromuscular disorders and combat arenaviral infections.

All are welcome to attend. Registration is at no-cost, but sign-up is required:
https://us02web.zoom.us/webinar/register/WN_EvYD9mh6QuGUDbJg20hFhA

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.