CryoEM Current Practices Webinar

Decoding mechanisms that control PPP specificity

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The large majority of ser/thr dephosphorylation is performed by the PPP family, comprised of just seven families: PP1, PP2A, PP2B/PP3/calcineurin (CN), PP4, PP5, PP6 and PP7. While it has been known for more than two decades that PP1 and CN engage their regulators using short linear motifs (SLiMs), the emerging view is that regulator and substrate engagement via SLiMs is likely conserved throughout the entire PPP family, with SLiMs now also identified for PP4 and PP2A-B56. Remarkably, new mechanisms that modulate regulator and substrate binding continue to be discovered. For example, we recently discovered that dynamic charge-charge interactions modulate the affinities of PPP-specific SLiMs for their cognate PPPs. We also discovered that similar dynamic electrostatic interactions can, in some cases, actively direct substrate specificity. Here, we present recent data, based on cryo-EM structures of PP2A:B55 bound to inhibitors, substrates and regulators, that illustrate the diverse and novel mechanisms used by regulators and substrates to engage their cognate PPPs and, in turn, direct PPP holoenzyme formation and activity.

All are welcome to attend. Registration is at no-cost, but sign-up is required:
https://us02web.zoom.us/webinar/register/WN_ZbHoCTb6SCe7zhCKb8uMvA

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.