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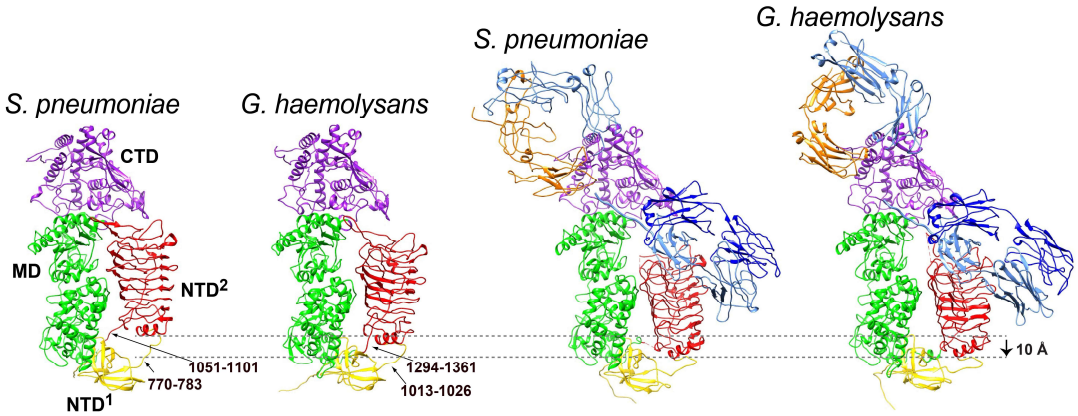
CryoEM Current Practices Webinar

The bacterial pathogen/host interface: Cutting up the host

The M26 family of IgA1 Proteases



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12PM EDT / 9AM PDT Thursday, April 27th, 2023

The Eisenmesser lab is interested in how macromolecular structure and dynamics are coupled to function, particularly for pathogenic enzymes that manipulate the host innate immune response. To address these interests, we utilize multiple biophysical methods that include cryo-EM and NMR.

Bacterial pathogens have developed deadly mechanisms to thwart the human host response and our lab has elucidated the molecular details of several pathogen/host interactions. The first example will focus on how Gram-positive bacteria utilize the M26 family of giant proteases for infection, which are ~2000 residue, multi-domain proteins that specifically cleave human IgA1. Cleavage by these IgA1 proteases (IgA1P) is specific to the IgA1 "hinge" region that is a long linker connecting the FAB and Fc domains that serve multiple roles for infection that we will discuss. Using cryo-EM, our lab has elucidated the first two near-atomic-resolution structures of M26 family members from both Streptococcus pneumoniae and a Gemella haemolysans. These IgA1Ps undergo a conserved gating mechanism facilitated by the host IgA1 that will be described. The second example will focus on preliminary biochemistry and solution studies aimed at understanding how Staphylococcus aureus exfoliative toxins (ETs) function. Specifically, we have begun to elucidate the molecular basis of exfoliative toxin A (ETA) function that serves to cleave the human desmosome for deeper infections. Such studies have begun to lay the foundation for cryo-EM studies aimed at determining the structure of ETs with their host targets. Both examples of pathogen/host interactions discussed will help us understand the exquisite specificity of these bacterial enzymes for their human targets.

All are welcome to attend. Registration is at no-cost, but sign-up is required:
https://us02web.zoom.us/webinar/register/WN_B-115ocHRF2FjwPG2oyzrA

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.