

## Center for Structural Biology

Transforming our understanding of molecular biological structures and their movements through interdisciplinary collaboration.



**PennState**  
Huck Institutes of  
the Life Sciences

# Center for Structural Biology Seminar



## **“Structural and biophysical studies into the picornaviral main protease 3C and its polyprotein precursor 3CD”**

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**Abstract:** The picornaviral 3C protein plays a critical role as a protease, facilitating the cleavage of both the viral polyprotein and host cell defense proteins. In addition to its proteolytic function, the 3C protein engages with RNA replication elements in the viral genome, and is recruited to replication organelles enriched with phosphoinositide (PIP) lipids. This seminar highlights recent structural and biophysical investigations aimed at understanding the specificities of the protease, RNA and lipid-binding activities. The 3CD precursor, comprising a 3C protease and 3D RNA-dependent RNA polymerase domains, is a key factor in generation of virus replication organelles through its interactions with PIP-enriched membranes. Building on our earlier work that identified PIP-binding surfaces on both 3C and 3D, we have recently used paramagnetic relaxation enhancement (PRE)-based NMR approaches using modified lipid nanodiscs to refine this interaction map and demonstrate that membrane binding is primarily electrostatic. To probe 3C-RNA interactions, we examined a broad panel of RNA oligonucleotides. These studies revealed two RNA-binding sites, confirming the previously described RNA-binding region and uncovering a second site near the protease active site. Unexpectedly, RNA engagement triggered liquid-liquid phase separation (LLPS), likely due to 3C's ability to interact with multiple RNA strands simultaneously. This behavior suggests that 3C and its precursor 3CD may help regulate LLPS-driven assemblies, such as stress granules, during infection. Collectively, these studies suggest that 3C and its precursor 3CD are key factors in the generation of virus replication organelles, and may also help modulate membraneless LLPS-based assemblies, including stress granules and processing bodies, observed during viral infection.

**Wednesday, December 17, 2025**

**W-203 Millenium Science Complex Building**

**2 – 3 pm**

**Hosted by Katsu Murakami (kum14@psu.edu)**