NUS National University of Singapore | Department of Biological Sciences, Faculty of Science

VIRTUAL BIOLOGY COLLOQUIUM

Friday, 15 Oct 2021 | 4 pm | Online Zoom Session

Hosted by A/P Lu Gan

A capsid with a twist: Assembly mechanism of the pleomorphic immature poxvirus scaffold

By **Matthias Wolf**

Okinawa Institute of Science and Technology Graduate University, Japan

The poxvirus family is a unique group of nucleo-cytoplasmic large DNA viruses (NCLDVs), characterized by formation of a non-icosahedral scaffold surrounding the viral membrane during the initial stage of virus assembly1. In Vaccinia virus (VACV), the prototype poxvirus, scaffold protein D13 forms a loosely connected, honeycomb-like lattice on the viral membrane that results in formation of the pleiomorphic, spherical, immature virion (IV). The structure of D13 is similar to those of major capsid proteins that readily form icosahedral NCLDVs. However, D13 does not, and the detailed assembly mechanism of the pleiomorphic poxvirus scaffold has never been understood. Here we show the cryo-EM structures of D13 trimers, trimer doublets, and the tubular assembly of an expanded honeycomb lattice produced in vitro. The structures reveal that the short N-terminal α-helix is critical to initiation of D13 self-assembly. The assembly mechanism revealed in this study explains the semi-ordered capsid-like arrangement of D13 that is distinct from homologous capsid proteins of icosahedral NCLDVs. Our structures explain how a single protein can self-assemble into different capsid morphologies, induced by a small conformational change of a peripheral helix, which represents a local exception to the universal Caspar-Klug theory of quasi-equivalence.

About the Speaker

Dr. Wolf joined OIST as Assistant Professor in 2012, where he is leading the Molecular Cryo-Electron Microscopy Unit. He was a postdoctoral research fellow at Harvard Medical School in the laboratory of Prof. Steven Harrison with an emphasis on molecular virology. Matthias received a PhD in Biophysics and Structural Biology from Brandeis University (MA , USA) working with Prof. Nikolaus Grigorieff on the structure of viruses and ion channels using cryo-EM. Previously, he studied pharmaceutical chemistry with an emphasis on computer-aided drug design and holds a Master's degree in Pharmacy from the University of Innsbruck, Austria. In early 2020, he has been promoted to tenured full Professor at OIST, and began a joint appointment as Associate Research Fellow at Academia Sinica in Taiwan.

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