“Structural studies of mature virions of poxviruses using cryo-electron tomography and subvolume averaging”

Keywords: poxviruses, electron microscopy, cryo-electron tomography, subvolume averaging

Description:

Viruses are obligate intracellular parasites with an interesting variety of viral particles exhibiting diverse morphotypes. Of special interest for our team at the Institute for Integrative Biology of the Cell (I2BC, Gif-sur-Yvette, France) are poxviruses that represent a diverse group of enveloped DNA viruses that include Variola virus, the causative agent of smallpox. Smallpox was eradicated using Vaccinia virus (VACV) as the first live vaccine. However, our knowledge about poxvirus biology and pathogenicity remains limited, and only a few antivirals have been developed against poxviruses. Along these lines, emerging poxviruses still continue to pose a threat to human and animal populations as recent outbreaks of Mpox and Lumpy skin disease show.

Poxviruses have large genomes encoding up to 200 proteins, with more than 80 proteins make up the infectious mature virion (MV) or viral particle. Due to this complexity and pleomorphic shape of the virion, the precise structure and molecular composition remain unclear. Recently, our lab could show that in VACV, one substructure, called the palisade layer, is composed of flexible trimer made of the major core protein A10. We now want to investigate whether similar architectures are conserved for members of different genera within the poxvirus family. To this end, we are mainly using cryo-electron tomography (cryo-ET) to analyze purified MVs of different strains of poxviruses.

The proposed internship project will focus on the computational aspects of the analysis of cryo-ET datasets. In the framework of this project, the characterization of the composition and architecture of MVs from different poxviruses will be the main focus. Large datasets have already been acquired, and a pipeline for their analysis has been established in the lab. This internship will offer the opportunity to learn tomogram reconstruction from tilt series and segmentation of tomography data. The student will be trained to recognize relevant features in tomograms, perform post-processing treatments, and work towards determine the structure of these features by subvolume averaging. Ultimately, the expected findings are likely to provide new insights into virus-host interactions, that could inspire antiviral strategies and enhance our understanding of poxviruses.

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