USER MEETING 2016
24-25 NOVEMBER
National Centre for Synchrotron Science

Contribution ID : **283** Type : **Oral**

Structural Insights into the Assembly and Regulation of Distinct Viral Capsid Particles

Thursday, 24 November 2016 14:45 (15)

The assembly and regulation of viral capsid proteins into highly ordered macromolecular complexes is essential for viral replication. Recent reports have elucidated the ability of capsids to switch between T1 and T3 symmetry, however little is known regarding how capsid proteins can switch between smaller, non-icosahedral macromolecular complexes. Here we utilize crystal structures of the capsid protein from the smallest and simplest of all known viruses capable of autonomously replicating in animal cells, circoviruses, to establish structural and mechanistic insights into capsid morphogenesis and regulation. The beak and feather disease virus is responsible for infecting critically endangered parrots, and remarkably, like many circoviruses, these viruses encode only two genes, a capsid protein, and a replication initiation protein. The capsid protein forms distinct macromolecular assemblies during replication and here we elucidate these structures at high resolution, showing that these complexes reverse the exposure of the N-terminal arginine rich domain responsible for DNA-binding and nuclear localization. We show that assembly of these complexes is regulated by single-stranded DNA (ssDNA), and provide a structural basis of capsid assembly around single stranded DNA, highlighting novel binding interfaces distinct from the highly positively charged N-terminal ARM domain. These structures of the world's smallest viral capsid assemblies serve as an important basis for enhancing our understanding viral capsid assembly and regulation.

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Session Classification : Concurrent Session 2: Structural Biology I - Sponsored by DECTRIS

Track Classification : Structural Biology