Poster Presentation

MS110.P06

Structure and function of cement proteins in human adenovirus

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Human adenoviruses (HAdVs) are large (~150nm in diameter, 150MDa) nonenveloped double-stranded DNA (dsDNA) viruses that cause respiratory, ocular, and enteric diseases. The capsid shell of adenovirus (Ad) comprises multiple copies of three major capsid proteins (MCP: hexon, penton base and fiber) and four minor/cement proteins (IIIa, VI, VIII and IX) that are organized with pseudo T=25 icosahedral symmetry. In addition, six other proteins (V, VII, μ, IVa2, terminal protein and protease) are encapsidated along with the 36Kb dsDNA genome inside the capsid. The crystal structures of all three MCPs are known and so is their organization in the capsid from prior X-ray crystallography and cryoEM analyses. However structures and locations of various cement proteins are of considerable debate. We have determined and refined the structure of an entire human adenovirus employing X-ray crystallpgraphic methods at 3.8Å resolution. Adenovirus cement proteins play crucial roles in virion assembly, disassembly, cell entry and infection. Based on the refined crystal structure of adenovirus, we have determined the structure of the cement protein VI, a key membrane-lytic molecule and its associations with proteins V and VIII, which together glue peripentonal hexons beneath vertex region and connect them to rest of the capsid. Following virion maturation, the cleaved N-terminal pro-peptide of VI is observed deep in the peripentonal hexon cavity, detached from the membrane-lytic domain. Furthermore, we have significantly revised the recent cryoEM models for proteins IIIa and IX and both are located on the capsid exterior. Together, the cement proteins exclusively stabilize the hexon shell, thus rendering penton vertices the weakest links of the adenovirus capsid. Adenovirus cement protein structures reveal the molecular basis of the maturation cleavage of VI that is needed for endosome rupture and delivery of the virion into cytoplasm.

Keywords: adenovirus, structure, cement proteins