VIRAL TRANSCRIPTION

Locating reovirus polymerase

During particle morphogenesis, the double-stranded (ds) RNA genome of reovirus is packaged into virions together with viral RNA-dependent RNA polymerase (RdRp) molecules. Following cell entry and partial uncoating of the virion to yield a core particle, these RdRp molecules transcribe the genome into single-stranded plus-sense RNA for translation and packaging into new particles. The core particle comprises five viral proteins: λ1 (which constitutes the icosahedral inner-capsid layer), σ2, λ2 (a turret protein that mediates the final three of four RNA-capping reactions), μ2 (which mediates NTPase activities *in vitro*) and λ3 — the RdRp.

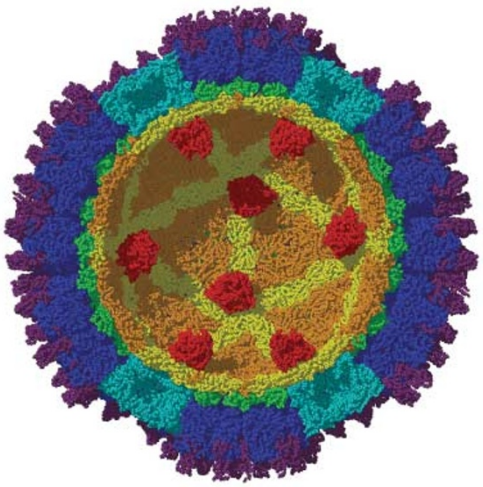
Previous structural studies have determined the X-ray crystal structures of the λ1, λ2 and σ2 proteins within the reovirus core particle, and of the RdRp λ3 protein in separate, recombinant form. But to fully understand how the core particle mediates both transcription and co-trancriptional capping and export of viral plus-strand RNAs, it is necessary to identify how the RdRp λ3 is positioned within viral particles.

In a new study published in *Nature Structural Biology*, Zhang *et al.* have now identified the precise location of the RdRp λ3 within the complete virion. Using cryo-electron microscopy (EM) and three-dimensional image reconstruction, the authors have determined the structure of the non-fusogenic mammalian reovirus virion to 7.6 Å, and fitted the X-ray coordinates of λ3 into this cryo-EM map — revealing one copy of λ3 to be positioned at one side of each of the five-fold axes of the λ1 shell.

The X-ray crystal structure of λ3 had previously revealed four channels for the entry and exit of substrates and products — namely, entry paths for the RNA template and NTPs, and exit paths for the RNA template and the plus-strand RNA transcript. Zhang *et al.* have identified a small channel in the λ1 shell of the core particle, beneath which the plus-strand exit channel of the RdRp λ3 subunit is positioned. Analysis of the surrounding side chains suggests that this channel might be widened during transcription to allow passage of the RNA transcript, and the outer end of the channel is positioned beneath the pentameric capping enzyme complex formed by λ2.

Taken together, these findings have led the authors to propose a mechanism for exit and capping of the RNA transcript, in which the nascent RNA transcript exits the icosahedral shell through this small channel, and is thereby directed into the larger channel of the pentameric capping enzyme complex.

Jane Saunders



Sectioned view of the pseudo-atomic structure of the mammalian reovirion showing the RdRp λ3 polymerase molecules. Image courtesy of Timothy Baker, Purdue University, USA, and Max Nibert, Harvard University Medical School, USA.

References and links

ORIGINAL RESEARCH PAPER Zhang, X. *et al.* Reovirus polymerase λ3 localized by cryo-electron microscopy of virions at a resolution of 7.6 Å. *Nature Struct. Biol.* (2003) doi: 10.1038/nsb1009

WEB SITES
Timothy S. Baker's laboratory:
http://bilbo.bio.purdue.edu/~baker/
Max L. Nibert's laboratory:
http://micro.med.harvard.edu/nibert/default.html