

HIGHLIGHT ADVISORS

ADRIANO AGUZZI

UNIVERSITY HOSPITAL OF
ZÜRICH, ZÜRICH, SWITZERLAND

NORMA ANDREWS

YALE UNIVERSITY SCHOOL OF
MEDICINE, NEW HAVEN, CT, USA

ARTURO CASADEVALL

THE ALBERT EINSTEIN COLLEGE
OF MEDICINE, BRONX, NY, USA

RITA COLWELL

UNIVERSITY OF MARYLAND
BIOTECHNOLOGY INSTITUTE,
BALTIMORE, MD, USA

STANLEY FALKOW

STANFORD UNIVERSITY
SCHOOL OF MEDICINE,
STANFORD, CA, USA

TIMOTHY FOSTER

TRINITY COLLEGE, DUBLIN,
IRELAND

KEITH GULL

UNIVERSITY OF OXFORD,
OXFORD, UK

NEIL GOW

UNIVERSITY OF ABERDEEN,
ABERDEEN, UK

HANS-DIETER KLENK

PHILIPPS UNIVERSITY,
MARBURG, GERMANY

BERNARD MOSS

NIAID, NATIONAL INSTITUTES OF
HEALTH, BETHESDA, MD, USA

JOHN REX

ASTRAZENECA, CHESHIRE, UK

DAVID ROOS

UNIVERSITY OF PENNSYLVANIA,
PHILADELPHIA, PA, USA

PHILIPPE SANSONETTI

INSTITUT PASTEUR,
PARIS, FRANCE

CHIHIRO SASAKAWA

UNIVERSITY OF TOKYO,
TOKYO, JAPAN

ROBIN WEISS

UNIVERSITY COLLEGE LONDON,
LONDON, UK

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: $\lambda 1$ (which constitutes the icosahedral inner-capsid layer), $\sigma 2$, $\lambda 2$ (a turret protein that mediates the final three of four RNA-capping reactions), $\mu 2$ (which mediates NTPase activities *in vitro*) and $\lambda 3$ — the RdRp.

Previous structural studies have determined the X-ray crystal structures

of the $\lambda 1$, $\lambda 2$ and $\sigma 2$ proteins within the reovirus core particle, and of the RdRp $\lambda 3$ protein in separate, recombinant form. But to fully understand how the core particle mediates both transcription and co-transcriptional capping and export of viral plus-strand RNAs, it is necessary to identify how the RdRp $\lambda 3$ is positioned within viral particles.

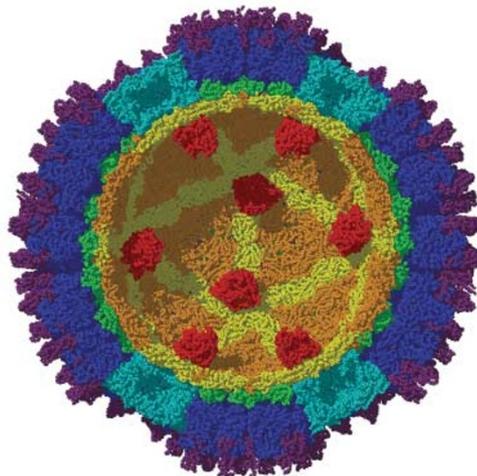
In a new study published in *Nature Structural Biology*, Zhang *et al.* have now identified the precise location of the RdRp $\lambda 3$ within the complete virion. Using cryo-electron microscopy (EM) and three-dimensional image reconstruction, the authors have determined the structure of the non-fusogenic mammalian reovirus virion to 7.6 Å, and fitted the X-ray coordinates of $\lambda 3$ into this

cryo-EM map — revealing one copy of $\lambda 3$ to be positioned at one side of each of the five-fold axes of the $\lambda 1$ shell.

The X-ray crystal structure of $\lambda 3$ 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 $\lambda 1$ shell of the core particle, beneath which the plus-strand exit channel of the RdRp $\lambda 3$ 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 $\lambda 2$.

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 $\lambda 3$ 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 $\lambda 3$ 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>