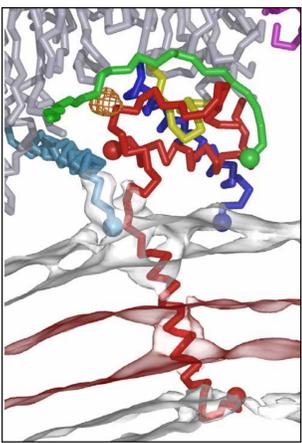


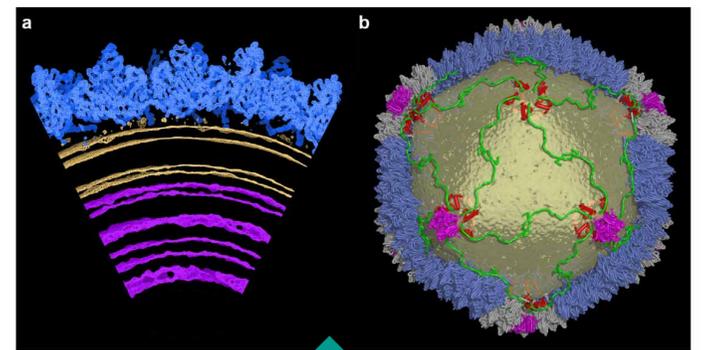
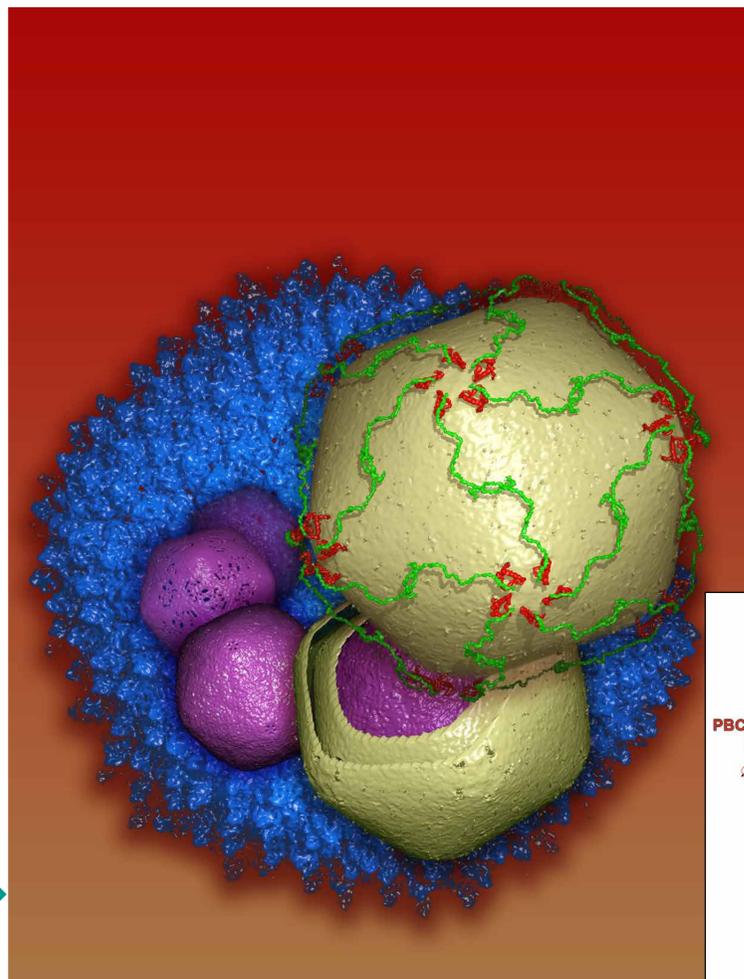
The Wellcome Trust Centre for
Human Genetics

First structure of a membrane-containing virus

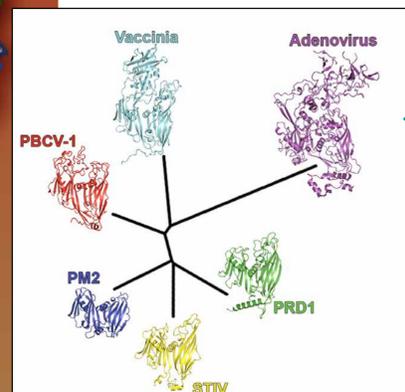


The structure reveals how the integral membrane protein P16 interacts with the viral capsid. The lipid tails are within the red envelope whilst the headgroups are in the two grey envelopes

The crystal structure of PRD1 reveals the lipid bilayer (yellow) and minor proteins that are involved in directing viral assembly (green and red)



a) A slice through the phage reveals the electron density for the lipid bilayer (yellow) and the DNA genome (purple), below the protein shell (blue). b) Peeling away the protein shell (blue) exposes the minor proteins that interact with the membrane (green and red)



PRD1 belongs to a viral lineage, members of which infect archaeal and eukaryotic viruses, suggesting that their common icosahedral ancestor existed before the emergence of the three domains of cellular life

WHAT WAS KNOWN

- Biological membranes and their associated proteins present considerable difficulties for structural analysis
- Many viruses with an icosahedral capsid also have an accompanying lipid membrane
- No detailed crystallographic analysis of a membrane system had been described
- PRD1 is a double stranded DNA bacteriophage, with a lipid bilayer and with multiple copies of over 20 different proteins

WHAT WE DID

- Used molecular genetics and gentle chemical treatment to stabilise a mutant form of the phage
- Grew crystals that diffracted X-rays very poorly
- Used further gentle treatment to re-anneal these crystals so that they gave good diffraction
- Solved the structure of PRD1 to a resolution of 4 Å, allowing us to visualise not only the phage proteins but also for the first time, the viral membrane

WHAT THIS ADDS

- The organisation of the membrane is unusual, ranging from local structure of the headgroups to lateral segregation within a leaflet and segregation between the leaflets
- The inner leaflet is composed predominantly of zwitterionic phosphatidylethanolamine molecules, facilitating a very close interaction with the viral DNA
- The outer leaflet is enriched in phosphatidylglycerol and cardiolipin, which show a marked lateral segregation
- We derive a model for virus assembly, which suggests a scalable assembly pathway that might apply to some of the largest known viruses
- PRD1 belongs to an extensive lineage, whose origin might predate the division of the bacterial, archaeal and eukaryotic domains of life

REFERENCES

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