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A link for unrelated viruses

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Apparently unrelated viruses that infect all three domains of life - Archaea, Bacteria, and Eukarya - could share a common ancestry, according to a report (*Mol Cell* 2004, **16:**673-685) by an international team of scientists in the December 3 Molecular Cell.

So far, researchers believe they have uncovered two lineages that infect all domains, with another virus line infecting two. In the *Molecular Cell* study, senior author Roger Burnett, of the Wistar Institute in Philadelphia, and colleagues have now shown through molecular modeling that many of these viruses' coat protein sequences are compatible with the major coat protein of bacteriophage PRD1. That builds on earlier evidence that a number of viruses are descended from that bacteriophage. "This new experimental evidence supporting the proposed PRD1-adenovirus lineage places the idea on a much firmer footing," Burnett told us.

Viruses were often viewed and studied as unrelated families until 5 years ago, when Burnett's lab and colleagues at the University of Helsinki in Finland made the discovery by X-ray crystallography that P3, the major coat protein of bacteriophage PRD1, strikingly resembled hexon, the major coat protein of human adenovirus. Both are trimeric molecules with two viral jelly rolls, with each such barrel containing eight beta strands in tandem folded back at the middle.

"The reasoning behind why we believe this structural similarity is not due to convergent evolution is there are four different ways to fold these barrels, and there's only one used in all these viral folds," Burnett said. Adenovirus and PRD1 are also structurally similar in architecture, vertex recognition spikes, and genomes with inverted terminal repeats and terminal proteins. As no detectable sequence similarity now exists between these viruses, Burnett suggested they diverged billions of years ago.

X-ray crystallography, electron microscope image reconstructions, or sequence similarities suggest other relatives of this double-barrel trimer lineage include algal phycodnavirus Paramecium bursaria Chlorella virus 1 (PBCV-1), bacteriophage Bam35, insect iridovirus Chilo iridescent virus, African swine fever virus, mimivirus, and perhaps even the poxviruses. This year, a research team found the major coat protein of an archaeal virus, Sulfolobus turreted icosahedral virus, matched well with PRD1 P3, providing an example from the third domain of life. All described viruses are icosahedral double stranded DNA viruses.

"The double-barrel trimer is an ideal building block for a protein array ideal for large surfaces. It can be used in principle to build a virus of any size," Burnett said.

Burnett said tenuous evidence existed for another virus lineage that may span all three domains consists of the herpesviruses and tailed bacteriophages, all double-stranded DNA viruses. Also, the double-stranded RNA reoviruses span Bacteria and Eukarya, with none yet known for Archaea.

"Convergent evolution can never be absolutely ruled out, but I think the amount of data they have makes a strong case for common ancestry," Roger Hendrix of the University of Pittsburgh, who did not participate in this report, told us. "The fact the sequences diverged as much as they have suggests the lineages are ancient, a good argument that viruses emerged earlier than the emergence of the three

domains. It argues that viruses have had a really big role in the evolution of life and had a more central role than most people might have imagined."

To cement their hypothesis, Burnett and colleagues aim to uncover further similarities in structure within the double-barrel trimer lineage, such as the special vertex both PRD1 and PBCV-1 have for packaging and perhaps injecting DNA.

"There is a lot of interest in using viral capsids as a delivery vehicle for nanotechnologies. So these findings could help learn more about the structure of these viruses, the biggest icosahedral viruses, and you could imagine them being useful someday for protein nanocontainers," Sherwood Casjens of the University of Utah, who did not participate in this study, told us.

Hendrix and Casjens cautioned that horizontal exchange of genes between viruses made determining linear ancestries extraordinarily complicated. "You could for instance have a virus that originally had a different coat protein that basically stole this double barrel from another virus," Casjens said.

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