THE ORIGIN and DIVERSITY of VIRUSES
Molecular clocks are calibrated against branches whose dates are known from the fossil record.

Individual genes vary in how clocklike they are.
Figure 26.19

Divergence time (millions of years)

Number of mutations

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Problems with Molecular Clocks

- The molecular clock does not run as smoothly as neutral theory predicts.
- Irregularities result from natural selection in which some DNA changes are favored over others.
- Estimates of evolutionary divergences older than the fossil record have a high degree of uncertainty.
- The use of multiple genes may improve estimates.
New information continues to revise our understanding of the tree of life

- Recently, we have gained insight into the very deepest branches of the tree of life through molecular systematics
From Two Kingdoms to Three Domains

- Early taxonomists classified all species as either plants or animals.
- Later, five kingdoms were recognized: Monera (prokaryotes), Protista, Plantae, Fungi, and Animalia.
- More recently, the three-domain system has been adopted: Bacteria, Archaea, and Eukarya.
- The three-domain system is supported by data from many sequenced genomes.
Is the Tree of Life Really a Ring?

- Some researchers suggest that eukaryotes arose as an fusion between a bacterium and archaean
- If so, early evolutionary relationships might be better depicted by a ring of life instead of a tree of life
Applying a Molecular Clock: The Origin of HIV

- Phylogenetic analysis shows that HIV is descended from viruses that infect chimpanzees and other primates.
- HIV spread to humans more than once.
- Comparison of HIV samples shows that the virus evolved in a very clocklike way.
- Application of a molecular clock to one strain of HIV suggests that that strain spread to humans during the 1930s.
Figure 26.20

HIV

Adjusted best-fit line (accounts for uncertain dates of HIV sequences)

Index of base changes between HIV gene sequences

Year

HIV

Range

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VIRUS
VIRUSES
PHAGE
Figure 19.3

(a) Tobacco mosaic virus
(b) Adenoviruses
(c) Influenza viruses
(d) Bacteriophage T4

- Capsomere of capsid
- RNA
- Capsid
- Membranous envelope
- DNA
- Glycoprotein
- Glycoproteins
- Head
- Tail sheath
- Tail fiber

Dimensions:
- 18 × 250 nm
- 70–90 nm (diameter)
- 80–200 nm (diameter)
- 80 × 225 nm
- Virion
- Virial particle
- Pro-virus
- Pro-phage
- Capsid
- Capsomere
- Membrane envelope
Transposon
Transposable elements
Viriod
Prion
Simple component: NA and proteins

NA: nucleic acid (DNA or RNA)

Proteins: structure (capsid), functional (enzymes)

Enzymes: RNA polymerase, DNA polymerase
Nucleocytoplasmic large DNA virus
NCLDV

Pox virus (0.19 - 0.3 Mbp, already a large virus genome)
Mimivirus (1.1 Mbp)
Megavirus (1.2 Mbp)
Now 2013 Pandoravirus (1.9 - 2.5 Mbp)
A) Mimivirus (arrows) in cytocentrifuged *A. polyphaga* cells, seen as Gram-positive particles about mycoplasma size and appearance.

B) Electron microscopy of stained mimivirus and *U. urealyticum* (a cell).

C) Phylogenetic tree from alignment of ribonucleotide reductase small subunit sequences.
Genome Size Comparison

Number of bases (in millions)

- Viruses
  - Phage
  - Mimivirus
  - Pandoravirus

- Eukaryotes
  - Parasitic
  - Free-living

- Bacteria
  - Parasitic
  - Free-living

- Archaea
  - Parasitic
  - Free-living

Science 341, 226
Acanthamoeba *polyphaga*, the host eukaryote cell

- Most common protist in soil
- Bacterivores
- Cause amoebic keratitis and encephalitis
N. Philippe et al. (19 July 2013) Pandoraviruses: amoeba viruses with genomes up to 2.5 Mb. Science 341 (6143 cover), 281-286.

Transmission electron microscopy of a Pandoravirus particle (length: 1.2 μm)

Explanation: Despite obeying all criteria to discriminate viruses from cells (no ribosomes, no ATP production, no cell division), these *Acanthamoeba* viruses, unrelated to previously recognized virus families, have genomes of up to 2.5 megabases, and more genes (CDSs) than some microsporidia eukaryotic cells.
Phylogeny of the DNA polymerases hinting at the existence of 4th domain in the Tree of Life
Hypothesis: Viral origin of DNA

(a) Several successive cycles of mutation and selection resulted in the appearance of viral nucleic acids more resistant to degradation by the host cell: DNA-U, DNA with uracil; DNA-T, DNA with thymine (i.e. normal DNA); DNA-hmC, DNA with 5-hydroxymethyl cytosine.

All four types of nucleic acids are found in present-day viruses, although DNA-U and DNA-hmC are rare.

Conversion of RNA cellular genomes to DNA postulates lysogeny by a DNA “founder virus” followed by movement of host genes onto the DNA genome.
Three founder viruses, fvB, fvA, fvE, are hypothesized to have infected the ancestors of the *Bacteria*, *Archaea*, and *Eukarya*, respectively.

Note that viruses fvA and fvE are more closely related to each other than to fvB. As a result of viral infection the genomes of these three ancestral lines were eventually converted from RNA to DNA.

Other cellular lineages derived from the last universal common ancestor (LUCA) that retained RNA genomes are presumably extinct.
Mimivirus dsDNA nucleocytoplasmic large DNA *Mimiviridae* mimivirus

- dsDNA virus
- 90% coding capacity
- 10% Junk DNA
- 1.2 million base pairs
- ~911 protein coding genes
- Additional genes (inc. aminonatyl RNA synthetases, sugar, lipid, and amino acid metabolism)

acanthamoeba polyphaga mimivirus
the *P. salinus* genome


White – MORN repeats, ankyrin repeats, and F-box domain motifs.

Gray – no match.

(3) CDSs indentified in the proteome (PAGE gel) from *P. salinus*.
Specific features are marked on concentric circles using Circos as follows:

Ring 1, CDSs positions on the direct (blue) and reverse (red) strands.

Ring 2, CDSs with a best match within eukaryotes (in orange), bacteria (in green), and viruses (in purple). CDSs with MORN repeats, ankyrin repeats, and F-box domain motifs are shown in white; CDSs with no match are shown in gray.

Ring 3, CDSs identified in the proteome of purified P. salinus particles.
1. Akyrin repeats (blue), F-box domains (red) and MORN repeats (green).

2. Highly conserved DNA sequence regions between *P. salinus* and *P. dulcis*.

The four repeat rich regions of the *P. salinus* genome absent from *P. dulcis* are clearly visible, centered at positions 1000 kb, 1400 kb, and 1750 kb and 2300 kb.
(A&B) Purified *Pandoravirus* particles and (C) their proteomic profiles
Electron microscopy images of ultrathin sections of *P. salinus* within the amoebal cell. (A early, B middle and C mature), stages of maturation are presented, illustrating the progressive knitting together of the particles starting from the apex and ending up as mature virions fully encased in their tegument-like envelope.
Infection cycle of virophage

Virophage

Traditional satellite virus
Sputnik Virion

Sputnik Virion encapsidated in Helper Mimivirus particle
肝臟的功能

人體最大的化學工廠
Here is another example of macronodular cirrhosis. Viral hepatitis (B or C) is the most common cause for macronodular cirrhosis. Wilson's disease and alpha-1-antitrypsin deficiency also can produce a macronodular cirrhosis.
Hepatocellular Carcinoma with Satellite Nodules
Microscopically with Liver Tissue

- Normal
- Fibrosis
- Hepatitis
- Cirrhosis
Geographic Distribution of Chronic HBV Infection

HBsAg Prevalence
- ≥ 8% - High
- 2-7% - Intermediate
- <2% - Low

Downloaded & adapted from CDC, USA
HBV MAP

- Core/precocere (HBc/eAg)
- Polymerase
- Envelope (HBsAg)
  - PreS1
  - PreS2
  - Small S
- HBxAg
cccDNA: Covalently Closed Circular DNA