Viruses: tireless, undisciplined explorers of life

Daniel Marc

Viruses: tireless, undisciplined explorers of life

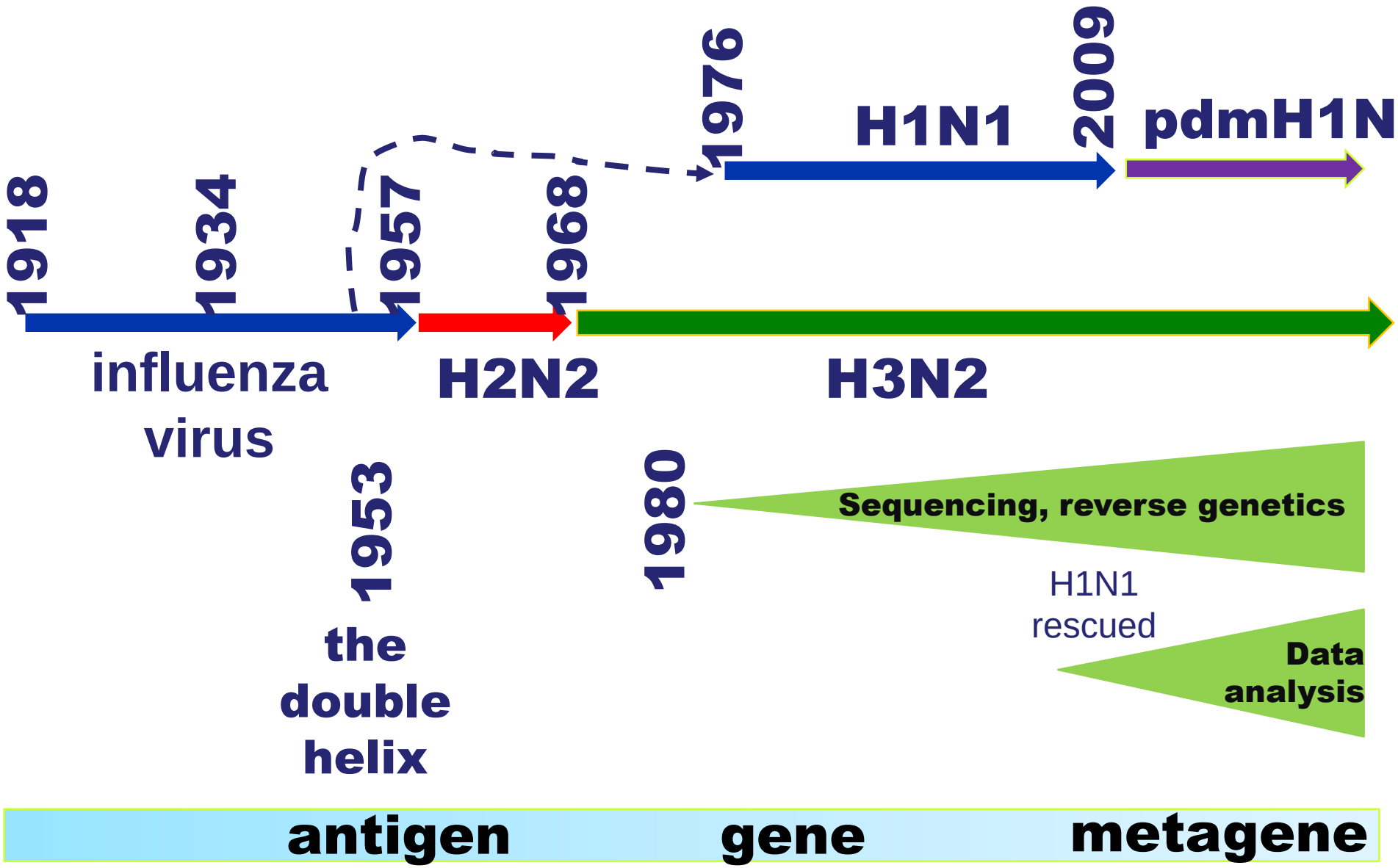
Daniel MARC
INRA - Infectiologie et Santé Publique

INRA SCIENCE & IMPACT

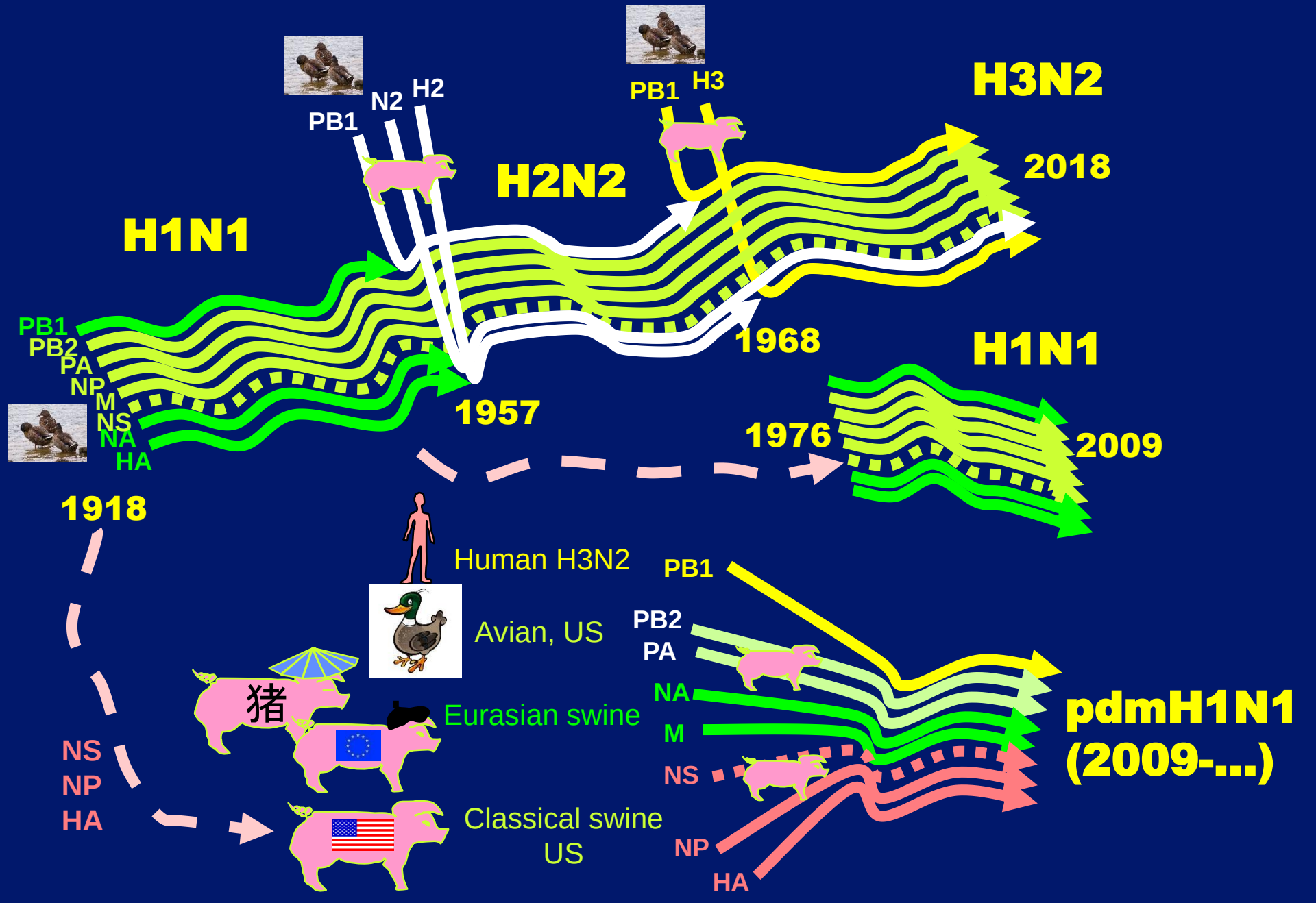
Viruses: reservoir of gene diversity

Chosen example: influenza viruses

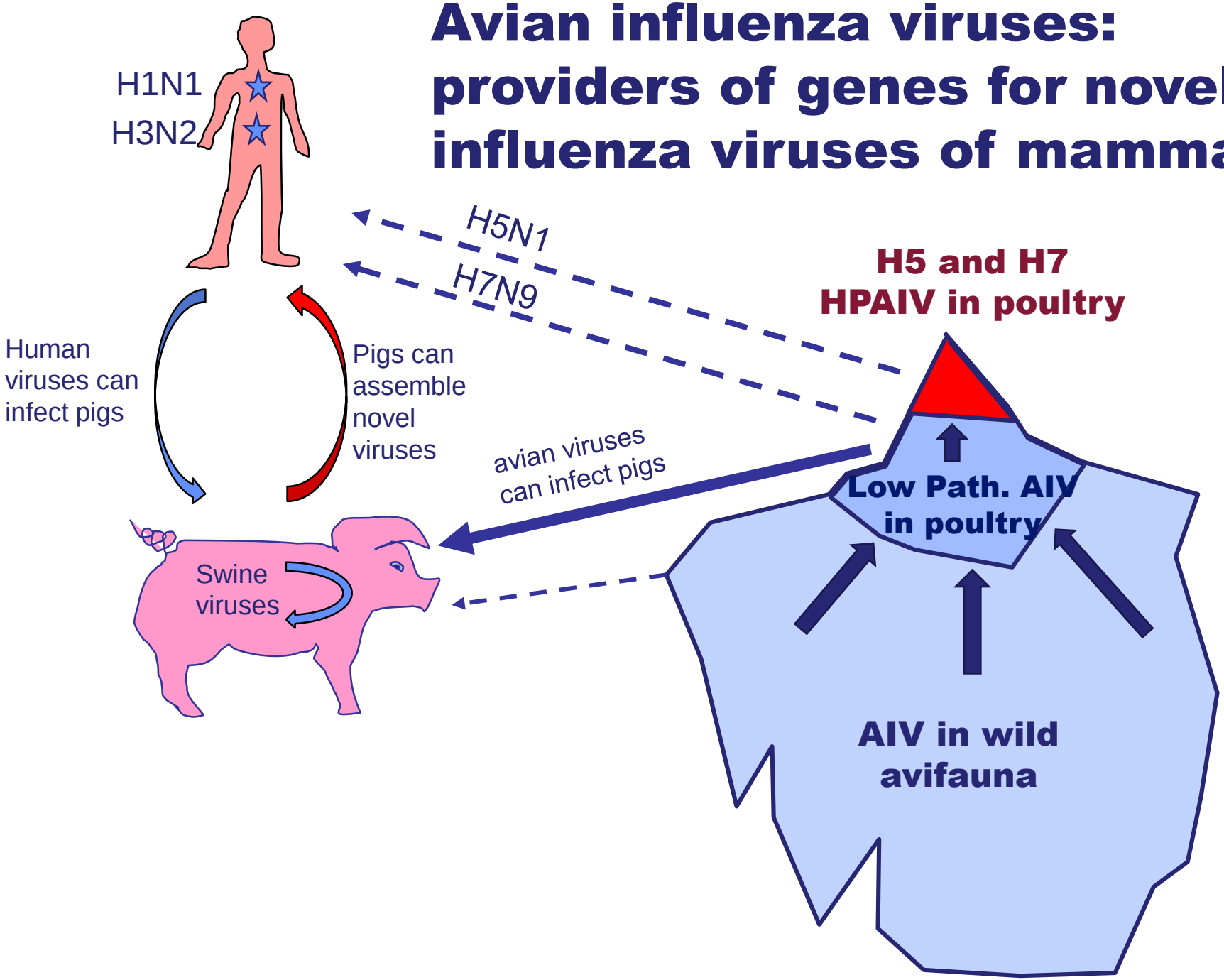
Events that shaped our current knowledge



Human influenza viruses, 1918 - 2019

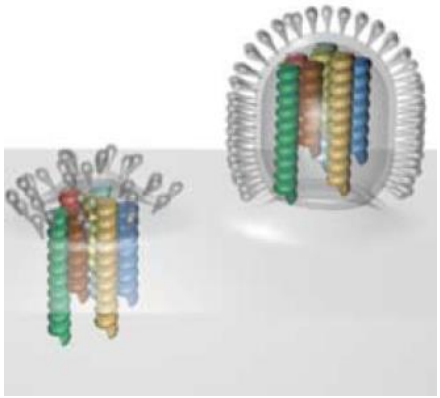


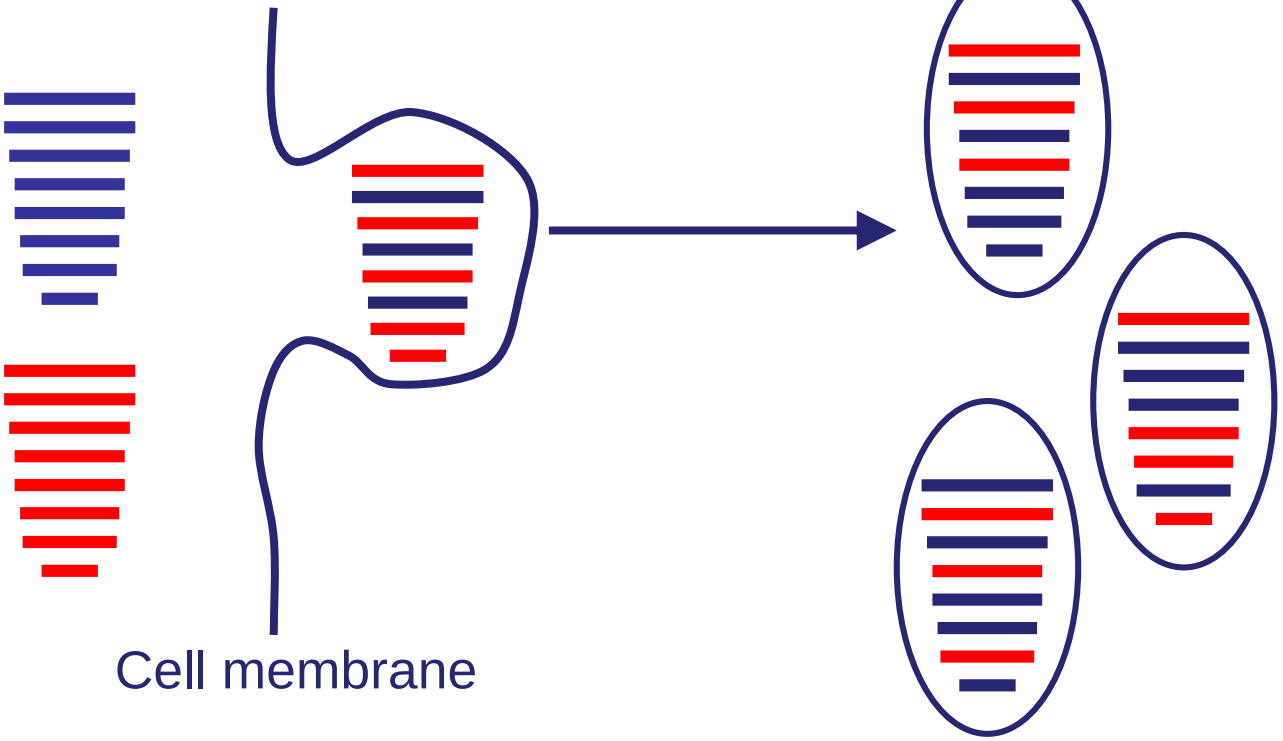
Avian influenza viruses: providers of genes for novel influenza viruses of mammals



Reassortments between influenza viruses permanently produce novel viruses

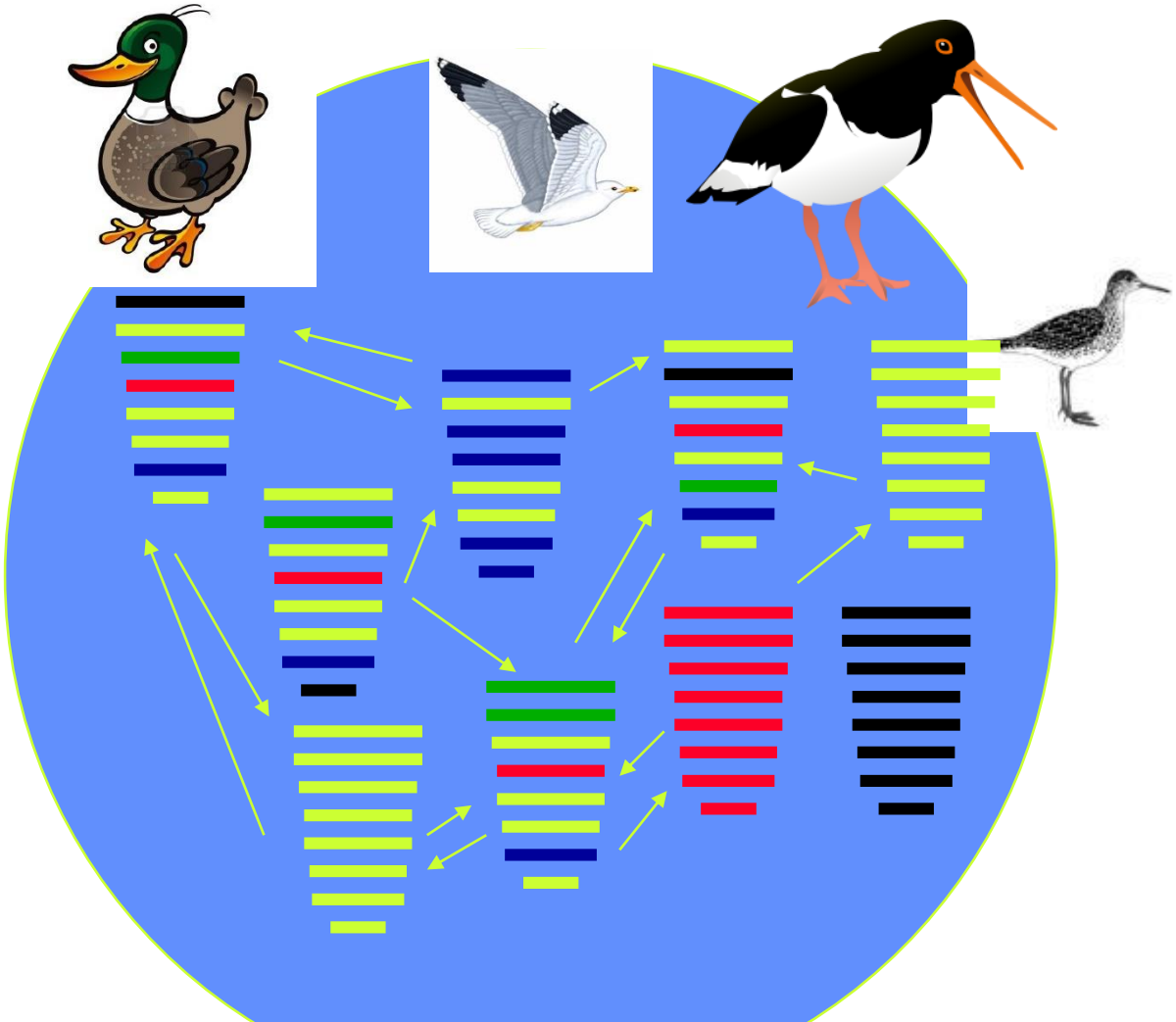
cell infected
by two viruses





A frequent event – and a major driver of the evolution of influenza viruses

In wild waterfowl, circulation of viruses within and between host species, permanent exchanges of segments



Similar, or even larger diversity in other virus families

Pathogenic viruses
Picornaviridae: polio, coxsackie, rhinoviruses
Pneumoviruses, Coronaviruses,

Non-Pathogenic viruses
Numerous viruses discovered in virome explorations

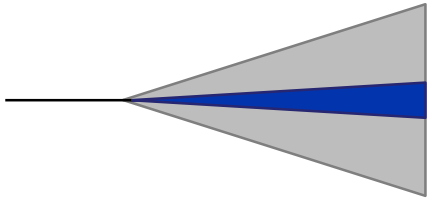
Wherever we look, a huge diversity of viruses

- **in domesticated organisms (mammals, plants)**

- **in hitherto unexplored biological systems**
  - Aquatic environments
  - Bats
  - amoebas → giant viruses

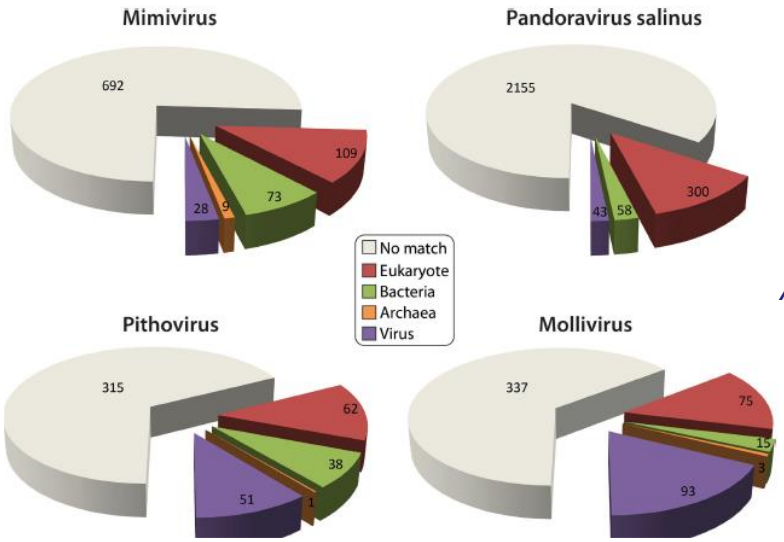
Knowable diversity

Viruses that were previously unknown, and expand the known viral families



Unknowable diversity

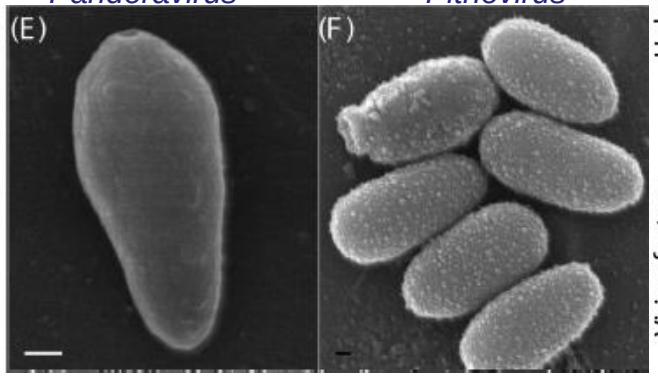
Novel families, with lots of novel unknown genes



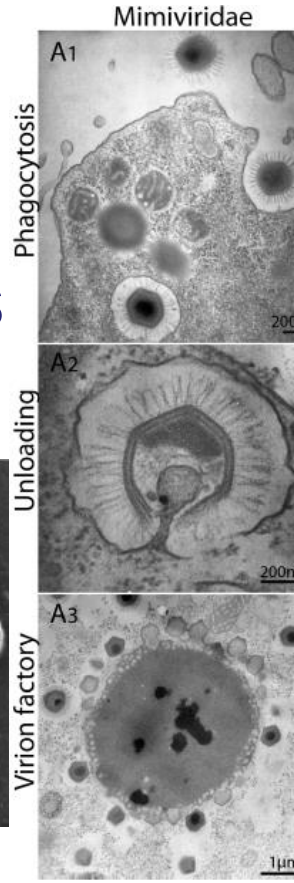
65 to 85% of ORFans

Abergel 2015

Pandoravirus *Pithovirus*

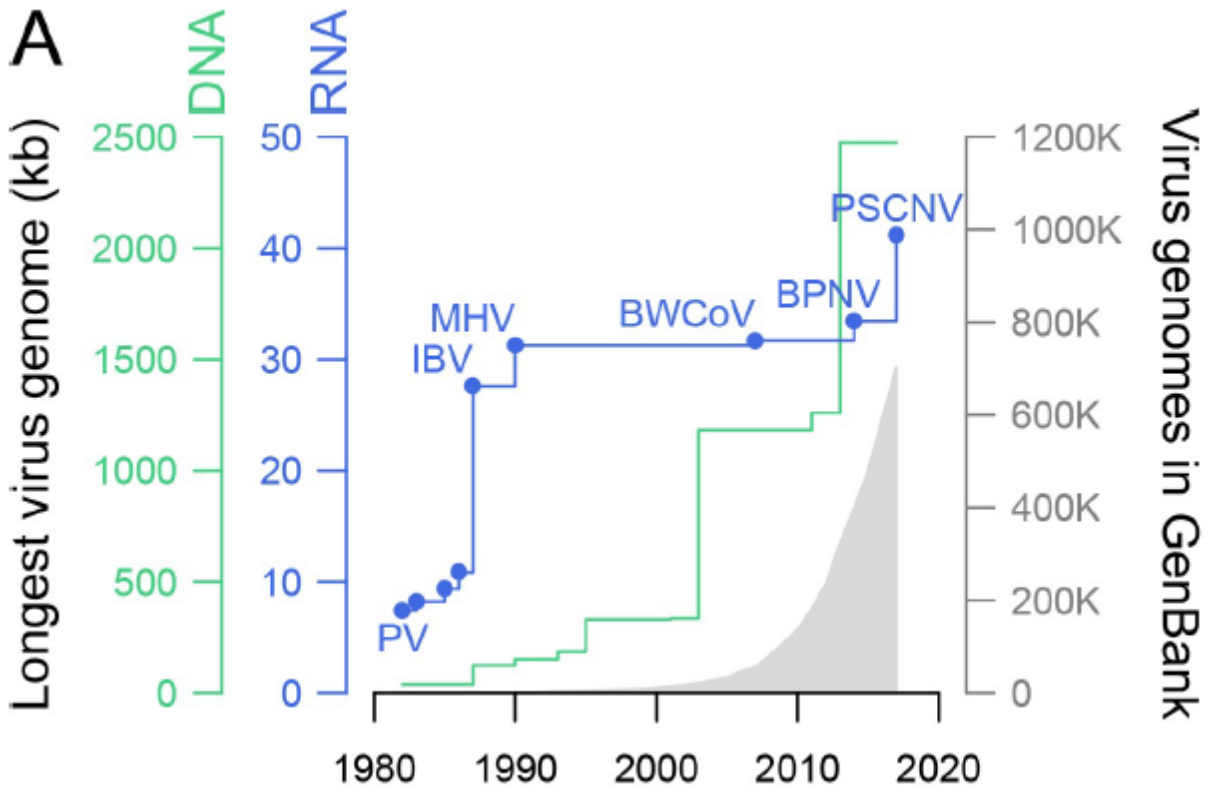


scale bar 100 nm



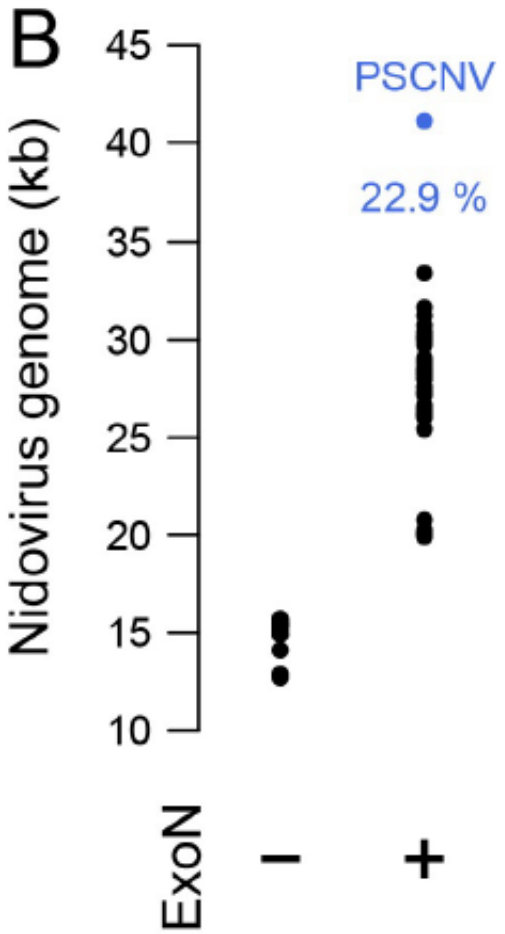
"…We also know there are **known unknowns**; that is to say we know there are some things we do not know. But there are also **unknown unknowns** -- the ones we don't know we don't know." Donald Rumsfeld, US Defense Secretary

More and more viral genomes sequenced
Unexpectedly large genomes

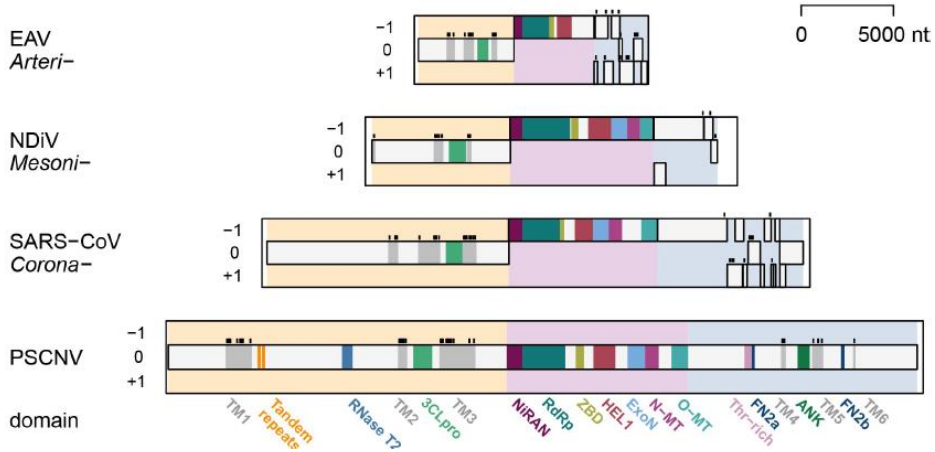


Saberi et al, Plos Path 2018

Large RNA viruses acquired a proofreading activity (ExoN), allowing still larger genomes



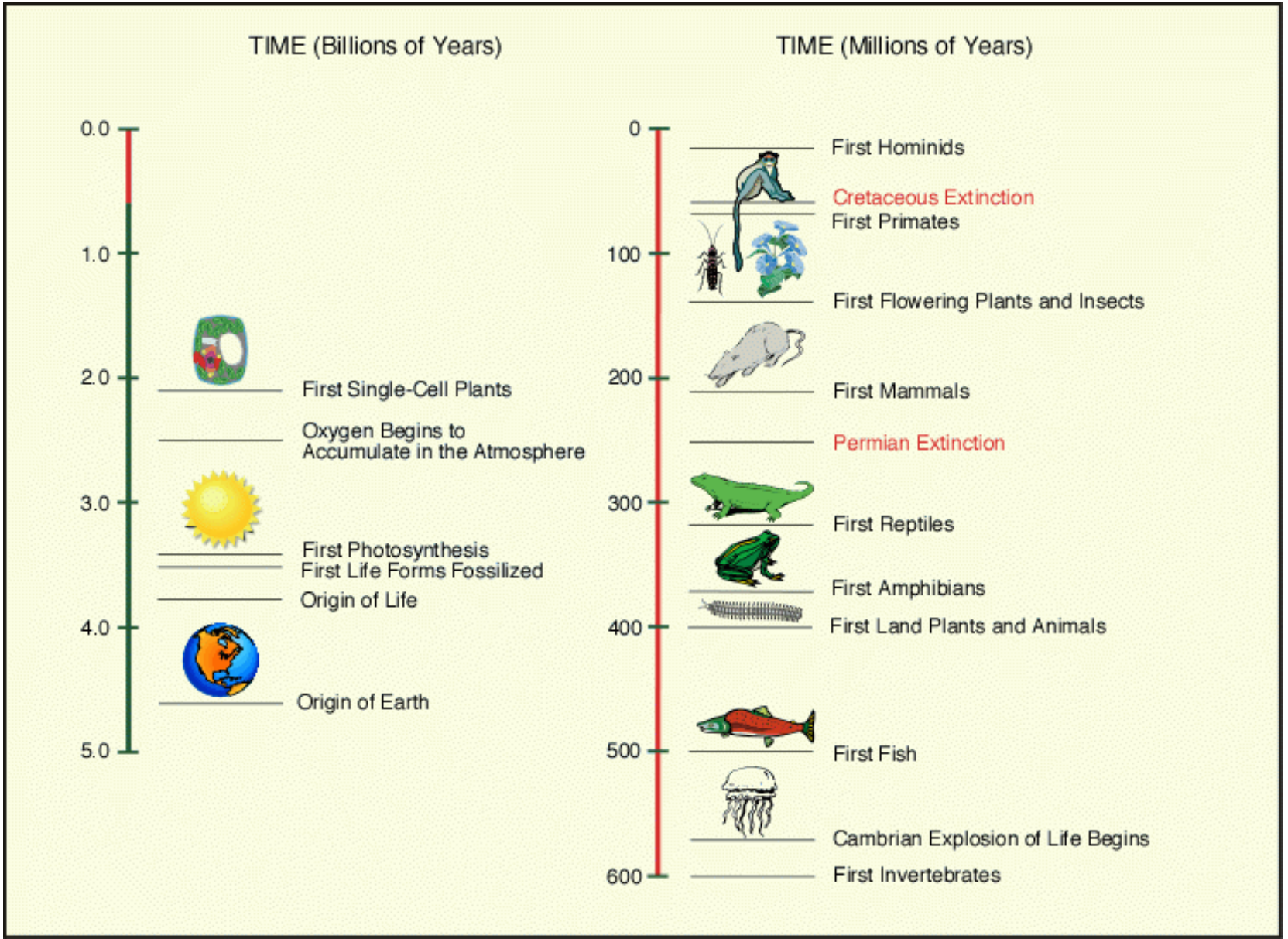
← Large Nidoviridae (incl. **Coronaviridae**)



← Small-genome Nidoviridae (**Arteriviridae**)
No ExoN activity

Saberi et al, Plos Path 2018

Viruses probably date back to the origins of life
They have had plenty of time to evolve / diversify



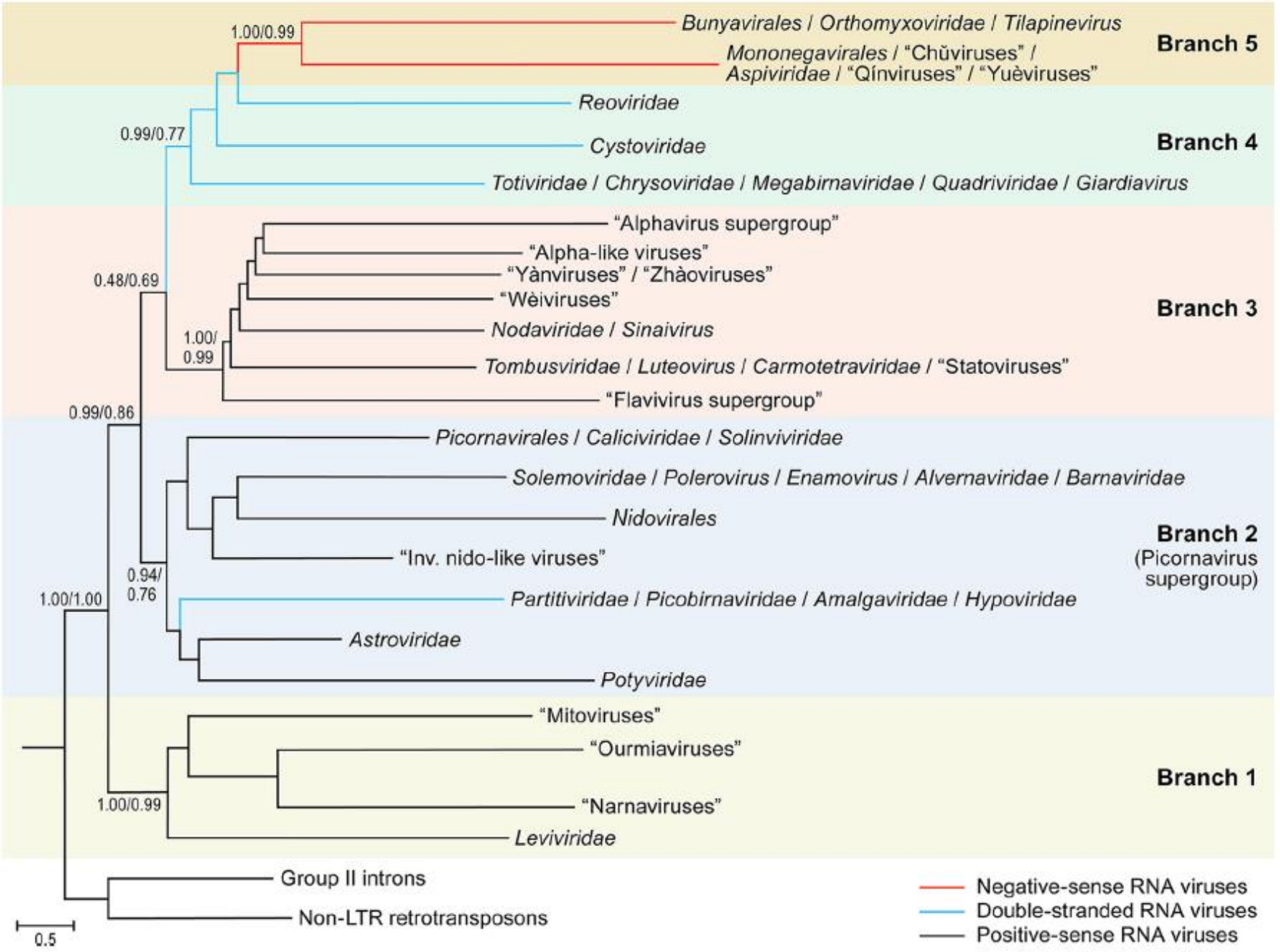
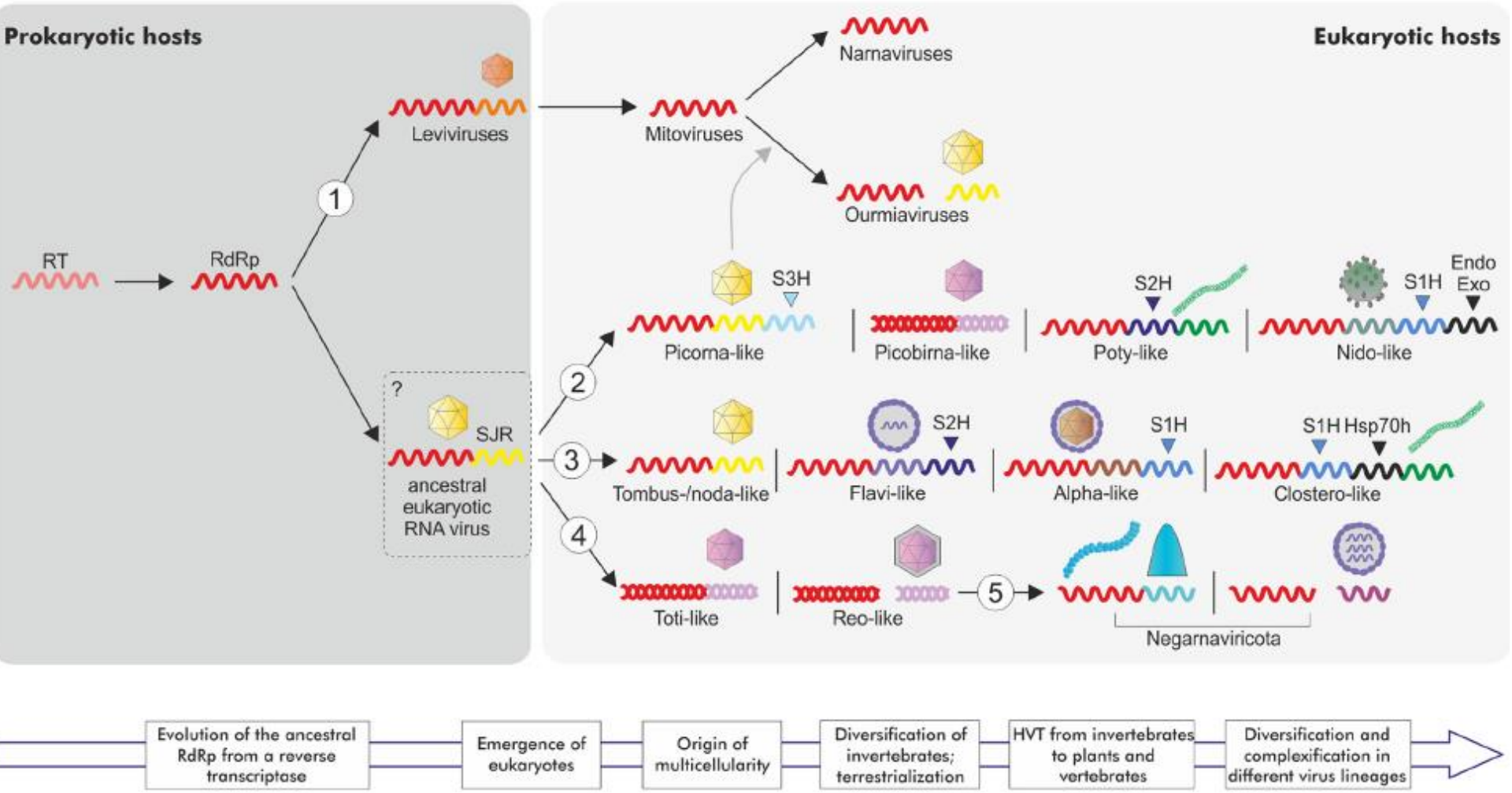


FIG 1 Phylogeny of RNA virus RNA-dependent RNA polymerases (RdRps) and reverse transcriptases (RTs): the main branches (branches 1 to 5).

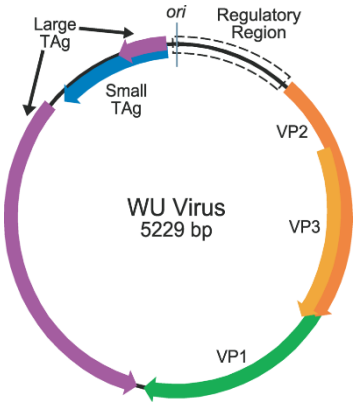
Wolf, mBio 2018

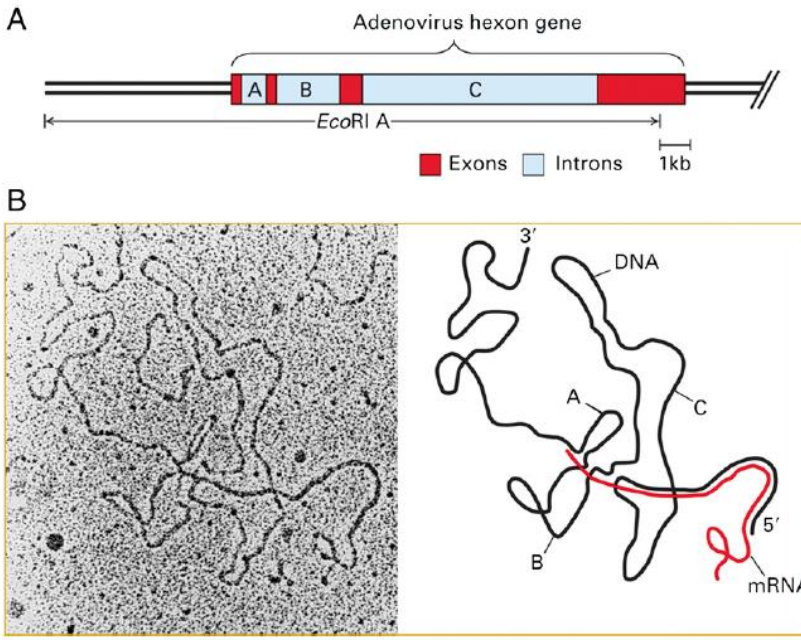


A proposed scenario of evolution of RNA viruses, based on their RdRp gene *(Wolf, mBio 2018)*

Opportunities to enrich the genetic information

- Overlapping reading frames
- Splicing / alternative splicing
- Ribosomal frameshifting
- Polymerase stuttering
- Recombination / reassortment



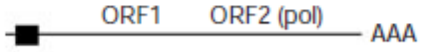
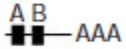
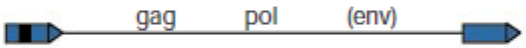


Everything that you can imagine,
life has probably already put it to use

Viruses contribute to host genetics

Directly: viral remnants in our genomes

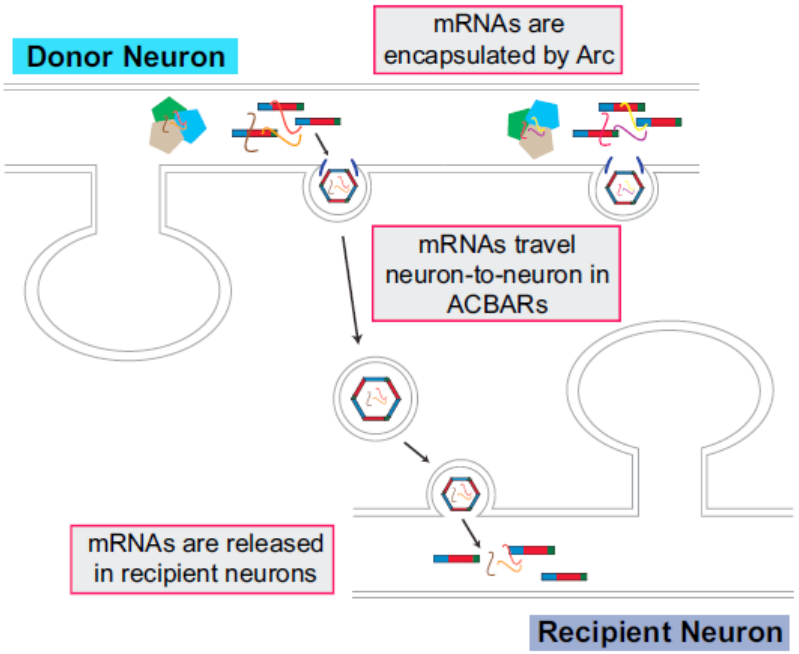
Classes of interspersed repeat in the human genome

			Length	Copy number	Fraction of genome
LINEs	Autonomous		6–8 kb	850,000	21%
SINEs	Non-autonomous		100–300 bp	1,500,000	13%
Retrovirus-like elements	Autonomous		6–11 kb	450,000	8%
	Non-autonomous		1.5–3 kb		
DNA transposon fossils	Autonomous		2–3 kb	300,000	3%
	Non-autonomous		80–3,000 bp		

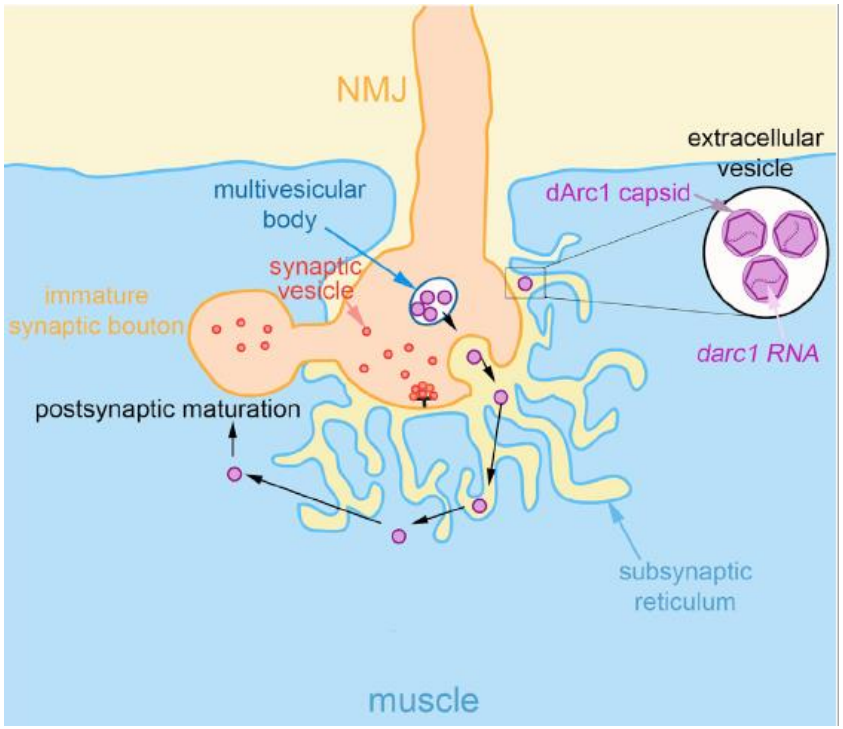
International Human Genome Sequencing Consortium, 2001
These repeats account for >45% of the genome

Viruses contribute to host genetics

Viral remnants providing functional proteins



Pastuzyn, Cell 2018



Ashley, Cell 2018

Ancestral capture of *syncytin-Car1*, a fusogenic endogenous retroviral *envelope* gene involved in placentation and conserved in Carnivora

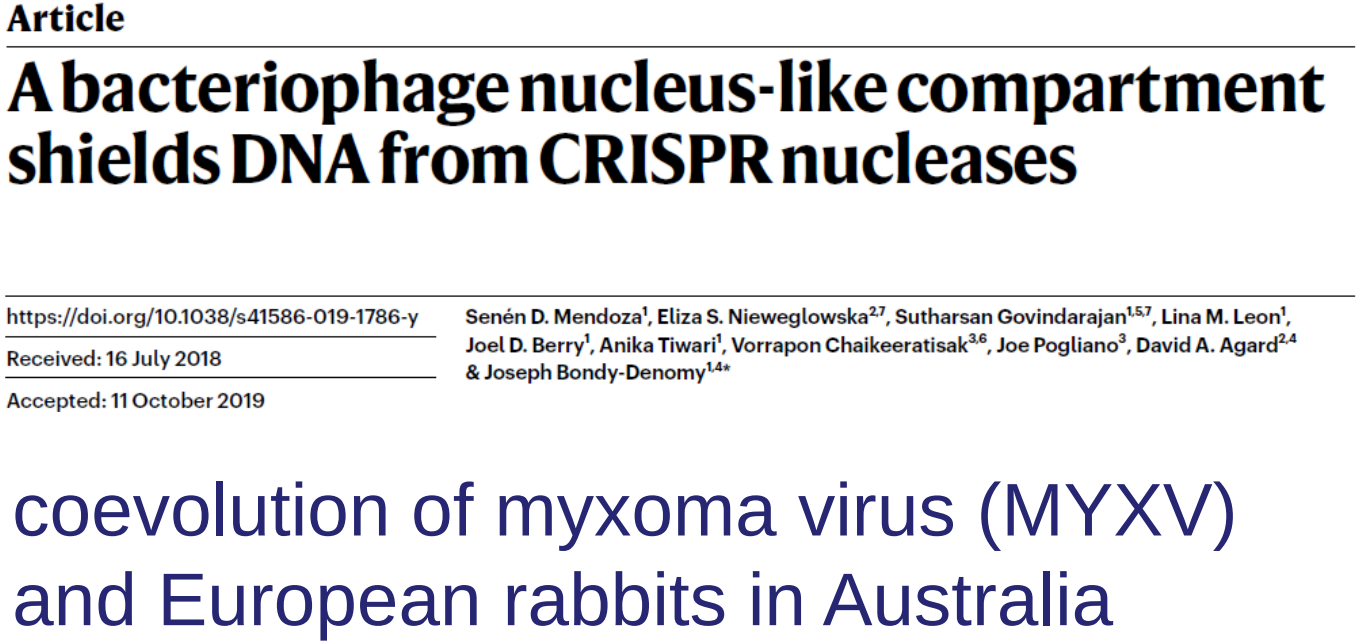
Guillaume Cornelis[a,b], Odile Heidmann[a,b], Sibylle Bernard-Stoecklin[a,b,1], Karine Reynaud[c], Géraldine Véron[d], Baptiste Mulot[e], Anne Dupressoir[a,b,2,3], and Thierry Heidmann[a,b,2,3]

Viruses contribute to host genetics

Indirectly: arms race between viruses and host

- **innate immunity**
- **acquired immunity**
  - acquired immunity in vertebrates
  - acquired immunity in bacteria (CRISPR-Cas systems)

Exemples of arms race



Article

A bacteriophage nucleus-like compartment shields DNA from CRISPR nucleases

https://doi.org/10.1038/s41586-019-1786-y

Received: 16 July 2018

Accepted: 11 October 2019

Senén D. Mendoza[1], Eliza S. Nieweglowska[2,7], Sutharsan Govindarajan[1,5,7], Lina M. Leon[1], Joel D. Berry[1], Anika Tiwari[1], Vorrapon Chaikeeratisak[3,6], Joe Pogliano[3], David A. Agard[2,4] & Joseph Bondy-Denomy[1,4*]

coevolution of myxoma virus (MYXV) and European rabbits in Australia

What is the purpose of viruses?

- **A large fraction of non-pathogenic viruses**
- **Have they (have they had) any function in life?**
- **As we have seen, they played a major role in evolution**
- **If in a biological system I were to diffuse a message, I would opt for a virus, not a chemical component**
- **Giant viruses : «** *the virion is not the virus … but only the vehicle by which the virus (i.e. the virion factory) is propagated from cell to cell* **»** Abergel, 2015

THANK YOU

MERCI pour votre ATTENTION