



# Viruses: tireless, undisciplined explorers of life

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# **Viruses: tireless, undisciplined explorers of life**

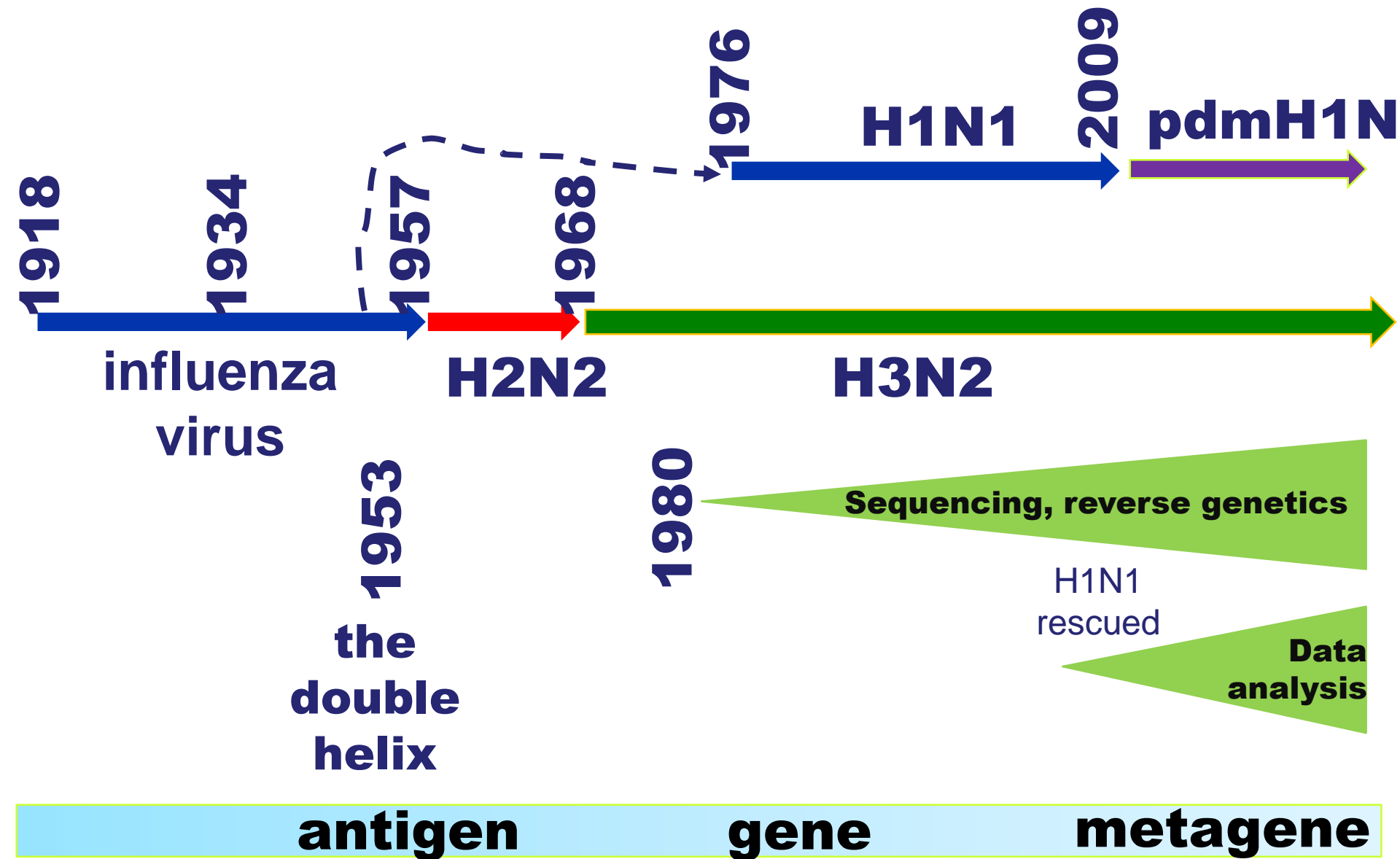
**Daniel MARC**

**INRA - Infectiologie et Santé Publique**

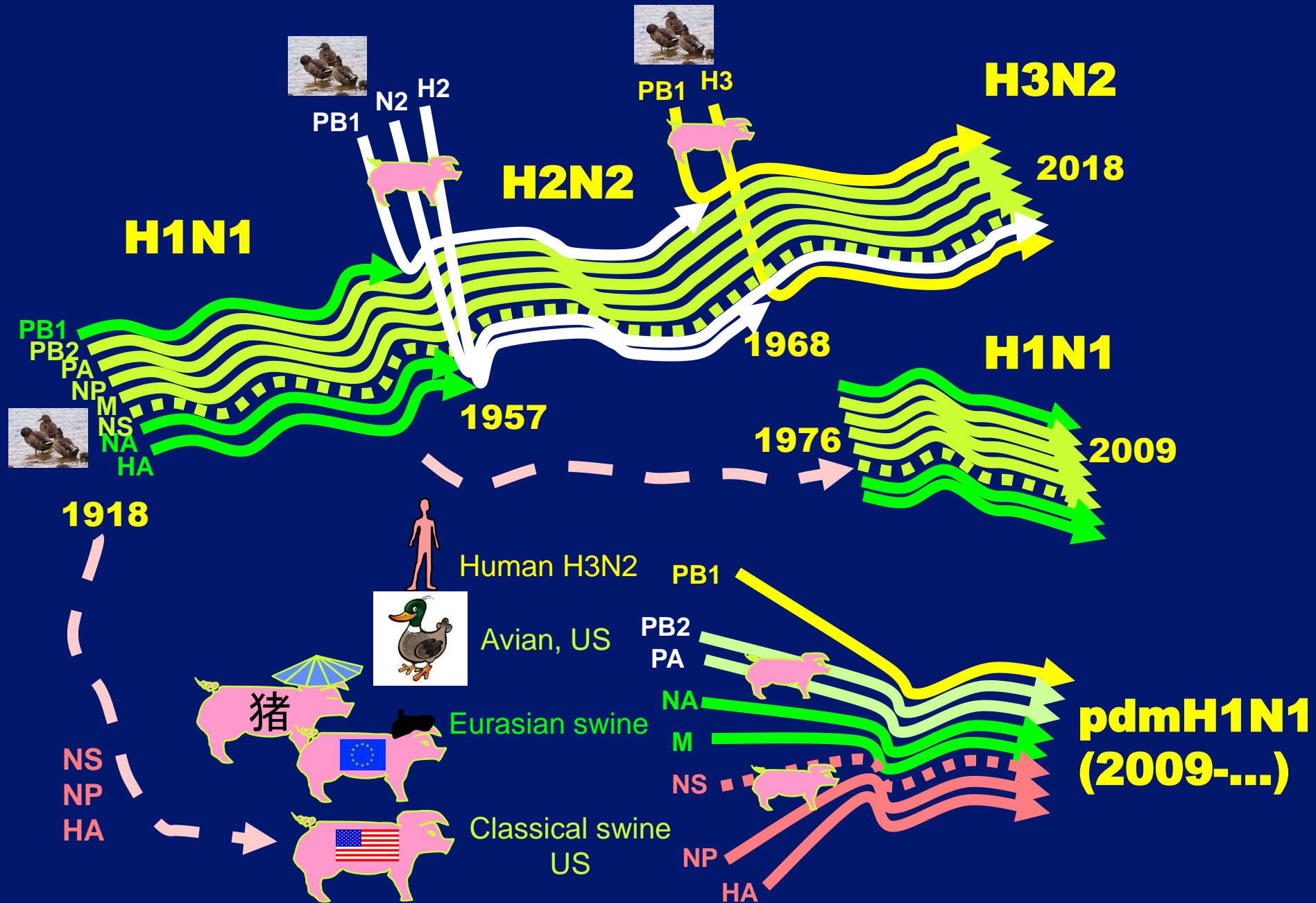
**Viruses: reservoir of gene diversity**

**Chosen example: influenza viruses**

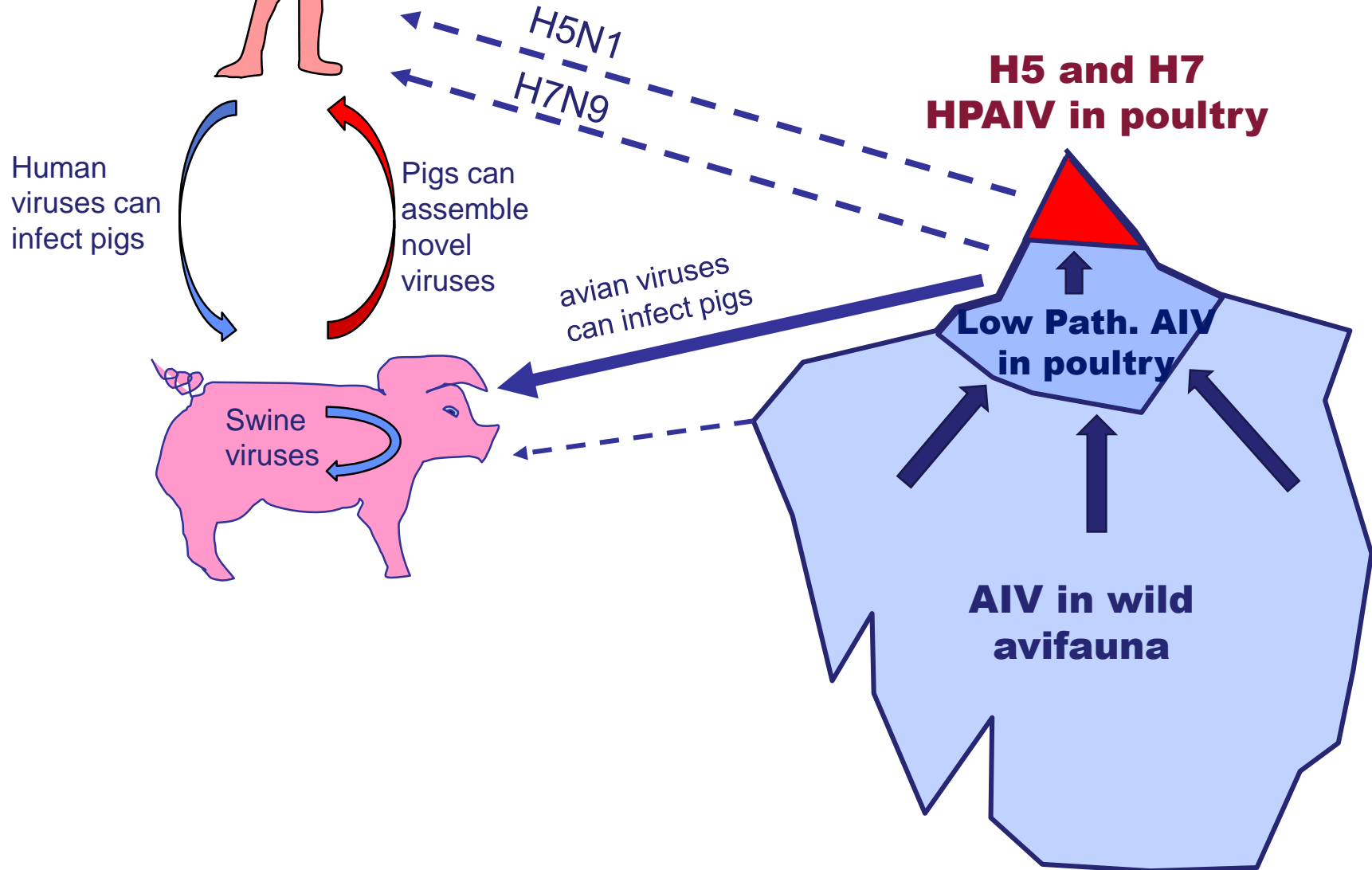
# Events that shaped our current knowledge



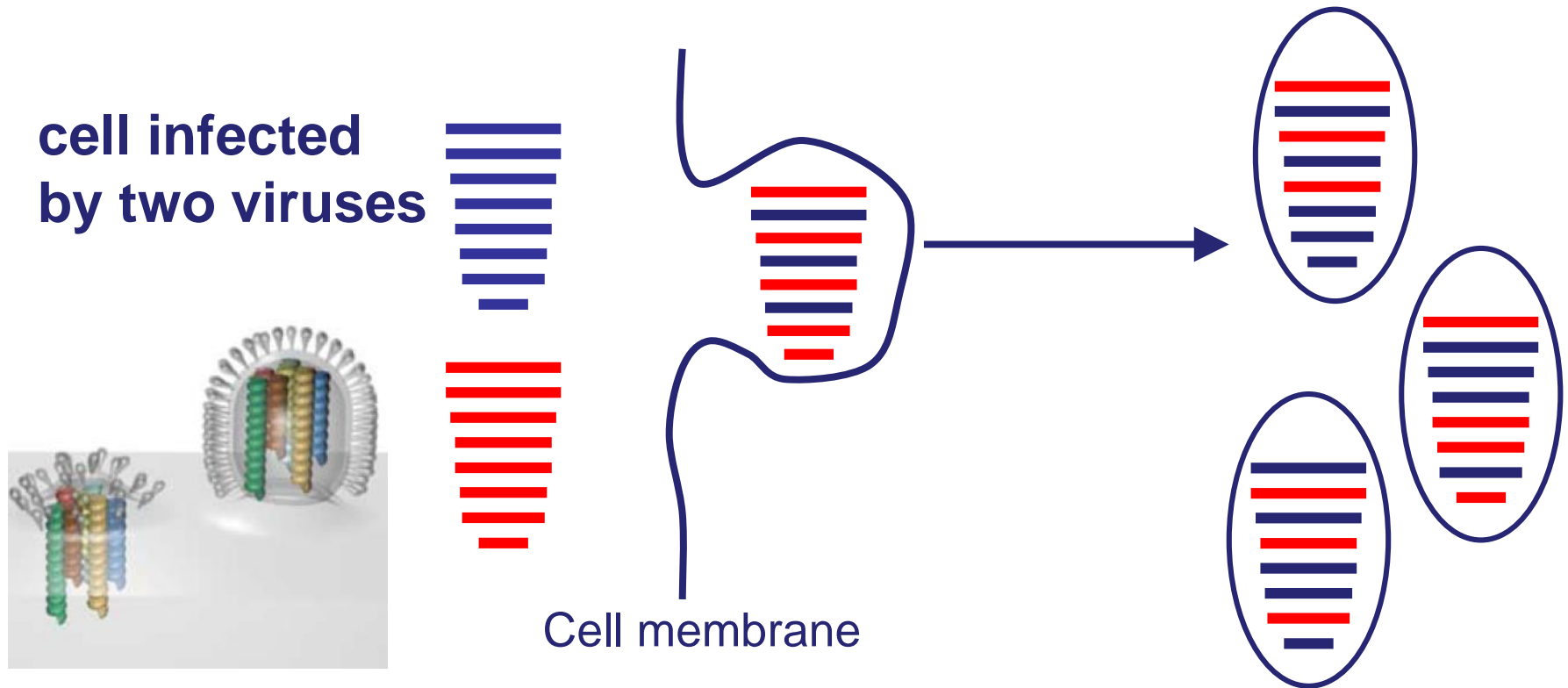
# Human influenza viruses, 1918 - 2019



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

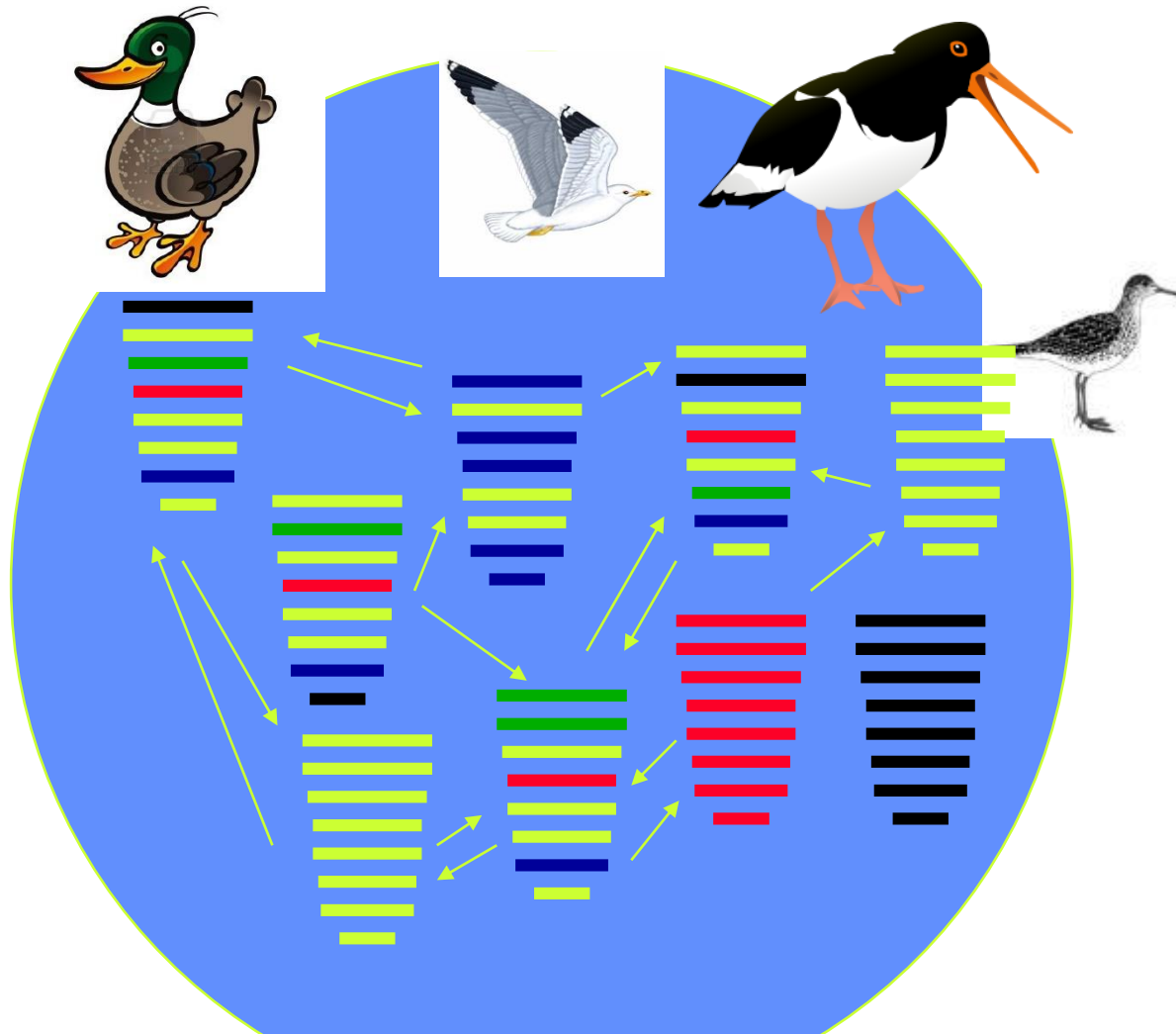


# Reassortments between influenza viruses permanently produce novel viruses



**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**

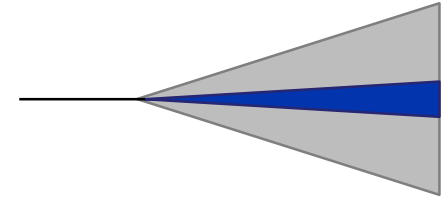
Numerous viruses discovered in virome explorations

## **Wherever we look, a huge diversity of viruses**

- **in domesticated organisms (mammals, plants)**
- **in hitherto unexplored biological systems**
  - Aquatic environments
  - Bats
  - amoebas → giant viruses

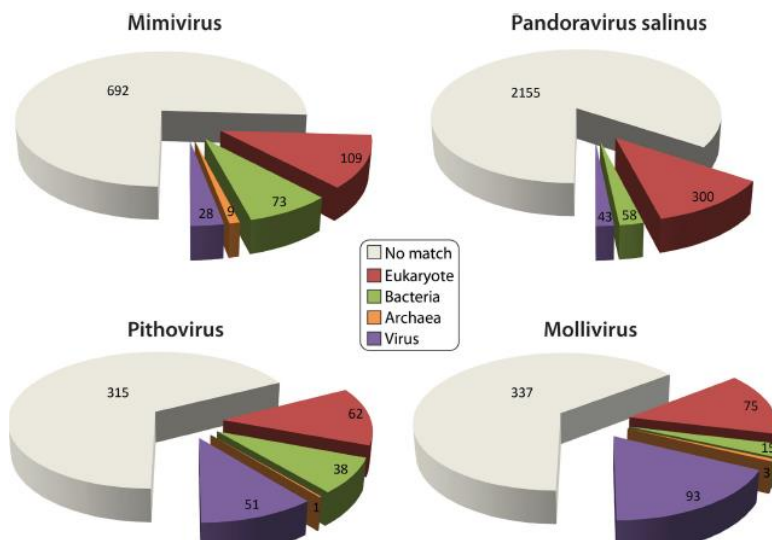
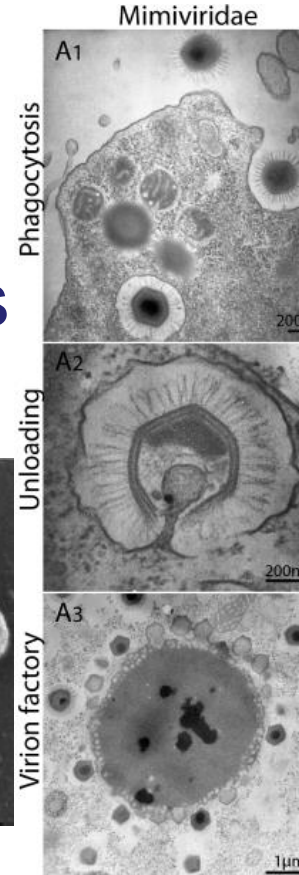
# Knowable diversity

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



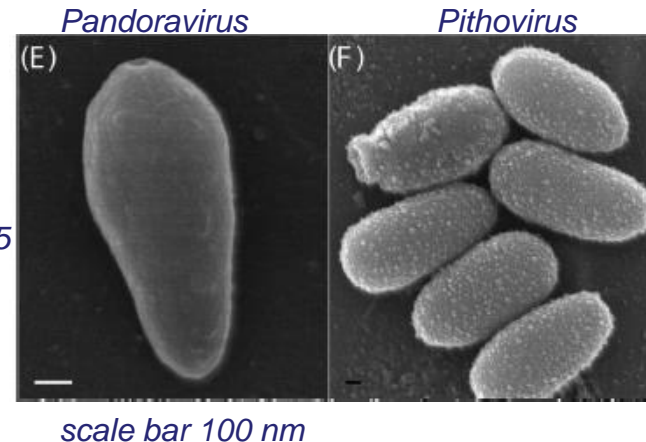
# Unknowable diversity

Novel families, with lots of novel unknown genes



65 to 85% of ORFans

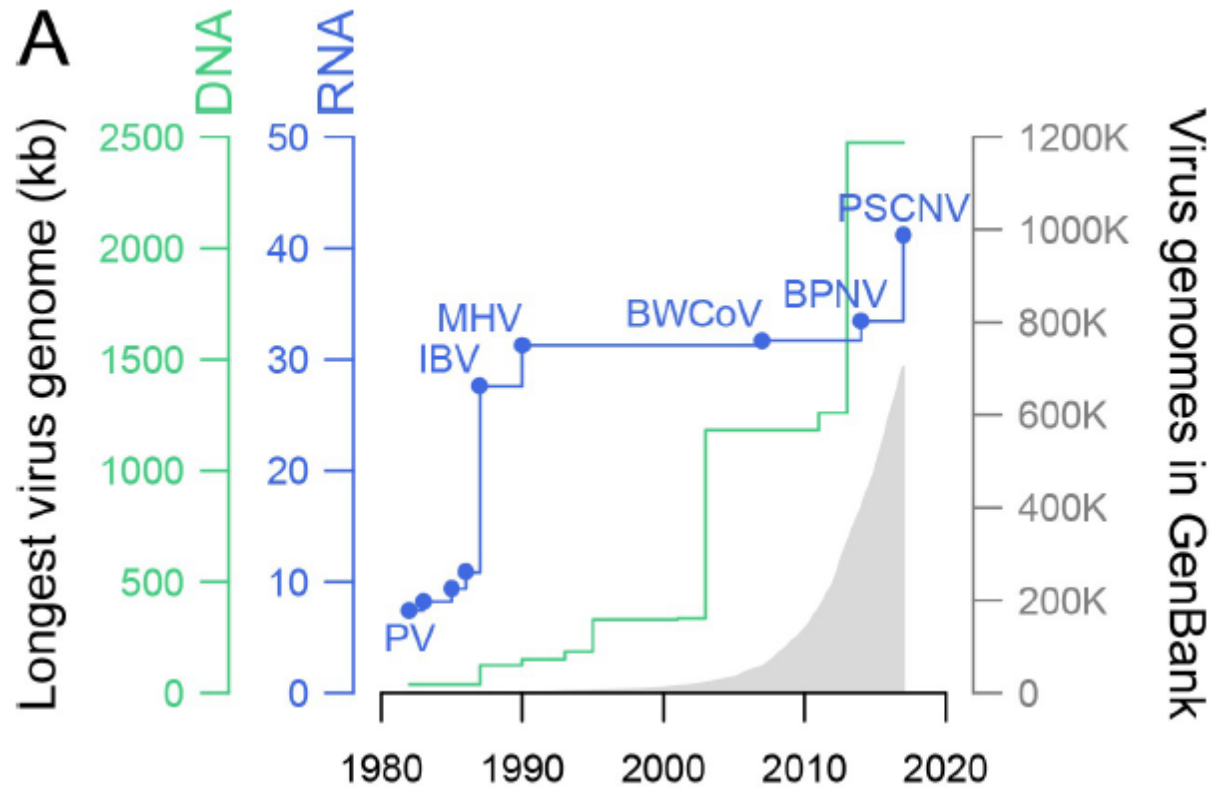
Abergel 2015



“...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

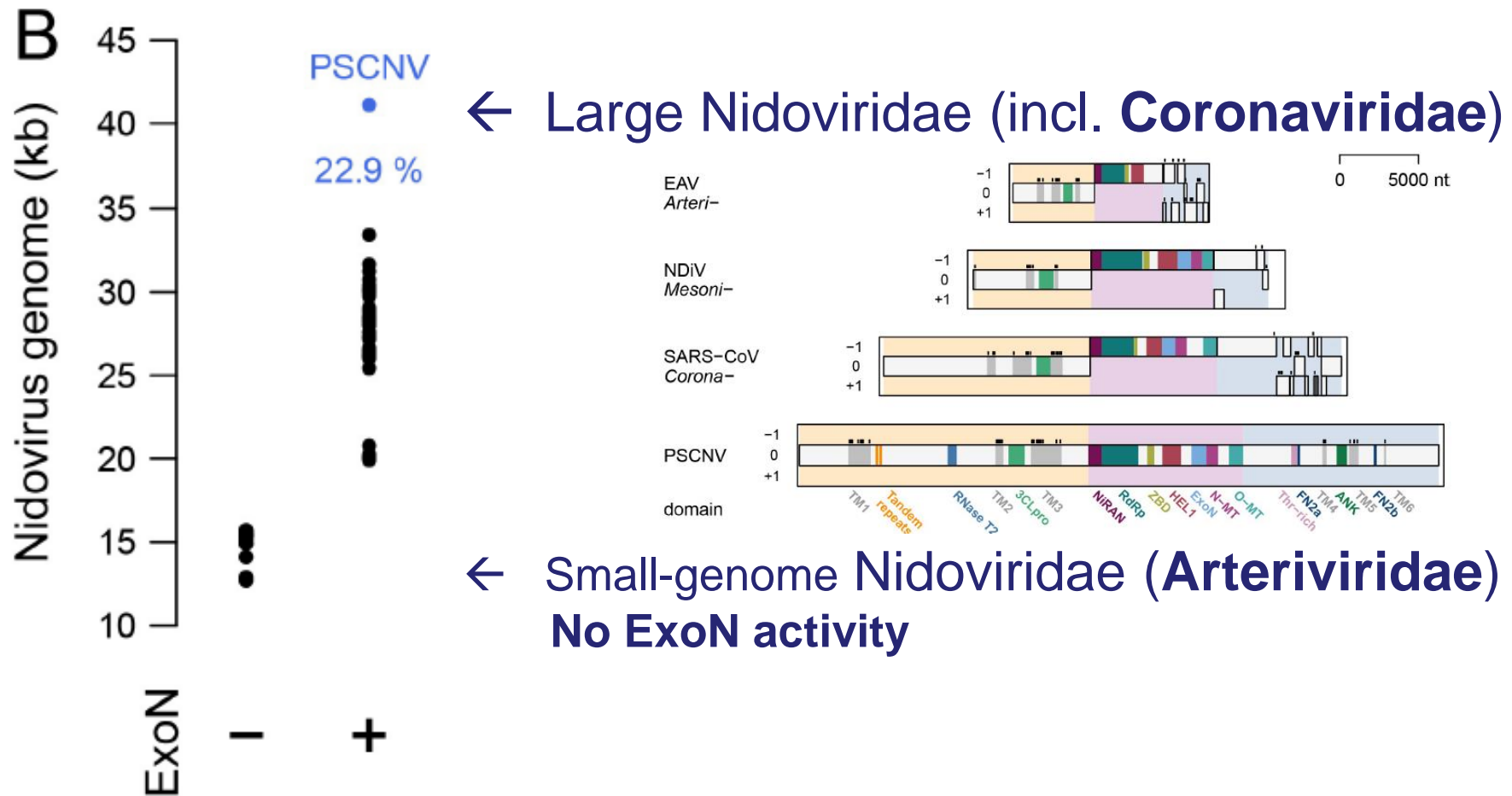
# More and more viral genomes sequenced

## Unexpectedly large genomes



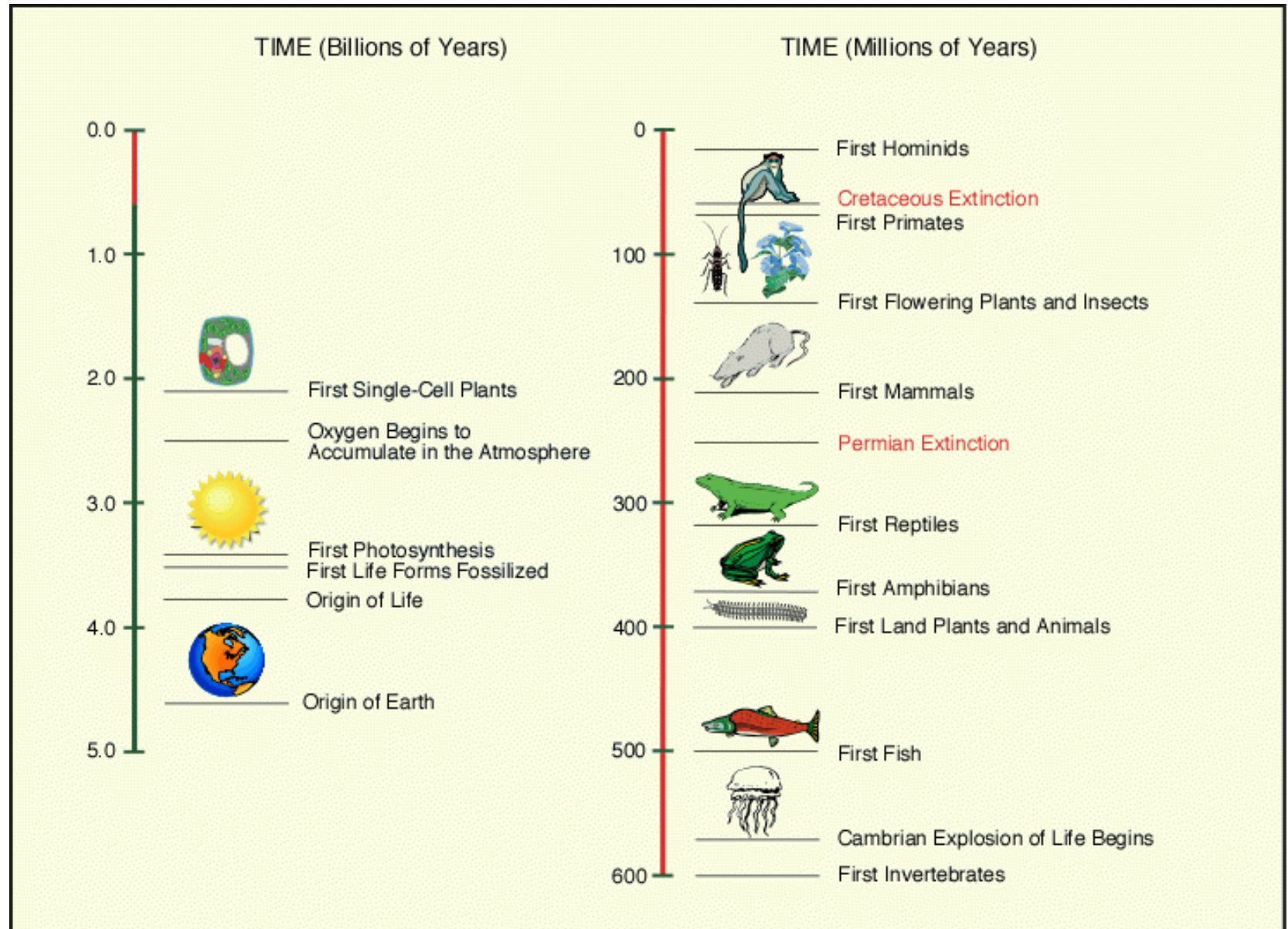
*Saberi et al, Plos Path 2018*

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

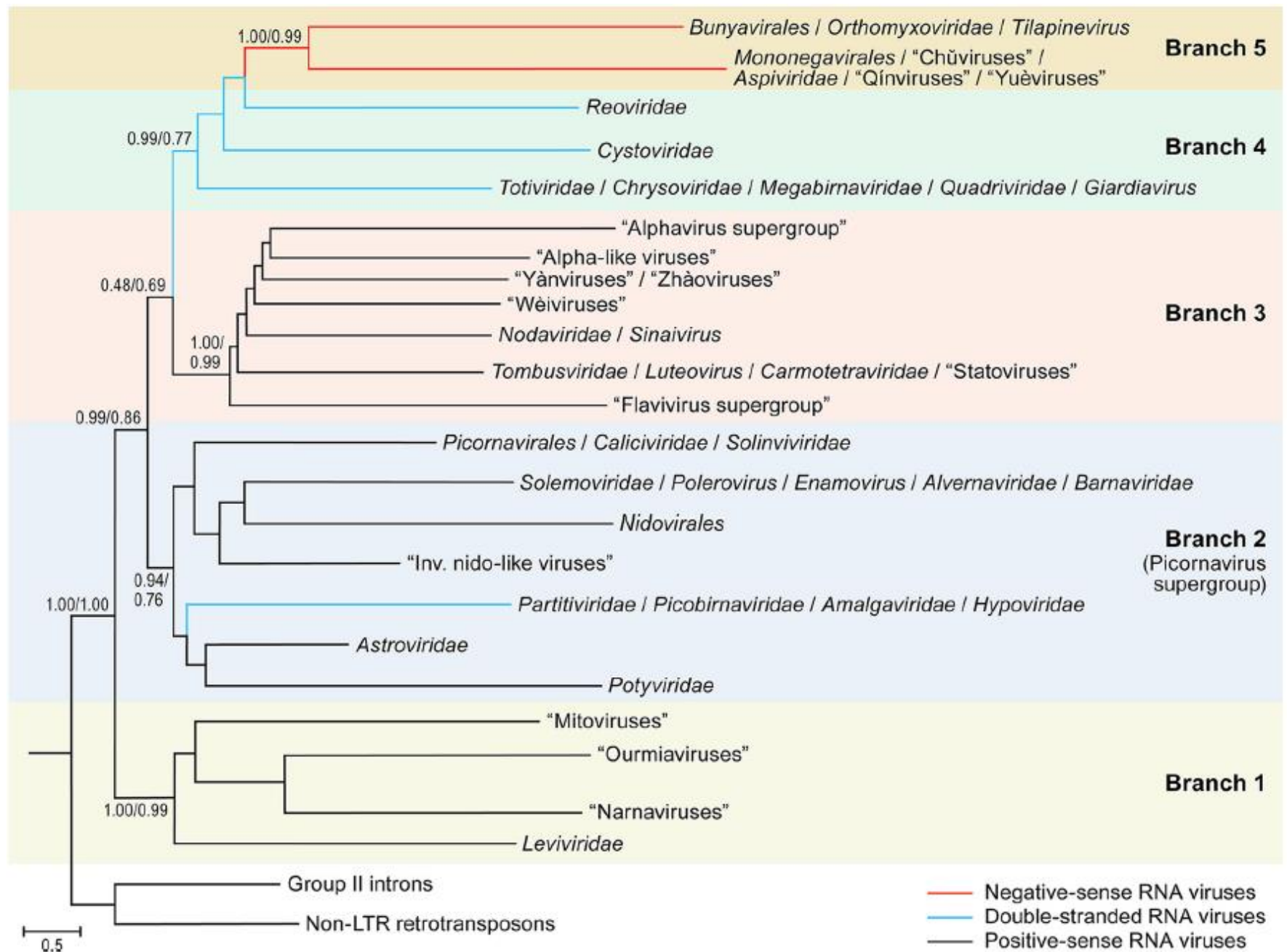


# Viruses probably date back to the origins of life

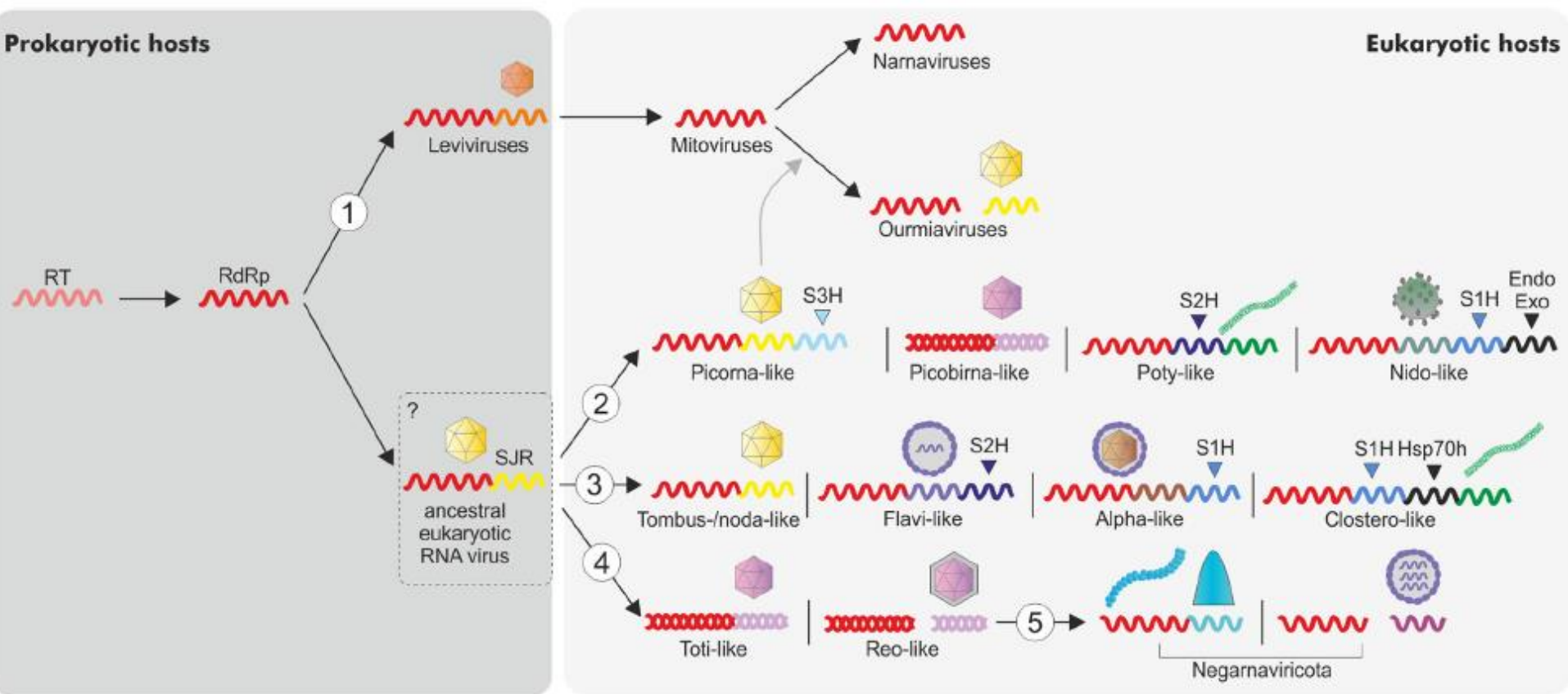
## They have had plenty of time to evolve / diversify







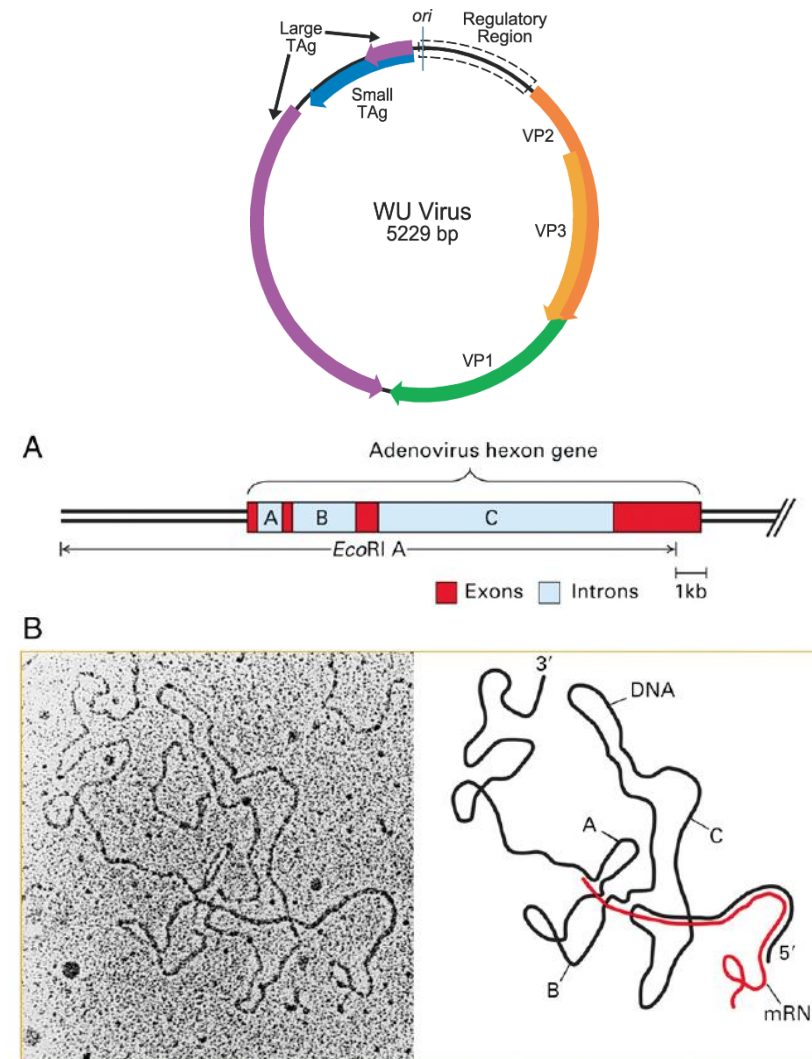
**FIG 1** Phylogeny of RNA virus RNA-dependent RNA polymerases (RdRps) and reverse transcriptases (RTs): the main branches (branches 1 to 5).



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



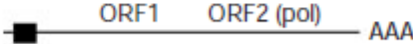
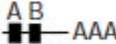
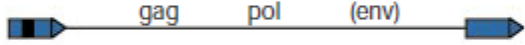

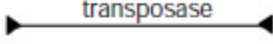

**Everything that you can imagine,  
life has probably already put it to use**



# Viruses contribute to host genetics

## Directly: viral remnants in our genomes

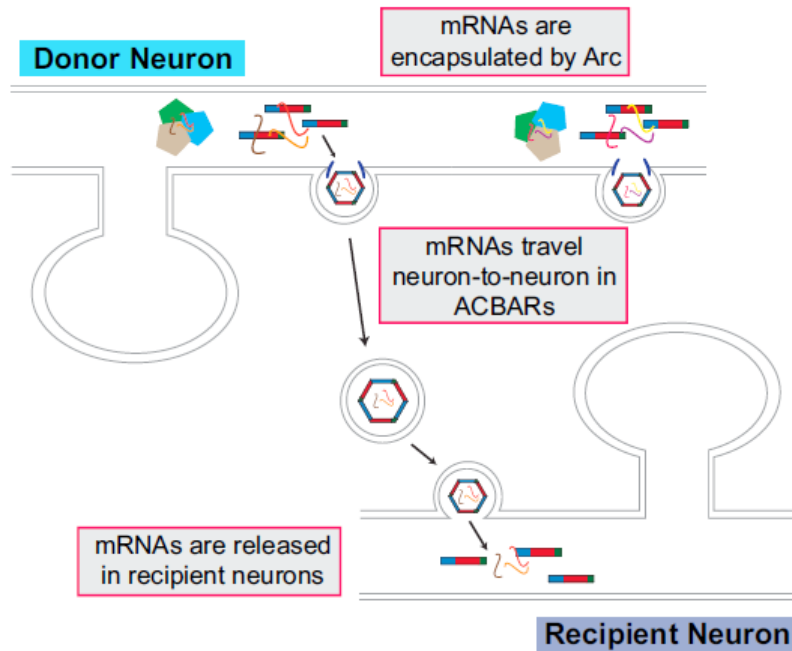
Classes of interspersed repeat in the human genome

|                          |                |   | 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 |             |                    |

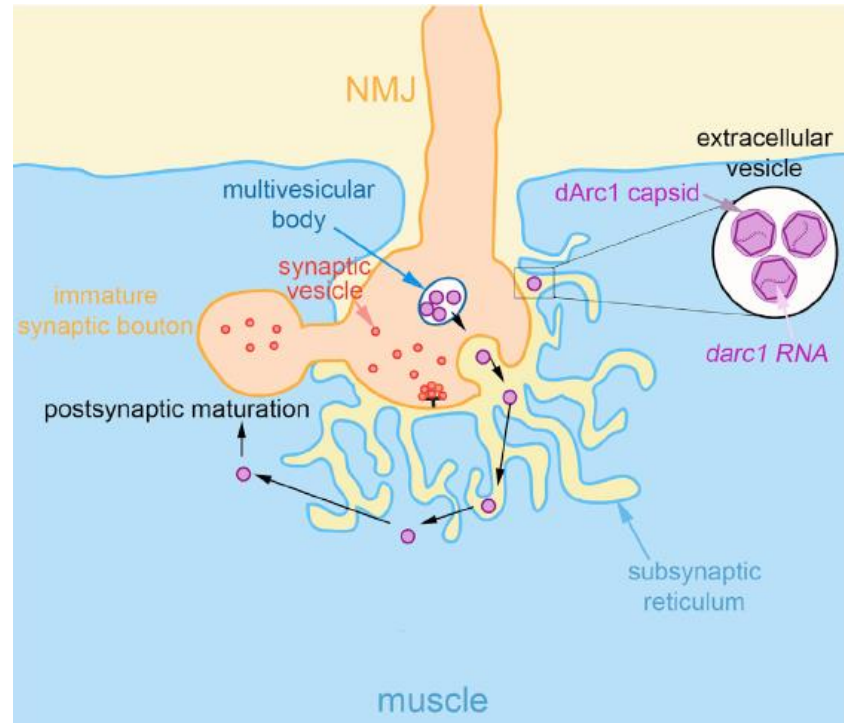
*International Human Genome Sequencing Consortium, 2001*  
*These repeats account for >45% of the genome*

# 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<sup>a,b</sup>, Odile Heidmann<sup>a,b</sup>, Sibylle Bernard-Stoecklin<sup>a,b,1</sup>, Karine Reynaud<sup>c</sup>, Géraldine Véron<sup>d</sup>, Baptiste Mulot<sup>e</sup>, Anne Dupressoir<sup>a,b,2,3</sup>, and Thierry Heidmann<sup>a,b,2,3</sup>

# 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>

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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**