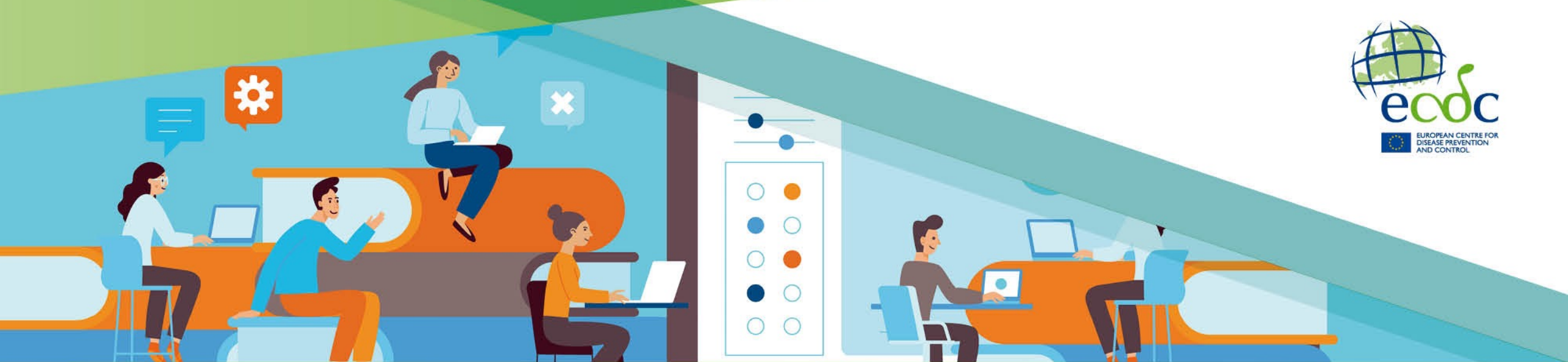




Virtual training 28

Genetic characterisation of poliovirus strains

<17 July 2026>

Maël Bessaud

The Global Polio Lab Network



Responsible for poliovirus surveillance in support of the Global Polio Eradication Initiative

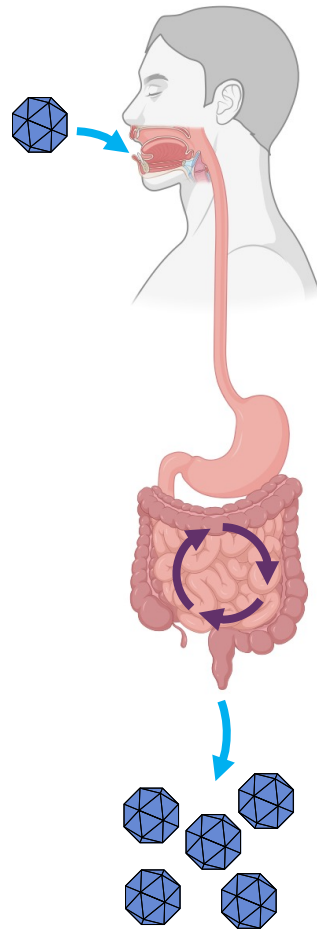
~150 laboratories in 90+ countries

Labs are accredited by WHO through annual audits and proficiency tests

Centralized reporting to WHO

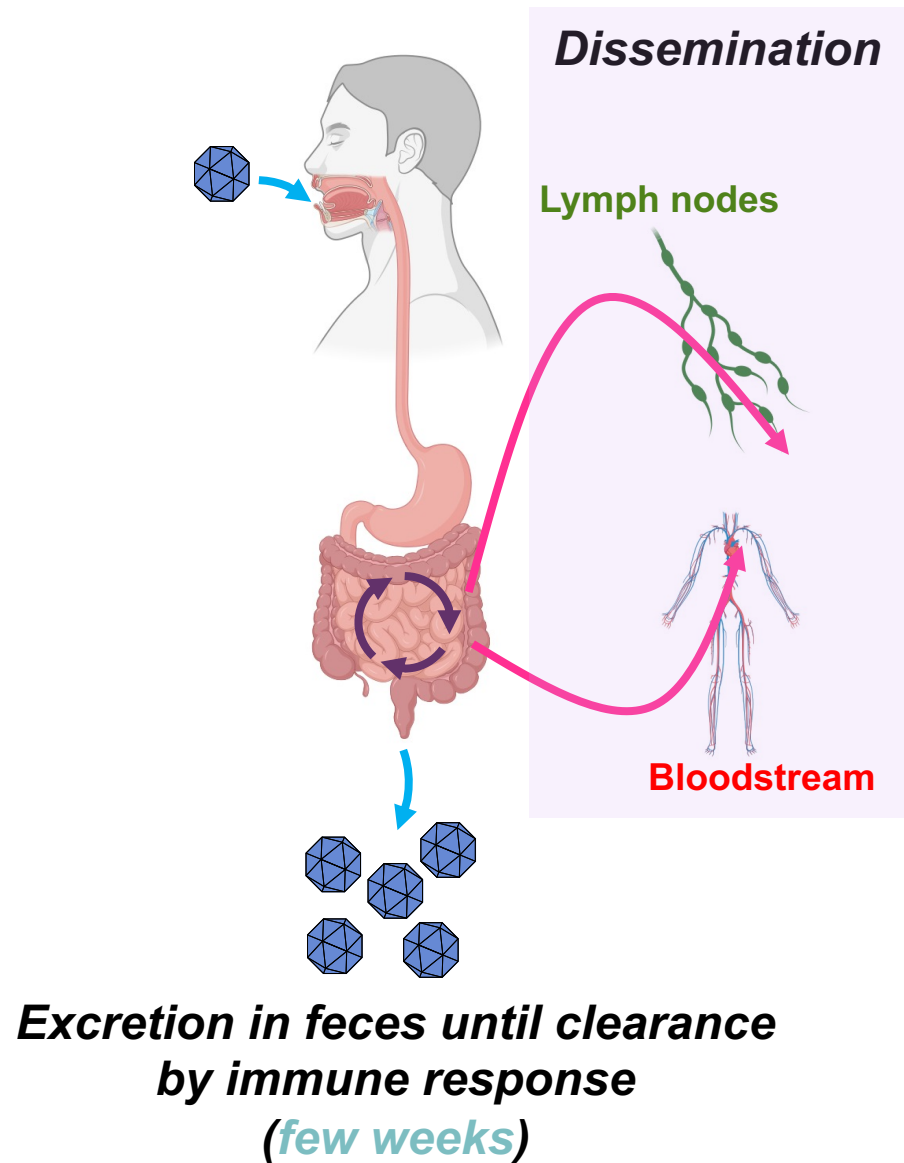
Since the 1980s, the *Institut Pasteur* has hosted a Global Specialized Lab of the GPLN

Polioviruses

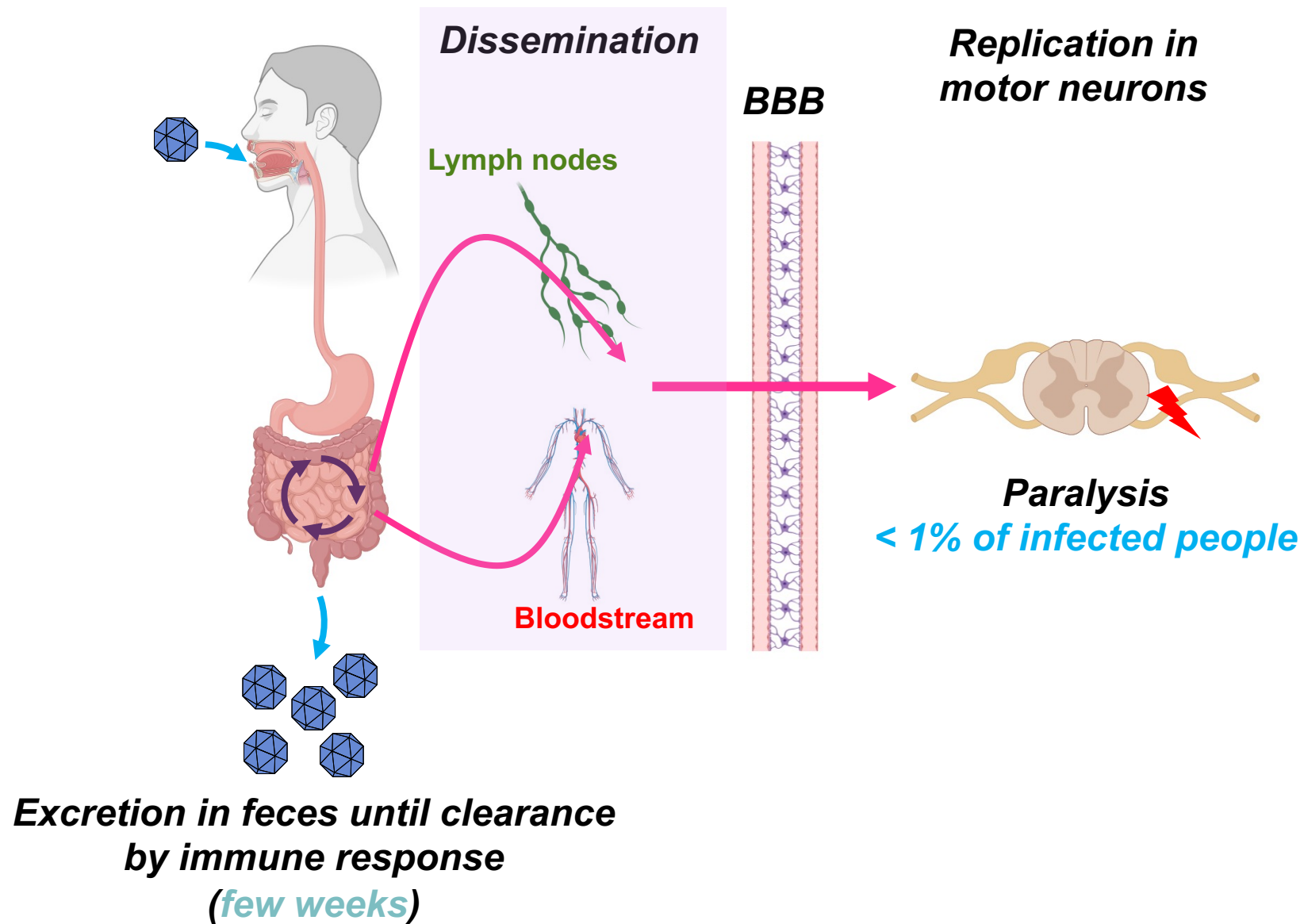


***Excretion in feces until clearance
by immune response
(few weeks)***

Polioviruses



Polioviruses



Paralytic poliomyelitis

Acute flaccid paralysis

All skeletal muscles can be affected (leg, head, neck, diaphragm...)

Fatality rate: 5-10%, due to inability to breathe
increases with age



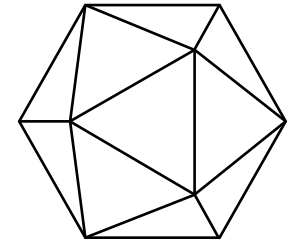
CDC/NIP/ Barbara Rice

Family *Picornaviridae*, genus *Enterovirus*

Small viruses (~30 nm)

Non-enveloped virus particles

⇒ **The capsid drives the tropism & the immune response**



Enteroviruses are described in humans, cattle, pigs, sheep, goats, camels, rodents...

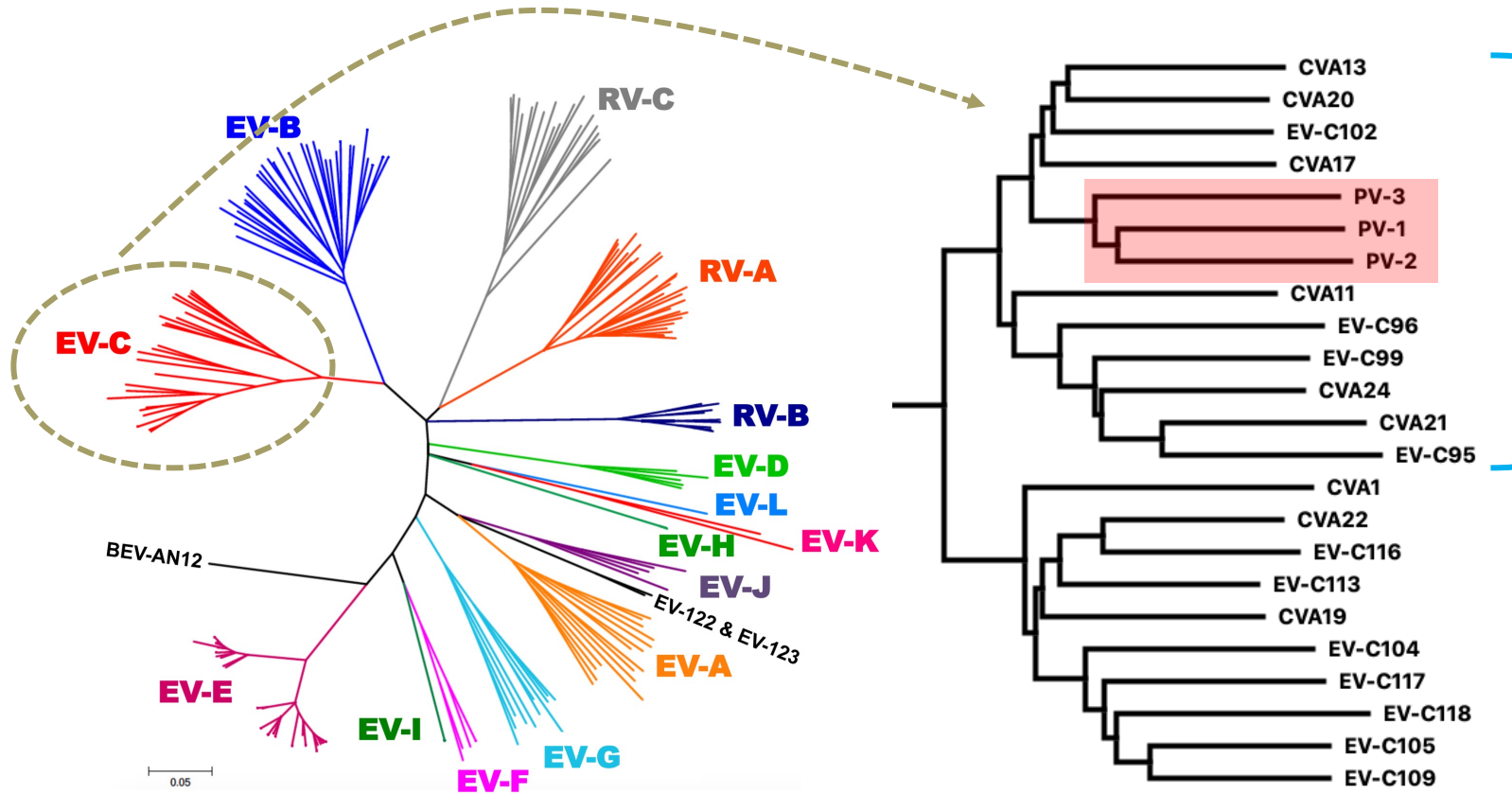
No animal reservoir of poliovirus (although non-human primates can be infected)

Currently, 15 enterovirus species, each containing different virus types

Enterovirus A-L

Rhinovirus A-C

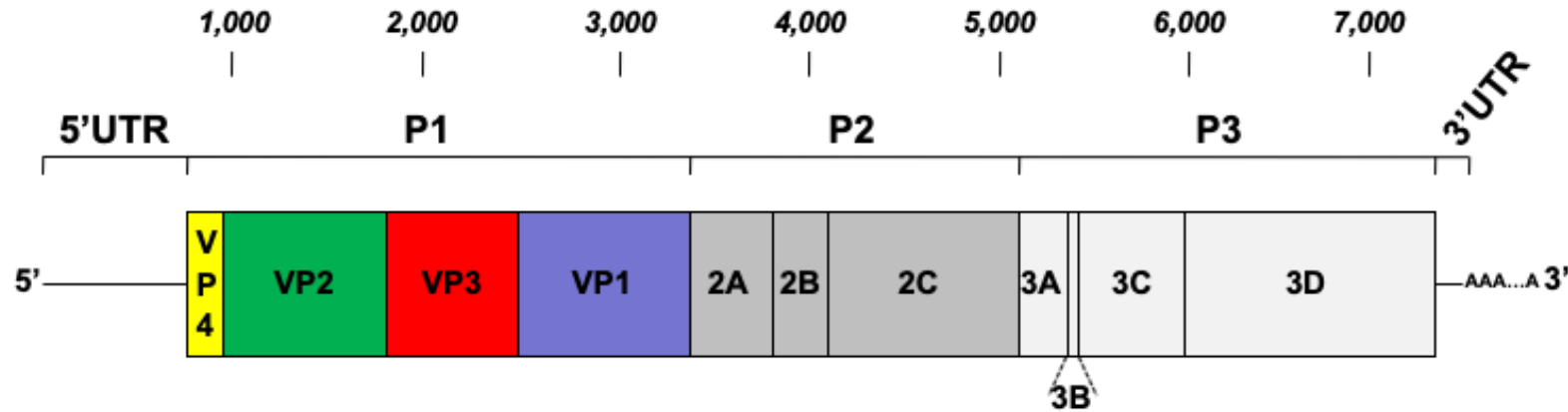
Polioviruses, members of species EV-C



3 serotypes of PV

Close to 10 types of non-polio EVs

Poliovirus genome



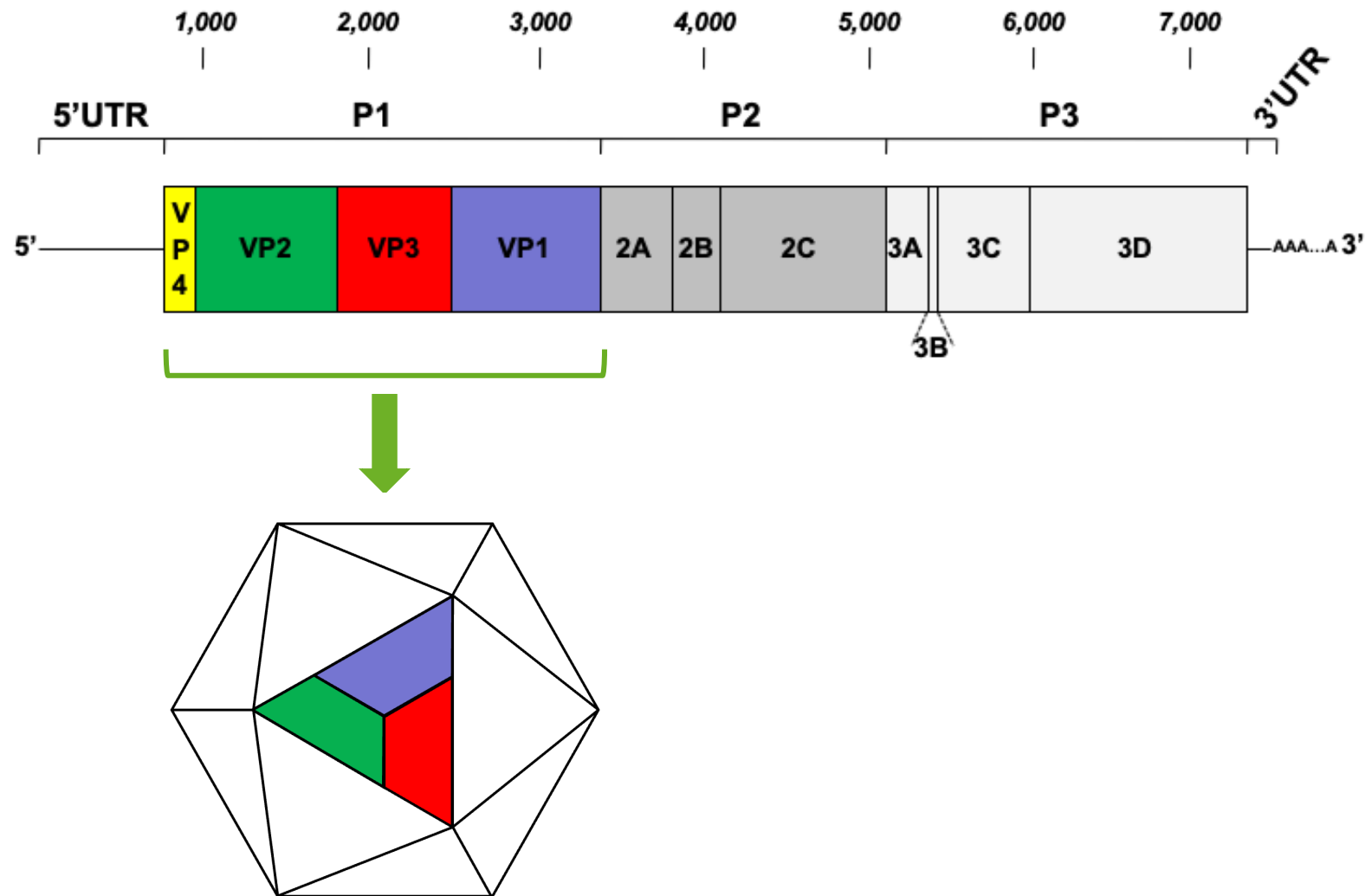
One single-stranded RNA molecule

Positive sense (directly translated)

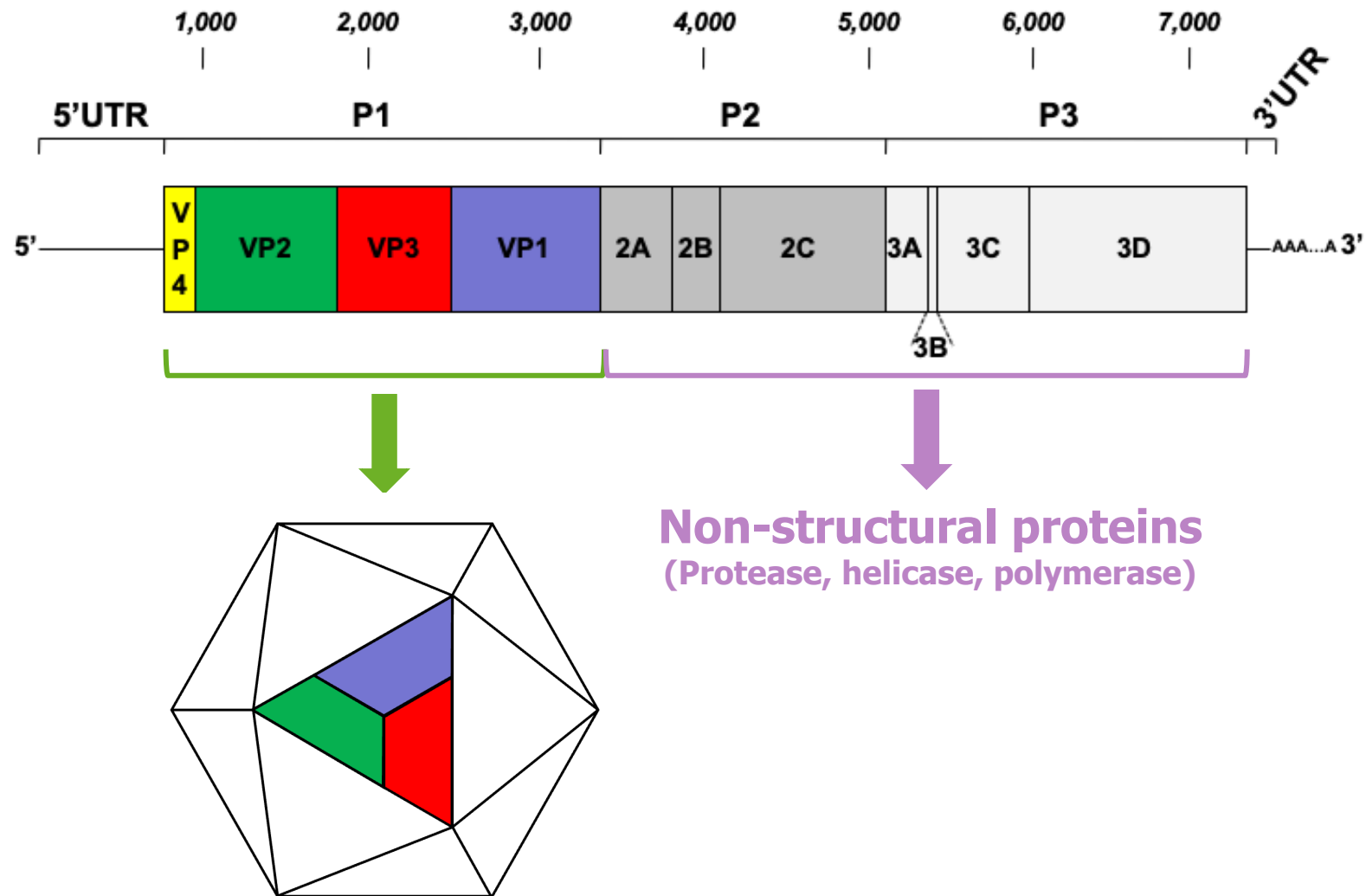
One large open reading frame (1 large polyprotein cleaved into functional proteins)

Two untranslated regions (involved in translation & replication)

Poliovirus genome



Poliovirus genome



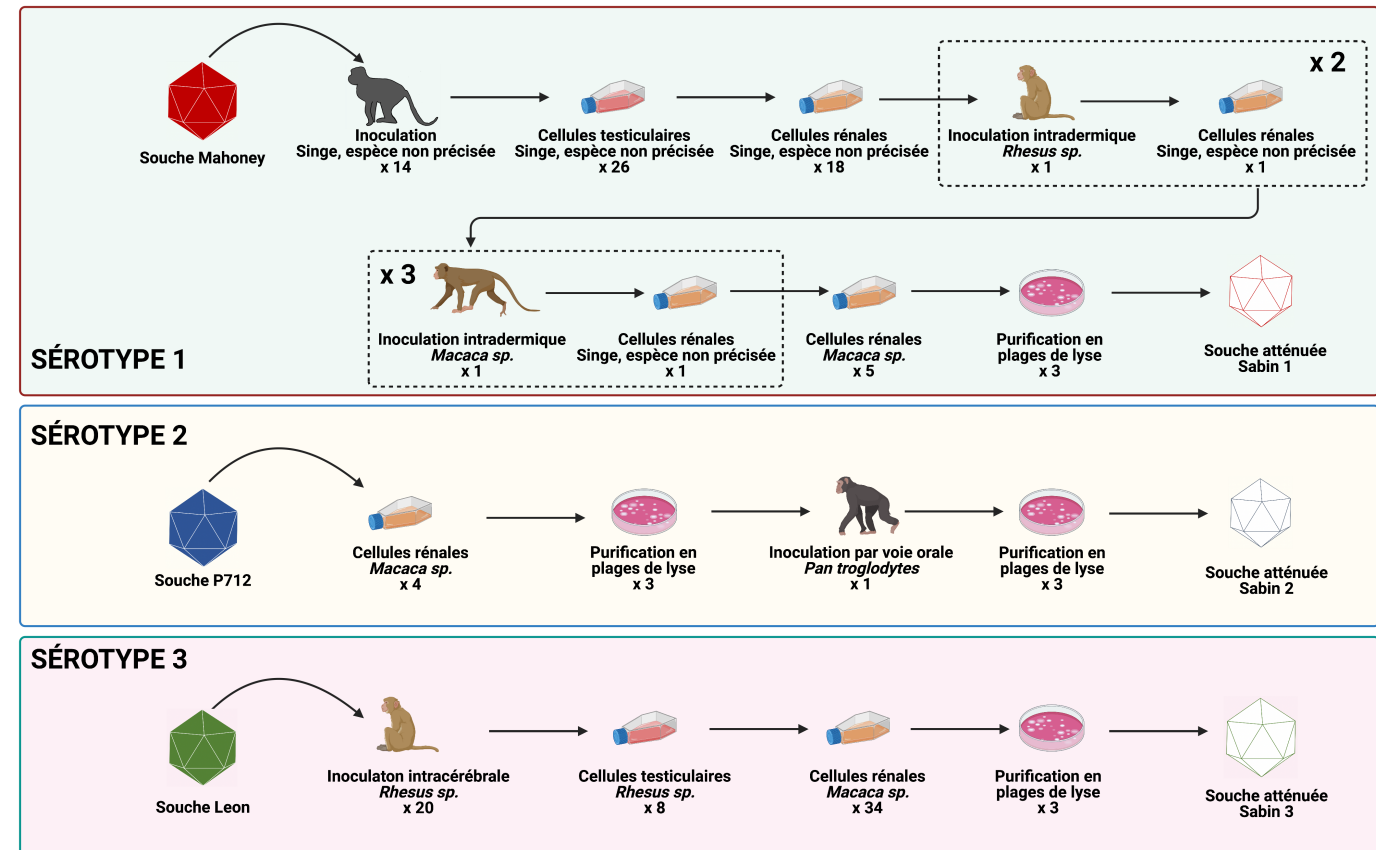
Oral polio vaccine ("Sabin strains"), 1950s

**Attenuation by serial passaging of
3 wild strains (1 of each serotype)**

Sabin strains are:

Able to replicate in the gut (⇒ immune response)

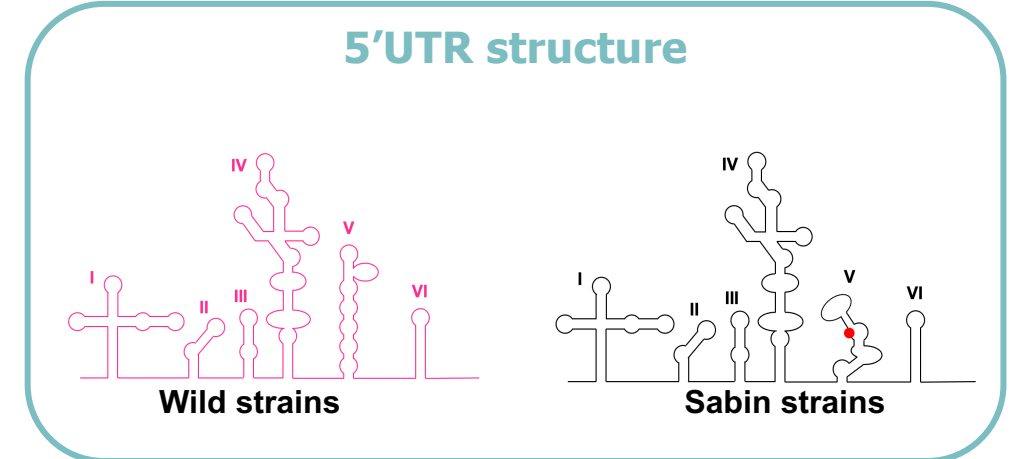
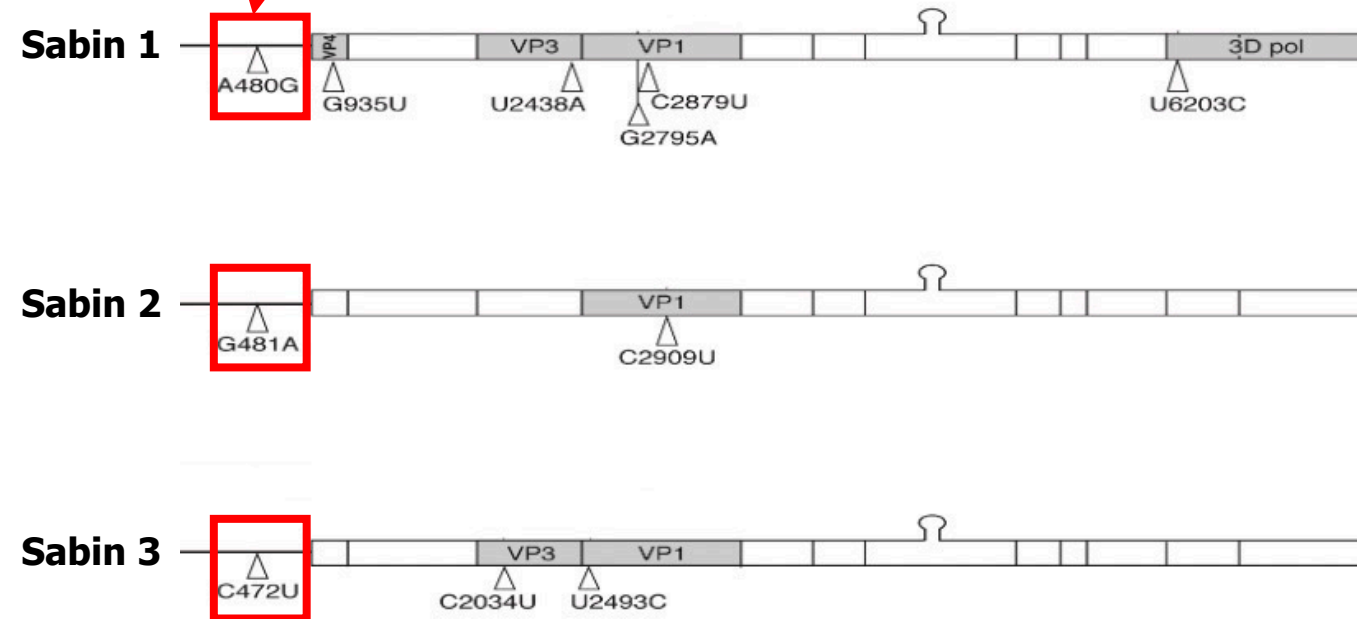
Unable to replicate in neural cells



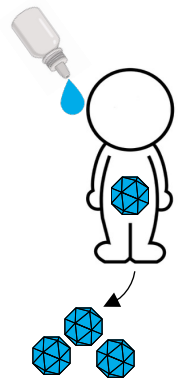
BESSAUD/MTSI/ <https://revuemtsi.societe-mtsi.fr/index.php/bspe-articles/article/view/191>

Oral polio vaccine ("Sabin strains"), 1950s

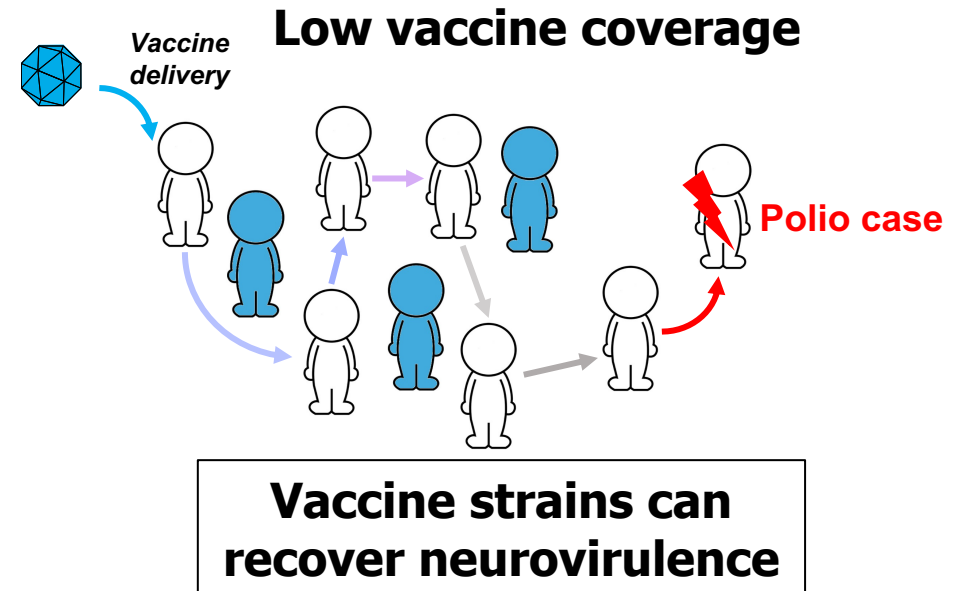
Few attenuation determinants
Most important one in the 5'UTR



Reversion of the vaccine strains

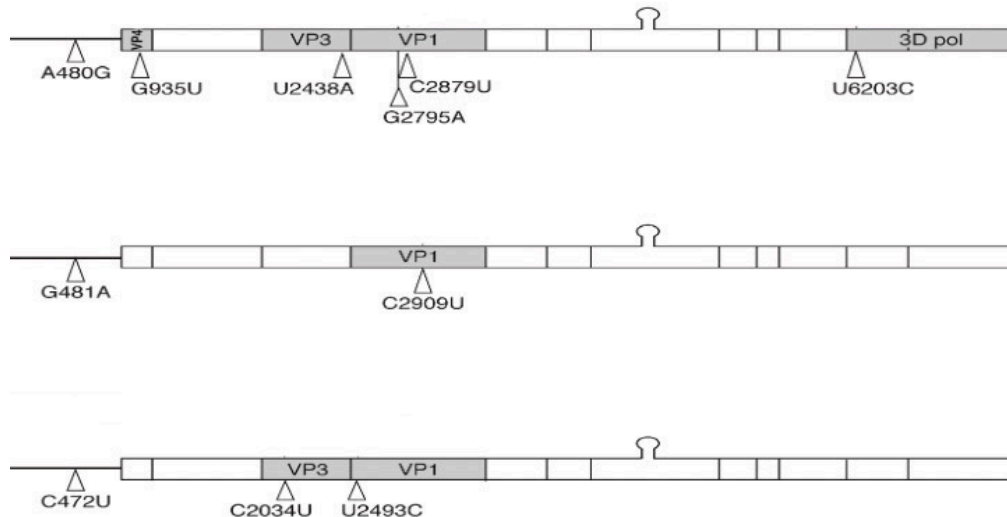


**Vaccine strains are excreted
for several weeks**
(until clearance by the immune response)



Reversion by point mutations

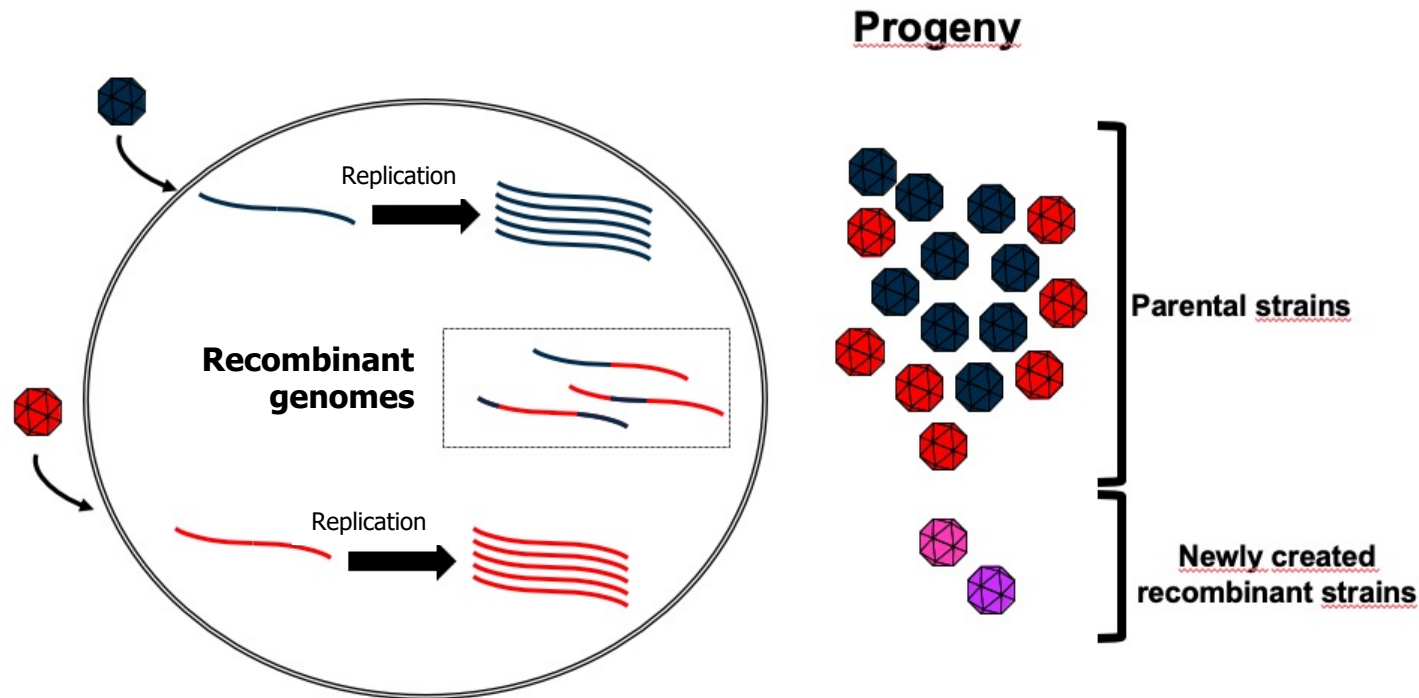
= errors during genome replication by the virus RNA polymerase
poliovirus polymerase error rate $\sim 10^{-4}$ (i.e. 1 mutation every 10,000 bases)



Small number of attenuation determinants

⇒ **reversion more likely**

Reversion by recombination

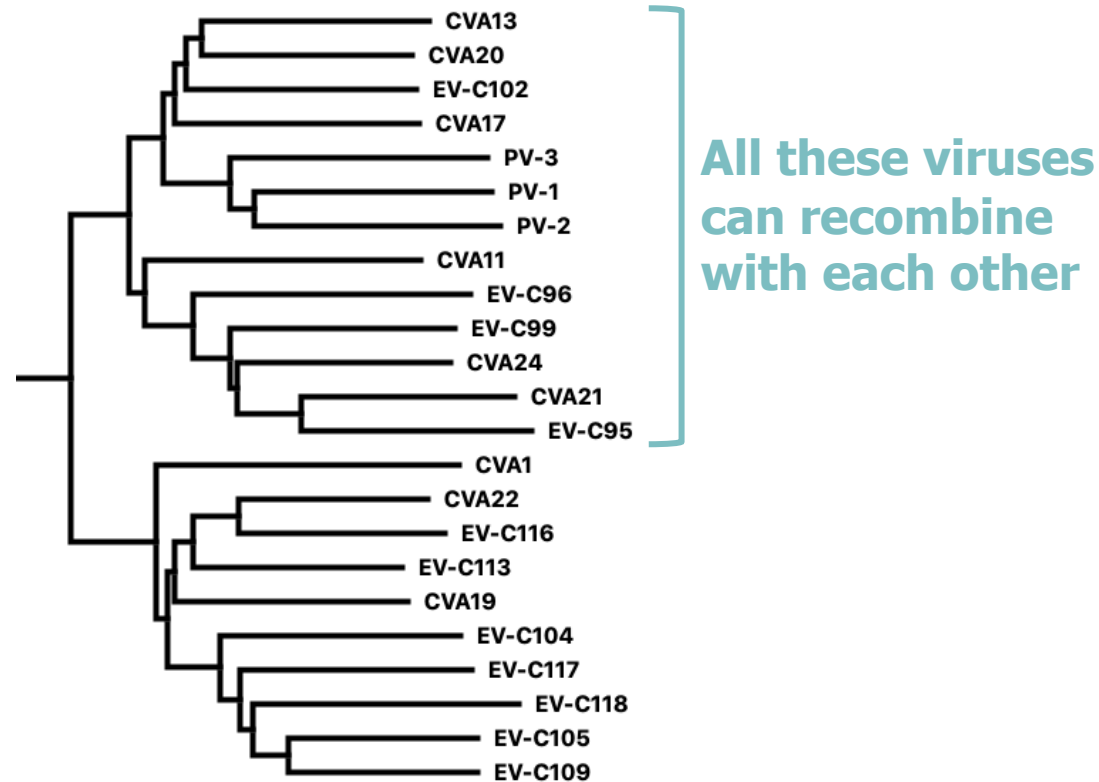


Recombinant genomes are chimeric genomes generated during co-infections

Reversion by recombination

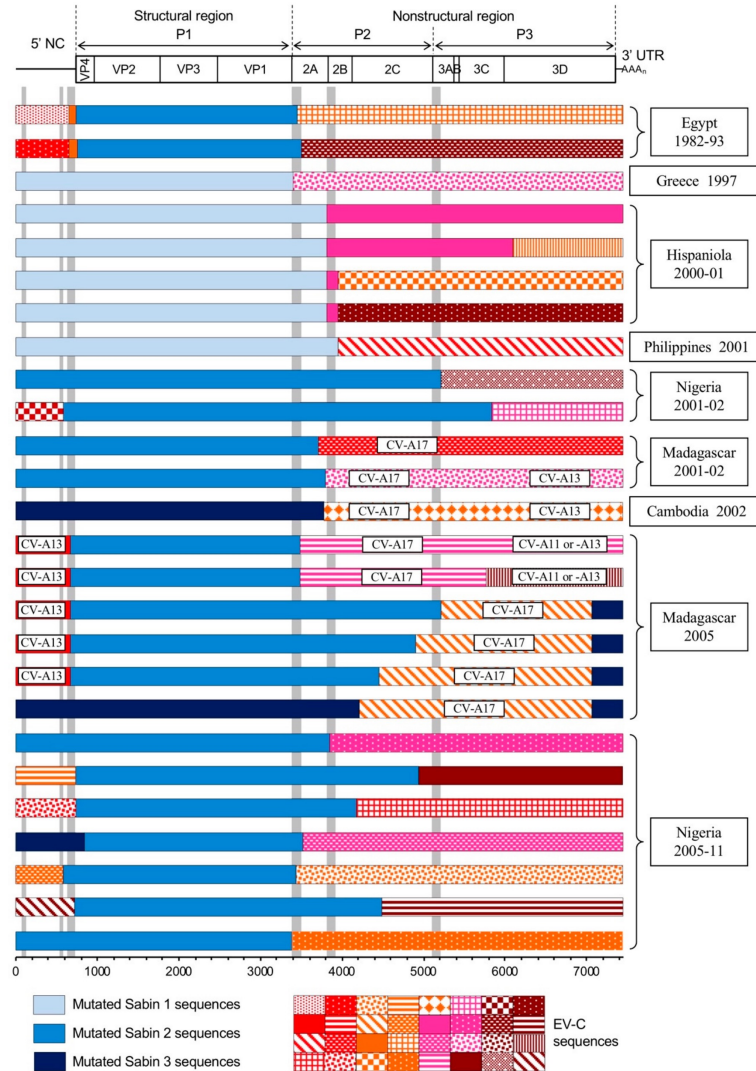
Recombination events are frequent among enteroviruses

Polioviruses can recombine with each other and with some other EV-Cs



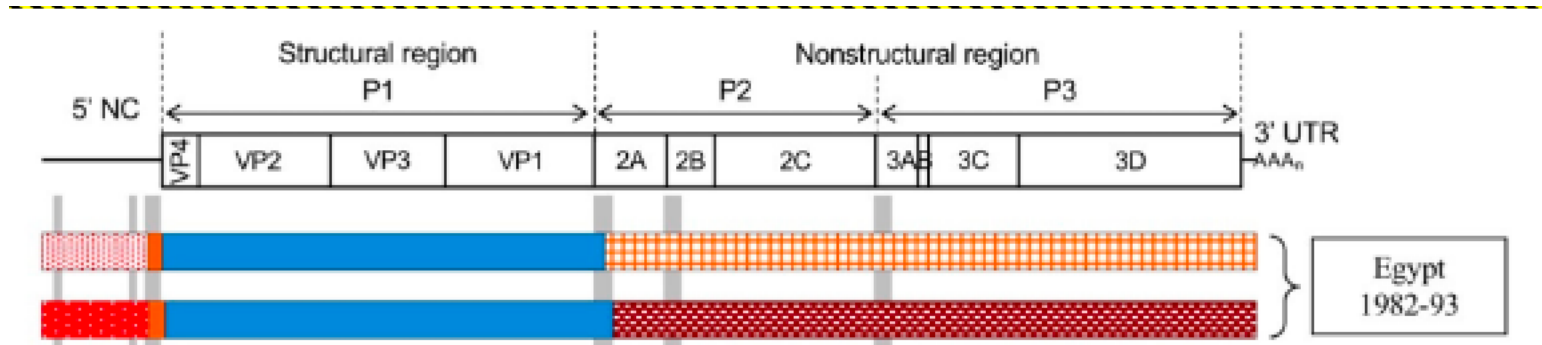
Muslin *et al.* doi: 10.3390/v11090859

Reversion by recombination



Attenuation determinants can be lost through recombination

Reversion by recombination



Muslin *et al.* doi: 10.3390/v11090859

In numerous vaccine-derived poliovirus strains, only the capsid-encoding sequence comes from the vaccine strain

⇒ **Poliovirus identification relies on the capsid-encoding region**

According to the Global Polio Lab Network algorithm, PV characterisation relies on the **VP1 region (~ 900 nt) as the VP1 protein carries the major antigens of PV**

PV genetic characterisation: overview



Poliovirus surveillance reveals both wild strains (i.e. natural strains still circulating) and strains from the vaccine

Wild strains

Serotypes 2 & 3 already eradicated (**highly concerning if detected**)

Serotype 1 circulates in Pakistan & Afghanistan only (**highly concerning if detected elsewhere**)

PV genetic characterisation: overview



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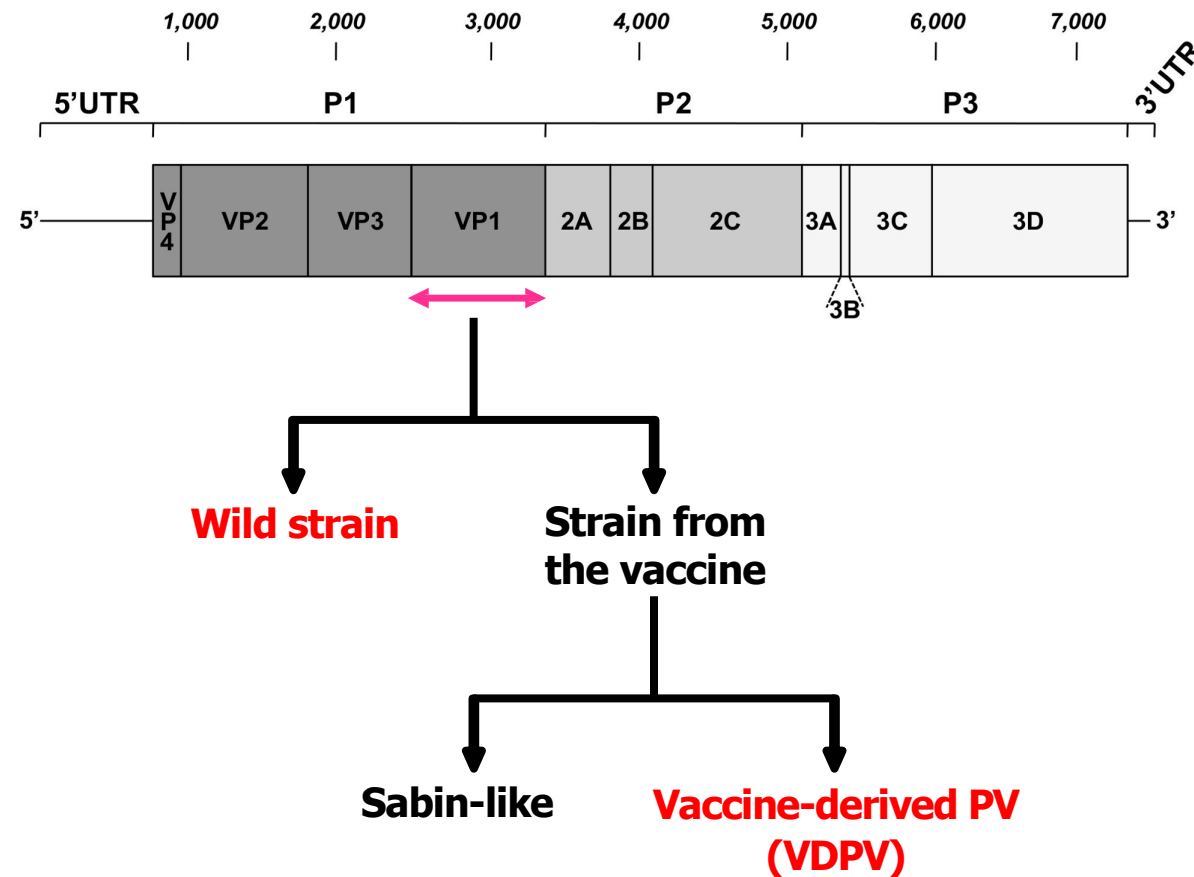
Vaccine strains

Expected, as long as the oral polio vaccine is used (can be used to monitor the vaccination campaigns)

Concerning if showing signs of phenotypic reversion

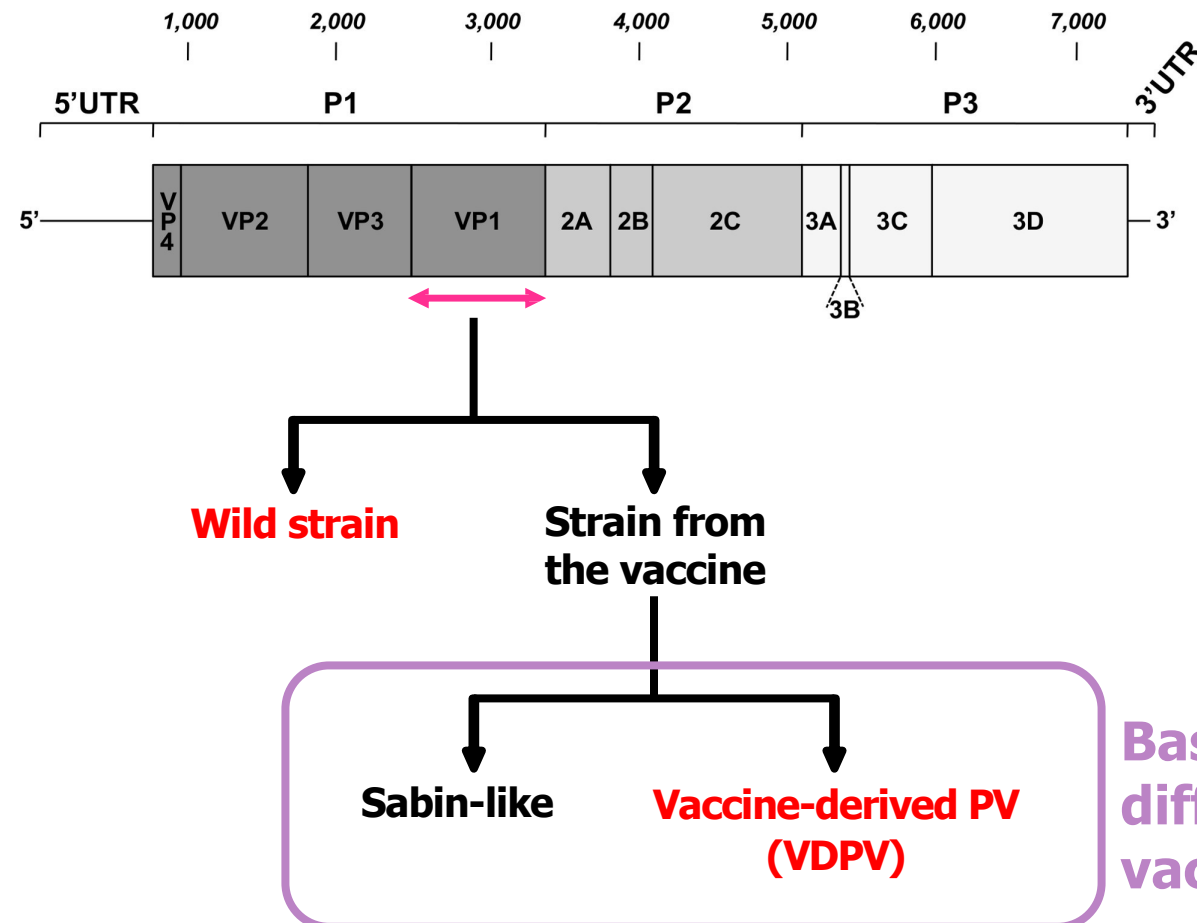
PV genetic characterisation: overview

Based on VP1 sequencing

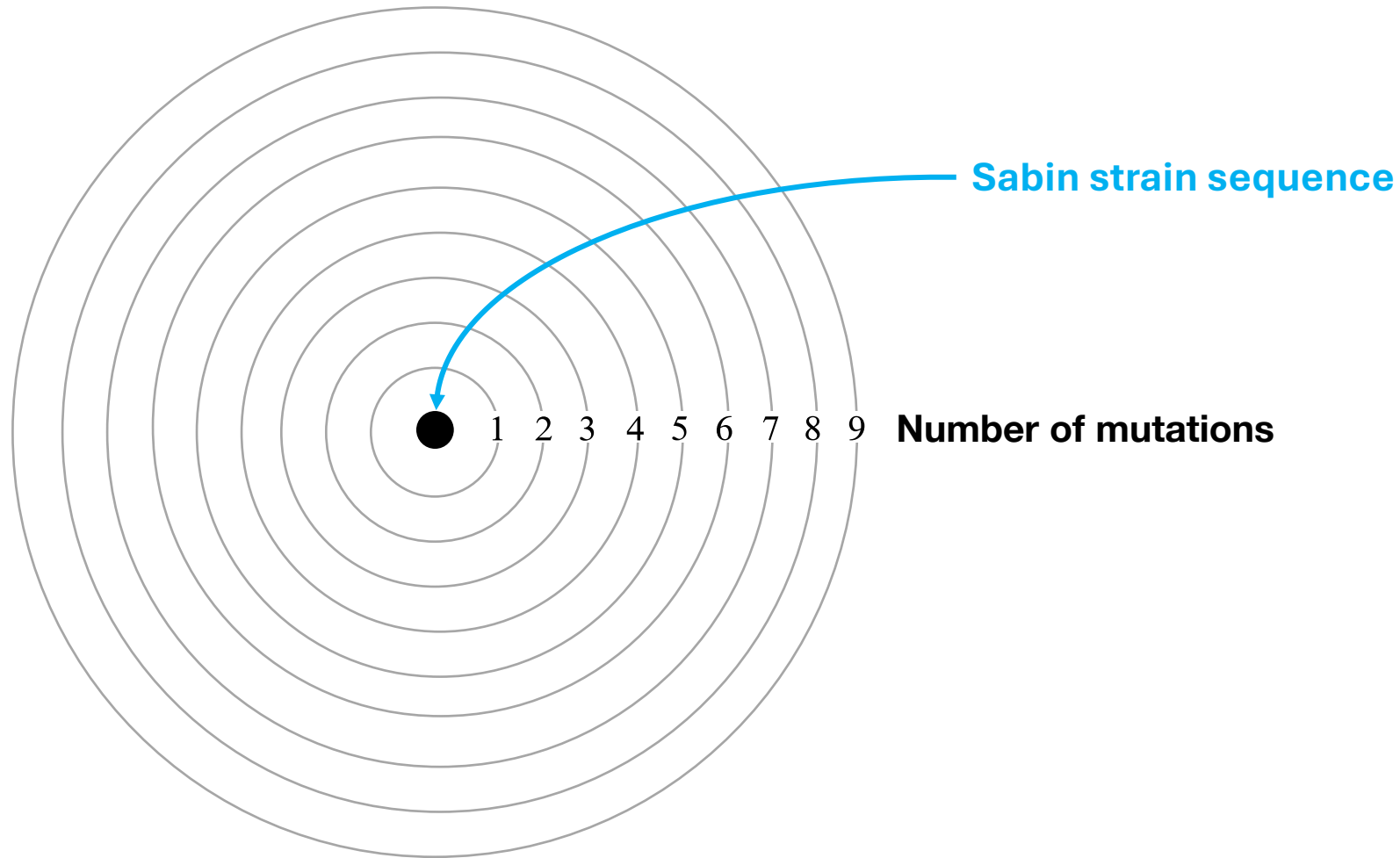


PV genetic characterisation: overview

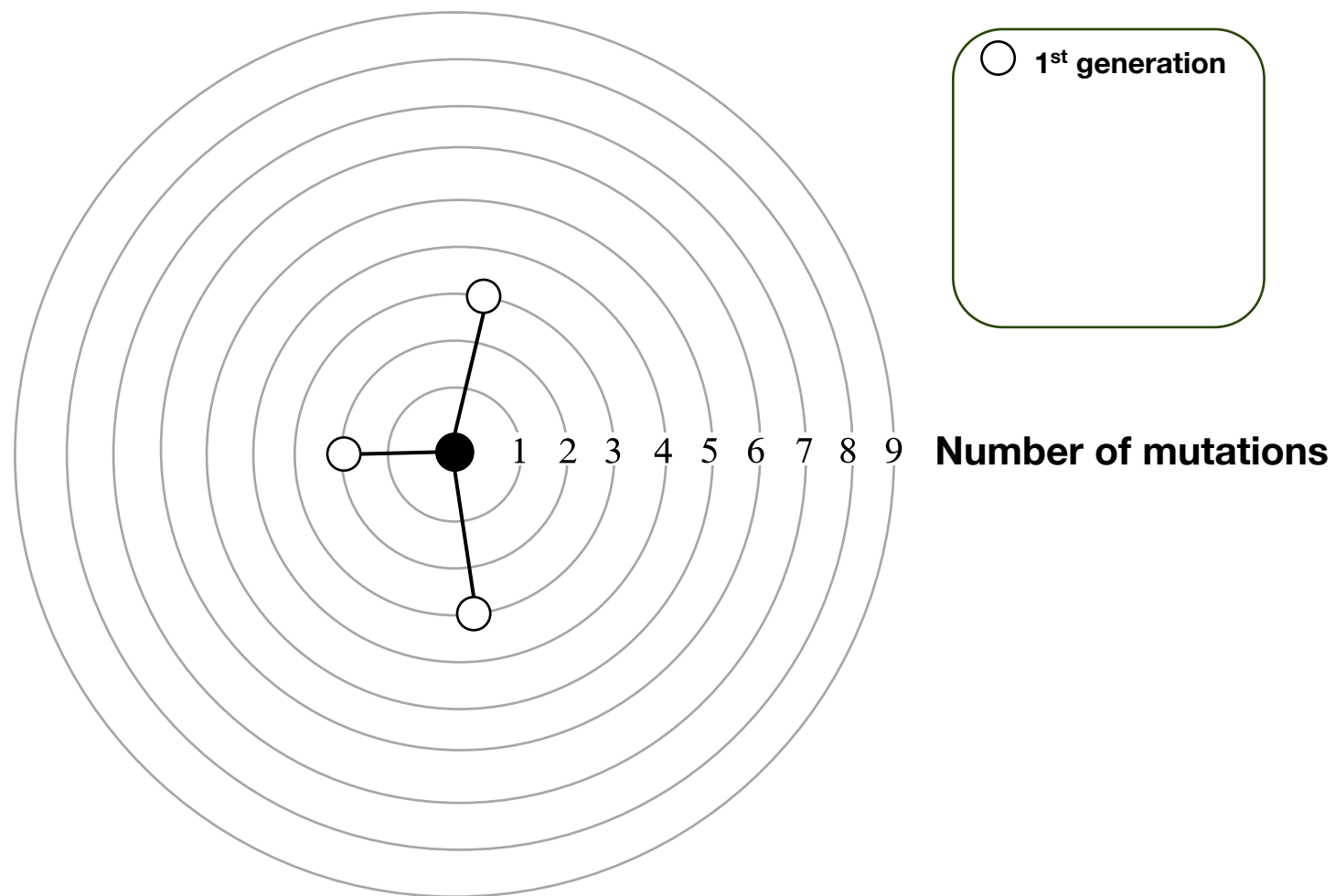
Based on VP1 sequencing



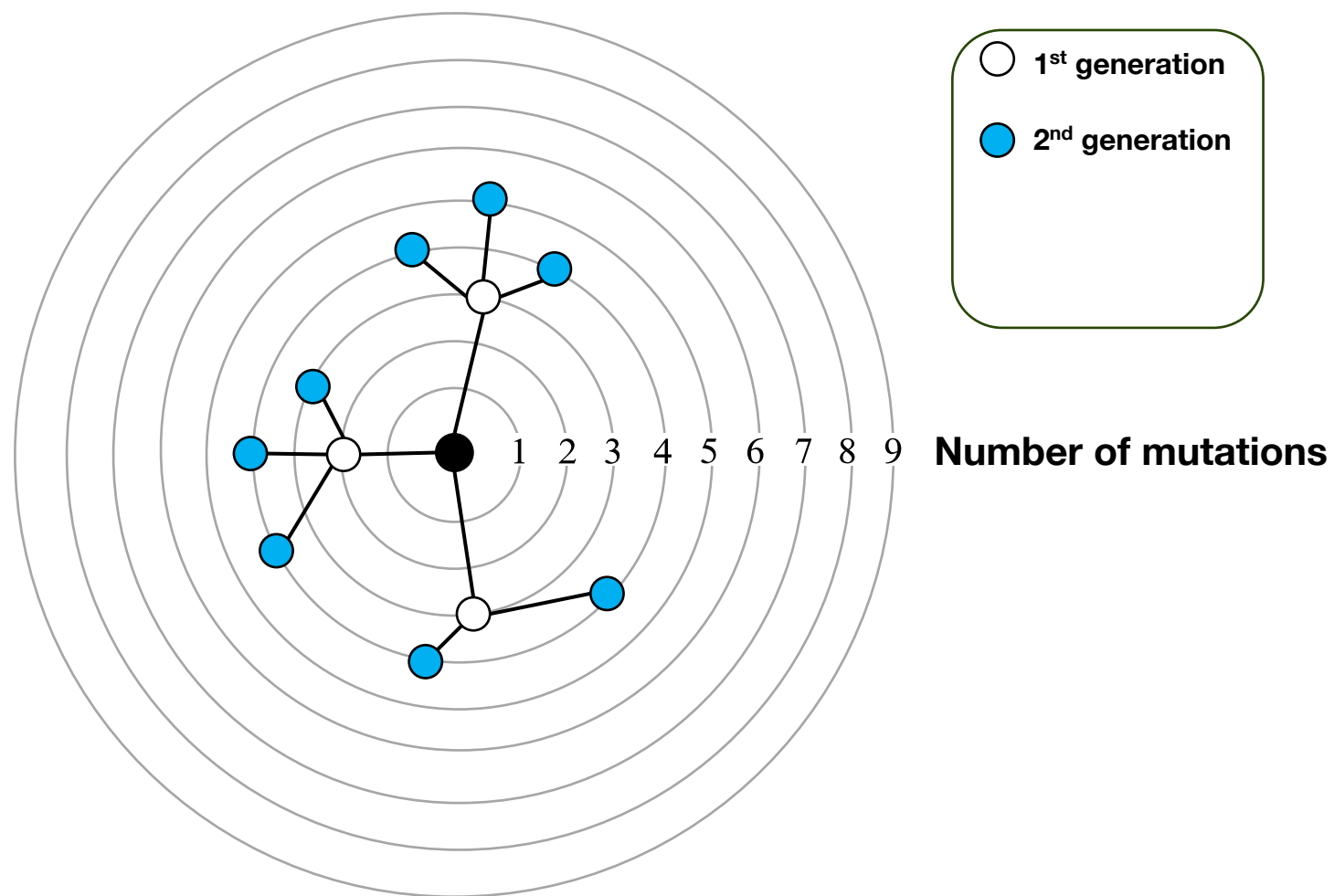
PV evolution: genetic drift



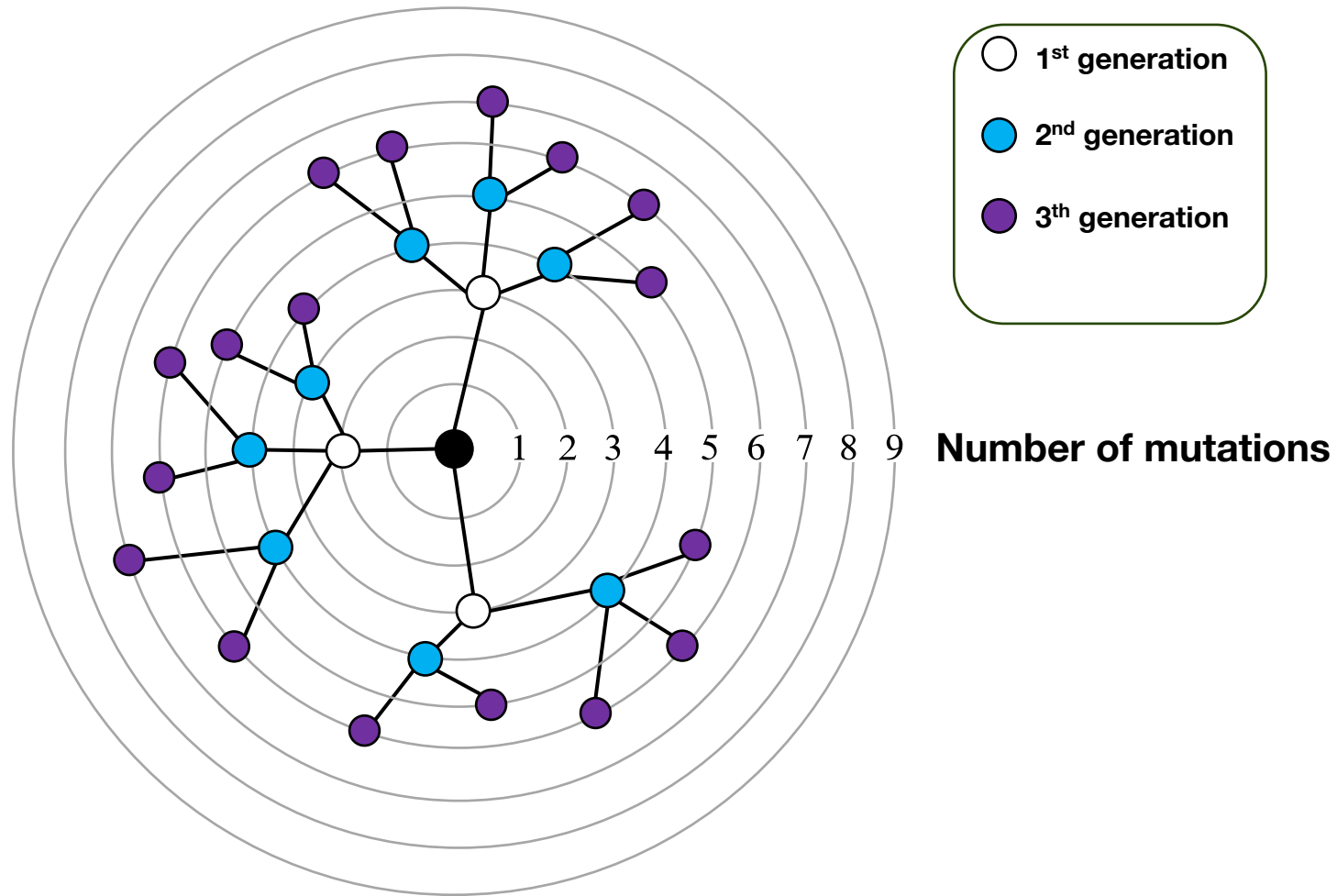
PV evolution: genetic drift



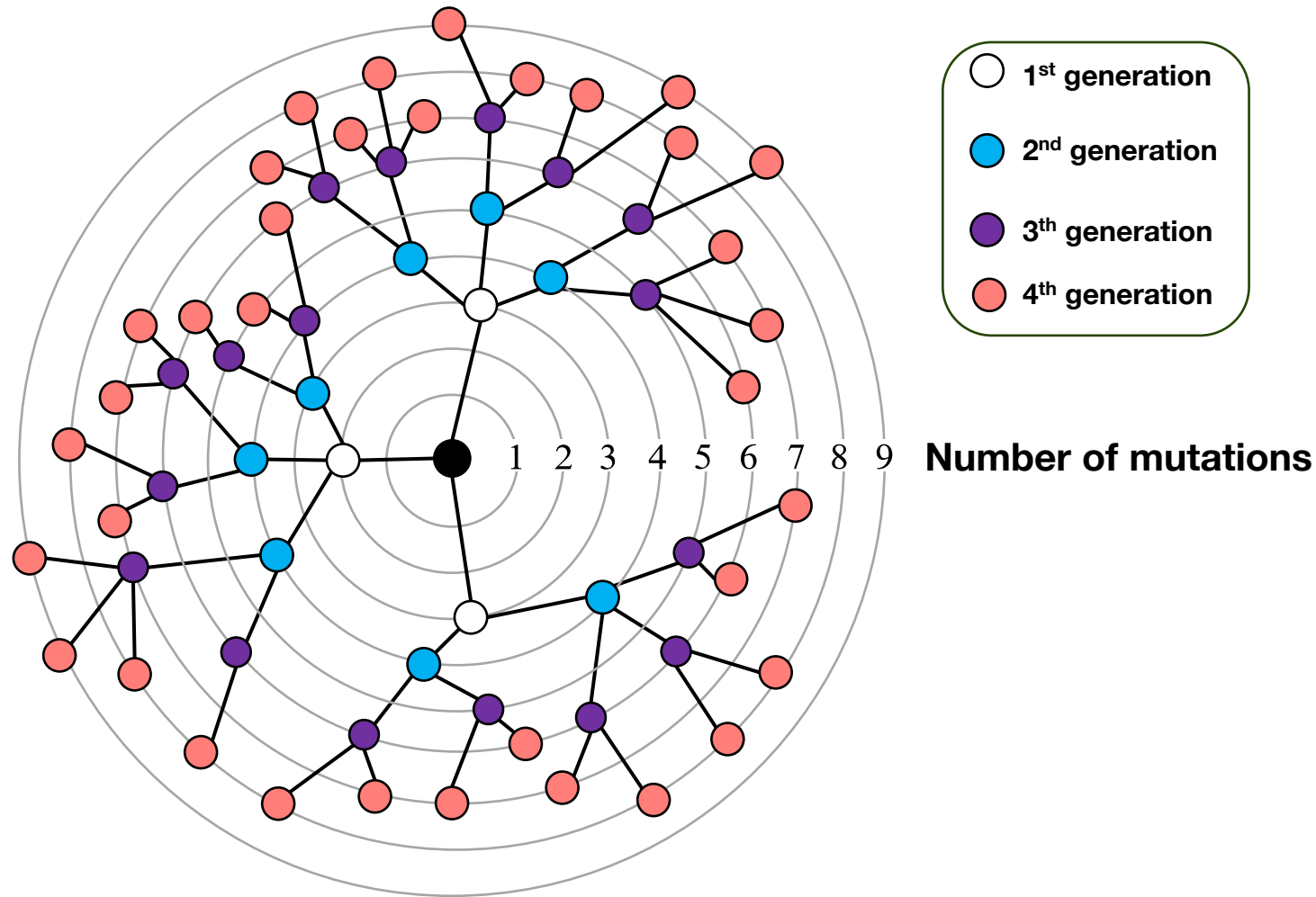
PV evolution: genetic drift



PV evolution: genetic drift

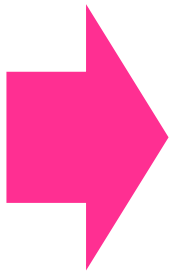


PV evolution: genetic drift



**Proxy for the
circulation time**

PV evolution: genetic drift

Number of mutations  Proxy for the
circulation time

Vaccine strains with **no or few mutations** are likely
excreted by a vaccine recipient or a close contact



"Sabin-like"

Vaccine strains with **numerous mutations**
probably stem from repeated reinfections



"Vaccine-derived poliovirus"

Sabin-like strains *vs* Vaccine-Derived polioviruses

Number of differences in **VP1** compared to the vaccine strain

≥ 10 for serotypes 1 & 3
 ≥ 6 for serotype 2

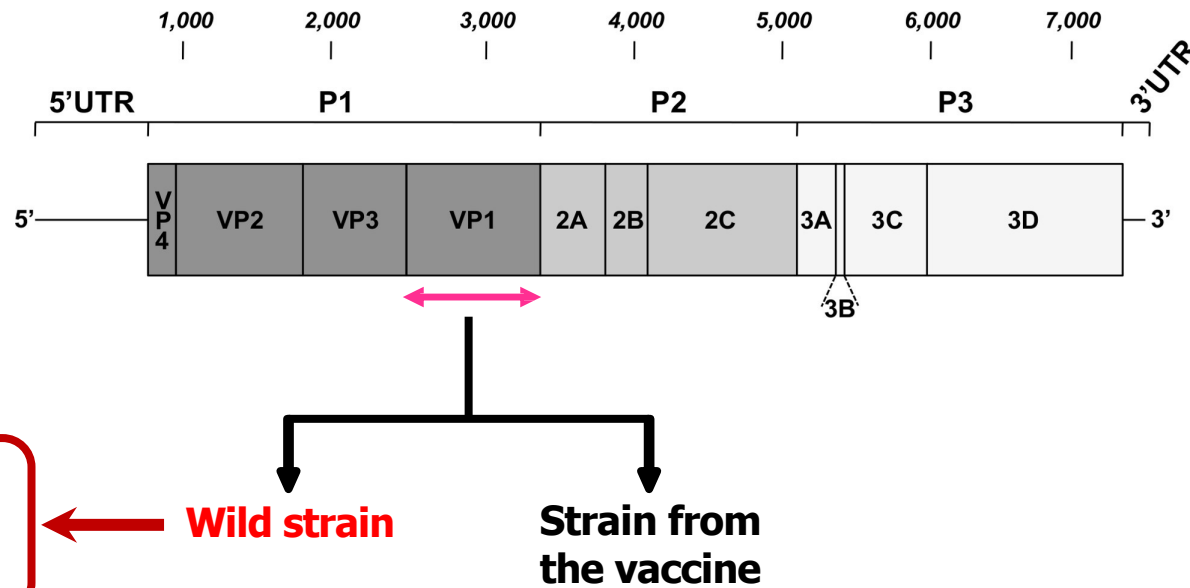


Vaccine-derived poliovirus (VDPV)

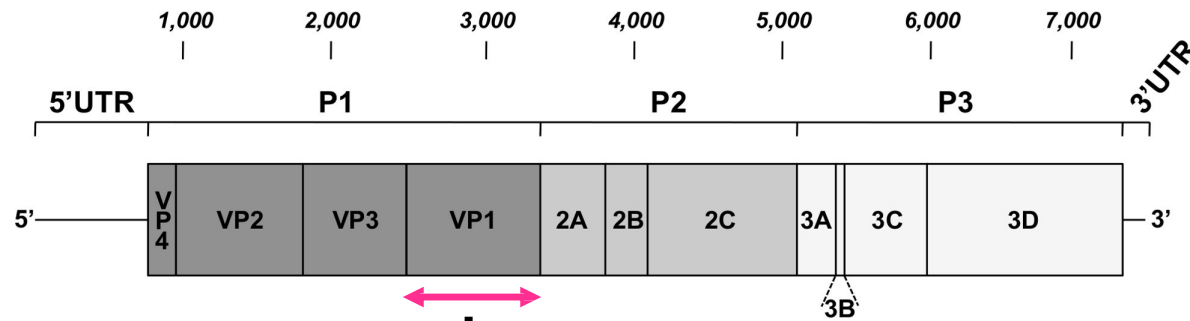
	[0-9]	10 and more
Serotype 1	SL1	VDPV1
Serotype 3	SL3	VDPV3

	[0-5]	6 and more
Serotype 2	SL2	VDPV2

PV genetic characterisation



PV genetic characterisation



Must be reported to
the Global Polio
Eradication Initiative

Wild strain

**Strain from
the vaccine**

< 10 differences for types 1 & 3
< 6 differences for type 2

≥ 10 differences for types 1 & 3
≥ 6 differences for type 2

Sabin-like

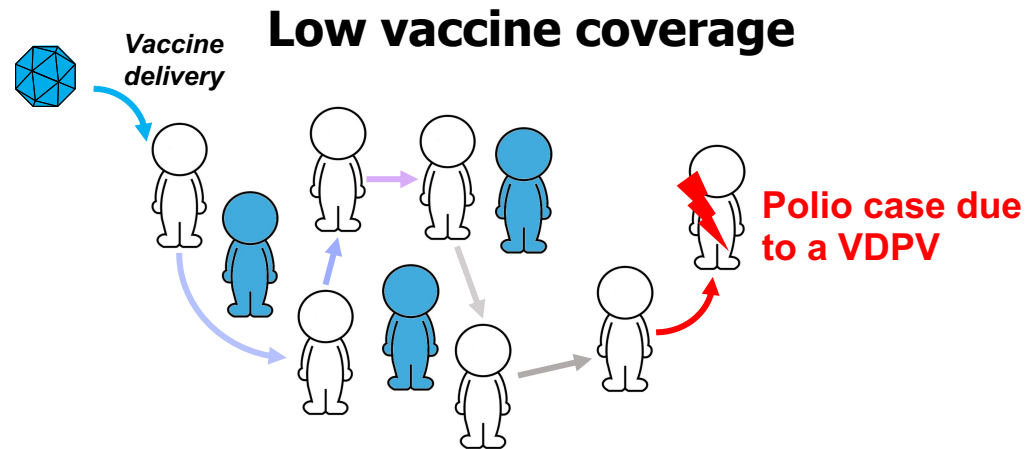
**Vaccine-derived PV
(VDPV)**

Must be reported to
the Global Polio
Eradication Initiative

Vaccine-derived polioviruses

VDPVs must be reported to the Global Polio Eradication Initiative because:

- 1- They have probably reverted towards neurovirulence (by genetic drift and/or by recombination);
- 2- They reveal immunity gaps.



A higher number of mutations in the VP1 suggests a longer transmission chain

In summary

PV vaccine strains have few attenuation determinants (most important one in the 5'UTR)

PV vaccine strains can revert through genetic drift and through recombination with other EV-Cs

Because of recombination, PV genetic characterisation must rely on the capsid-encoding region

VP1 sequencing is used to classify PV strains into three main categories:

- Wild** PV strains;

- Sabin-like** strains: less than 6 (for type 2) or 10 differences (for types 1 & 3);

- Vaccine-derived** strains: at least 6 (for type 2) or 10 differences (for types 1 & 3).

Wild strains and VDPVs must be reported to the Global Polio Eradication Initiative

Recommended material to explore further

Global Polio Lab Network guidelines

Guidance paper 5: Reporting Vaccine-derived Polioviruses (VDPVs). <https://polioeradication.org/wp-content/uploads/2024/05/GP5-VDPV-Reporting-for-GPLN-Sequencing-Laboratories-V2.0.pdf>

Classification and reporting of vaccine-derived polioviruses (VDPV). https://polioeradication.org/wp-content/uploads/2016/09/Reporting-and-Classification-of-VDPVs_Aug2016_EN.pdf.

Review focusing on recombination among enteroviruses

Recombination in Enteroviruses, a Multi-Step Modular Evolutionary Process. Muslin C, Mac Kain A, Bessaud M, Blondel B, Delpeyroux F. *Viruses*. 2019 Sep 14;11(9):859. doi: 10.3390/v11090859. <https://www.mdpi.com/1999-4915/11/9/859>

Article describing the primers that can be used to amplify and sequence the VP1 region

Molecular Properties of Poliovirus Isolates: Nucleotide Sequence Analysis, Typing by PCR and Real-Time RT-PCR. Burns CC, Kilpatrick DR, Iber JC, Chen Q, Kew OM. *Methods Mol Biol*. 2016;1387:177-212. doi: 10.1007/978-1-4939-3292-4_9

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Acknowledgements

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