

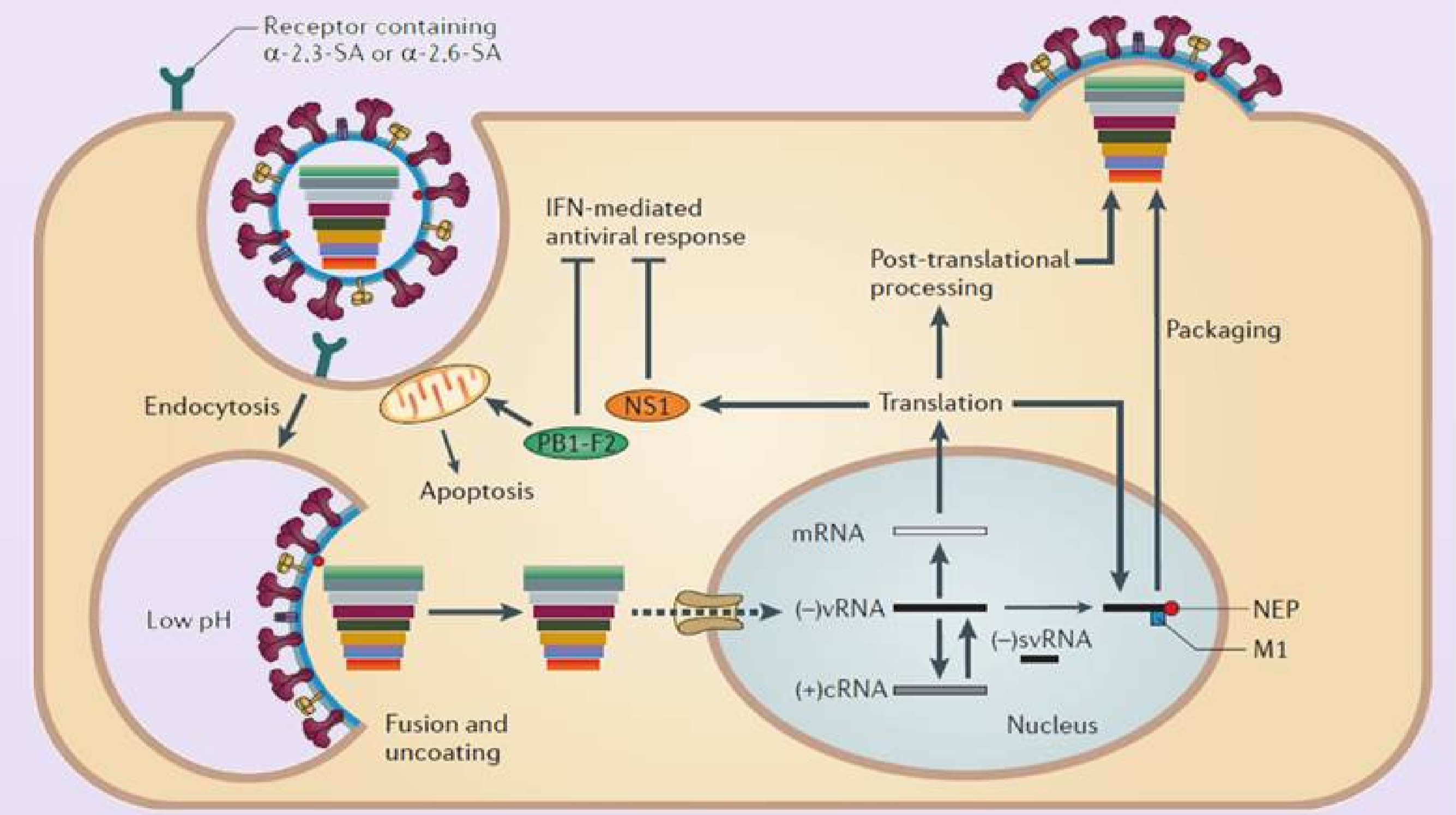
# Genetics of Cross-Species Influenza A Virus Transmission

**UAB**  
Universitat Autònoma de Barcelona

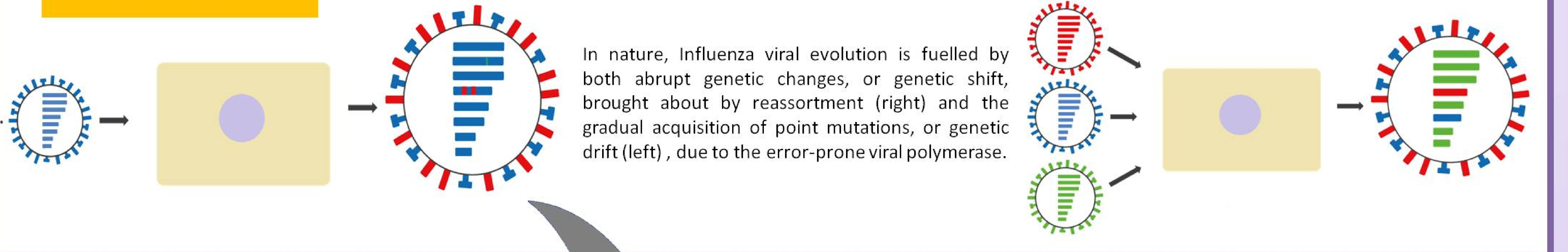
Miruna Elena Rosu  
Universitat Autònoma de Barcelona

## Objective

- To review the current understanding of the mechanisms through which Influenza A viruses (IAV) infect and replicate efficiently in a new host.
- To review mutations that allow the Influenza A avian virus to switch host and infect mammals and humans.



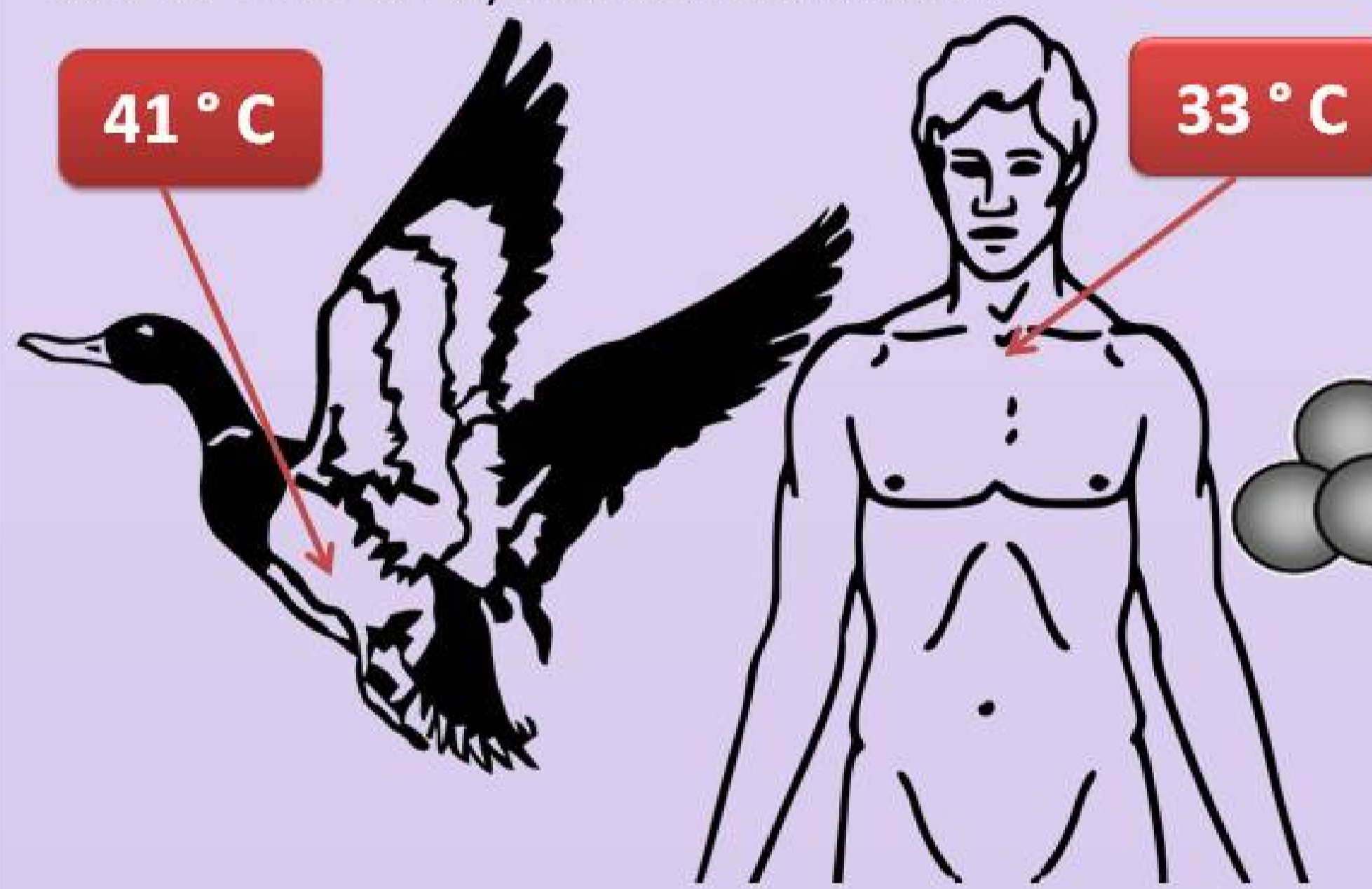
## Results



In nature, Influenza viral evolution is fuelled by both abrupt genetic changes, or genetic shift, brought about by reassortment (right) and the gradual acquisition of point mutations, or genetic drift (left), due to the error-prone viral polymerase.

## PB2

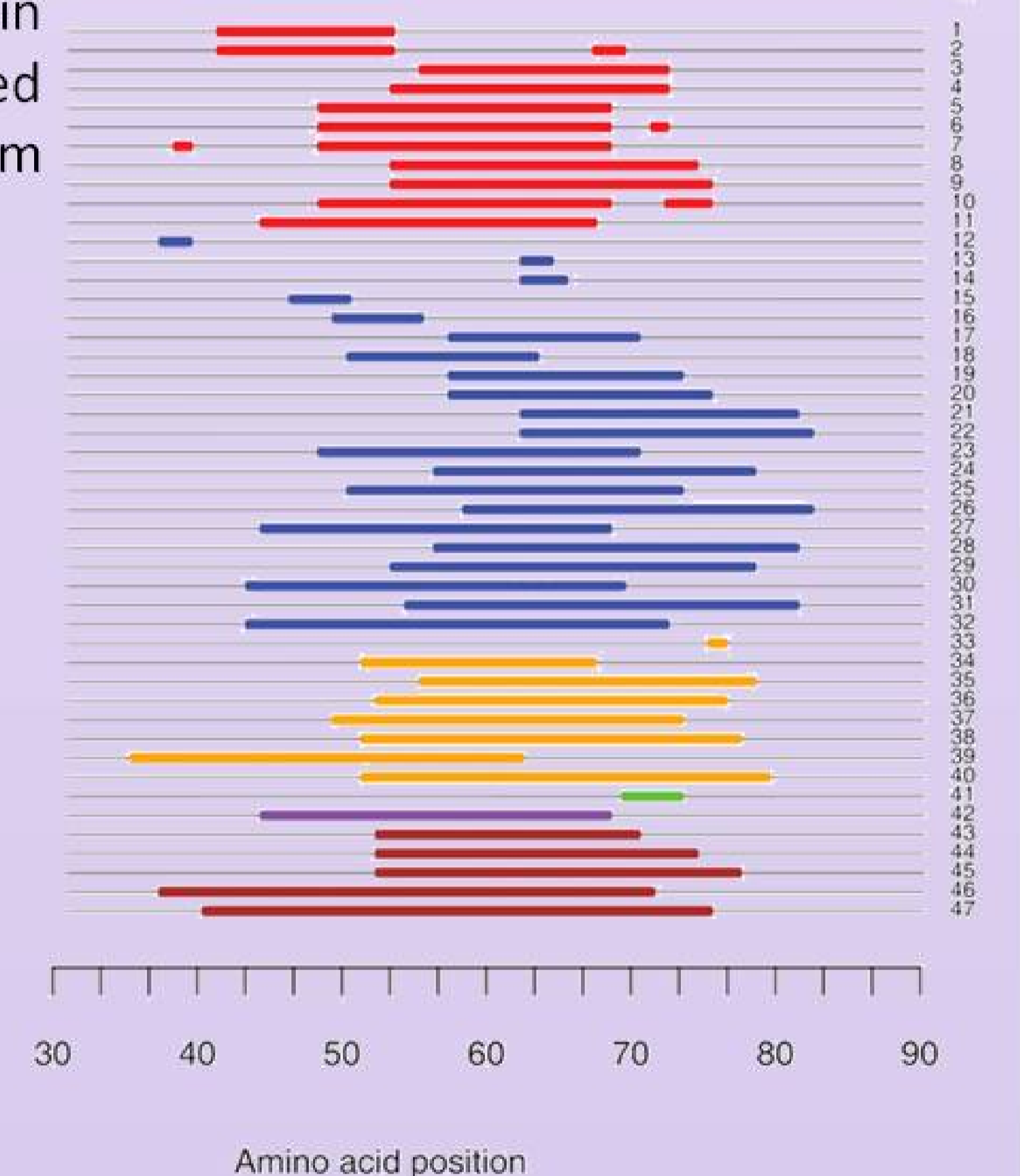
Human IAV replicate in the upper respiratory tract, which is approximately 33°C, whereas avian IAV replicate in the intestines of birds at a temperature of approximately 41°C. Several mutations confer higher replication efficiency at 37°C. Thus, the cold sensitivity of an avian Influenza polymerase could be controlled at least in part by the residue at position 627 in PB2 or by mimic mutations.



Deletions in the NA stalk region influence the virus replication efficiency in vivo, increase its host range, reduce its NA enzymatic activity, and in some cases increase the virus virulence. The longest deletion reported ever is 35 aa.

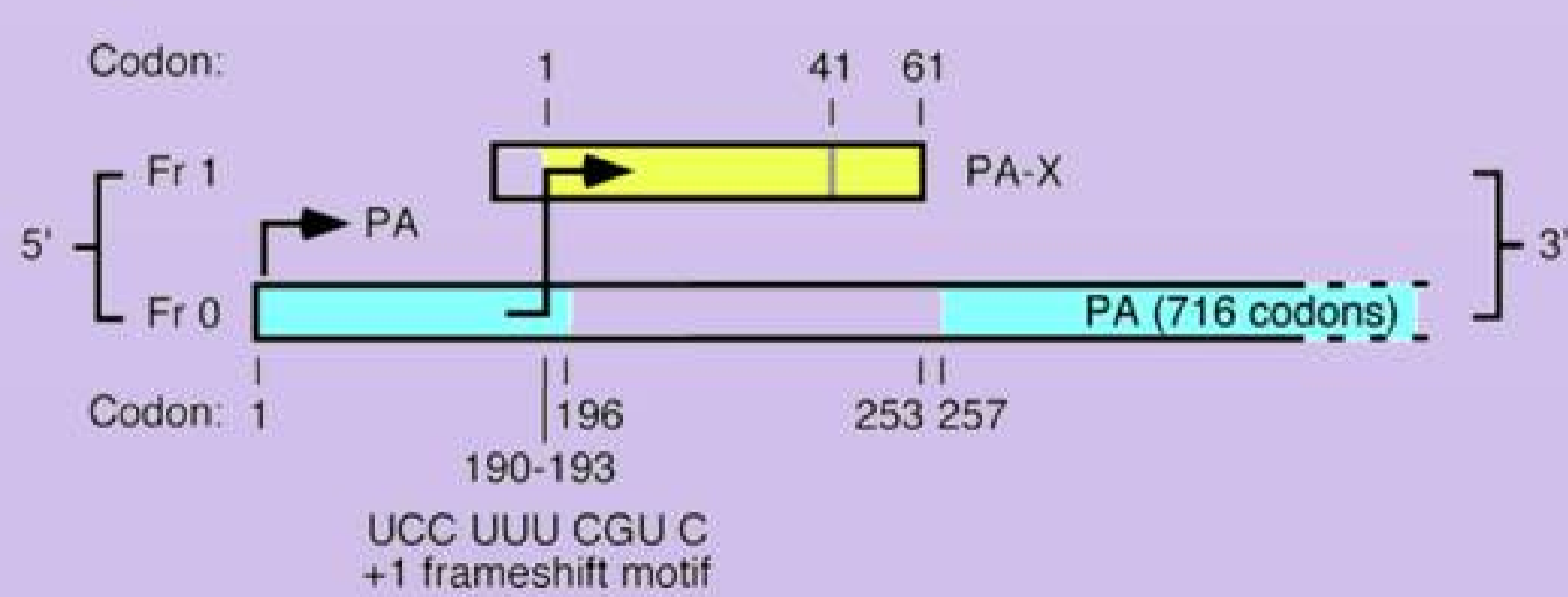
Amino acid deletions within the stalk domain are related to transmission of IAV from wild birds into chickens.

## NA



## PA

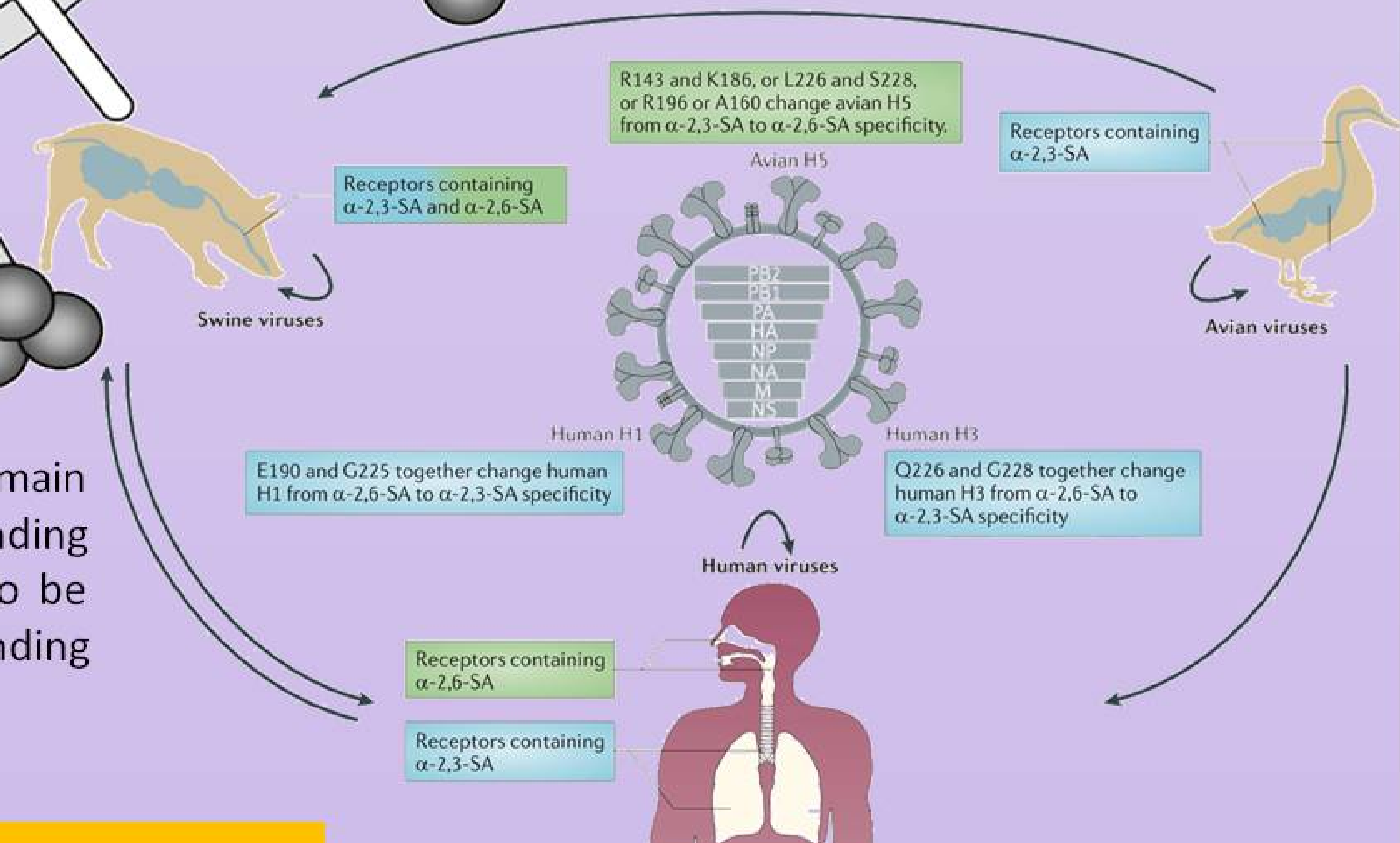
The role of PA in host adaptation is less well characterized than that of PB2 but exerts an important influence on host range. An important variant of the PA viral protein is PA-X that modulates host response and viral virulence.



Mutations in domain RBS (Receptor Binding Site) are taught to be responsible of binding preference.

## HA

Human viruses → Receptors α-2,6-SA  
Avian viruses → Receptors α-2,3-SA



## Conclusions

- RBS of HA gather many residues responsible for receptor binding preference and it is responsible of IAV infecting new hosts. In contrast, the stalk domain is the most conserved HA domain and it is thus an important target for vaccine design.
- PB2 protein has been found to carry the dominant determinants of host range.
- Reassortment may bring together two advantageous mutations that arose in different viruses or allow the separation of an advantageous change in one segment from a deleterious mutation in another.

## References

- Cauldwell, A. V., Long, J. S., Moncorgé, O. & Barclay, W. S. Viral determinants of influenza A virus host range. *J. Gen. Virol.* **95**, 1193–1210 (2014).
- Mair, C. M., Ludwig, K., Herrmann, A. & Sieben, C. Receptor binding and pH stability — How influenza A virus hemagglutinin affects host-specific virus infection. *Biochim. Biophys. Acta BBA - Biomembr.* **1838**, 1153–1168 (2014).