Vaccines for equine influenza (EI) and recent developments

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Today’s topic

1. Selection of equine influenza virus (EIV) strain for vaccine
2. Application of reverse genetics (RG) -derived inactivated vaccine

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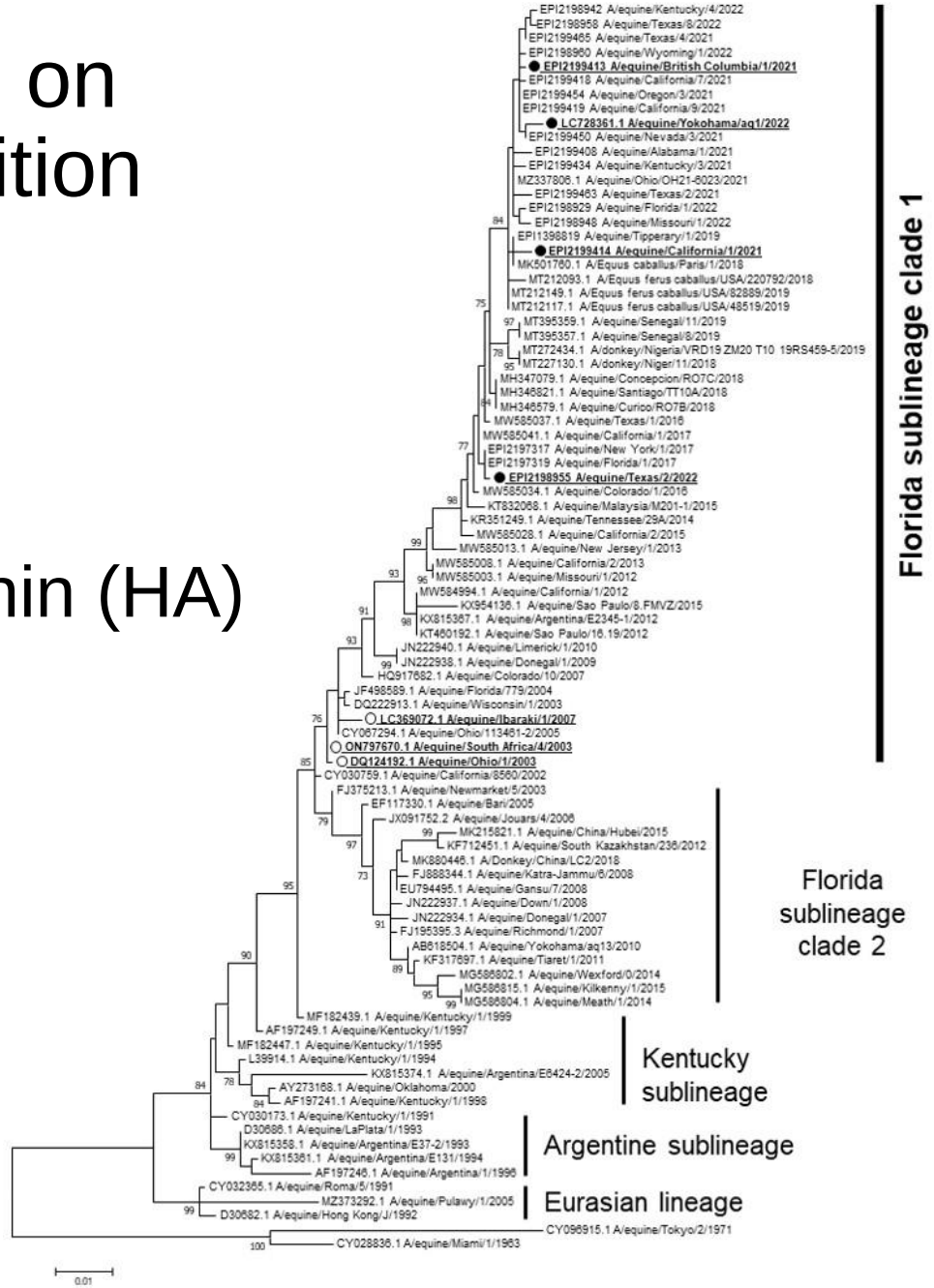
Vaccine strains should be changed regularly to maintain efficacy

- Vaccination is one of the most effective ways to prevent and control EI
- EIVs are getting new mutations with time

  ➡Current vaccine strain is getting less effective against strains with mutations

WOAH Expert surveillance panel on equine influenza vaccine composition

- Epidemiology
  - Recent outbreaks around the world
- Genetic characterisation of haemagglutinin (HA)
  - Phylogenetic analysis
  - Amino acid sequence of HA
- Antigenic characterisation
  - Hemagglutination inhibition (HI) assay
  - Virus neutralisation (VN) assay

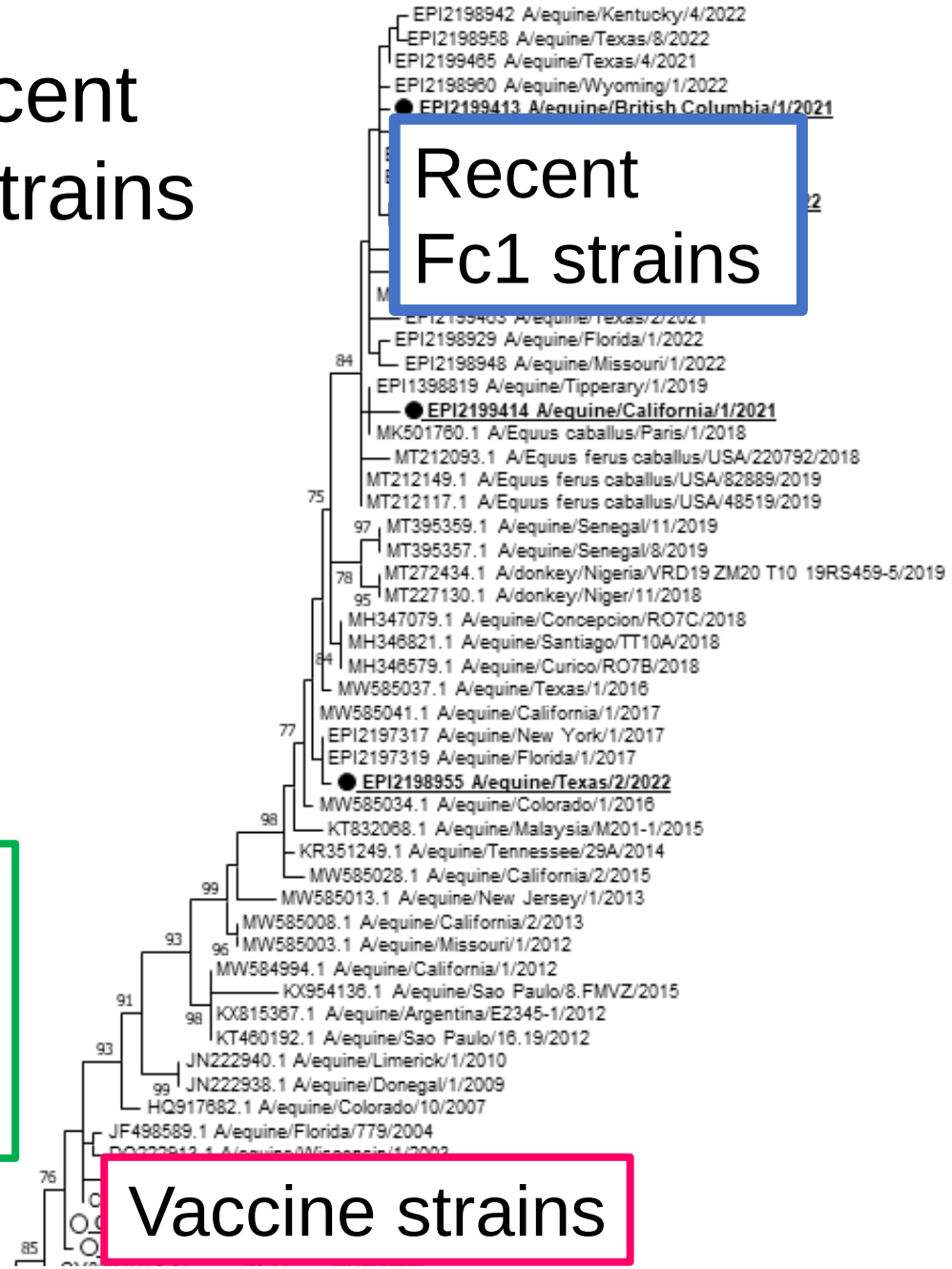


（Nemoto *et al*., Arch Virol 2023）

Phylogenetic tree of HA shows that recent strains were separated from vaccine strains

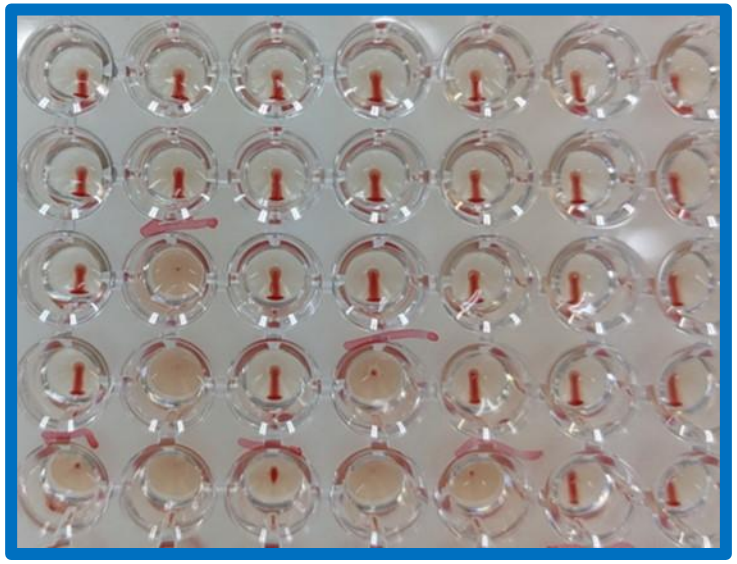
- Should be vaccine strains changed immediately? ➡ No!
- Genetic analysis shows just genotype, not phenotype

We must evaluate the antigenic characterizations between Vaccine and recent strains



Serological tests to compare antigenic differences

- HI assay
  - HI is more convenient than VN
  - HI is used for many laboratories



- Virus neutralisation (VN) assay
  - Eggs are used for VN
  - It is difficult to propagate in tissue culture

VN is more sensitive to detect antigenic differences

- Five horses got vaccines containing LaPlata/1993 (LP93)
- Antisera against LP93 were checked by LP93 and Carlow/2011 (CL11)

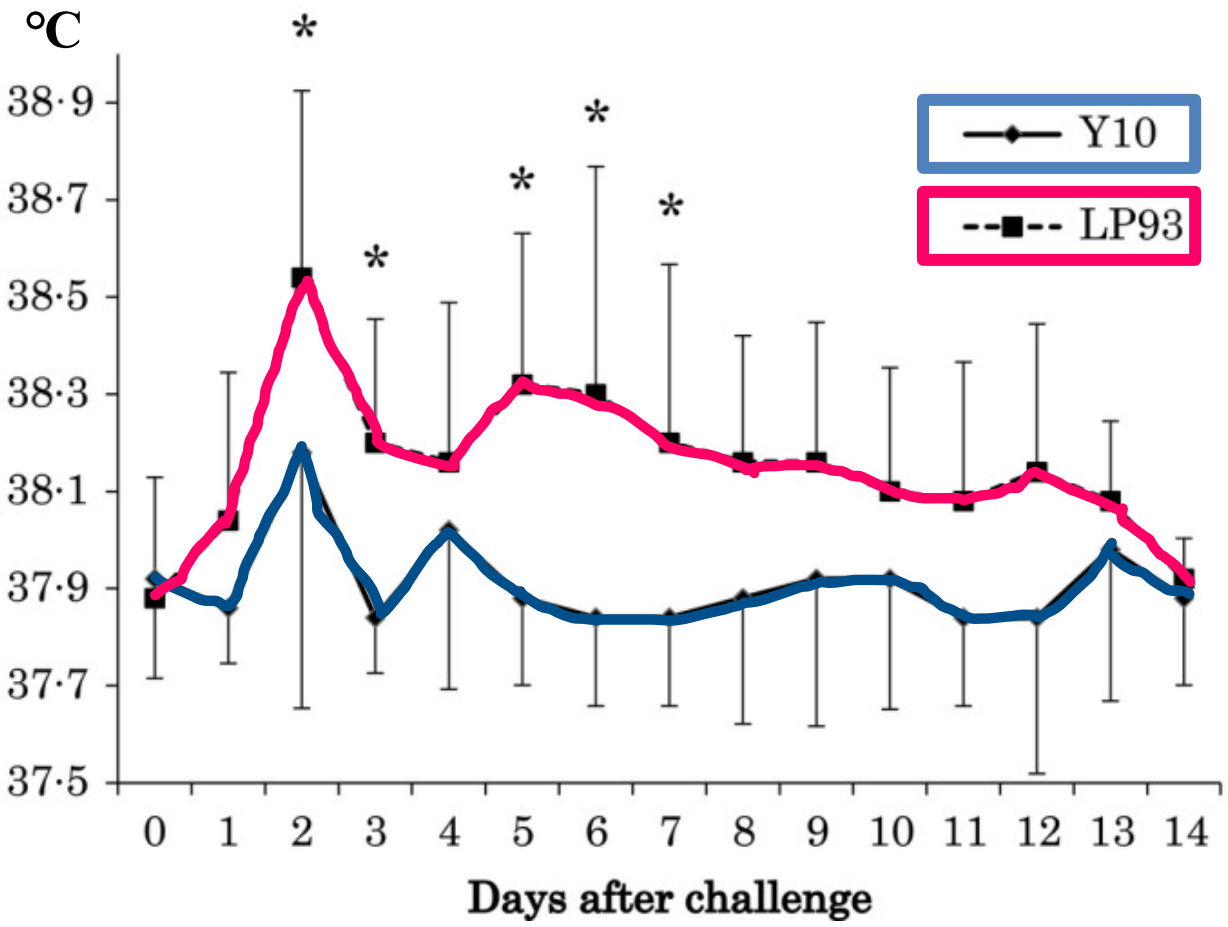
	HI titre		VN titre	
	LP93 (American)	CL11 (Fc2)	LP93 (American)	CL11 (Fc2)
Geometric mean titer	**36.8**	24.3	**168.9**	10.6

（Yamanaka *et al*., Influenza Other Respir Viruses 2016）

VN results correlate with clinical signs

	VN titre: Challenge virus		
Vaccinated group	**LP93** (American)	CL11 (Fc2)	**Y10 (Fc2)**
LP93	**168.9**	**10.6**	111.4
Y10	73.5	**55.7**	**48.5**

（Yamanaka *et al*., Influenza Other Respir Viruses 2016）



LP93 is less effective against CL11 than Yokohama/2010 (Y10)

Current Japanese vaccine strain is effective against recent Fc1 strains

	Antiserum against IBK07
Fc1 challenge virus	**VN** titre
Ibaraki/1/2007 (IBK07)	**203**
Tipperary/1/2019	51
California/1/2021	161
Texas/2/2022	128

（Nemoto *et al*., Arch Virol 2023）

- Antiserum against IBK07 cross-neutralized recent strains
- It is not necessary to change a vaccine strain

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Difficulty of changing vaccine strains smoothly in EIV-free countries

■ EIV-free countries does not have the latest strains

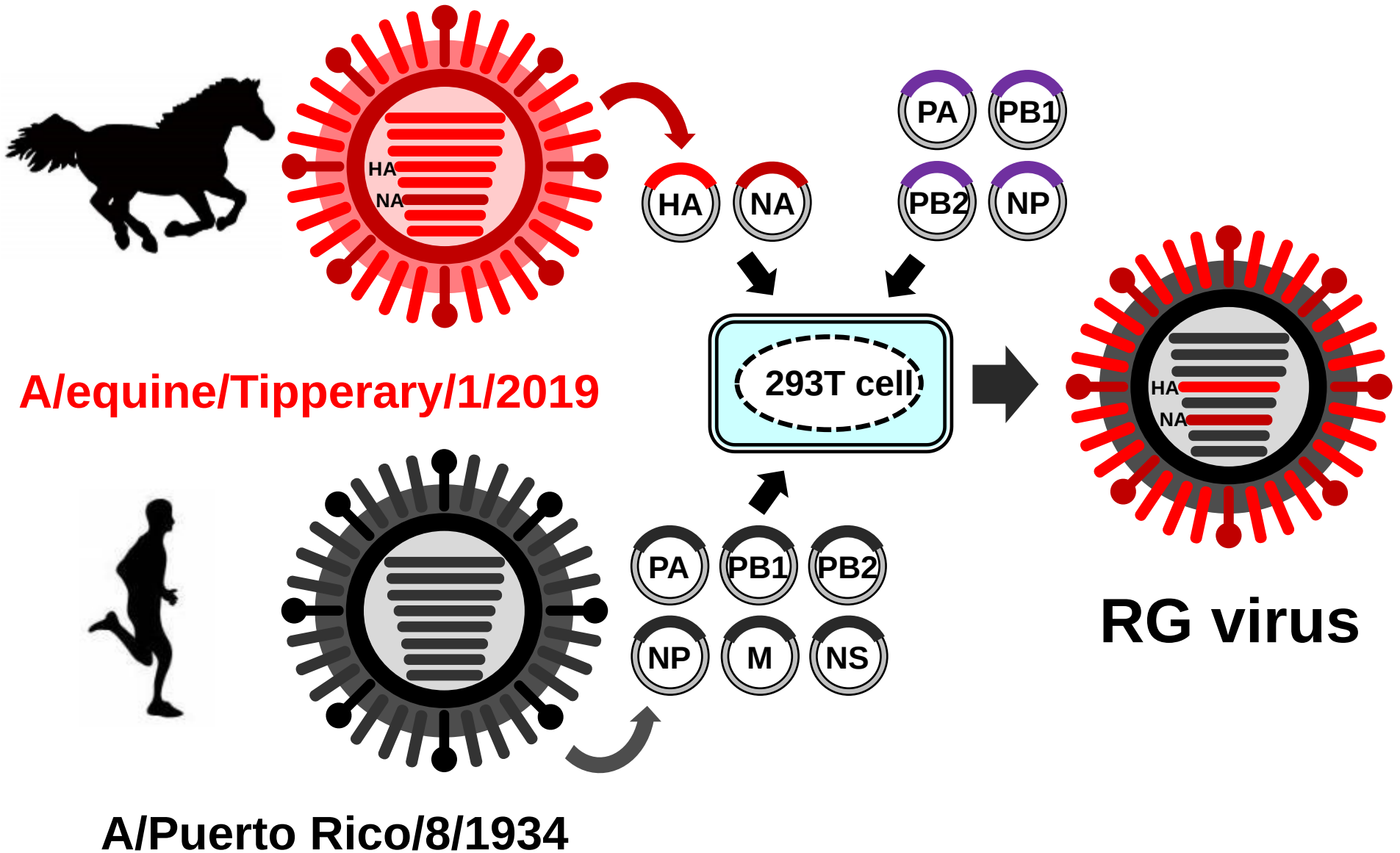
- To get viruses, we need paper works, transport, etc.
- It is not always possible to quickly get optimal strains for vaccines

Artificial virus generated by reverse genetics (RG) may be useful for updating vaccine strains

Purpose of the study

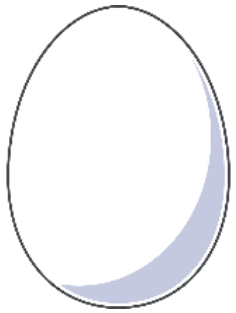
This study evaluated the protective efficacy of an RG-derived inactivated vaccine in horses

How to make artificial viruses by RG

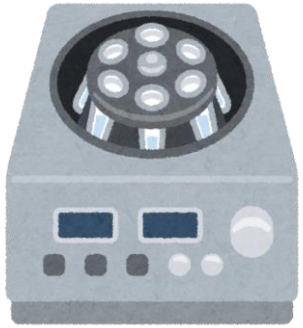


Inactivated vaccine preparation

- Wild-type (WT) vaccine: Tipperary/1/2019
- RG vaccine
  - HA/NA were derived from Tipperary/1/2019
  - Other genes were from human strain PR8/34 (H1N1)



Amplification



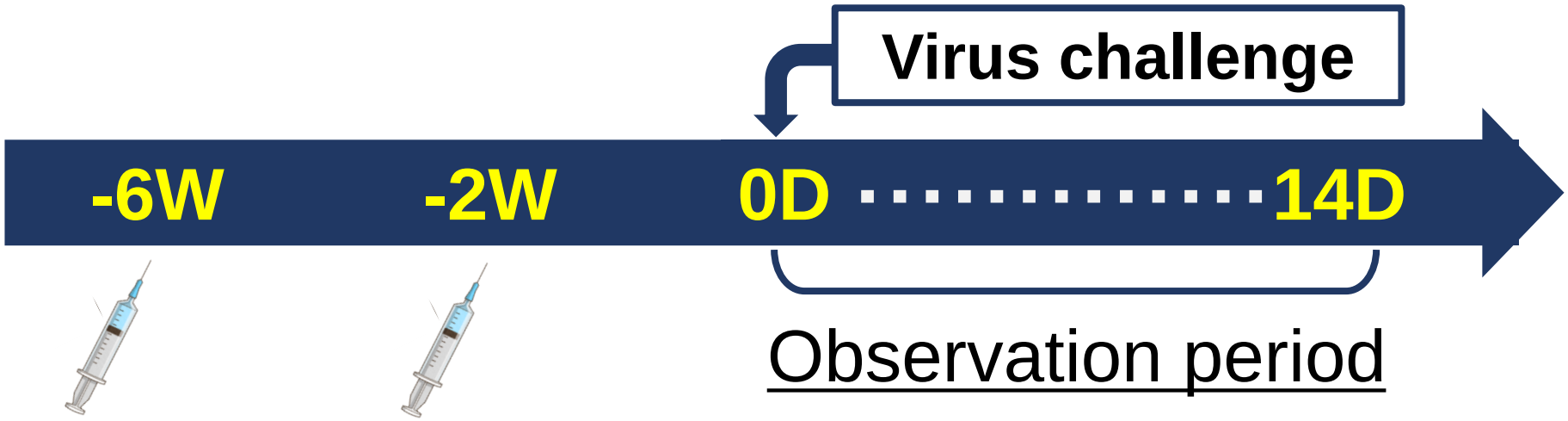
Ultracentrifugation

Inactivation

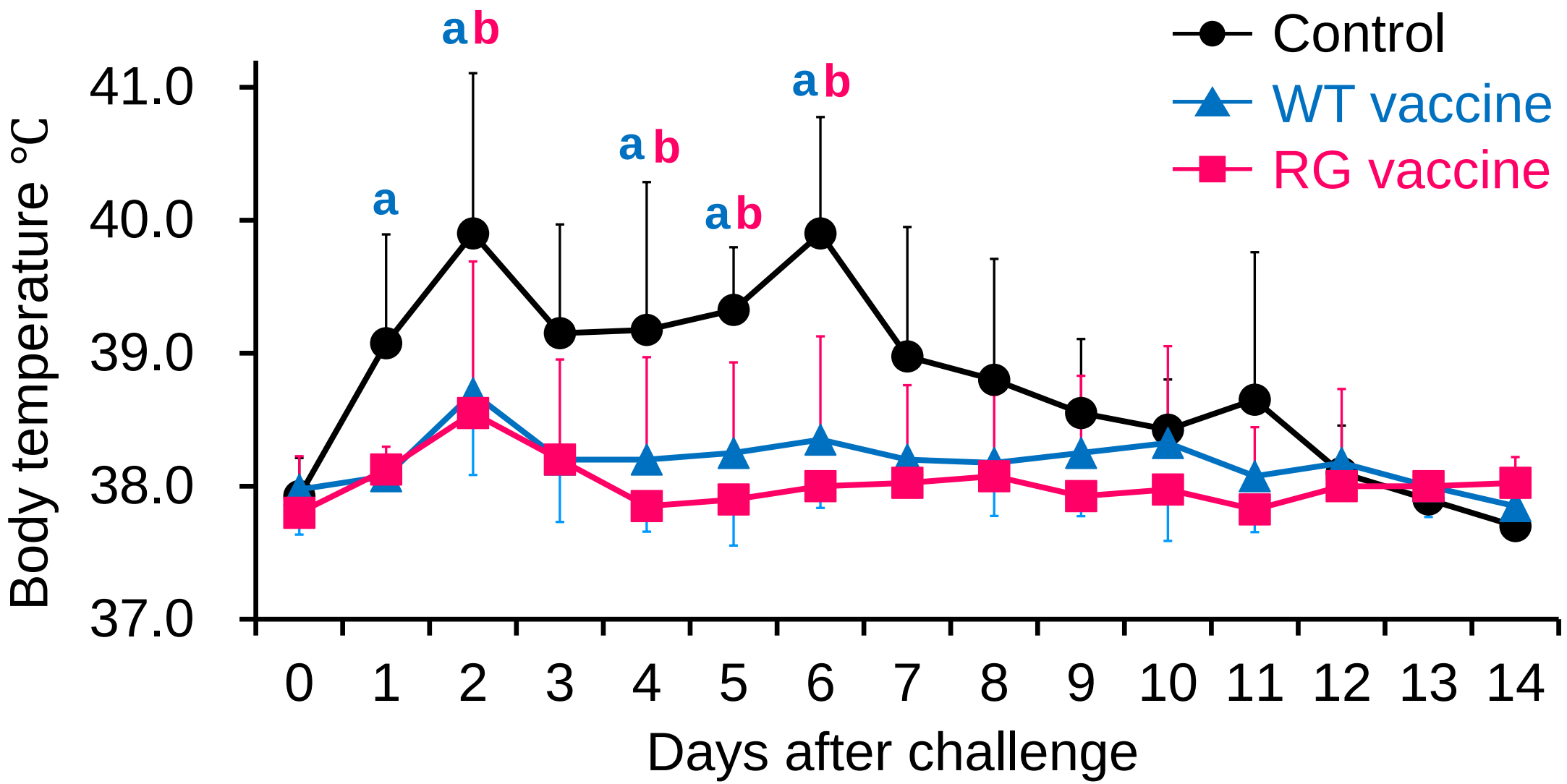
Experimental challenge study

- Grouping
  1. Control: 4 horses
  2. WT vaccine: 4 horses
  3. RG vaccine: 4 horses

- Challenge virus
  Tipperary/1/2019



Body temperature: WT≒RG



Clinical signs (Nasal discharge, Cough)

	Positive	Negative
Control	4/4 horses	0/4 horses
WT	1/4	3/4
RG	0/4	4/4

Relief of signs: WT≒RG vaccine

Protective efficacy of inactivated vaccine generated by RG

vaccine

RG can make it easy to update vaccine strains

（Ohta *et al*., Vaccine 2022）

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