Genome editing for animal health
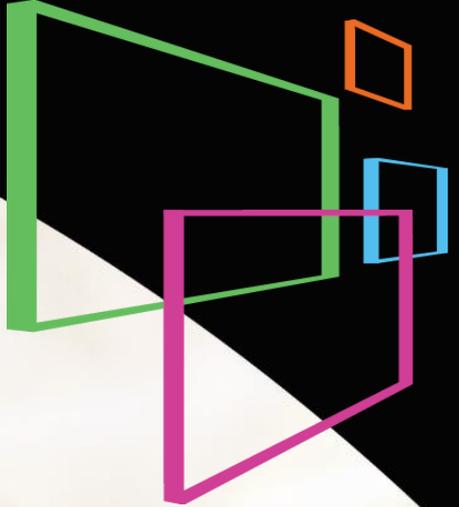
Dr Christine Tait-Burkard

The Roslin Institute, The University of Edinburgh

4th International Workshop on Regulatory

Approaches for Agricultural Applications
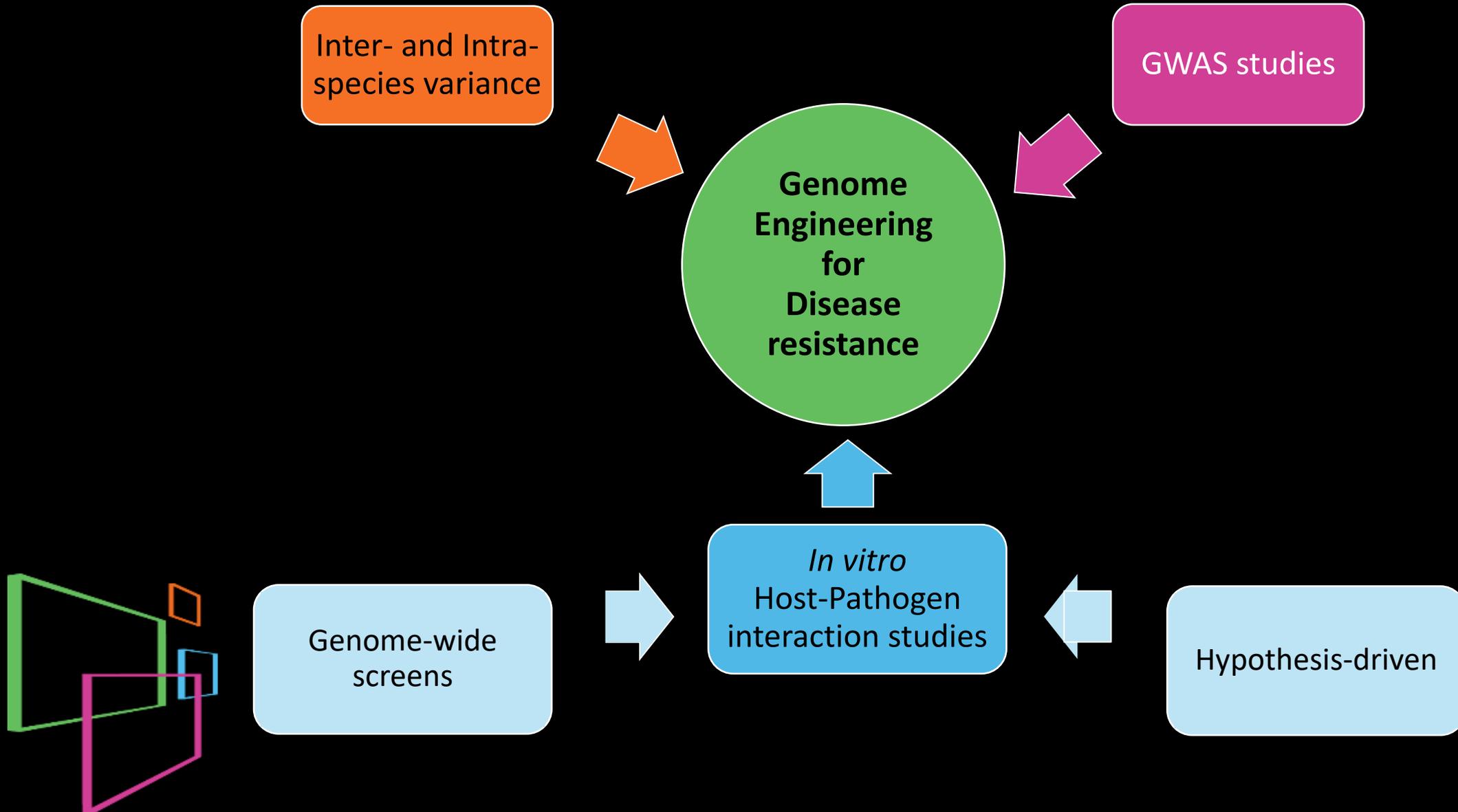
Genome editing for disease resistance
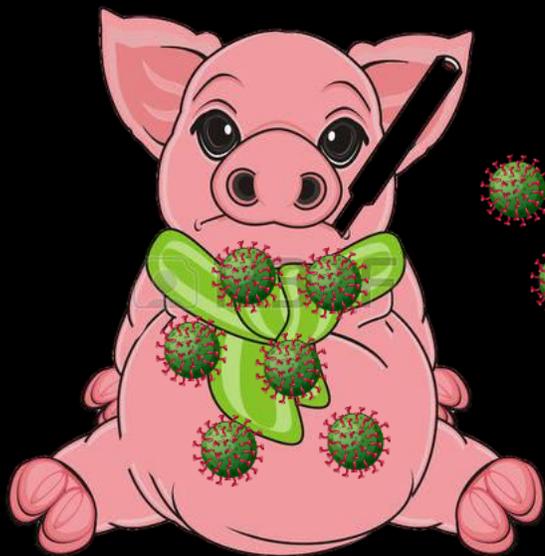
Dr Christine Tait-Burkard

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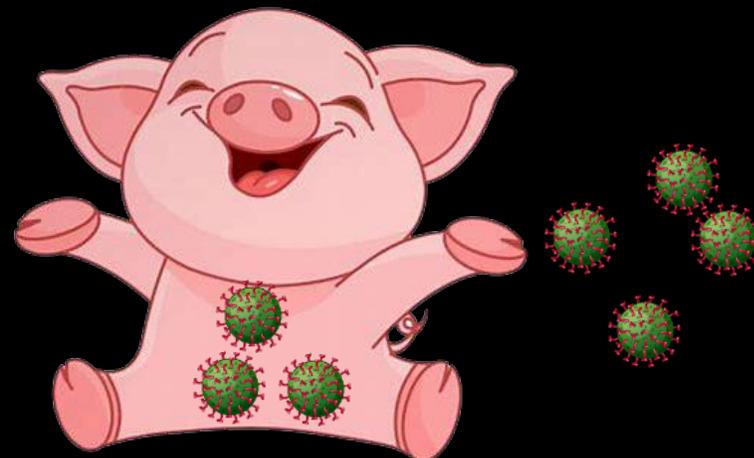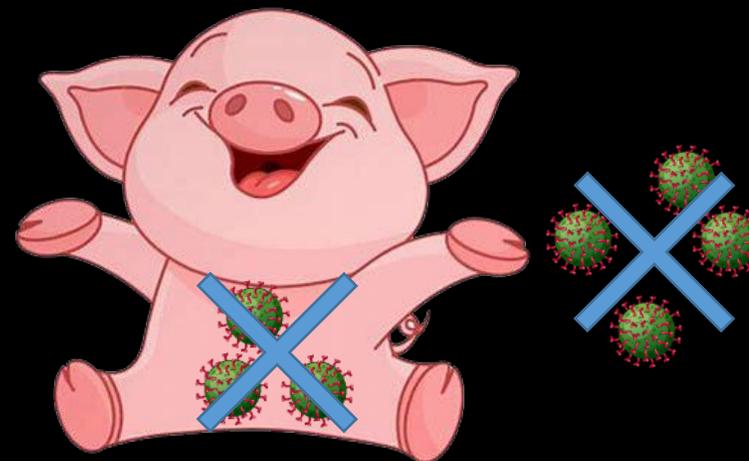
Finding targets
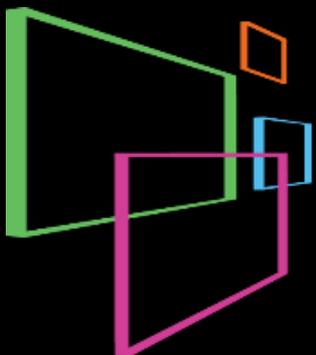
Finding targets

Susceptible

Resilient

Tolerant

Resistant

Porcine Reproductive and Respiratory Syndrome (PRRS)

All pigs
Respiratory distress, Fever, inappetence

Suckling piglets
Diarrhea, severe respiratory distress
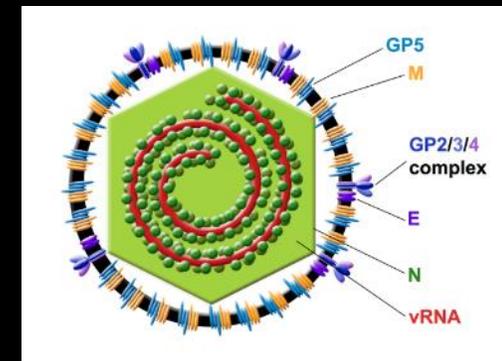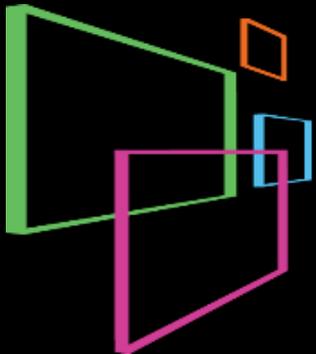Up to 100% lethality (strain dependent)

Pregnant Sows
Complete abortion or death of fetuses *in utero*
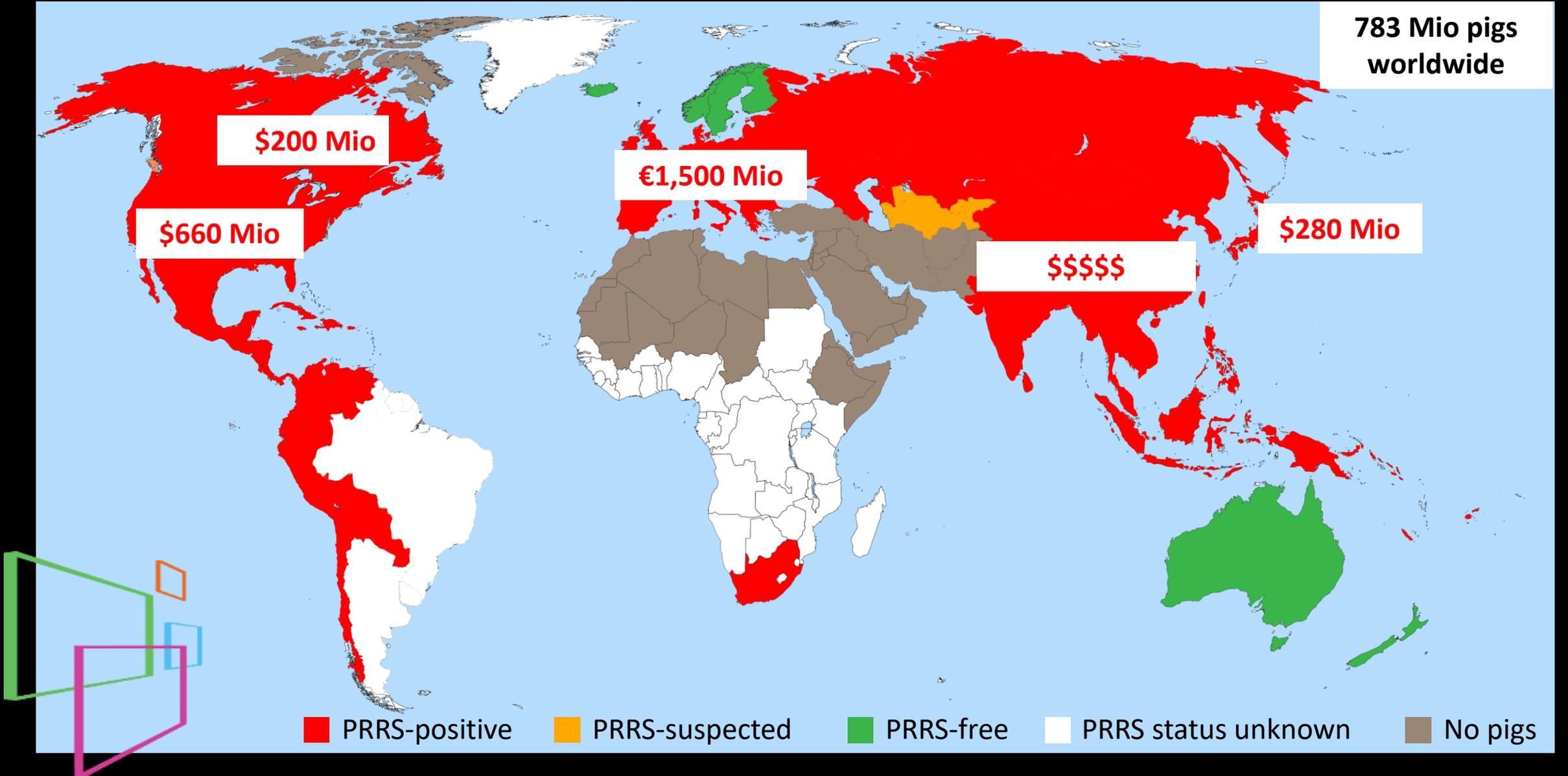
→**Animals suffering** from disease
→**Loss of animals / Growth / Food waste** in the production chain

→Viral infection **incapacitates immune system**
leaving the door open for **secondary infections** with **bacteria and pathogens**
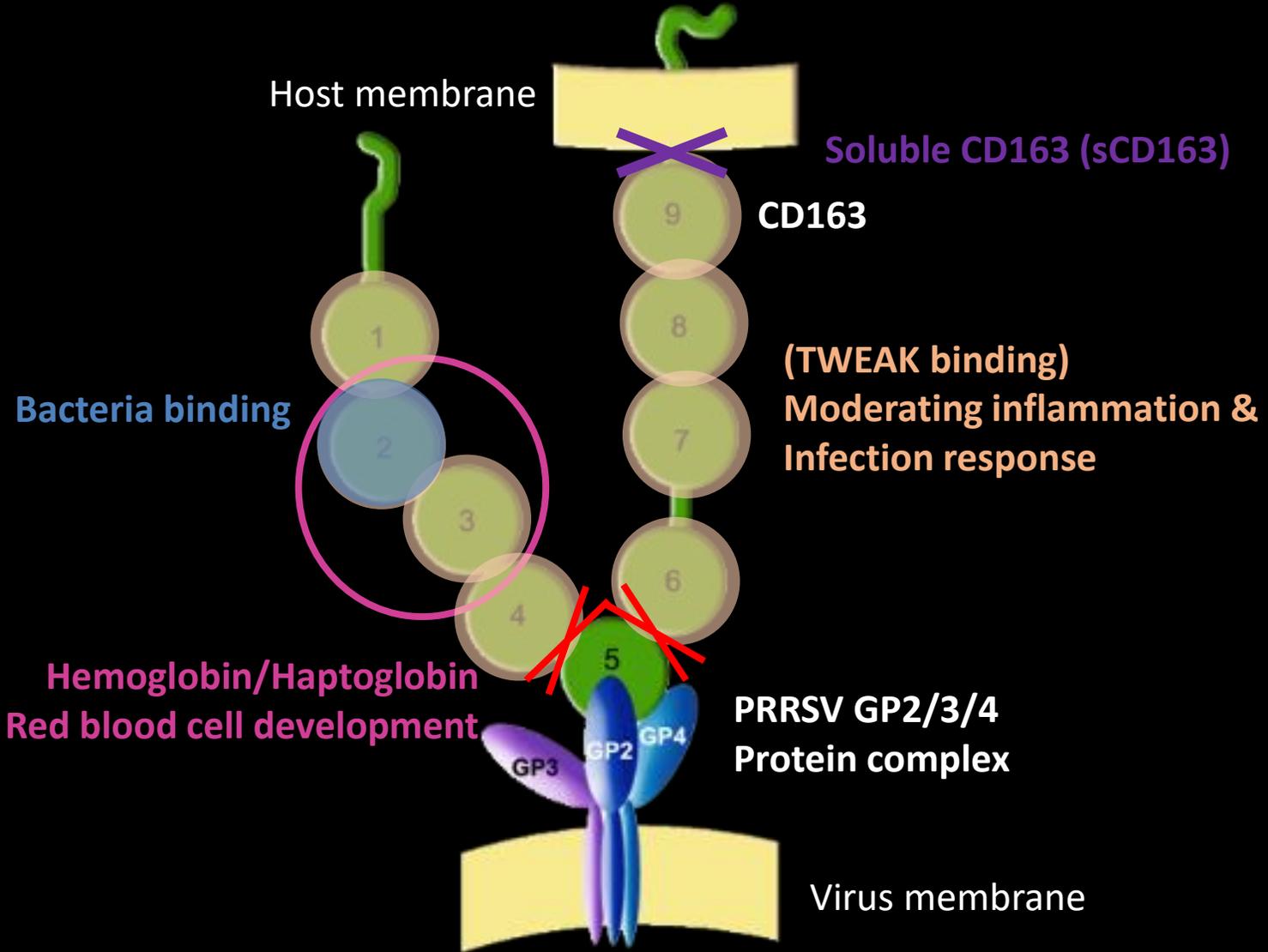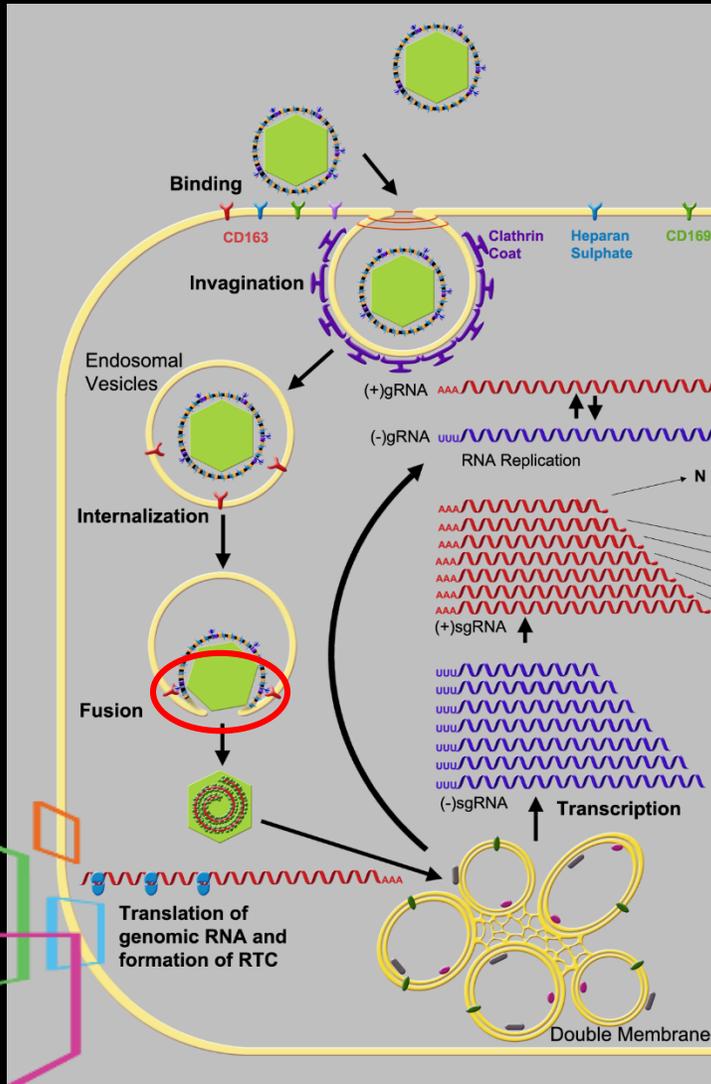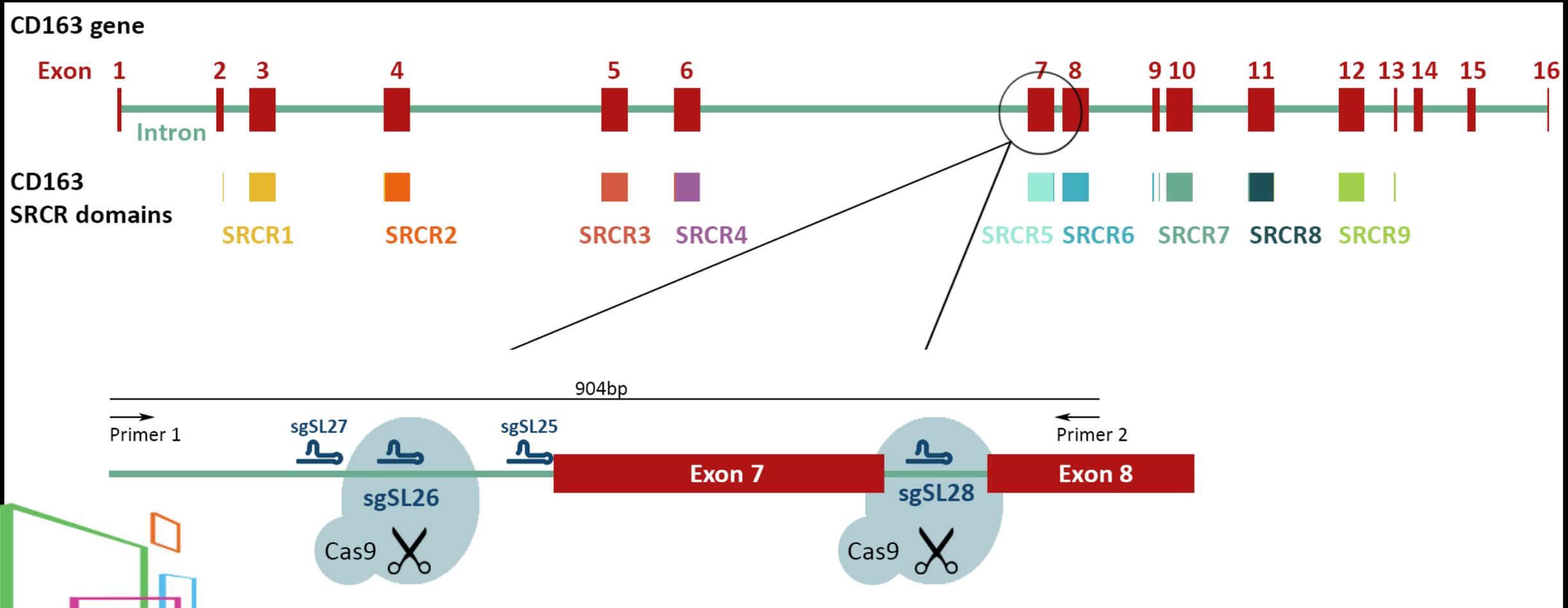
Genome editing for PRRSV resistance
The PRRSV panzootic

783 Mio pigs worldwide

$200 Mio

€1,500 Mio

$660 Mio

$$$$$

$280 Mio

PRRS-positive   PRRS-suspected   PRRS-free   PRRS status unknown   No pigs

The Background – PRRSV-host interaction

Host membrane

Soluble CD163 (sCD163)

CD163

Bacteria binding

(TWEAK binding)
Moderating inflammation &
Infection response

Hemoglobin/Haptoglobin
Red blood cell development

PRRSV GP2/3/4
Protein complex

GP3   GP2   GP4

Virus membrane

The Solution – Excising domain 5
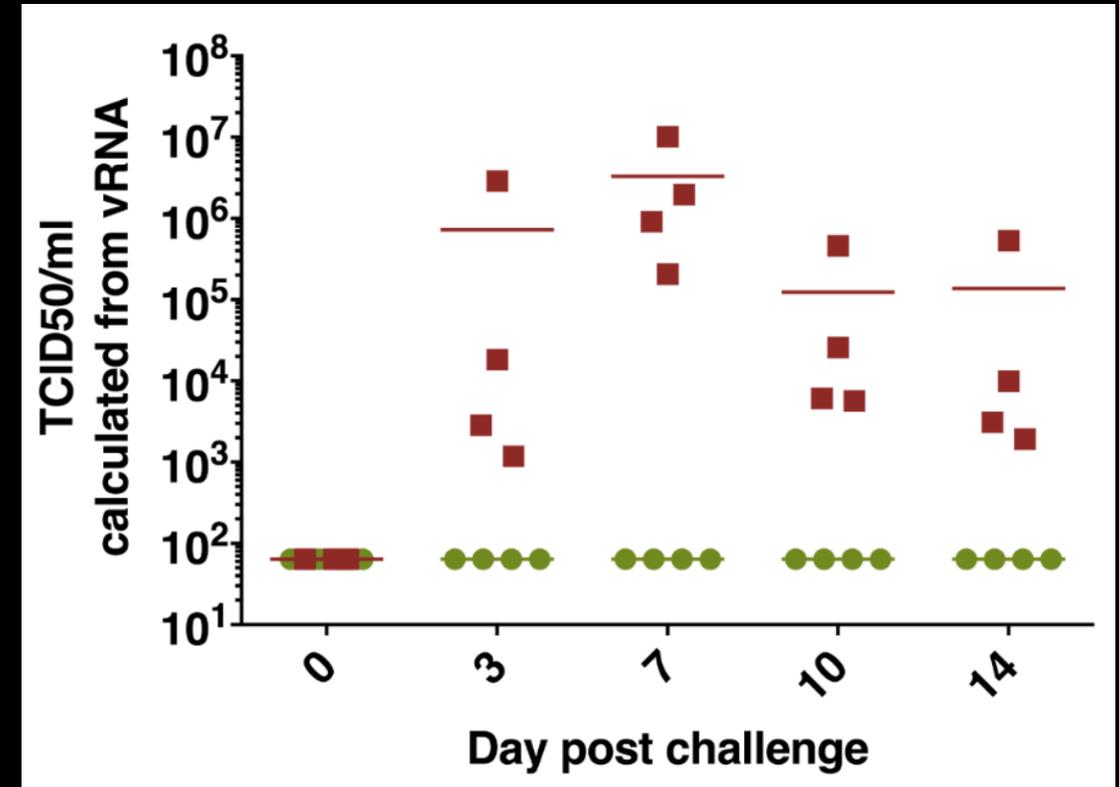

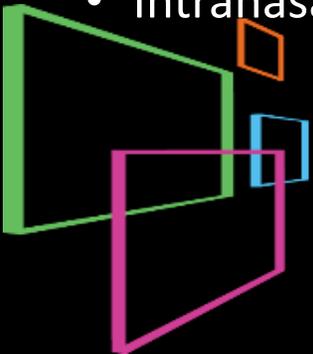**Burkard et al., 2017, PloS Pathogens**
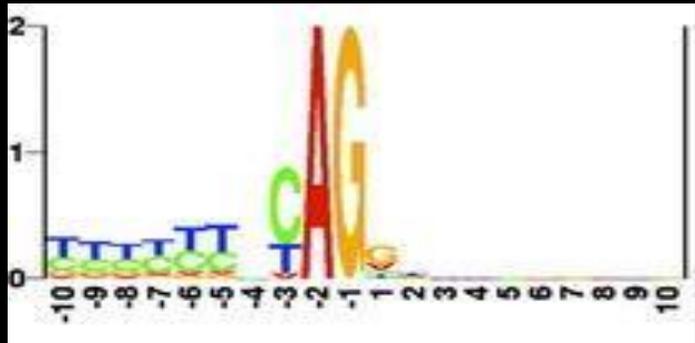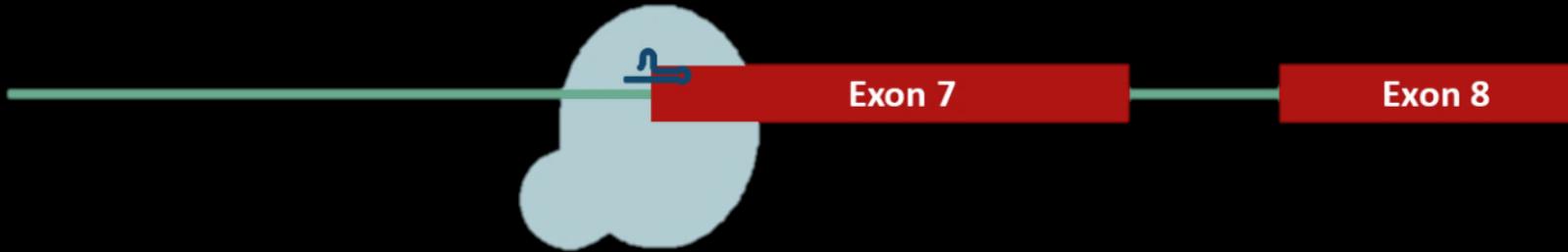
The Result – Healthy, resistant pigs

Experimental set-up

- **4x ΔSRCR5** & **4x wild type** animals at age 7-8 weeks
- Co-housing of animals to allow natural transmission
- Intranasal inoculation

Burkard et al., 2018, Journal of Virology

Many ways lead to Rome...
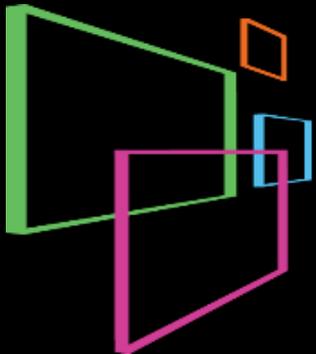

TATTTTTC**AG**CCCACAGGAAAC

11bp deletion

Option 1: Cas9
- Without template – random deletion
- HDR template – more efficient single base edit

Option 2: dCas9/UGI
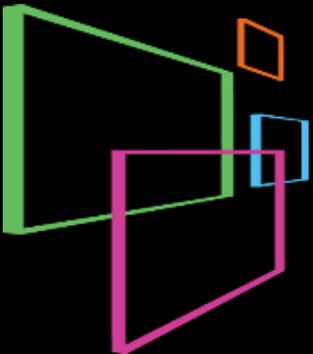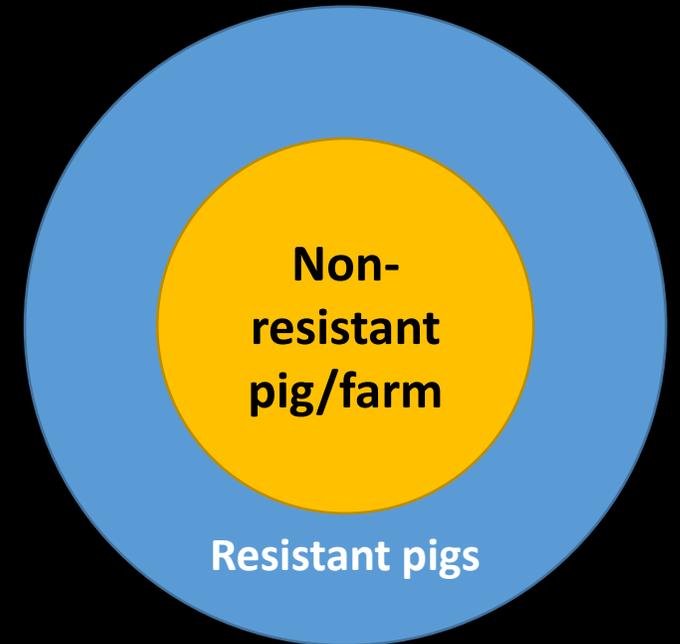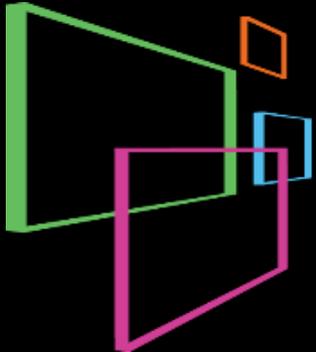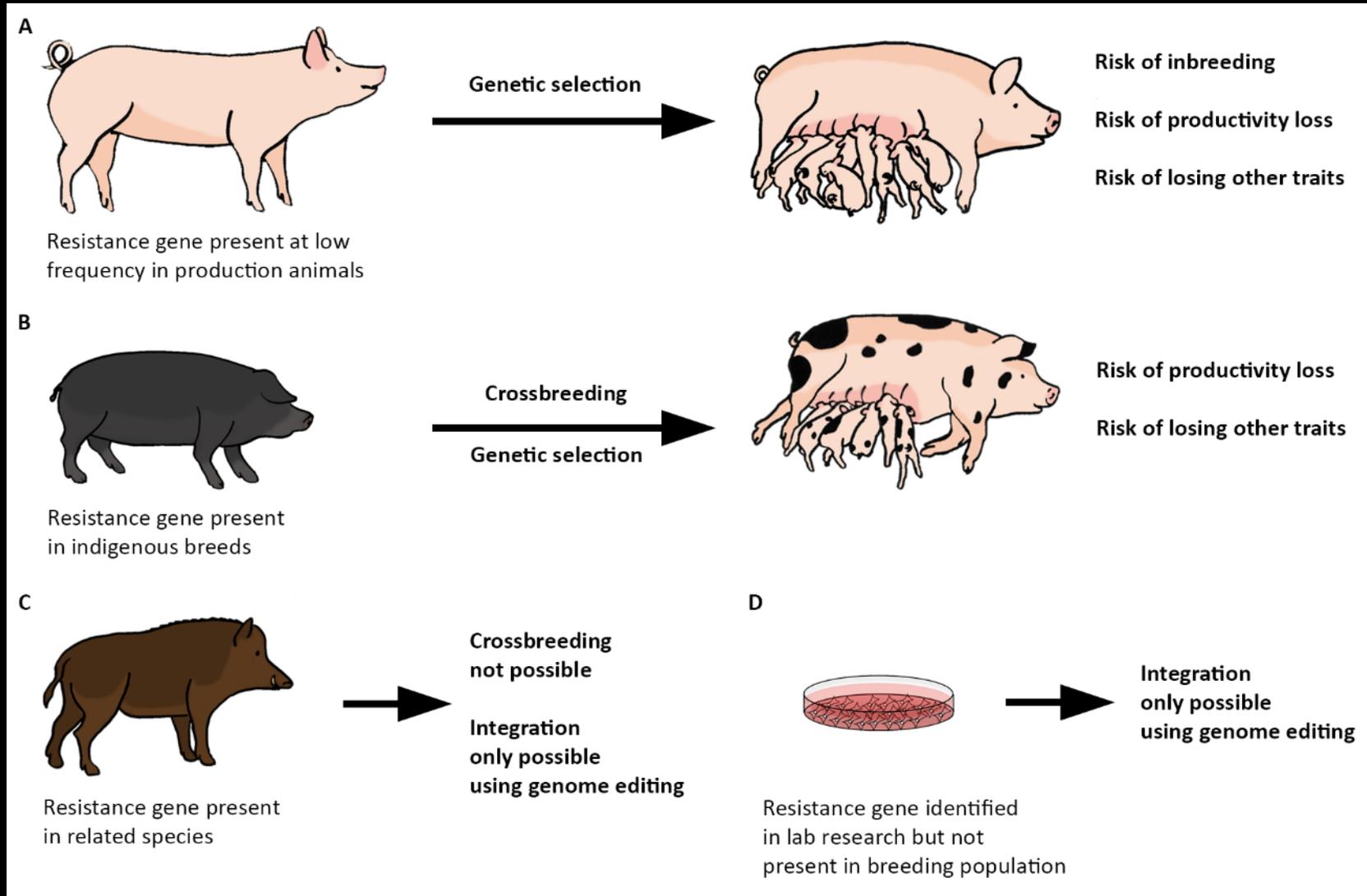Uracil Glycosylase Inhibitor
Targeted, non ds break base edit

Same phenotype but minimal genotype change

Opportunities for the PRRSV-resistant pig

- Improved animal welfare

- No secondary bacterial / pathogen infections
  - ➤ Less antibiotics use
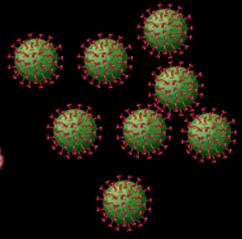
- No shedding / shielding other animals / farms

Non-resistant pig/farm

Resistant pigs

Why genome editing?
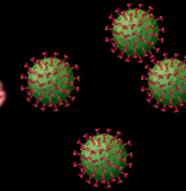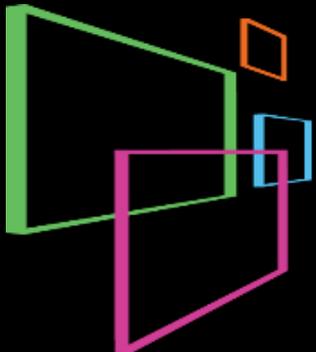
Risks, Benefits and Regulation

Tolerant

+ Improved production
+ Highly likely to react to live att. vaccines
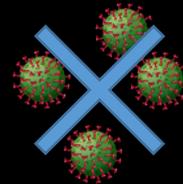- High pathogen load
- High evolution rate

Resilient
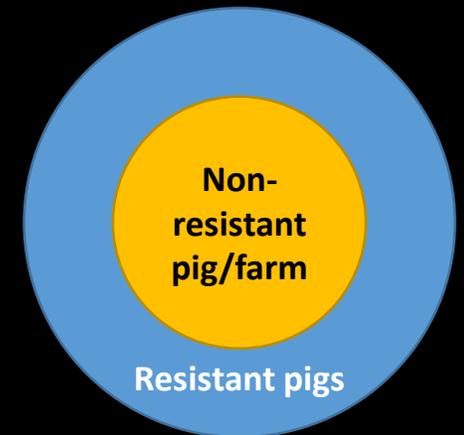
+ Improved production
+ Improved welfare
± Likely to somewhat react to LA vaccines
± Reduced pathogen load
± Reduced evolution rate

Resistant

+ Improved production
+ Improved welfare
+ No pathogen load
+ Low evolution rate
± Unlikely to react to LA vaccines
- More difficult to find targets

Non-resistant pig/farm

Resistant pigs

Risks, Benefits and Regulation

- Regulating traits vs. regulating methods?
  - Multiple technologies can lead to the same outcome

- Co-evolving methodology
  - RNA vaccines (self-amplifying)
  - Affordable antivirals
  - Antimicrobial alternatives

- Genome editing is one tool in the box

- Transgenesis may be a solution too
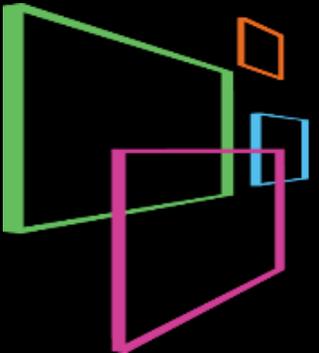
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