

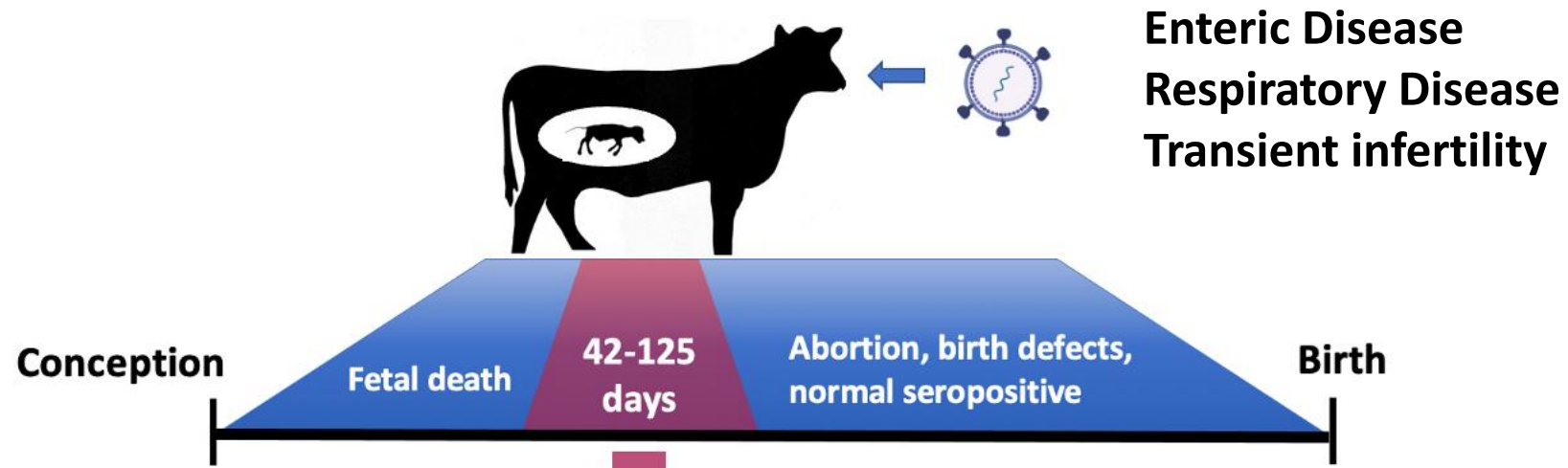
Producing Cattle with Genetic Resistance to Bovine Viral Diarrhea Virus

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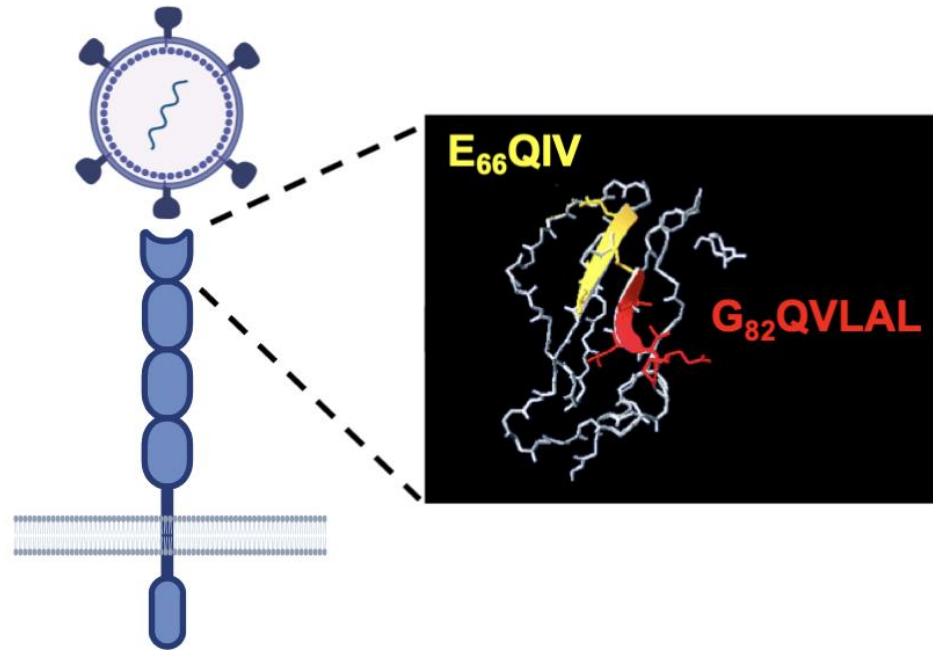
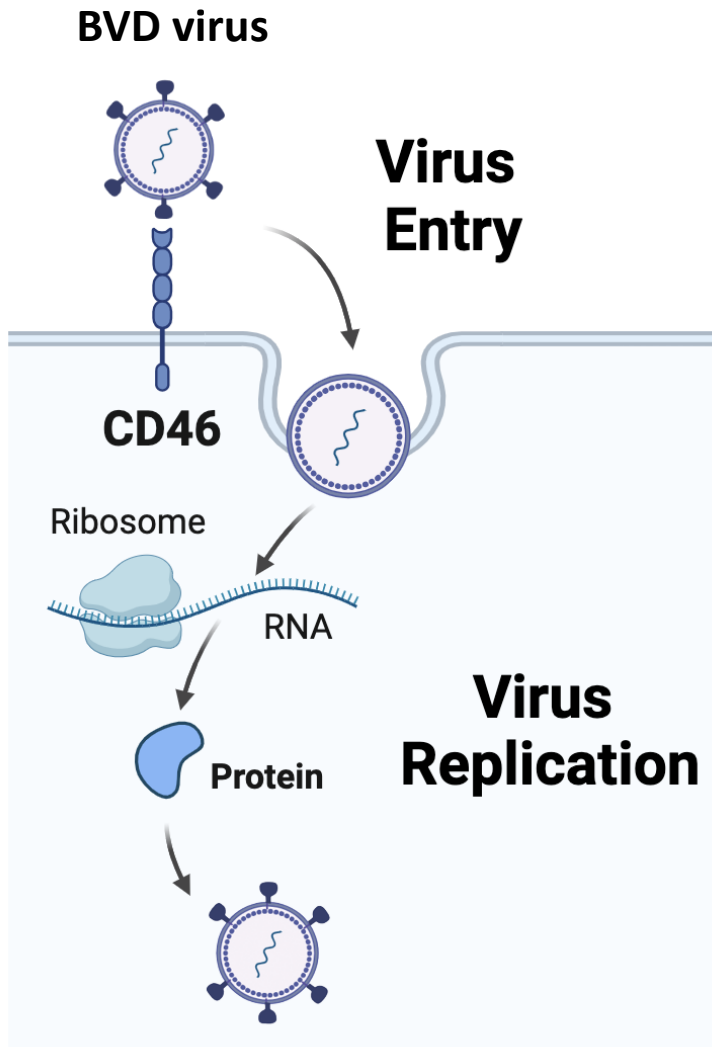


Bovine Viral Diarrhea Virus

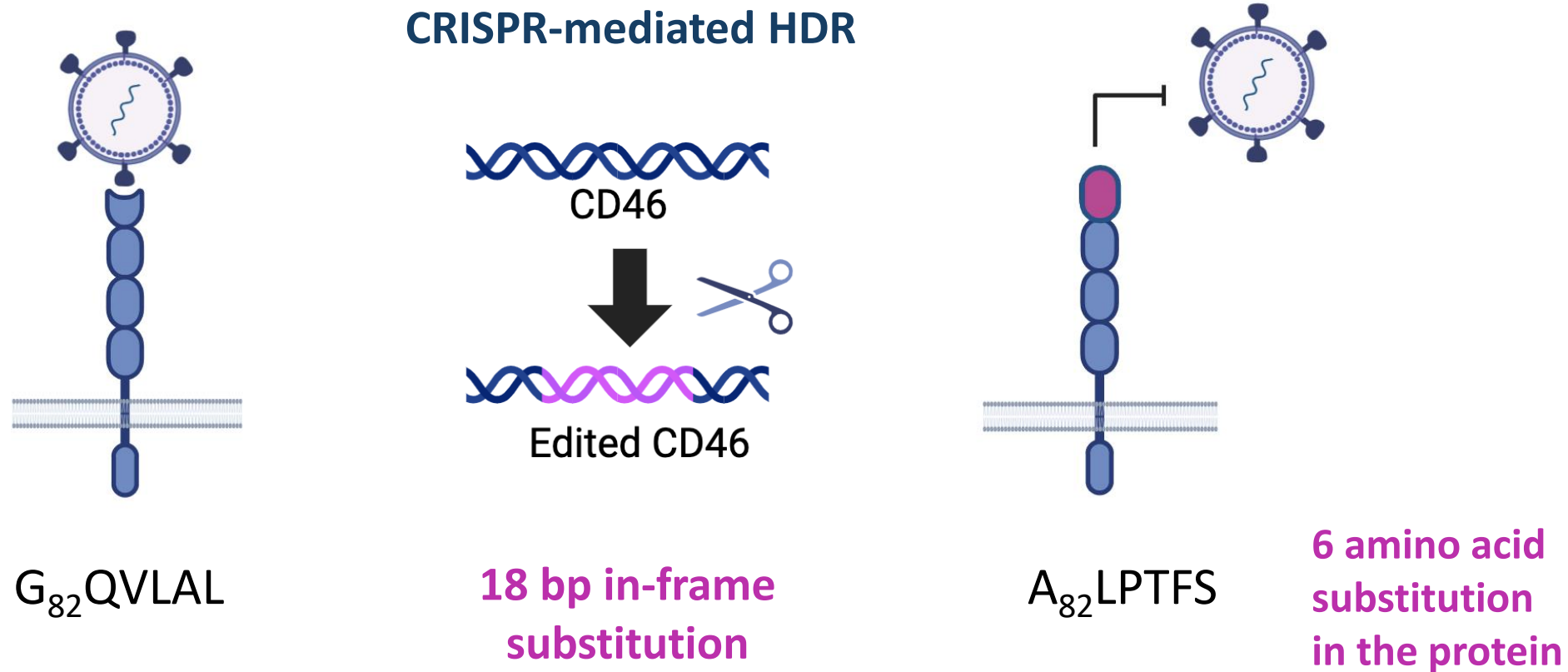


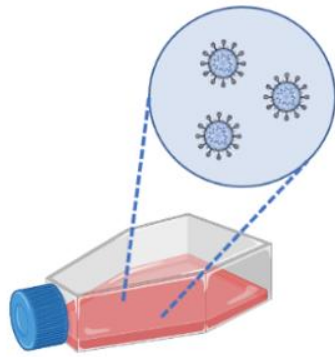
**Persistently Infected
"Trojan calf"**

Approach: Use CRISPR to produce a novel resistance allele



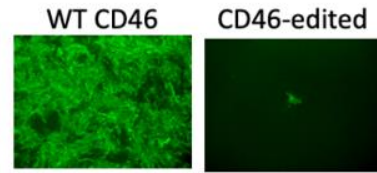
Approach: Use CRISPR to produce a novel resistance allele





Stage 1

in vitro
MDBK cells



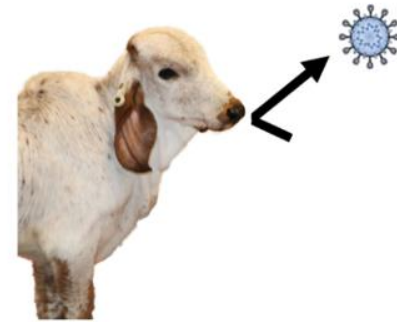
Stage 2

primary
fetal tissues



Stage 3

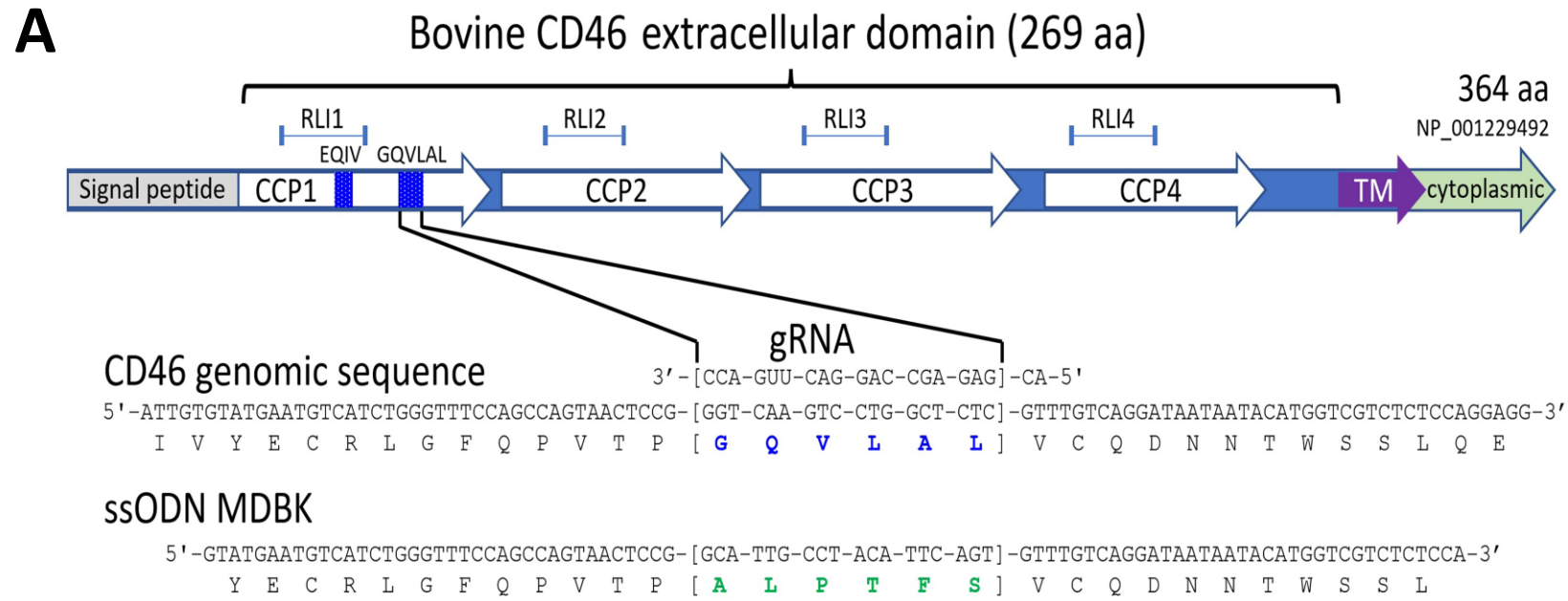
live calf
production



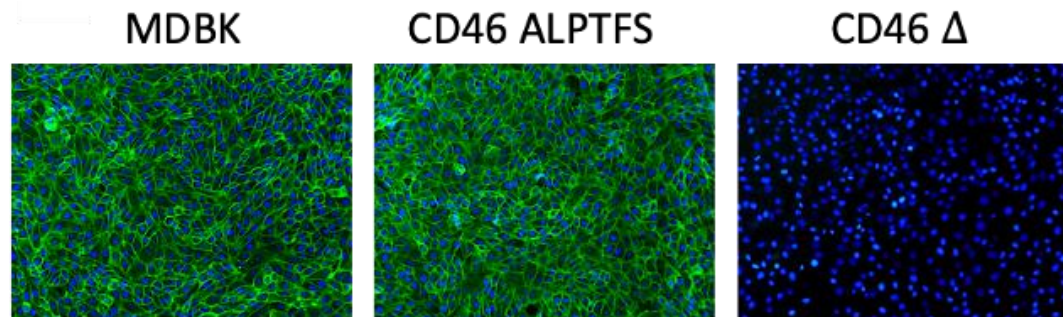
Stage 4

challenge
study

CRISPR/Cas9 editing of *CD46* in MDBK cells

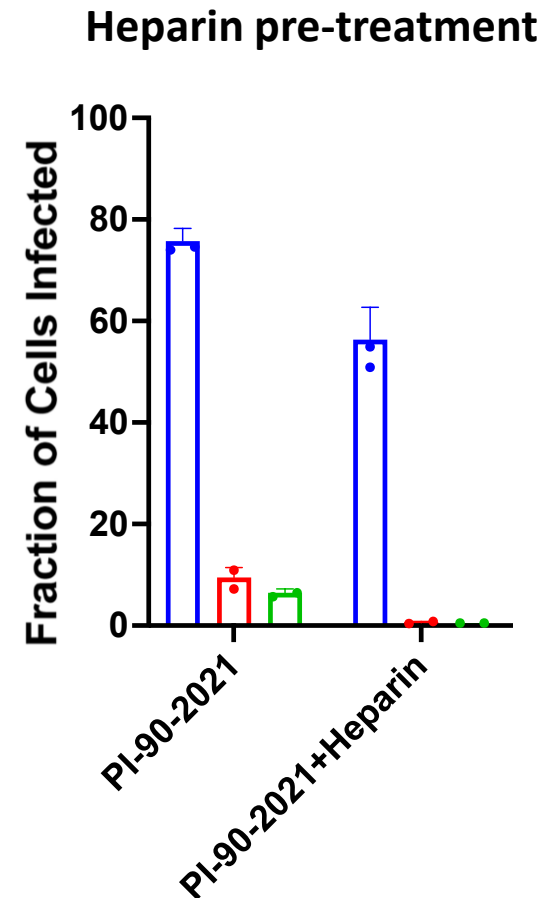
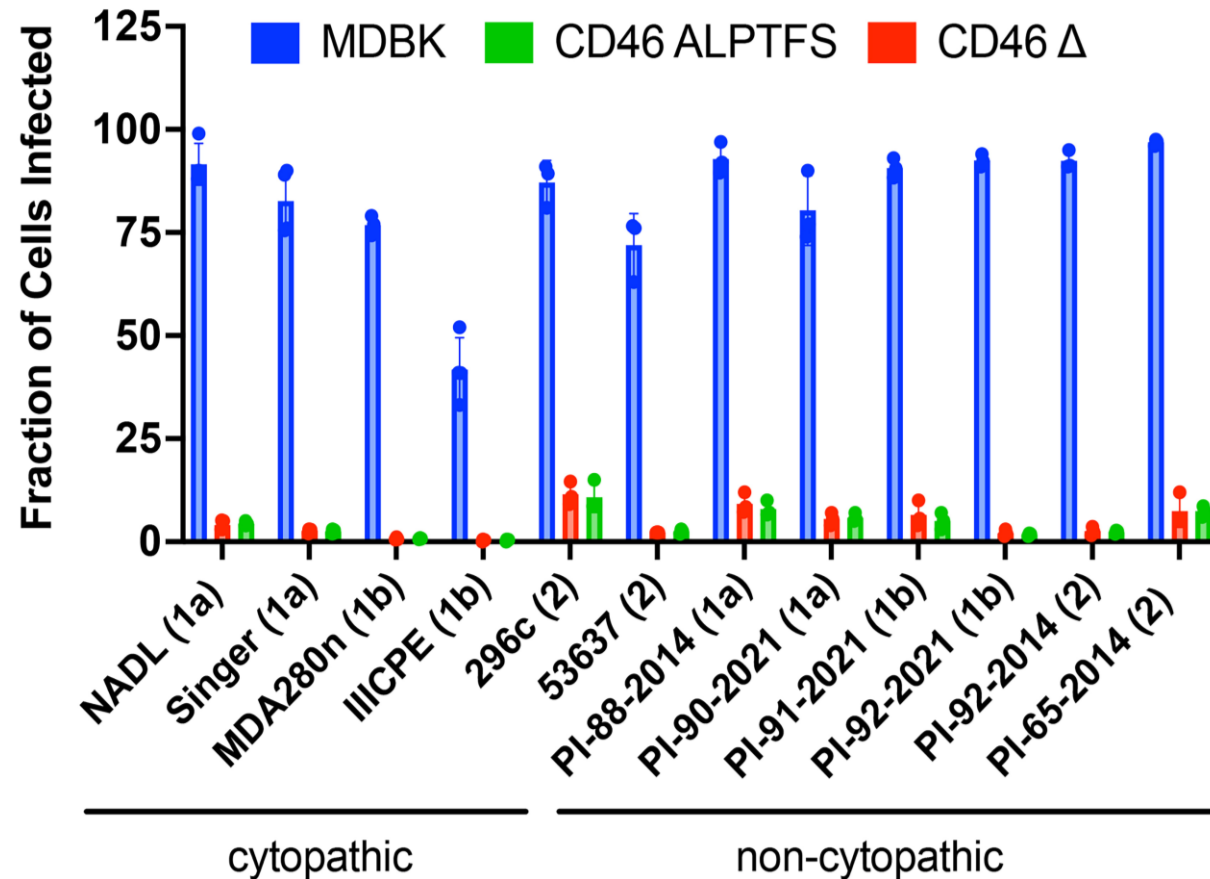


B



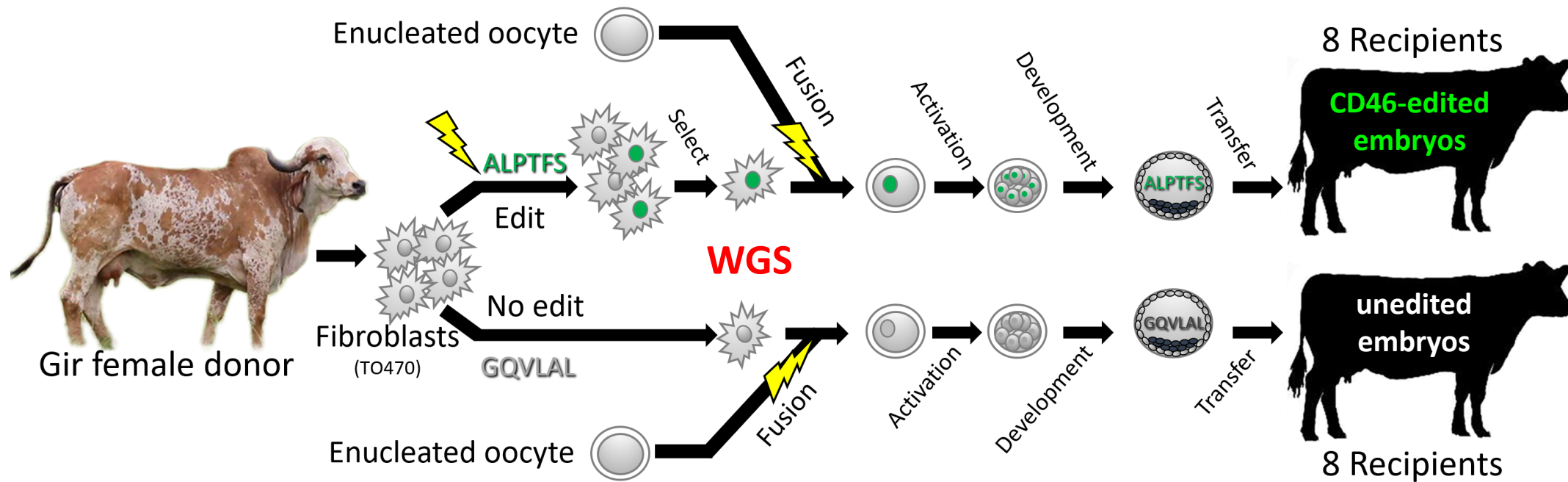
CD46, nucleus

Replacing six amino acids in CD46 eliminates CD46-dependent virus entry

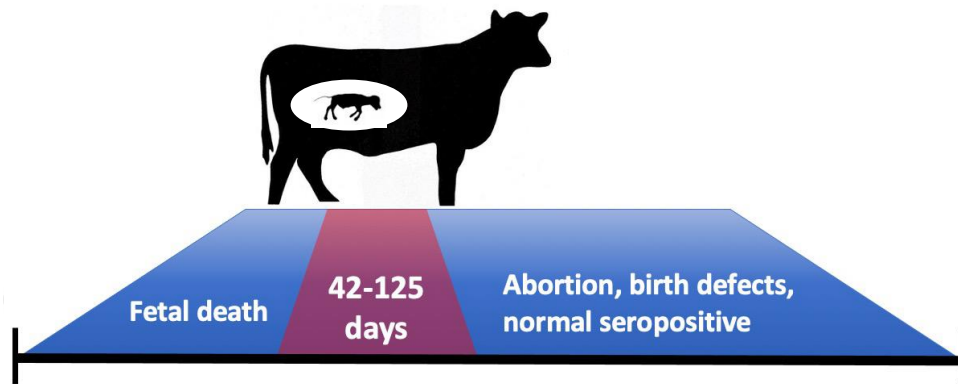


Cloning: Somatic Cell Nuclear Transfer

Test the impact of the edit on calf development and BVDV susceptibility

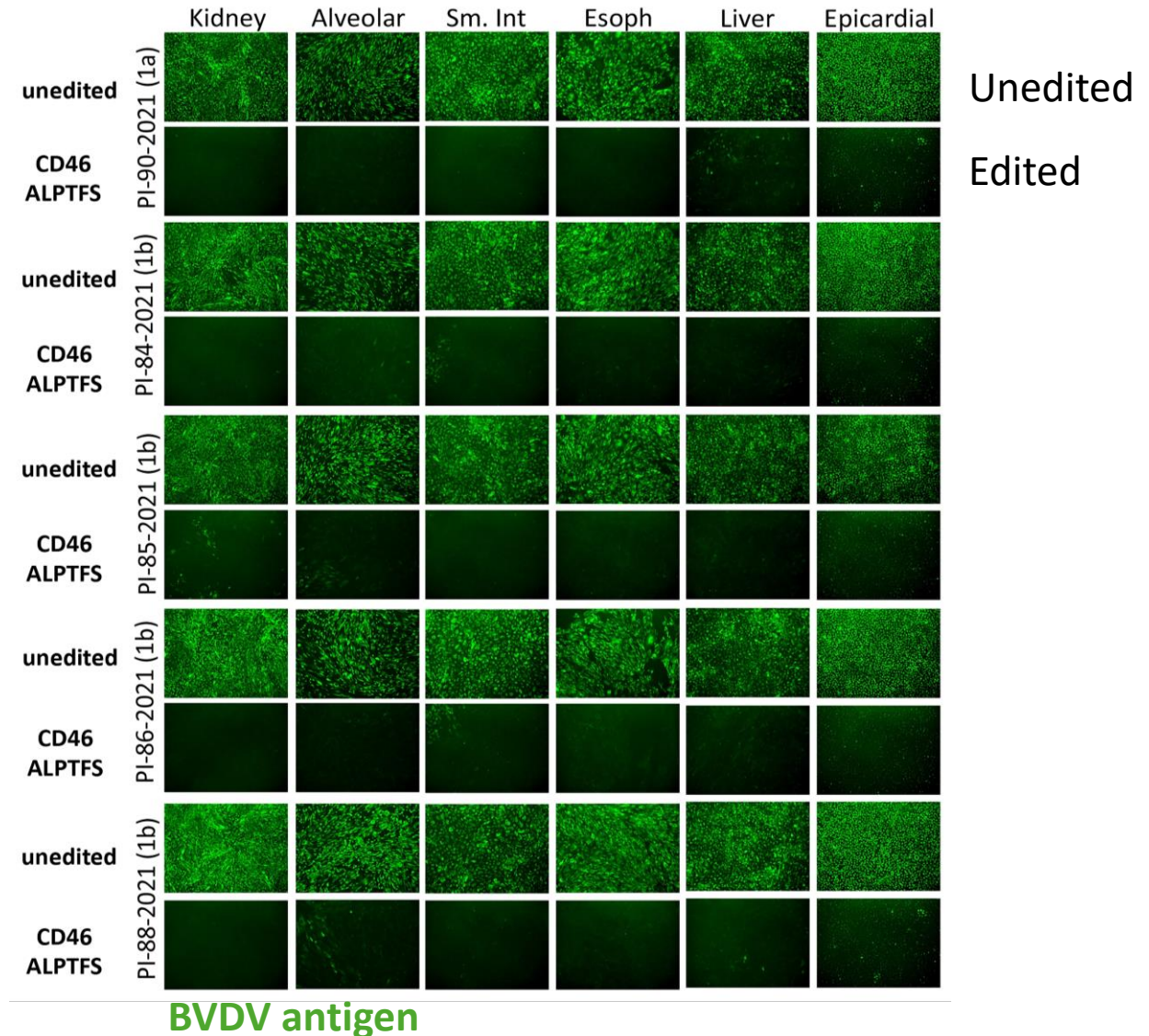


BVDV infection is reduced in CD46 ALPTFS primary cells from 100-day fetal tissues



100 days

- Lung
- Heart
- Small intestine
- Esophagus
- Kidney
- Liver

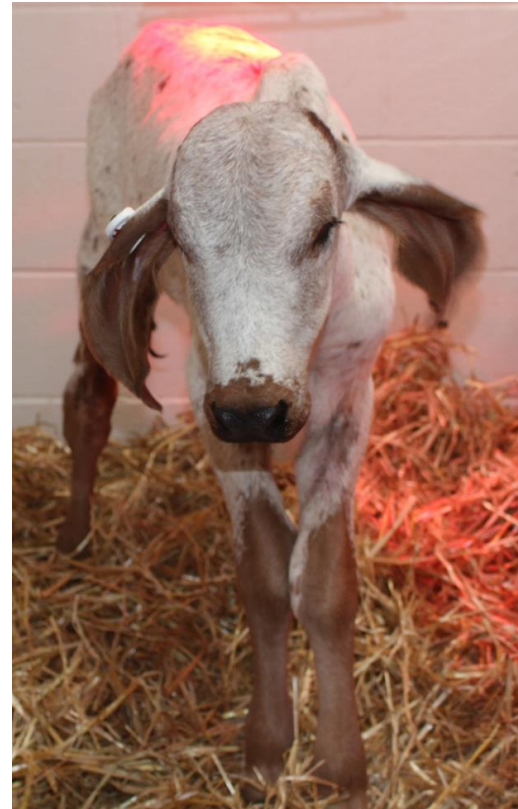


The *CD46*-edit did not prevent the birth of a live and healthy calf

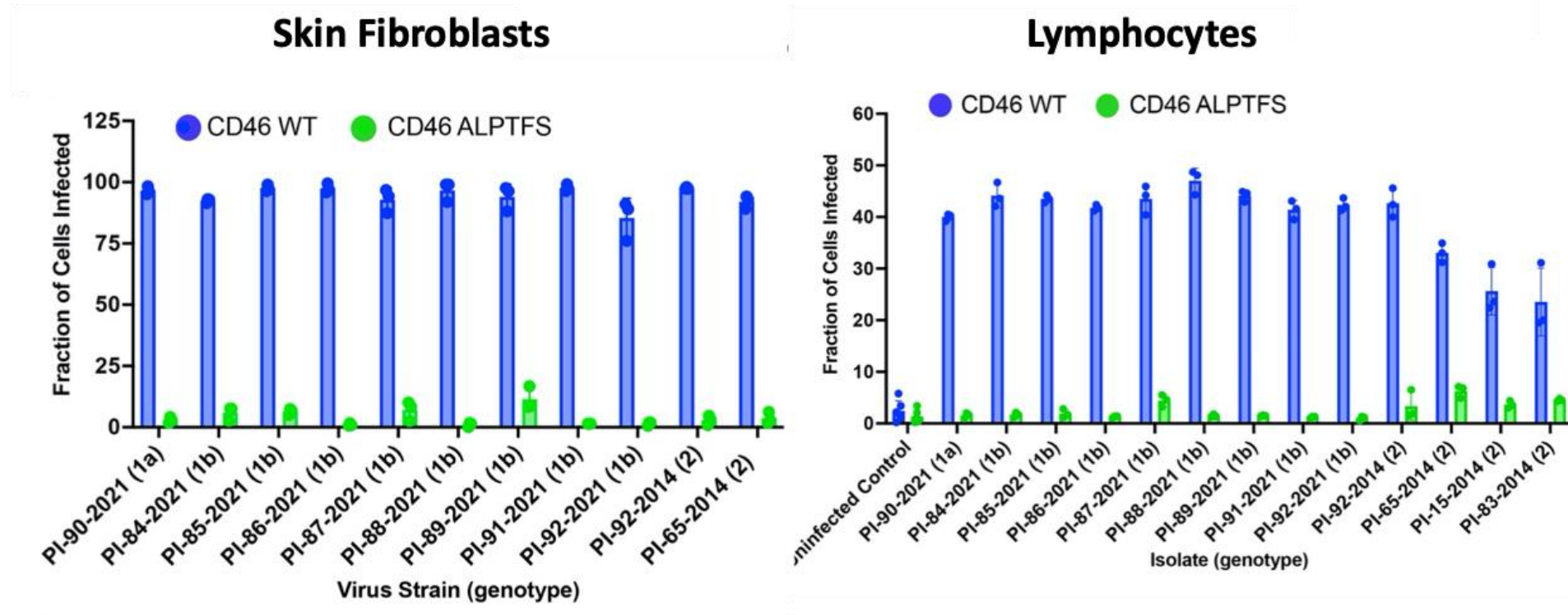


July 19, 2021

Ginger



Ginger's cells have significantly reduced susceptibility to BVDV when infected *ex vivo*



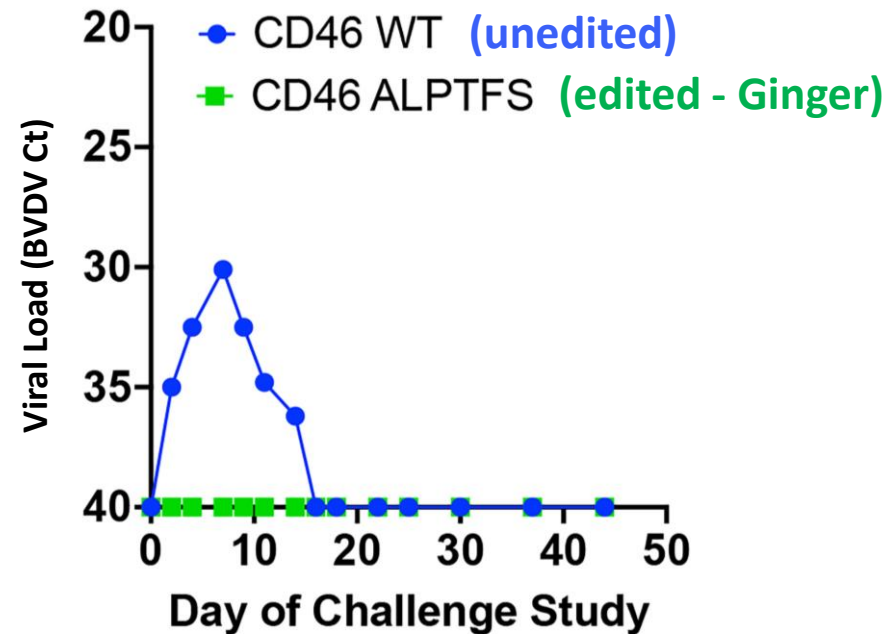
- CD46 WT (unedited)
- CD46 ALPTFS (edited - Ginger)

Ginger did not get sick and her white blood cells remained uninfected

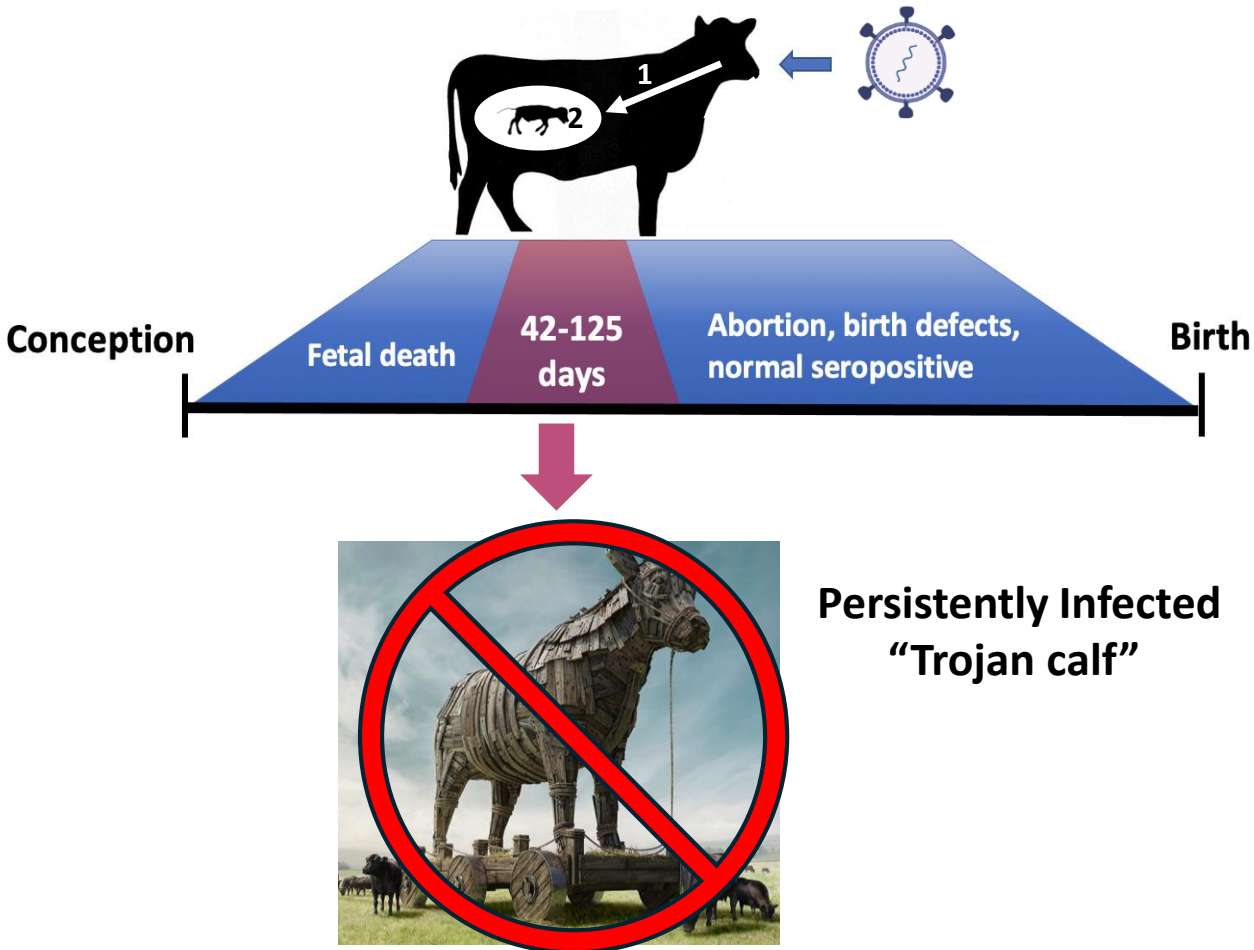
Natural exposure challenge study



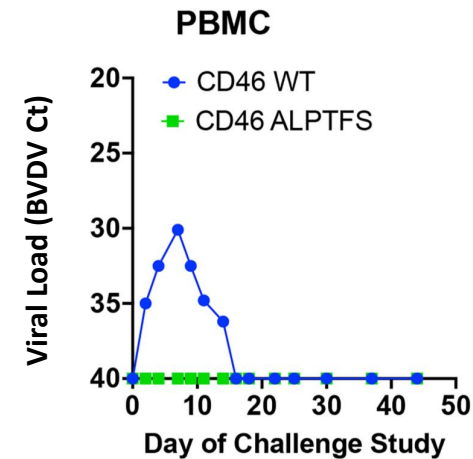
White Blood Cells



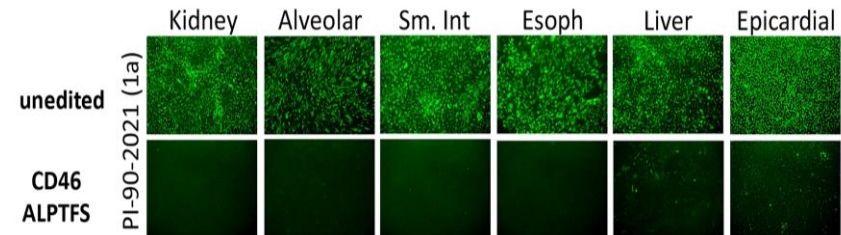
Reducing viremia in acute infections may significantly impact BVDV control efforts



1. Reduced viremia (virus spread) in the cow



2. Reduced susceptibility in fetal tissues



Acknowledgements



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Thank you!

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