Editing the future of Livestock

Chris Proudfoot

The Roslin Institute

University of Edinburgh

Domestication

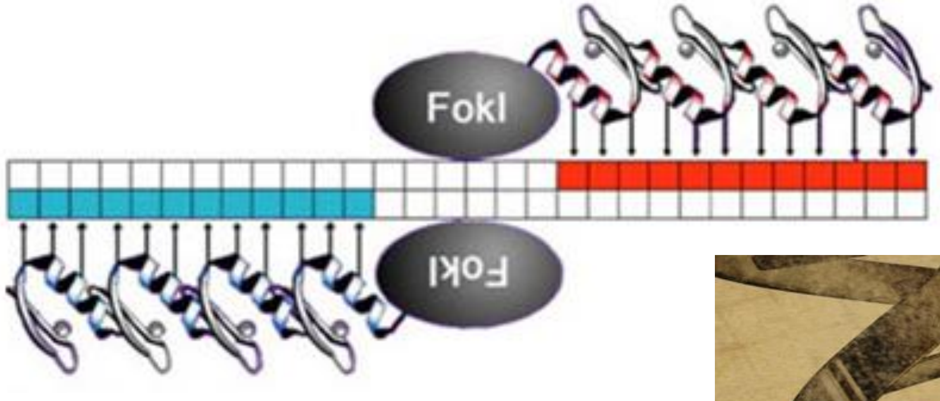




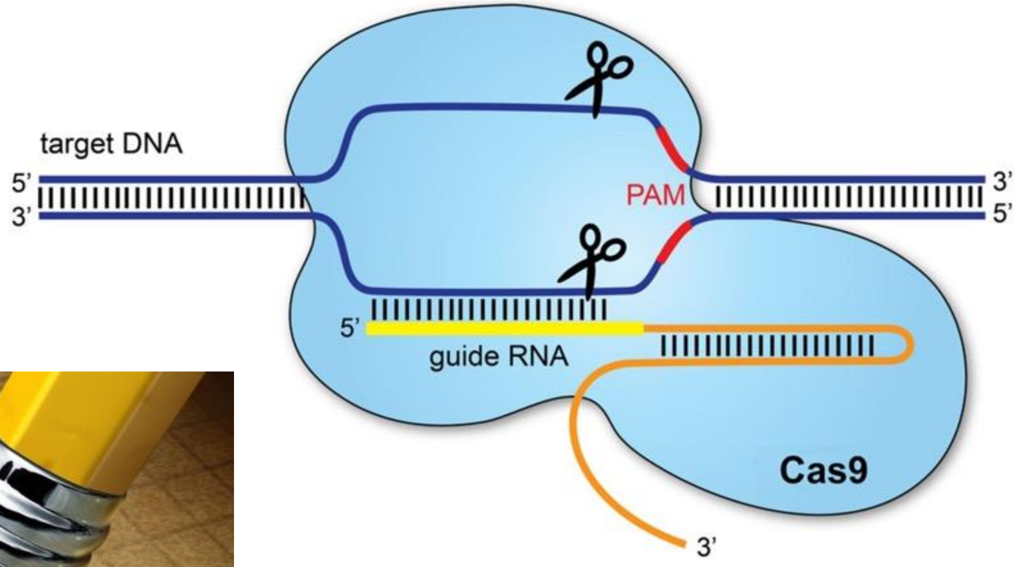



Selective breeding

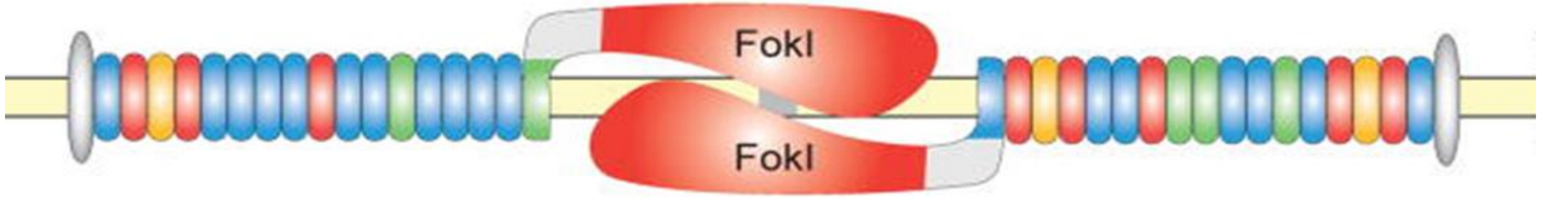
Genome Editing



ZFN



CRISPR/Cas9



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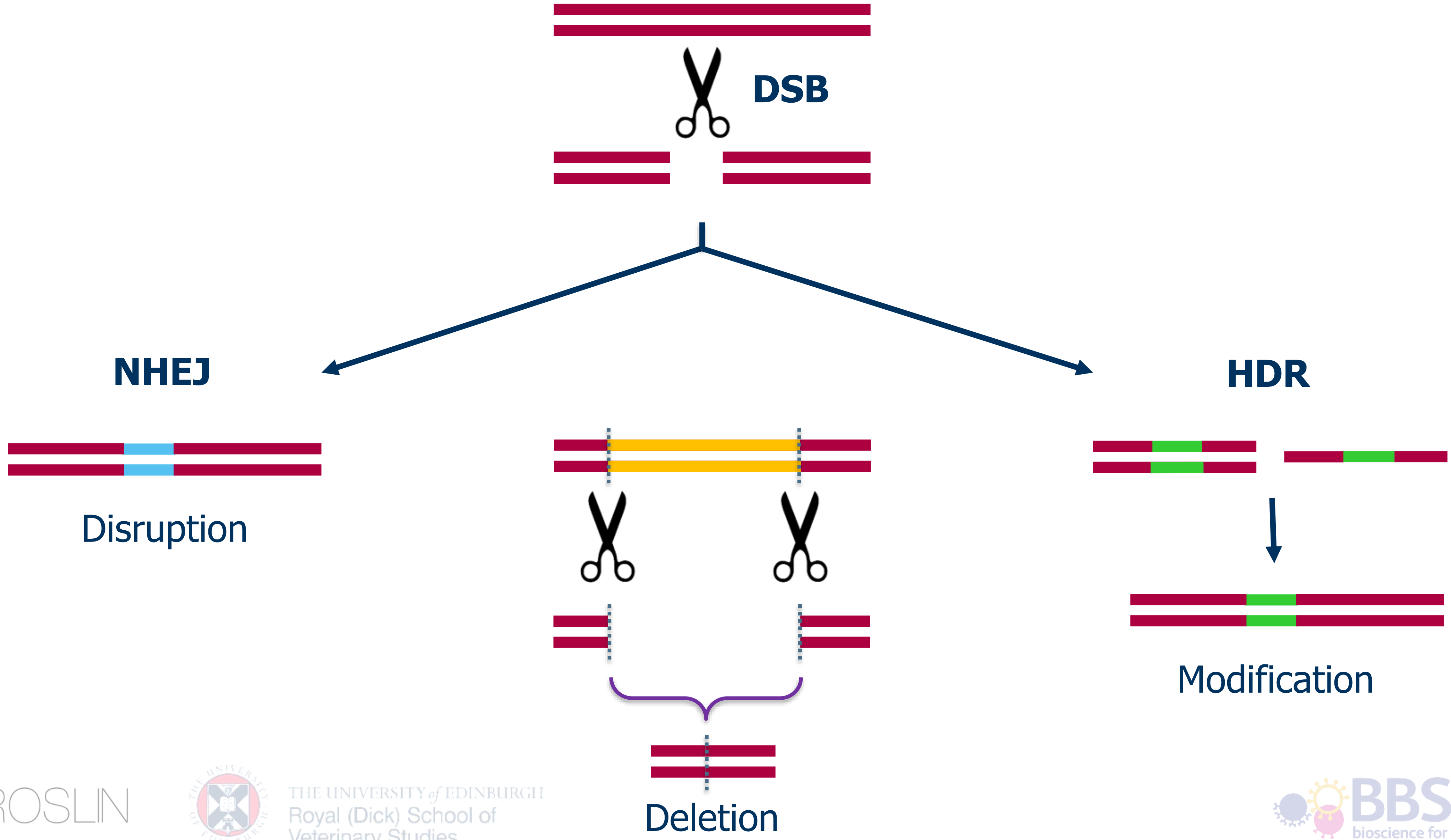
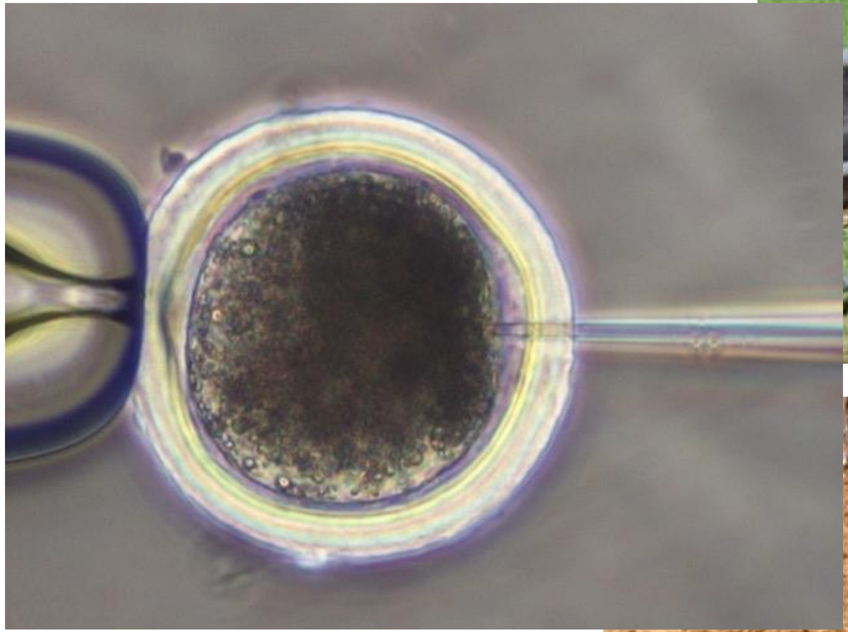
Types of editing events



Genome Editing in Livestock



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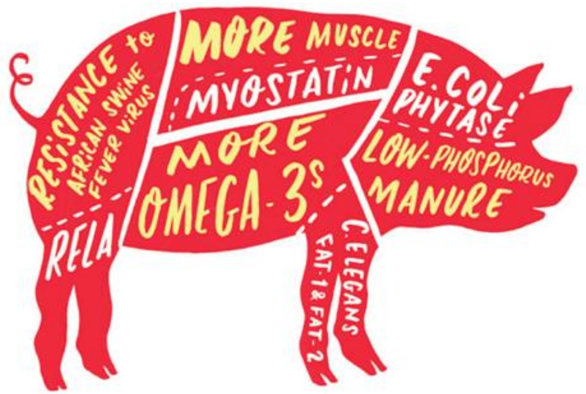
Why use Genome Editors?

Genome editing technology in breeding systems:

- to import traits… that are currently difficult to introgress

- introduce novel variation
- from outwith breeding population
- “capturing” rare breed alleles
- increasing fixation rate for low frequency variation
- eliminating deleterious alleles
- from different species

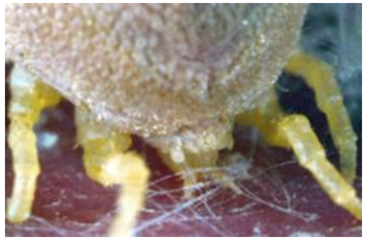


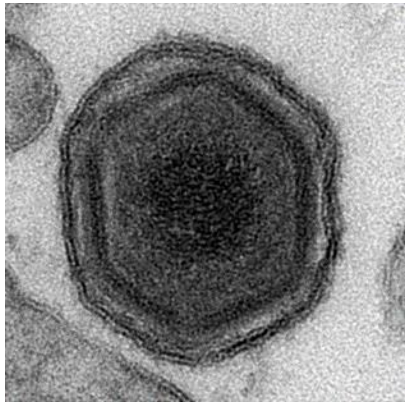
Target identification – Disease resistance/resilience

Genomics

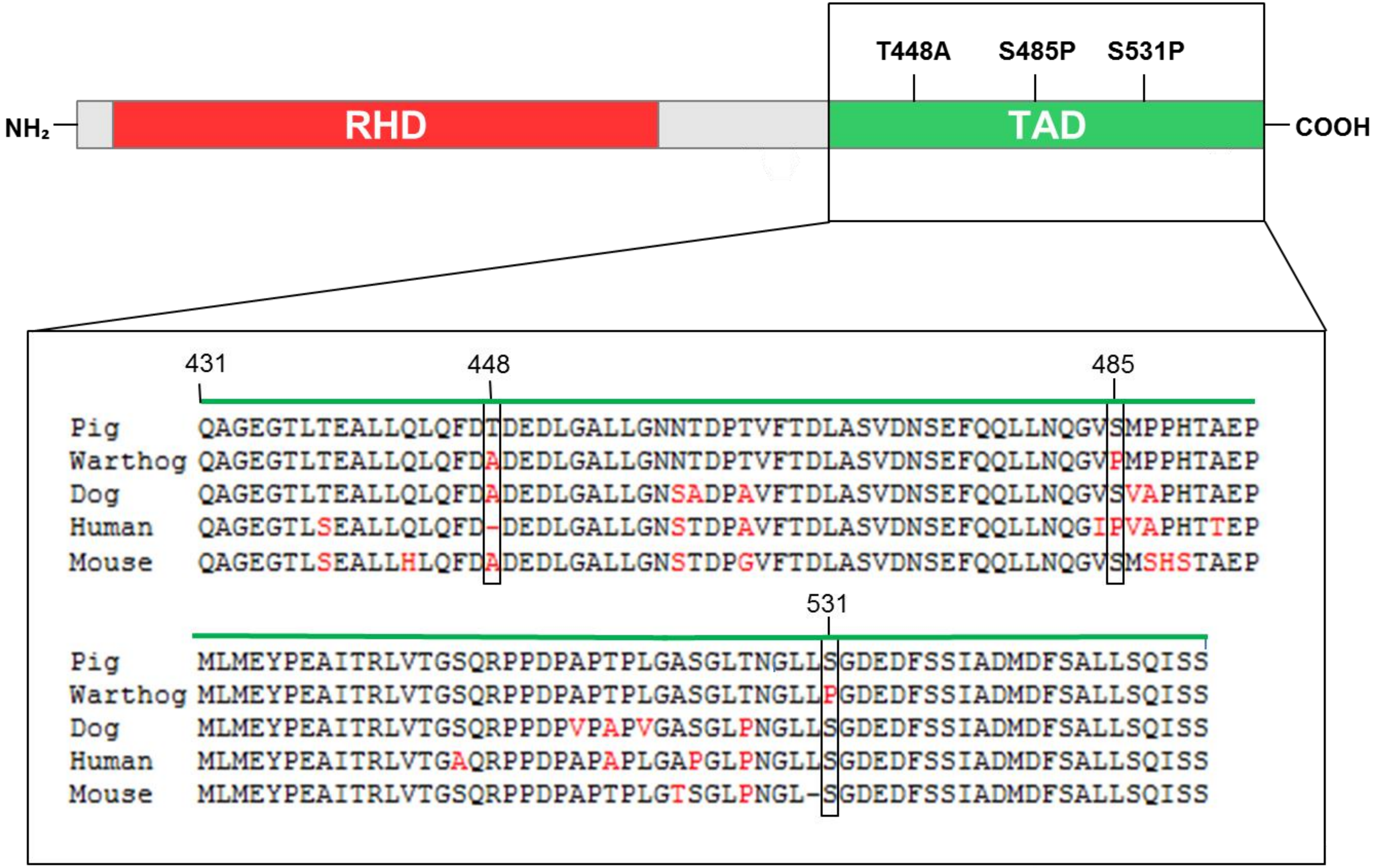
Species variation

African Swine Fever





RelA



J Virol. 2011 Jun;85(12):6008-14.

ZFN target site & HDR template

Sangamo BioSciences

Sus scrofa Rel A

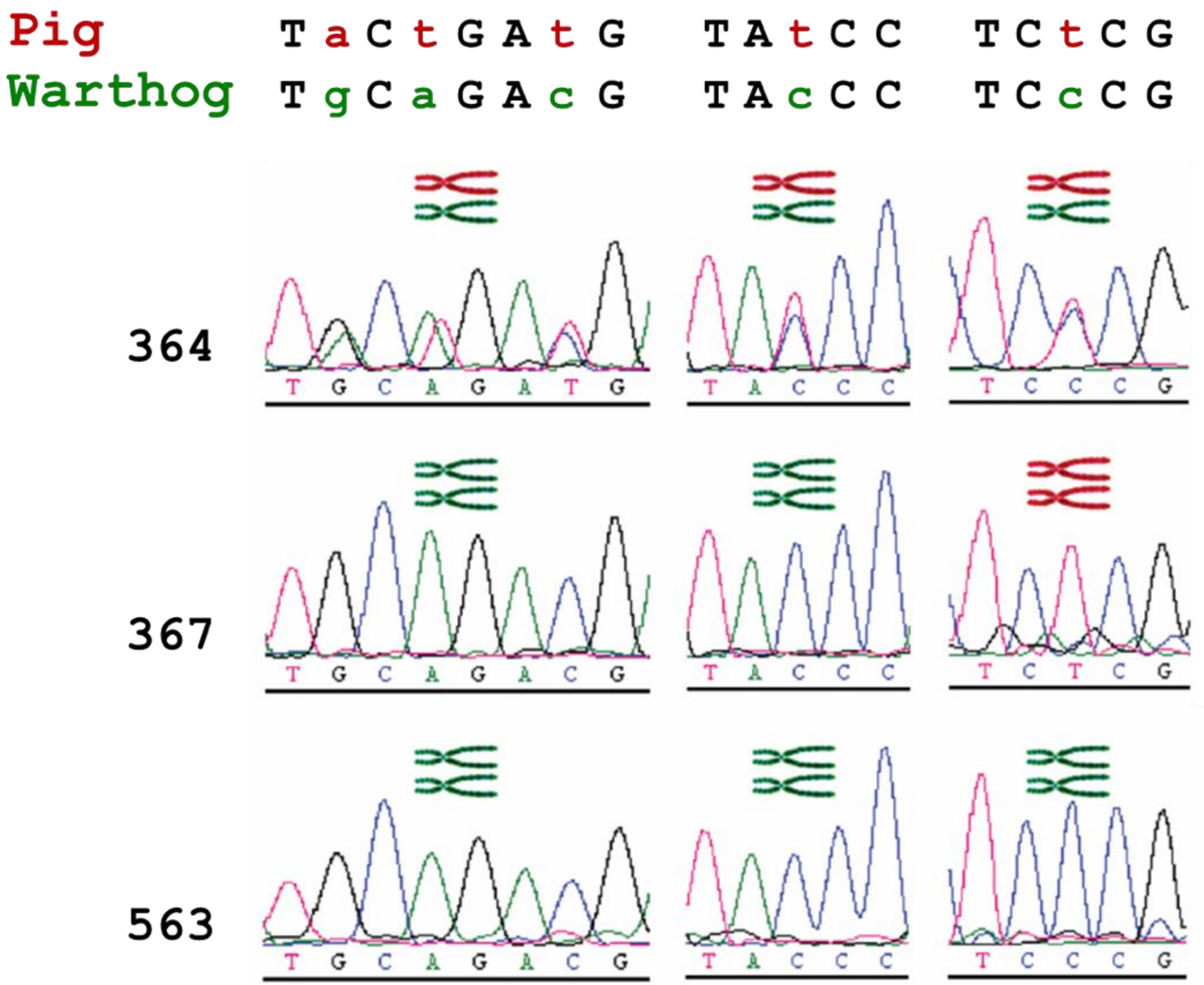
LQLQFD**T**DEDLGALLGNNTDPTVFTDLASVDNSEFQQLLNQGV**S**MPPHTAEPMLMEYPEAITRLVTGSQRPPDPAPTPLGASGLTNGLL**S**GDED

600-FD**A**DEDLGALLGNNTDPTVFTDLASVDNSEFQQLLNQGV**P**MPPHTAEPMLMEYPEAITRLVTGSQRPPDPAPTPLGASGLTNGLL**P**G-974

$\underbrace{\hspace{10em}}_{\text{262bp}}$

Sci Rep. 2016 Feb 22;6:21645.

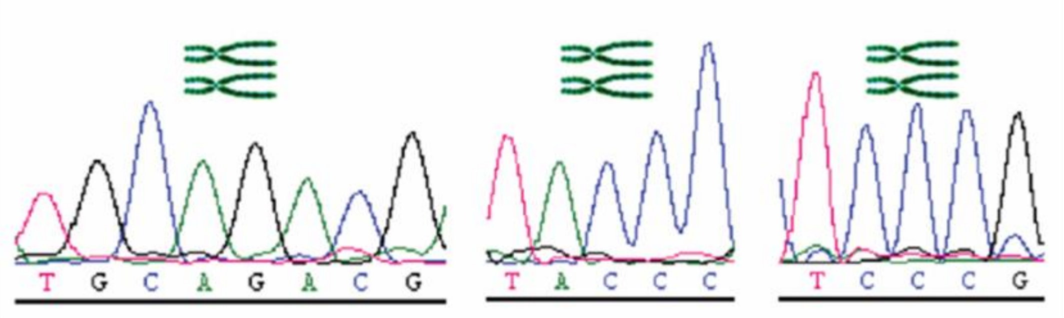
RelA Pigs - Genotype



Sci Rep. 2016 Feb 22;6:21645.

ASF Resilience?

563



Sci Rep. 2016 Feb 22;6:21645.

Target identification – Disease resistance/resilience

Genomics

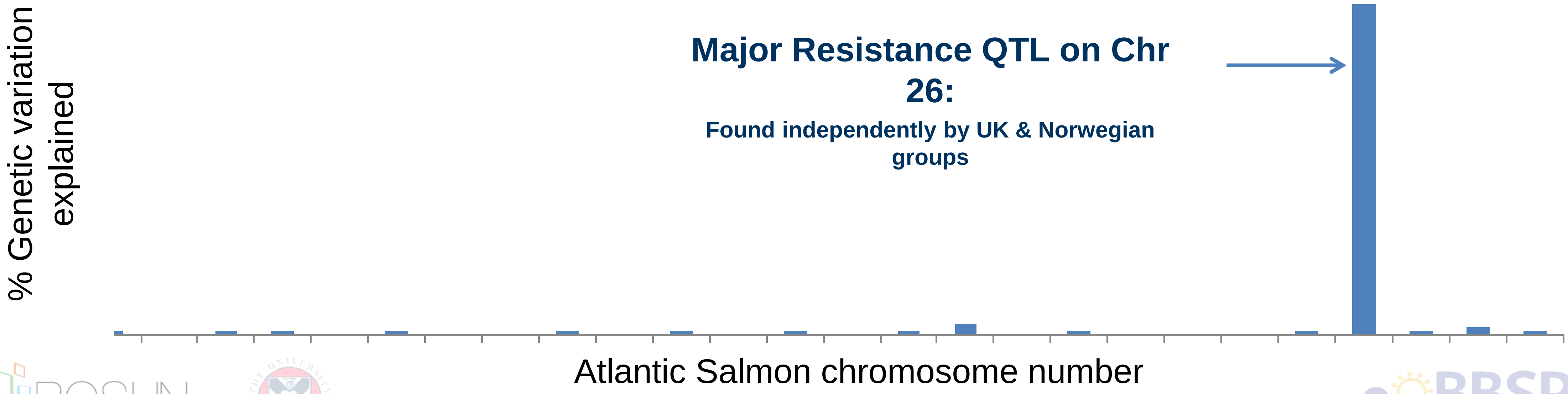
- Species variation
- WGS combined with phenotype data

Infectious Pancreatic Necrosis Virus

Atlantic salmon have varied resistance to IPNV

	Sire haplotype	
Dam haplotype	R	S
R	0%	2%
S	1%	63%

Resistance to IPNV maps to a single chromosome



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Houston et al. (2008) Genetics : Moen et al. (2009) BMC Genomics : Houston et al. (2010) Heredity

Target identification – Disease resistance/resilience

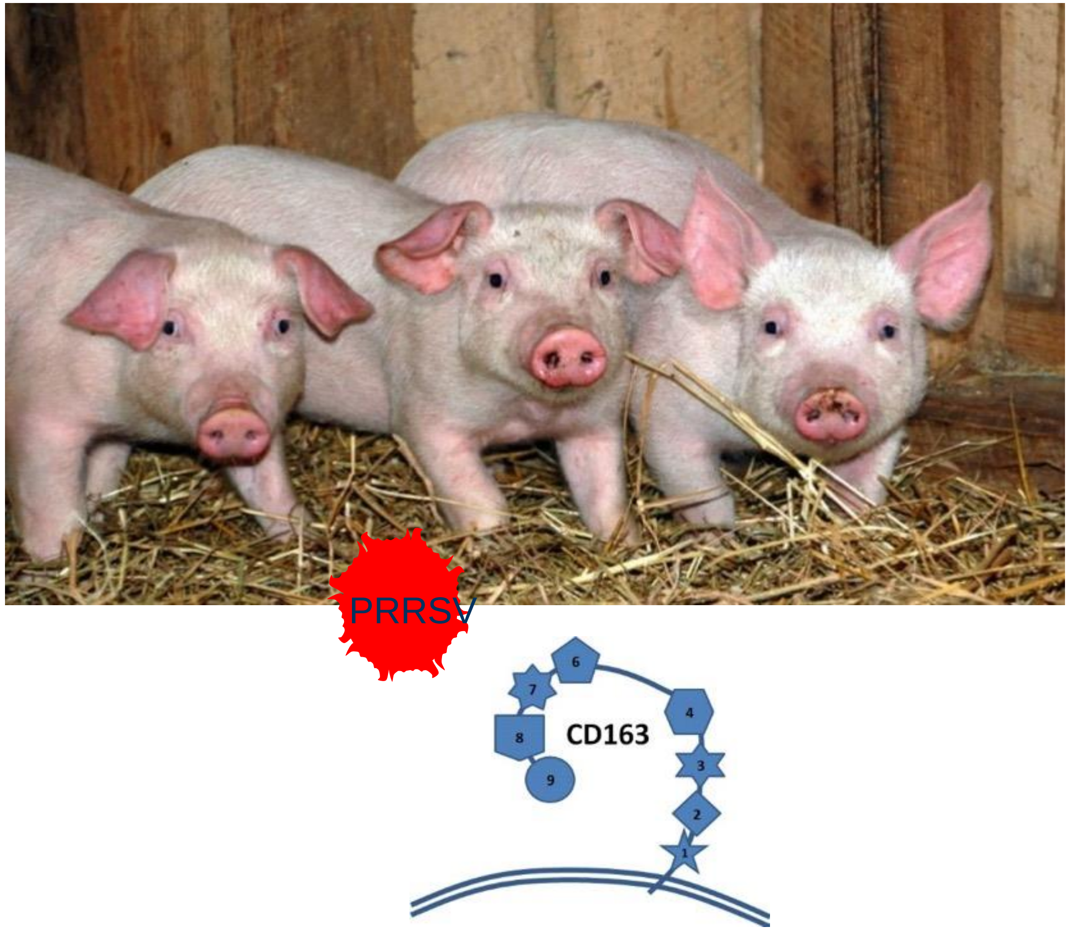
Genomics

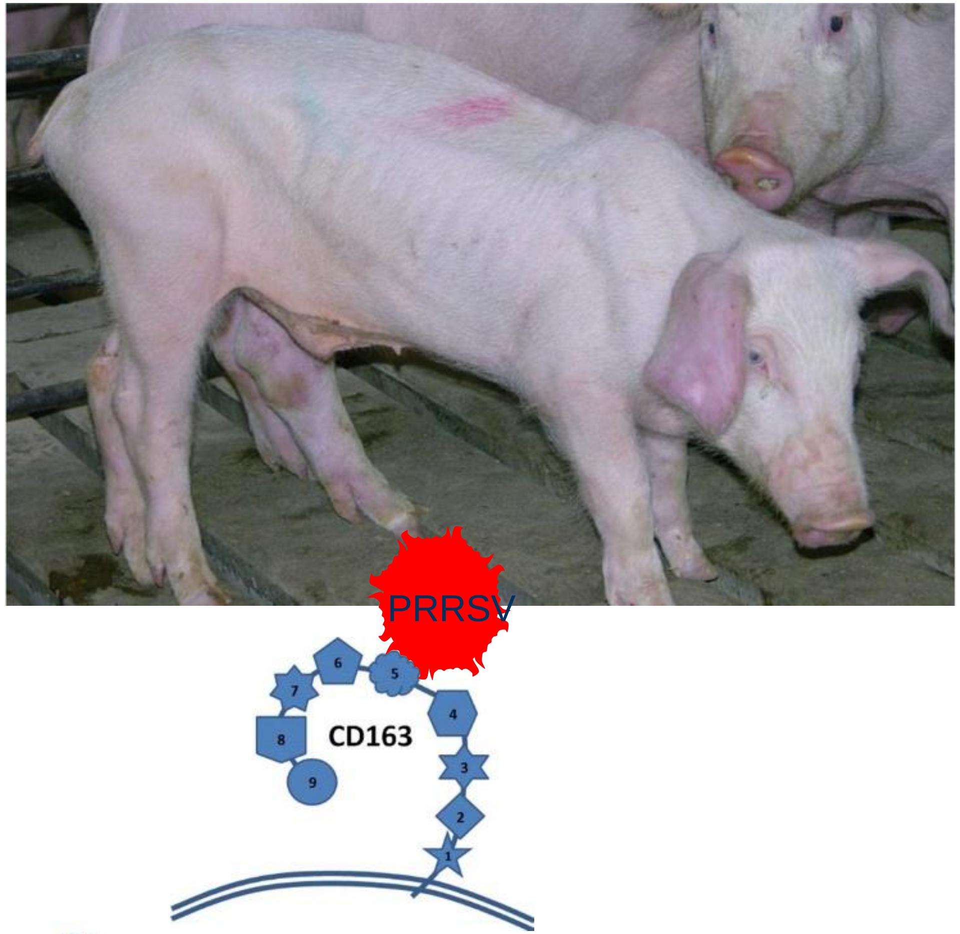
- Species variation
- WGS combined with phenotype data

Host Pathogen interaction

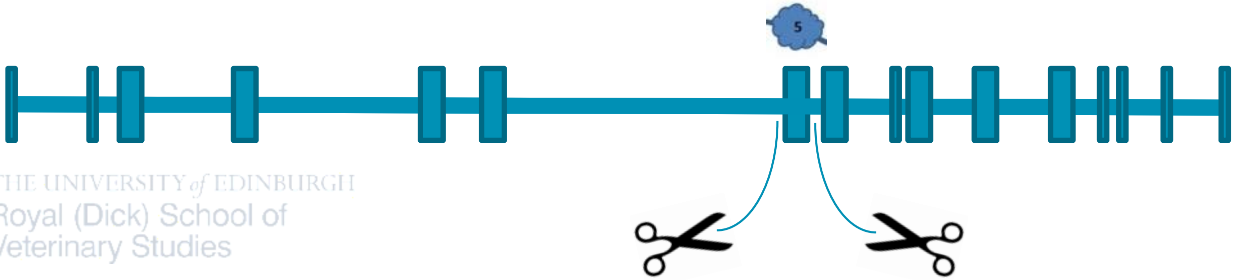
- Y2H

Porcine Reproductive and Respiratory Syndrome





CD163 gene

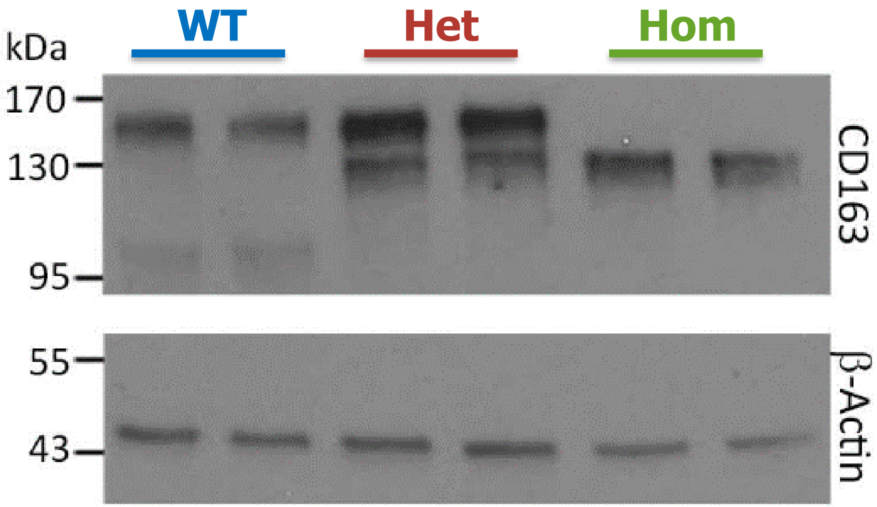


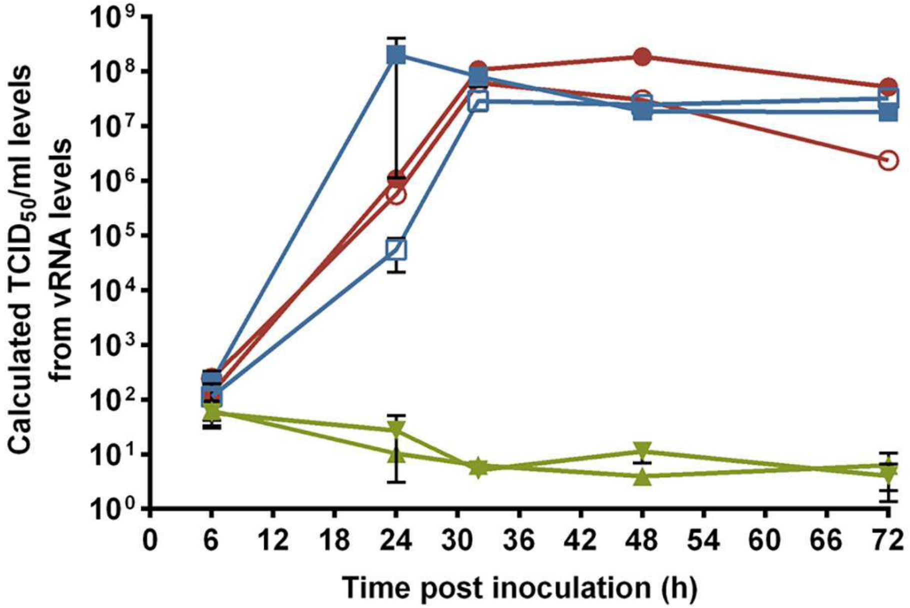
In vitro assessment of resistance

Wild Type

Heterozygous

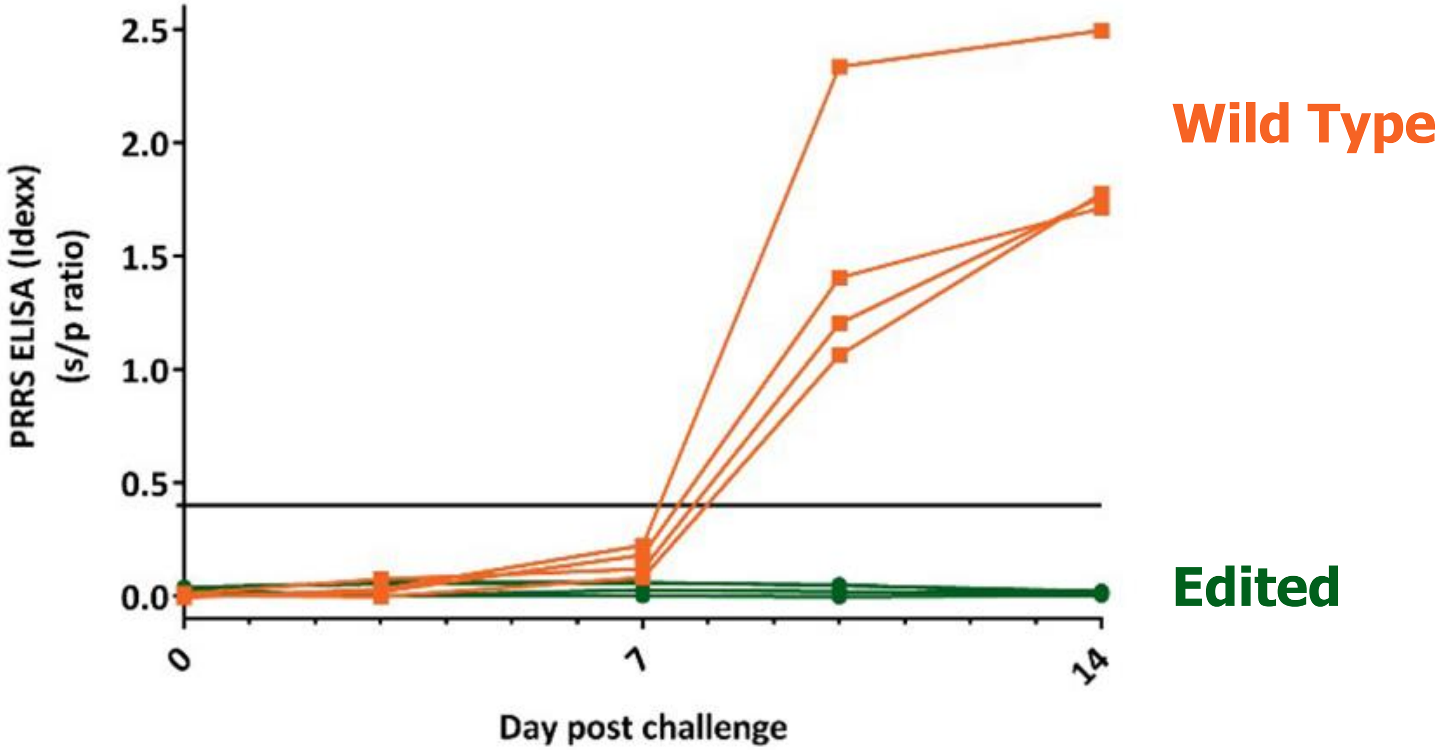
Homozygous

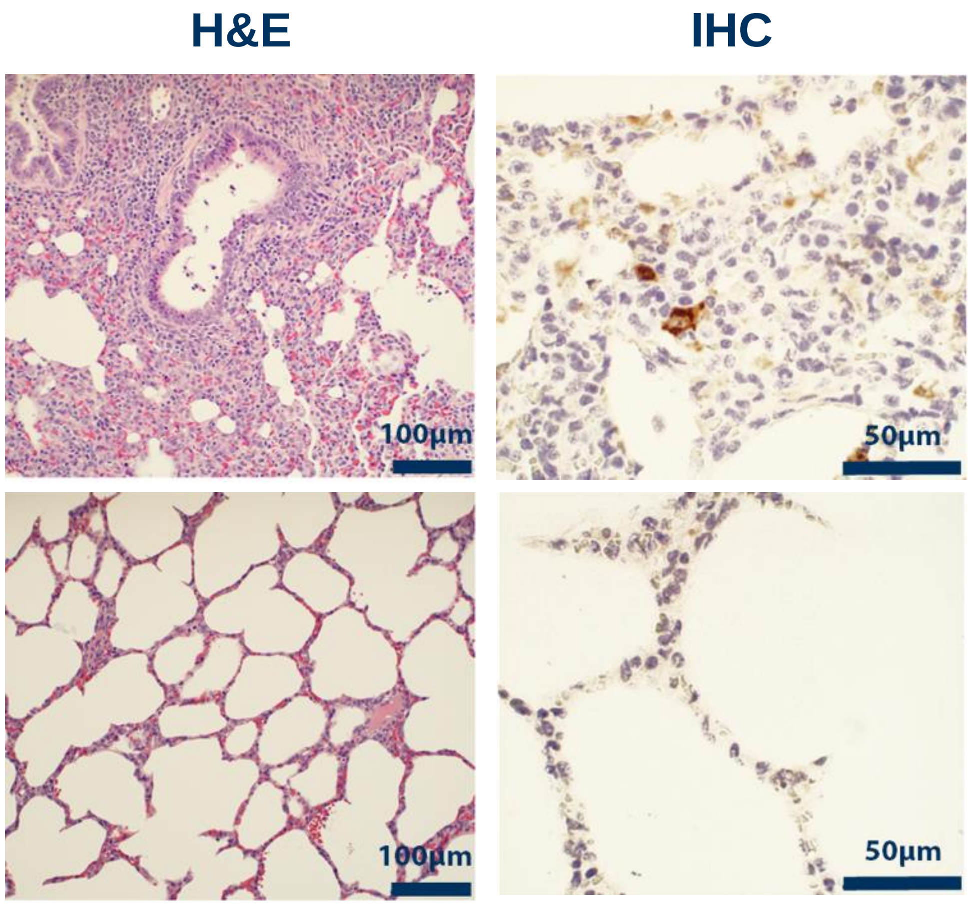




PLoS Pathog. 2017 Feb 23;13(2)

In vivo assessment of resistance





J Virol. 2018 Jul 31;92(16)

Target identification – Disease resistance/resilience

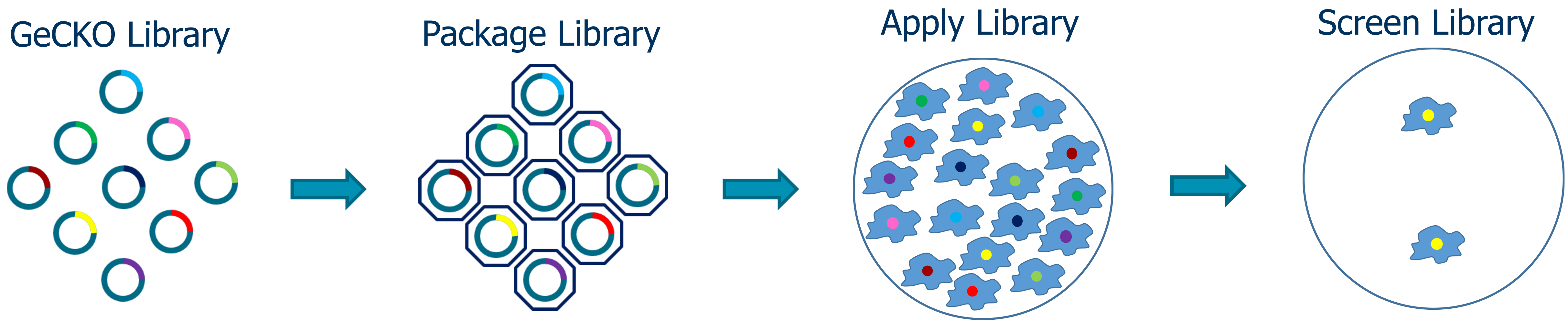
Genomics

- Species variation
- WGS combined with phenotype data

Host Pathogen interaction

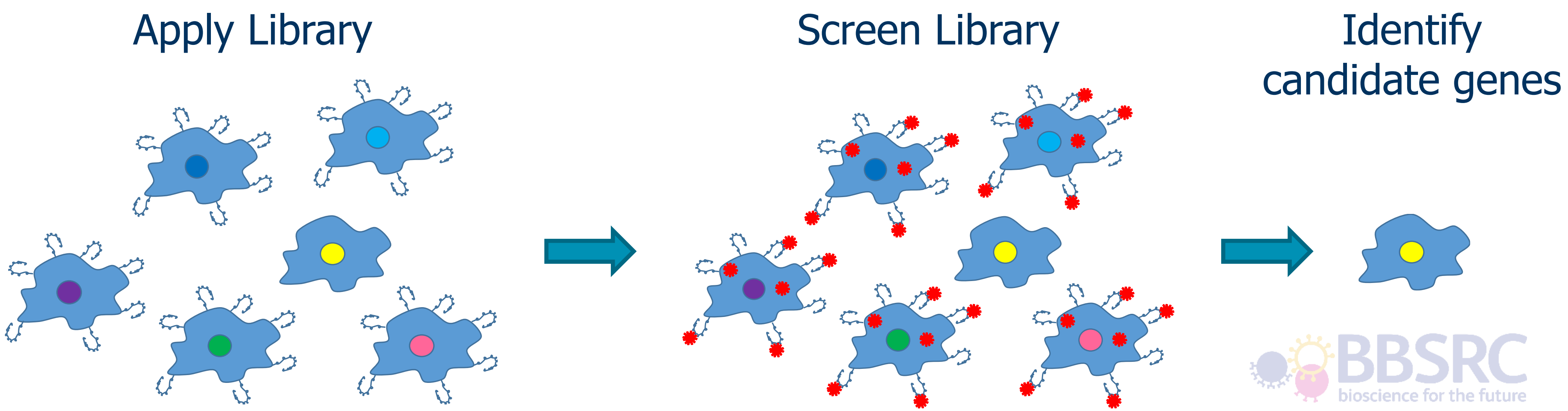
- Y2H
- GeCKO (Genome-Scale CRISPR Knock-Out)

GeCKO



GeCKO Library
Package Library
Apply Library
Screen Library

PRRSV



Apply Library
Screen Library
Identify candidate genes

The future?

The possibilities are endless

Acknowledgements

ROSLIN

Bruce Whitelaw

Simon Lillico

Claire Neil

Alan Archibald

Christine Burkard

Ross Houston

Alan Mileham

Dryden Farm Staff

THE UNIVERSITY of EDINBURGH
The Royal (Dick) School of Veterinary Studies

recombinetics

SANGAMO Sangamo BioSciences

Genus

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