



Editing allelic variation into the porcine genome

Bruce Whitelaw

Genus Chair of Animal Biotechnology
The Roslin Institute

EAAP2016, Belfast, 29th August 2016



THE UNIVERSITY of EDINBURGH



Inherited Genetic Change



Genetic Variation



Genetic Variation



**Spontaneous
(luck)**

or

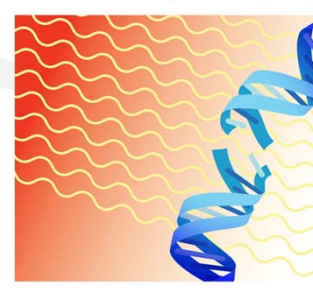
**Genome Editing
(precise)**

Genome Editors

rely on DNA repair



NHEJ

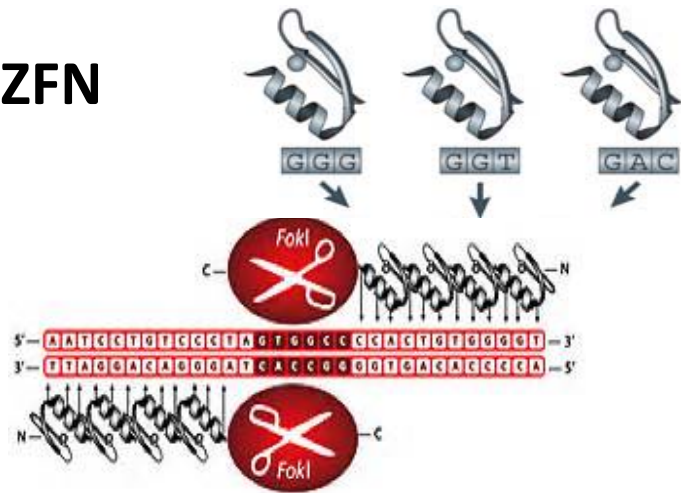


HDR

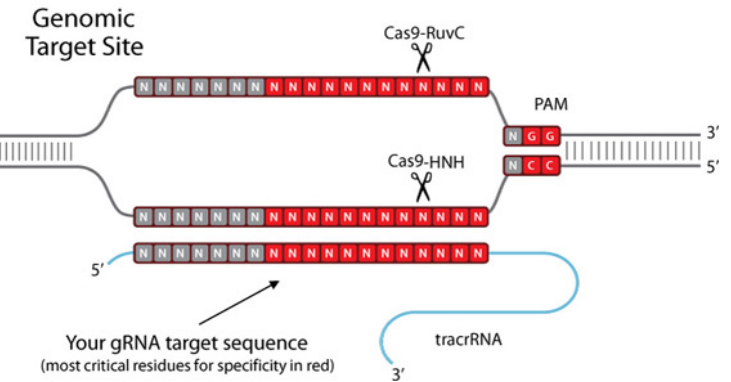
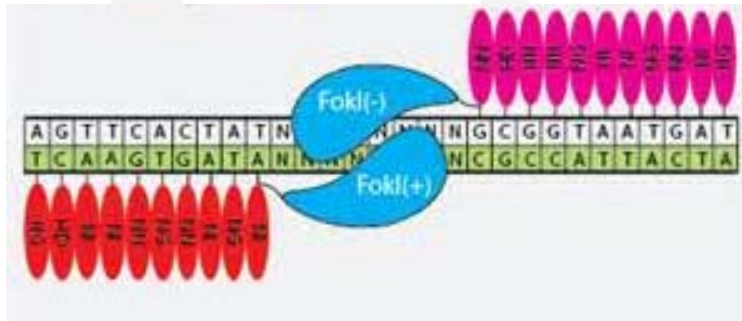


Engineer specificity into these editing tools:

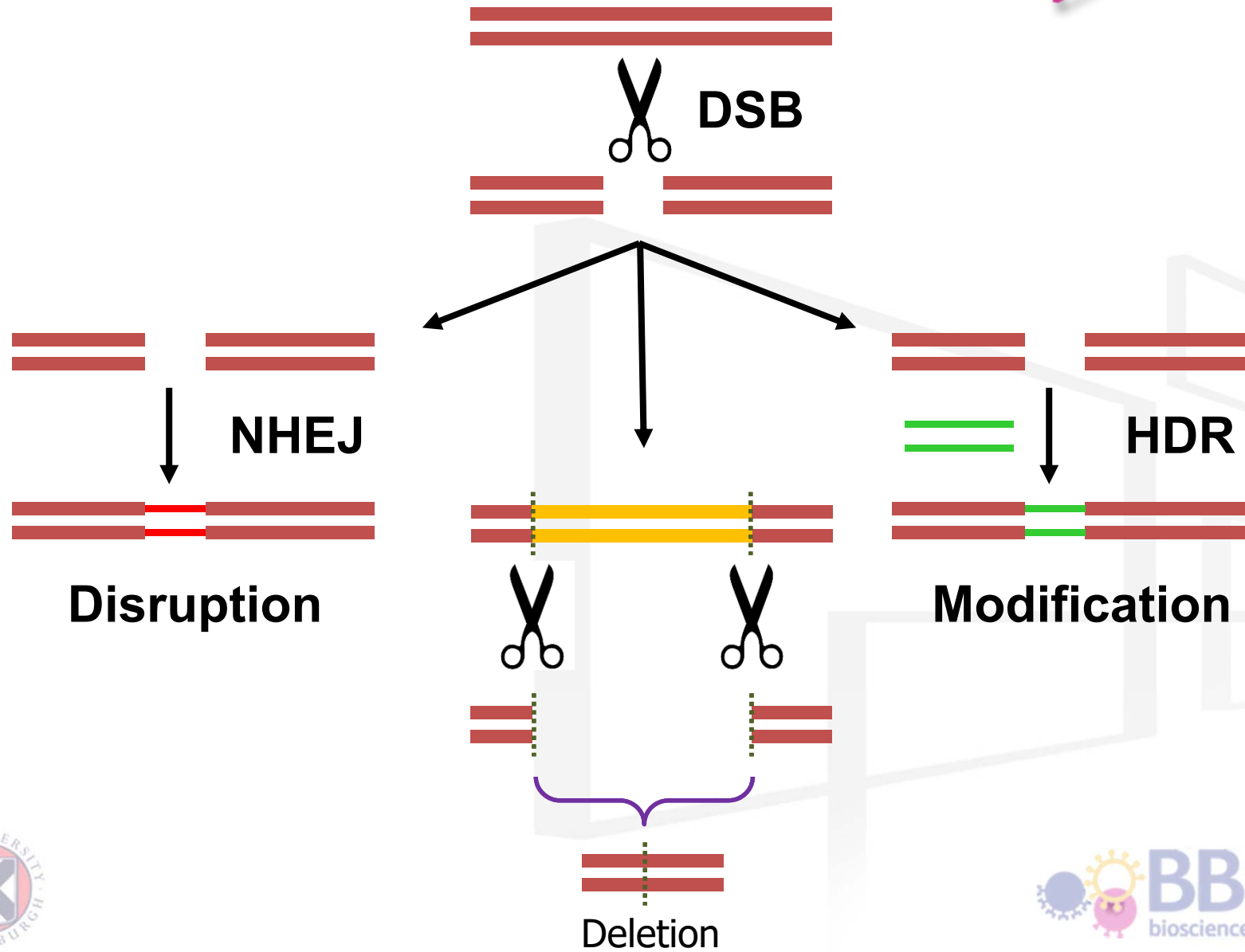
ZFN



TALEN



CRISPR/Cas9



When to use genome editing technology in breeding systems:

- to import variation ... that is otherwise challenging to introgress

- utilising ‘backyard genetics’
(from outwith breeding population)
“capturing” rare breed alleles
- introgress alleles from different species
- introduce novel variation
- increasing fixation rate for low frequency variation

e.g. polled



African Swine Fever



No vaccine

No drugs

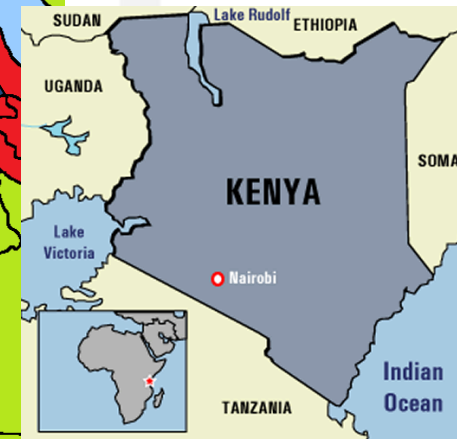
No treatment

CULL



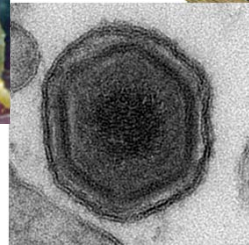


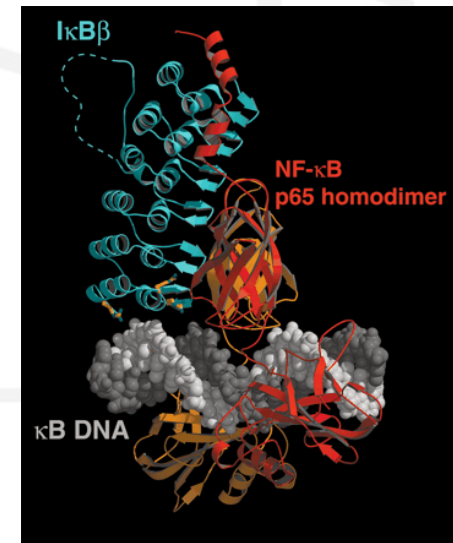
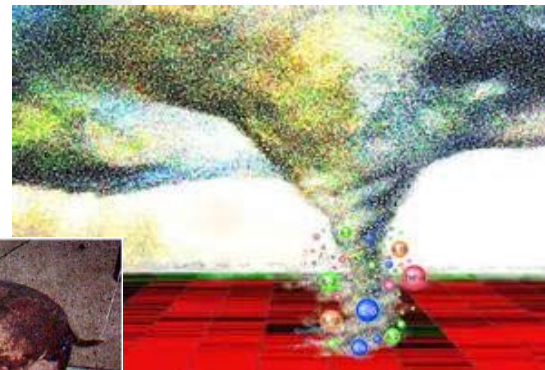
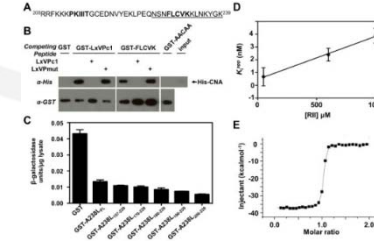
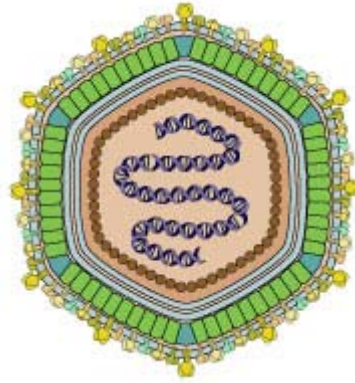
predicted
\$267m/year
loss in Russia

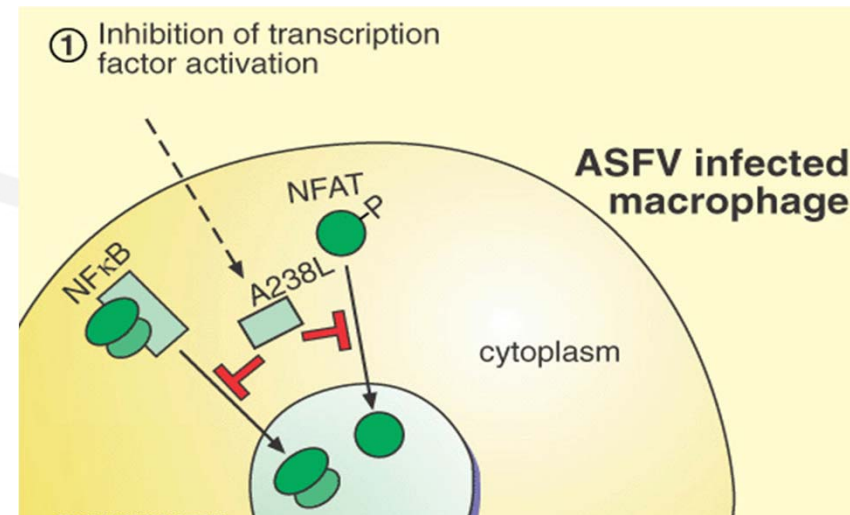
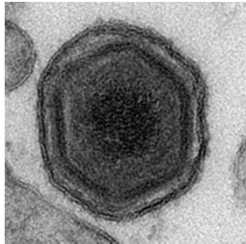


Georgia 2007 - within 60 days of first report 30,000 pigs died

Disease severity differs between pig species







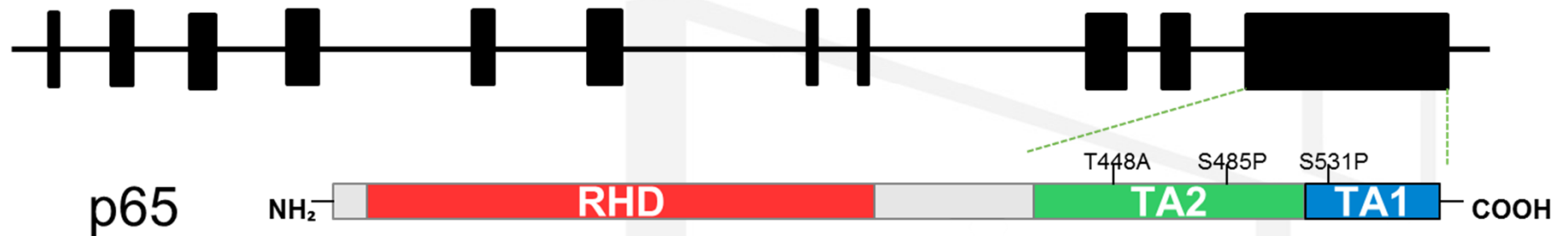
“domestic pig RELA”



“warthog RELA”

Gene Editors - TALEN and ZFN

RELA



NHEJ

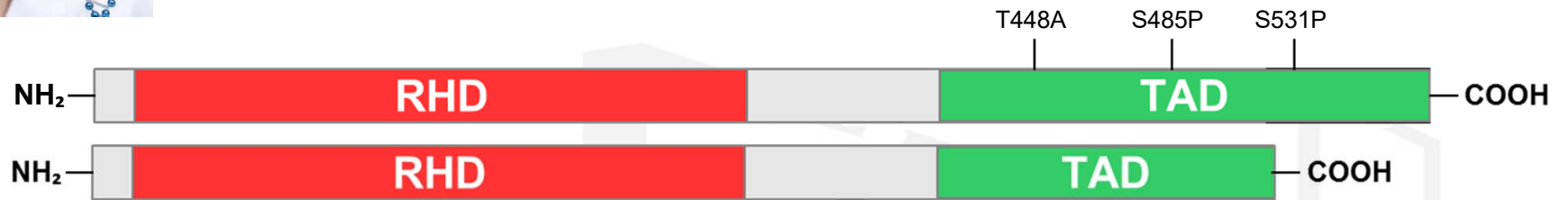


HDR

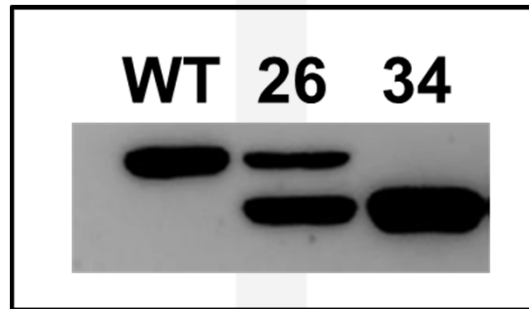




NHEJ

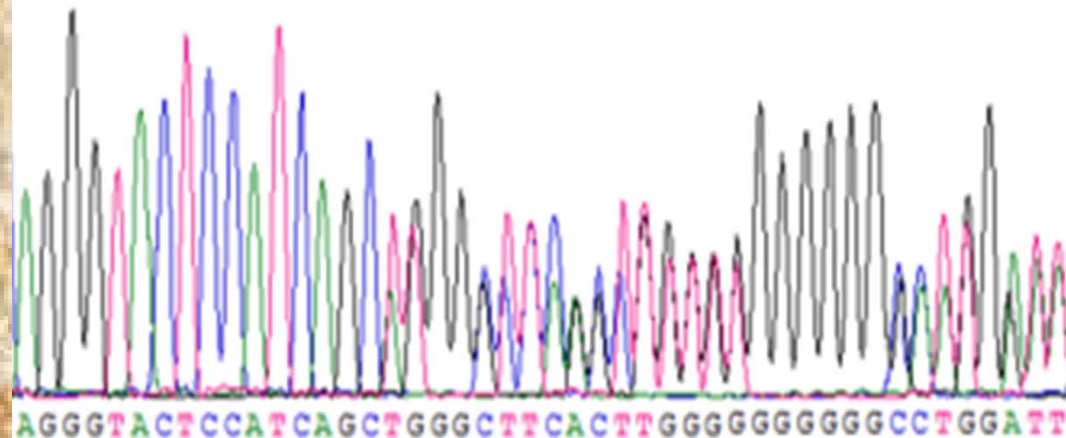


pig26





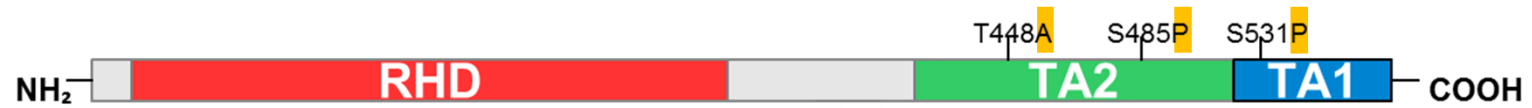
“Pig 26”



Monoallelic
1bp deletion

AGTTATAGCCTCAGGGTACTCCATCA(CAT)GGCTCAGCTGTGTGGGGGGGCA (wt)

AGTTATAGCCTCAGGGTACTCCATCA(C-T)GGCTCAGCTGTGTGGGGGGGCA (1 del)

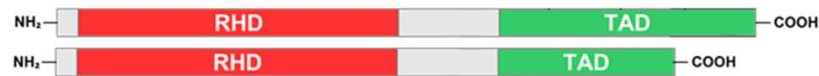


HDR

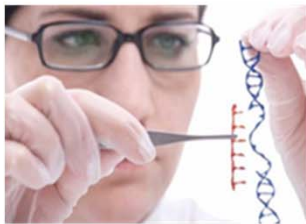
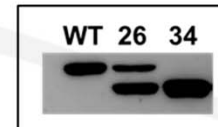




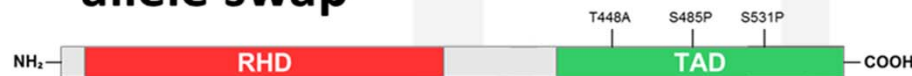
frameshift (premature stop)



deletion



allele swap







Simon Lillico

Chris Proudfoot

Wenfang (Spring) Tan

Claire Neil

Rachel Huddart

Maeve Ballantyne

Alex Brown

Sarah Fletcher

Du (Dina) Yue

Akshay Joshi

Caroline Krall

John Hickey

Gregor Gorjanc

Janez Jenko



SIGMA-ALDRICH

Innovate UK

Technology Strategy Board







2 days



**Over the next 50 years
the world's farmers
will be called upon to produce
more food than
has been produced
in the past 10,000 years combined,
and to do so
in an environmentally sensitive manner.**



Is gene editing a game changer?

