Science and Potential of Animal Biotechnology

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Animal Biotechnology Regional (Asia and Oceania) Workshop
31st August 2021

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Animal biotech plays an important role in research and development

Australian Centre for Disease Preparedness

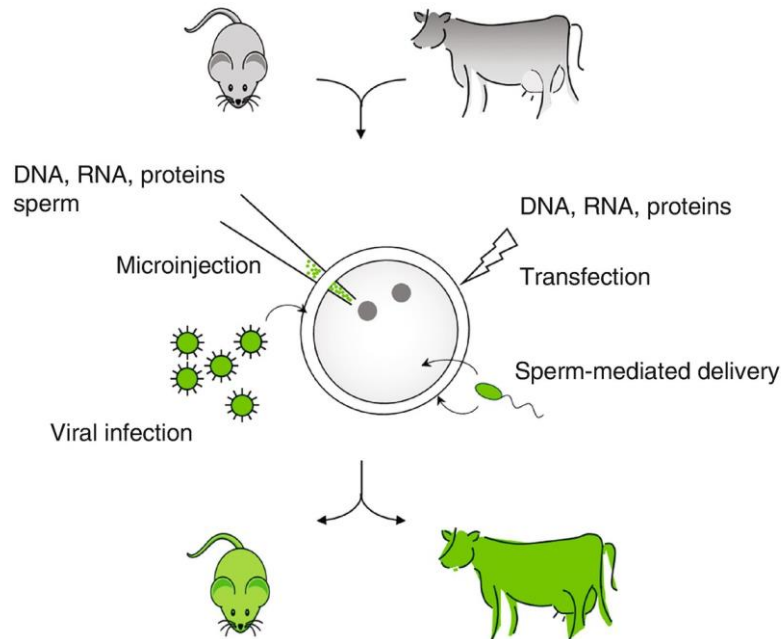Recombinetics, 2016

Shanghai Institute, 2018
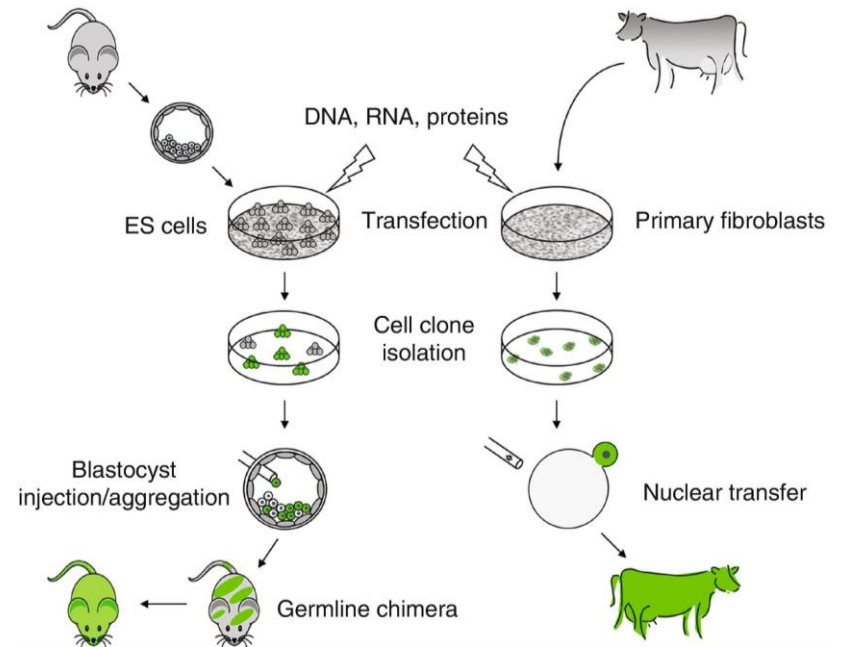
Xinjiang Academy of Zootechnical Science, 2016

Approaches for genetic modification

Embryo-mediated
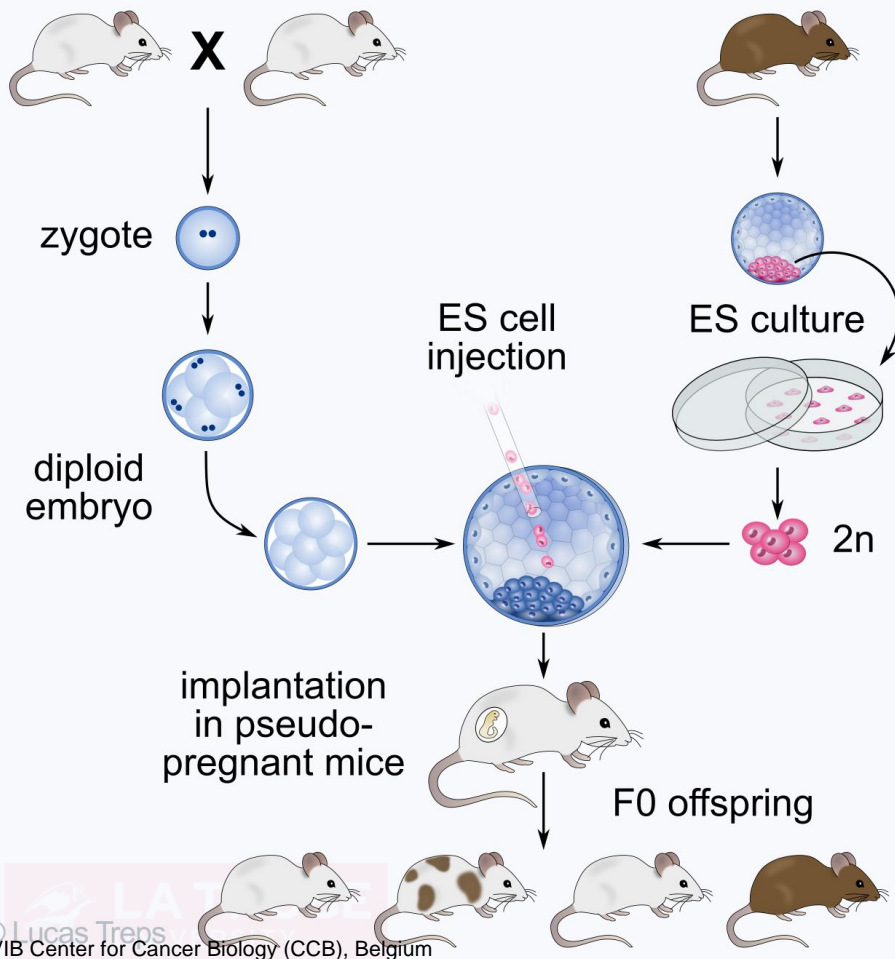

Cell-mediated

- Advantage of a relative high efficiency for the embryos to develop into live transgenic founder animals.

- Disadvantage of this approach lies in the lack of total control of when and what modification is introduced. Can lead to mosaic animals

- Advantages-sex selection, characterised modification before generating animals. Can avoid mosaics and produce multiple founders

- Disadvantage-Cloning step leading to other issues

Commercially available research models

BLASTOCYST INJECTION

zygote

diploid embryo

ES cell injection

ES culture

2n

implantation in pseudo-pregnant mice

F0 offspring

© Lucas Treps
VIB Center for Cancer Biology (CCB), Belgium

CByJ.Cg-$Foxn1^{nu}$/J

Photo courtesy of Mouse Mutant Resource at The Jackson Laboratory.

BALB/c Nude Mouse (1962 mutation)
Immunodeficient Inbred Line

C57BL/6-Tg(TcraTcrb)1100Mjb/Crl

Photo courtesy of Walter and Eliza Hall Institute, Victoria, Australia.

OT I Mouse (GM; Immunodeficient)
Transgenic inserts for mouse Tcra-V2 and Tcrb-V5 gene

What is commercially available?

AquAdvantage® Salmon

GloFish®

Photo: AquaBounty.com

"You are what you eat! Ban cloning now."
– PIERRE VICARY OF LIVERPOOL
BAN CLONING NOW
Source: foodwatereurope.org

take action
GMO
STOP 'Enviropig'™
NO GM ANIMALS
Write the Health Minister Today

LA TROBE UNIVERSITY

Key messages

- Animals are used extensively in R&D
- First nuclear transfer experiments undertaken in the early 1950s
- Dolly the sheep was cloned by Somatic Cell Nuclear Transfer in 1996
- Biotech animals have made significant contributions to our understanding of diseases, behaviour and developmental biology leading to numerous therapeutic treatments
- Technically challenging process-not precise, always improving
- Biotech animals as consumer products limited.

A new opportunity for animals….
Genome editing for precision
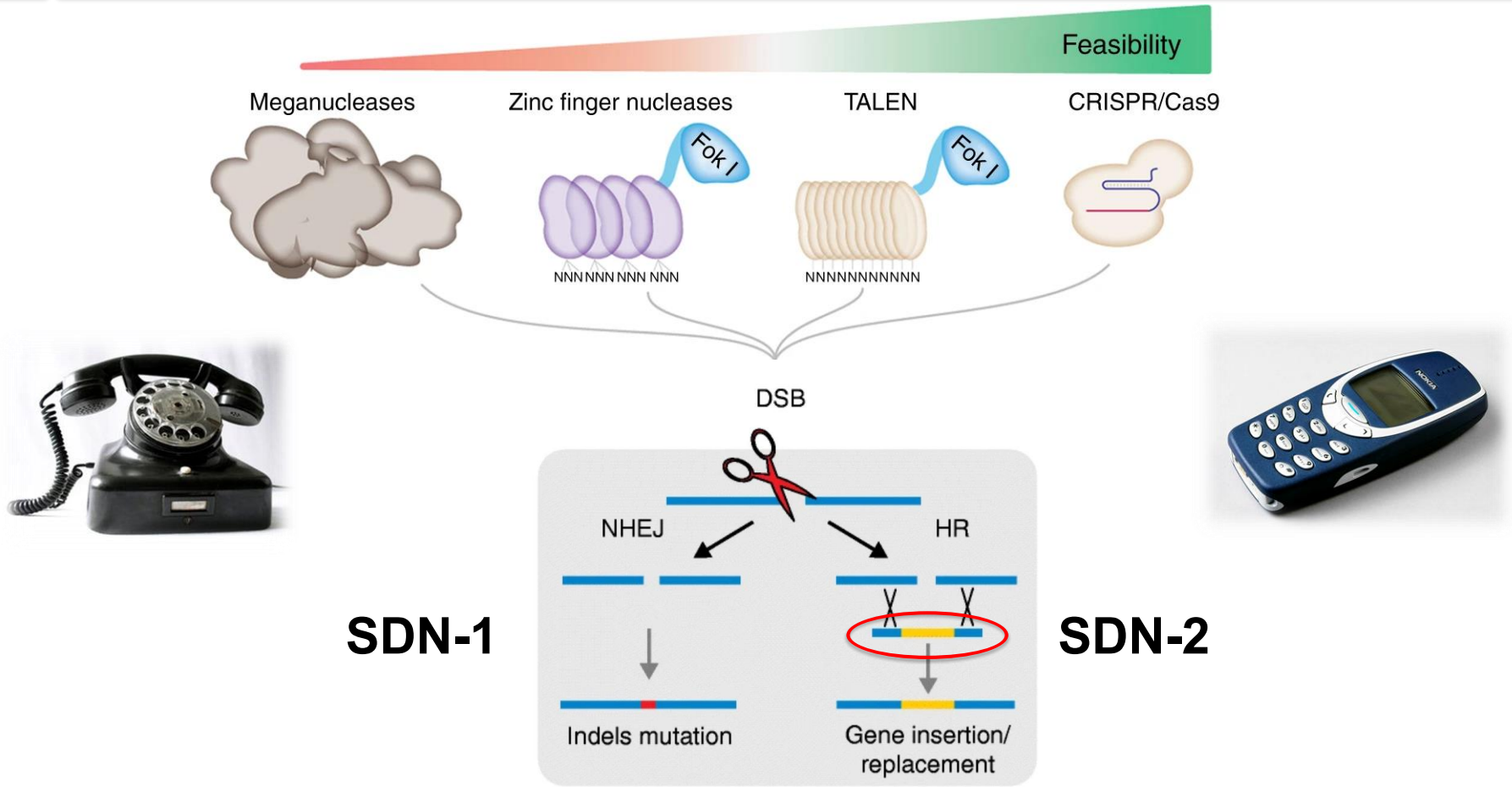
SDN-1

SDN-2

Adli, M. The CRISPR tool kit for genome editing and beyond. *Nat Commun* **9,** 1911 (2018).
https://doi.org/10.1038/s41467-018-04252-2
Zhang, Y., Massel, K., Godwin, I.D. *et al.* Applications and potential of genome editing in crop
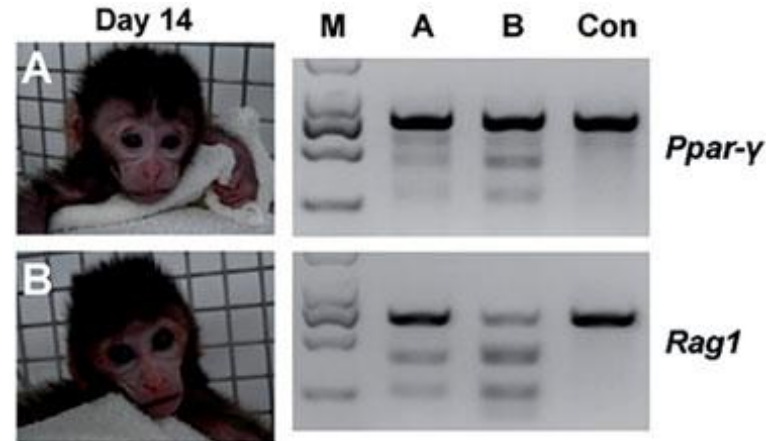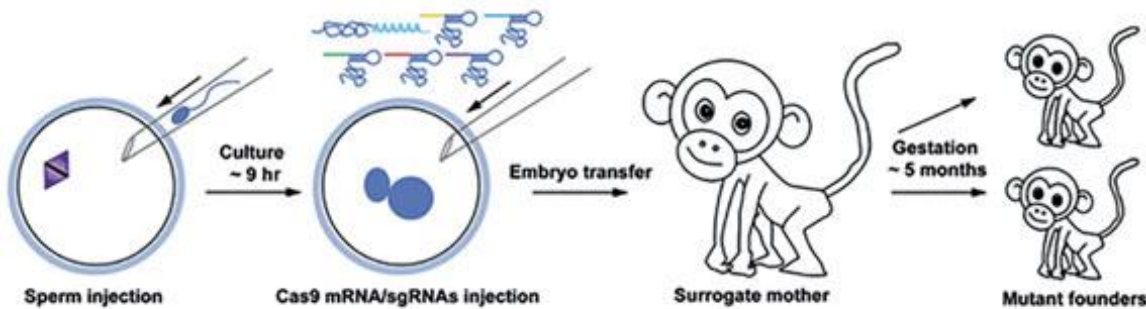improvement. *Genome Biol* **19,** 210 (2018). https://doi.org/10.1186/s13059-018-1586-y

The Genome editing 'Tool Kit'

CRISPR technology: Beyond genome editing

Adli, M. The CRISPR tool kit for genome editing and beyond. *Nat Commun* **9,** 1911 (2018). https://doi.org/10.1038/s41467-018-04252-2
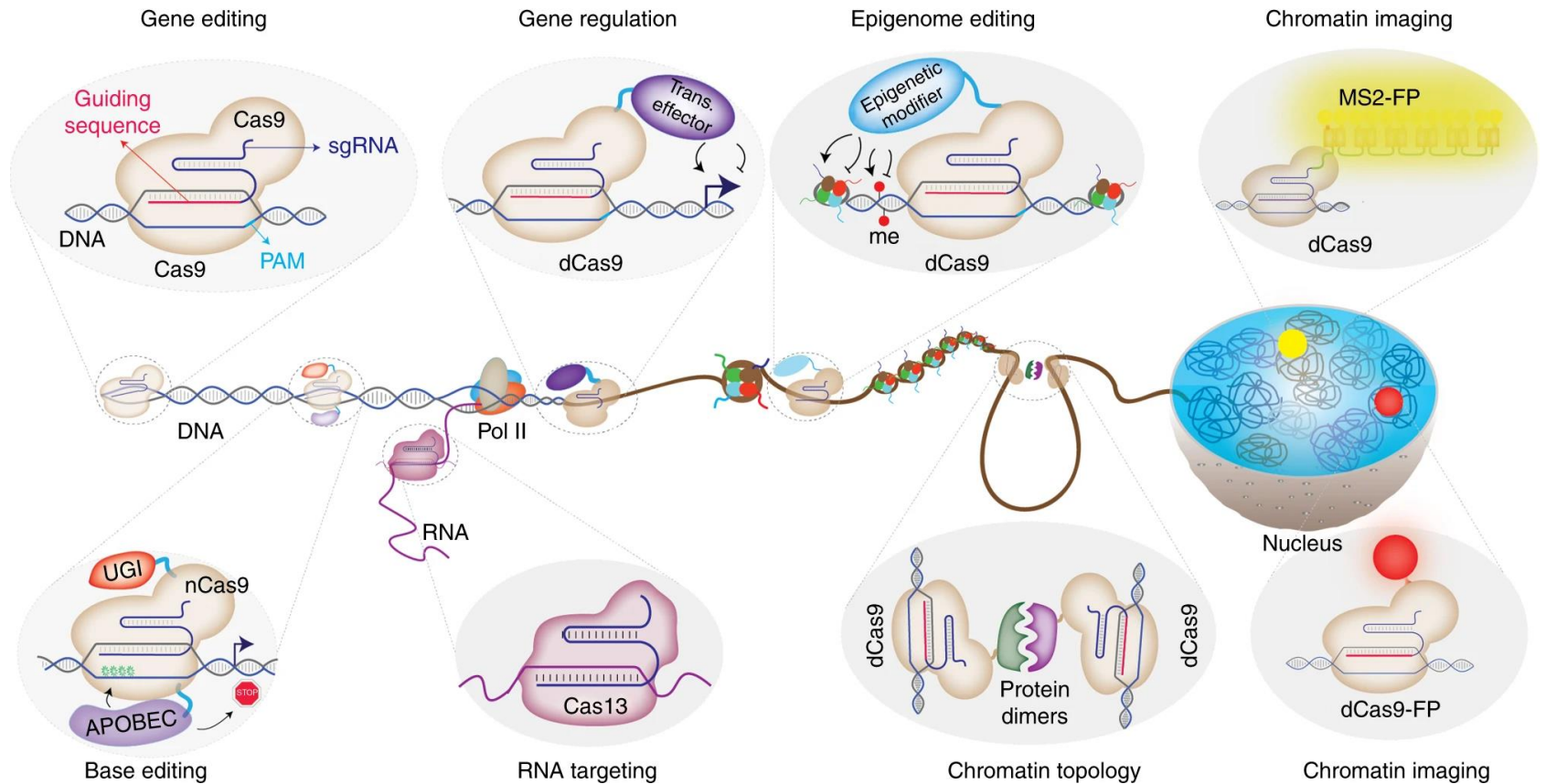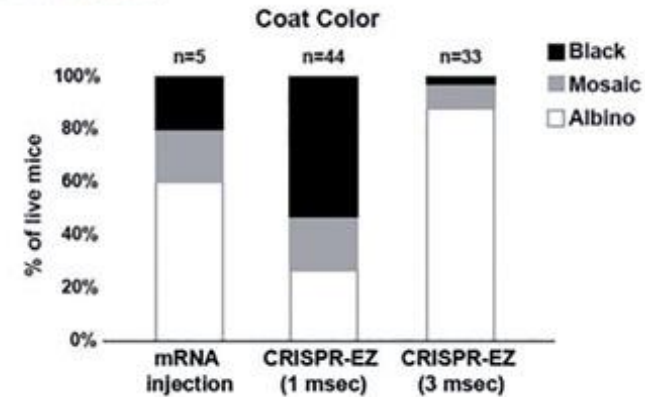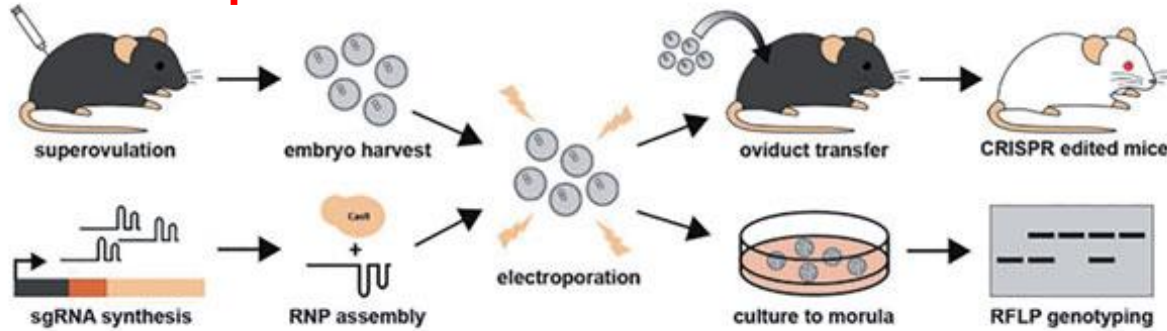
Traditional delivery methods
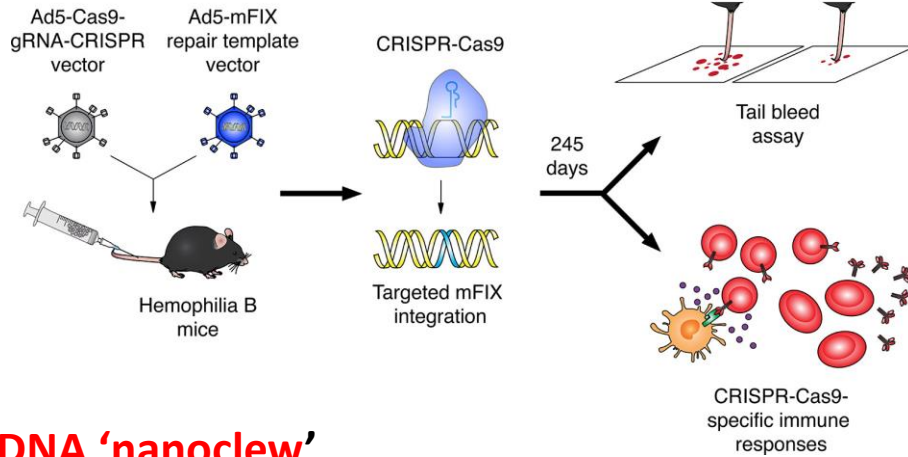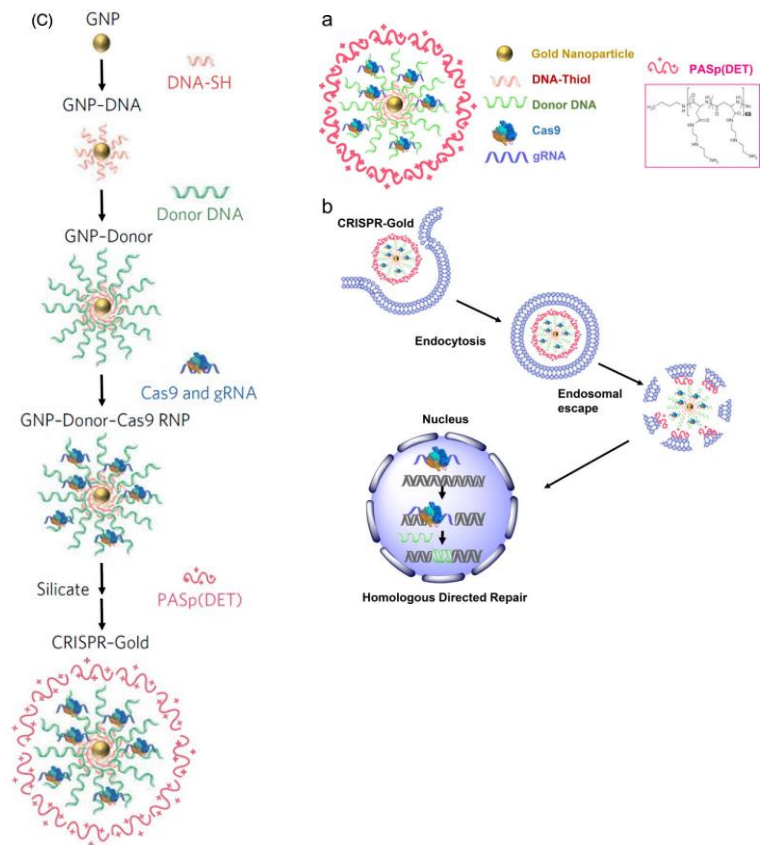

(A) **Microinjection**

(B) **Electroporation**
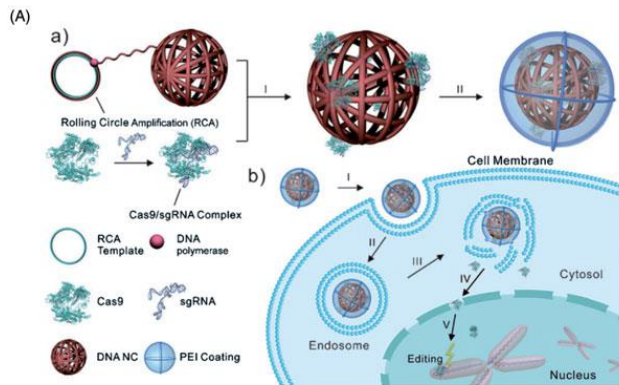
From Lino et al., (2018)

Additional delivery methods

Retroviral systems

Nano particle systems

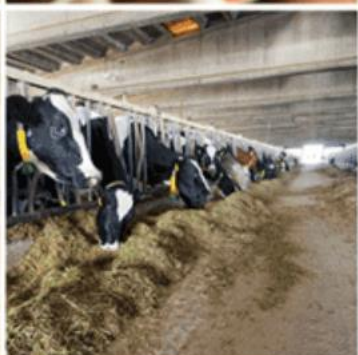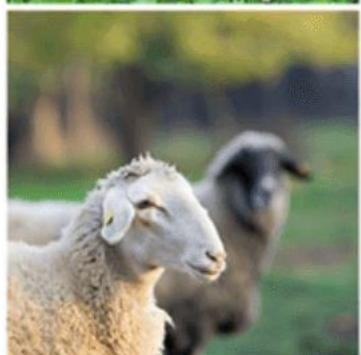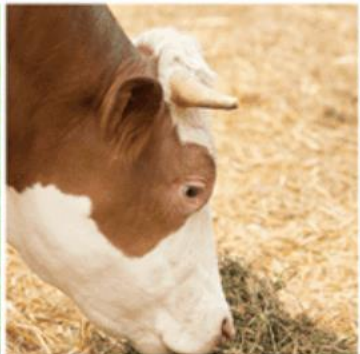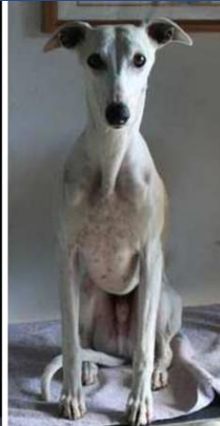**DNA 'nanoclew'**

Deciding on what to edit?
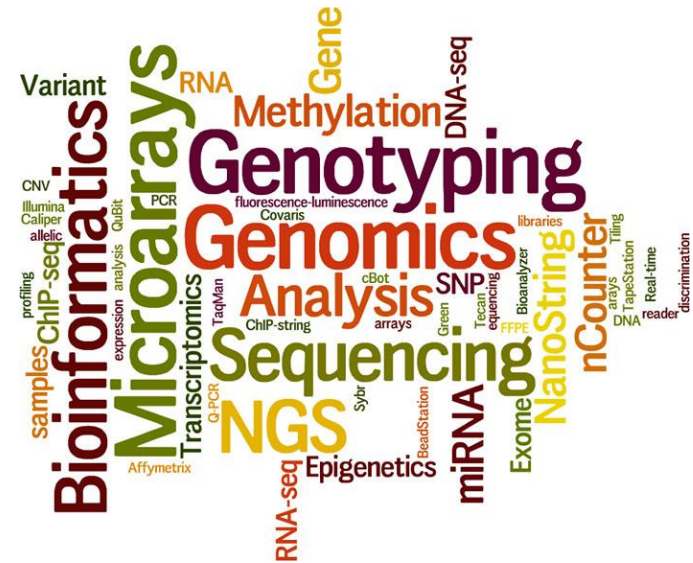
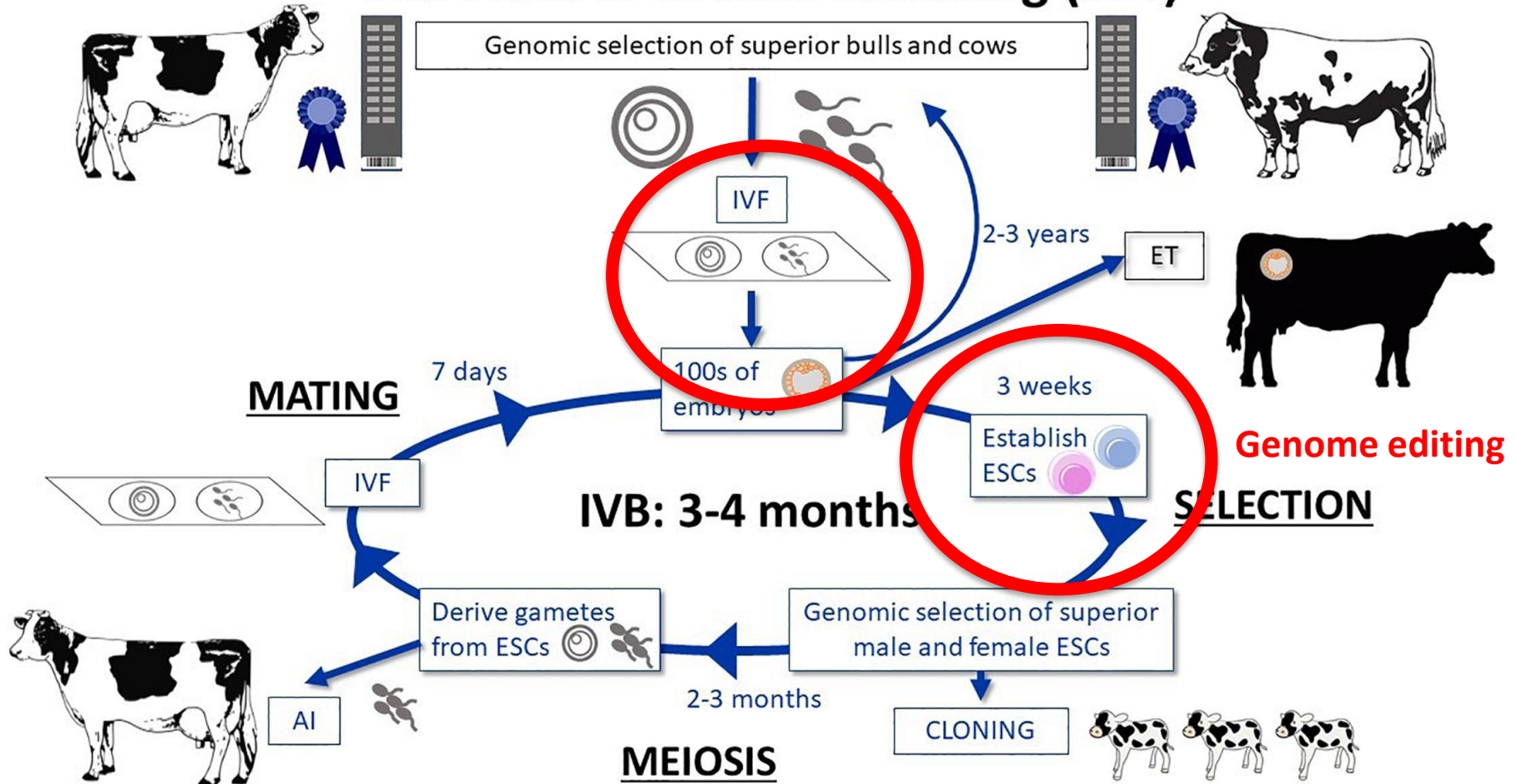# Genome editing improvements

- **New targets**
- **New methods/options for editing**
- **New delivery systems**
- **Towards multiple edits of complex traits**

Key messages

- GEd offers targeted changes for specific outcomes
- Many editing options and delivery methods are available and many more are being developed
- The entire 'process' brings together many technically complex systems and methods
- Expensive to identify targets, many traits are complex and will require multiple 'edits'
- Decisions on what to edit can be 'morally' and 'ethically' challenging.

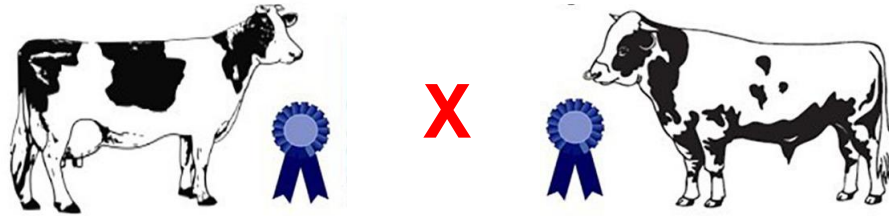# Pathway to market must compliment existing breeding programs

The Future: In vitro breeding (IVB)

Genomic selection of superior bulls and cows

IVF

2-3 years

ET

7 days

MATING

IVF

100s of embryos

3 weeks

Establish ESCs

Genome editing

IVB: 3-4 months

SELECTION

Derive gametes from ESCs

Genomic selection of superior male and female ESCs

AI

2-3 months

CLONING

MEIOSIS

Rexroad, et al. (2019). Genome to phenome: improving animal health, production, and well-being—a new USDA blueprint for animal genome research 2018-2027. Front. Genet. 10:327.

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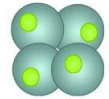# Pathway to market requires suitable value capture models
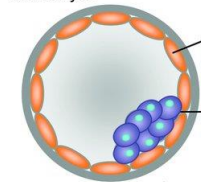

'Product Pull'

$$$

Genome editing → Fertilized egg

Few-celled embryo

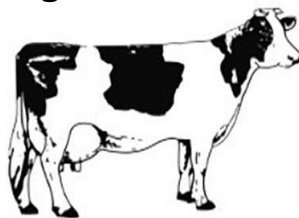Blastocyst — Trophectoderm

Genome selection → ICM

Surrogate

'Product Pull'

$$$

X

Rexroad, et al. (2019). Genome to phenome: improving animal health, production, and well-being—a new USDA blueprint for animal genome research 2018-2027. Front. Genet. 10:327.
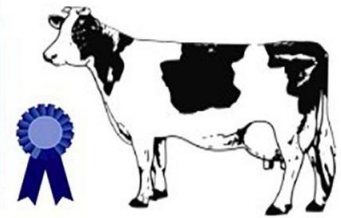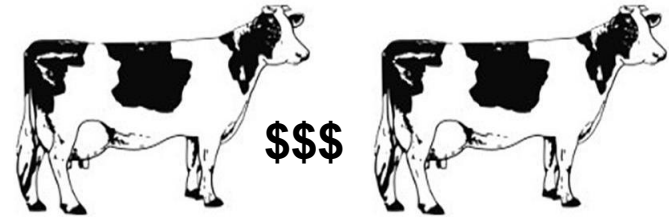
Example: Proof of Concept
GM / GEd 'Polled' in Australia

SDN-2

Buri's Grandchildren…
Are they / should they be regulated?

GM / GEd
Polled

Null
Segregant
Horned

Key messages

- Numerous GM and GEd targets have been identified and characterized for animals

- Many biomedical models are now generated using gene editing techniques

- Ornamental fish and high growth rate fish are the only products currently on the market

- There are significant opportunities for improved animal health and welfare, particularly in livestock

- Commercialisation will depend on a clear pathway to market and an effective value capture model.

Thank You