Gene drive technology for suppression of invasive mammals (rabbits)

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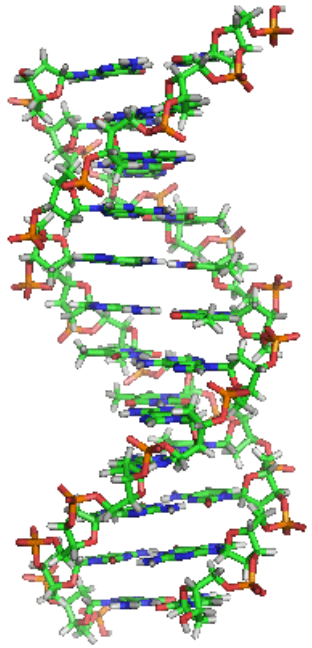
Overview

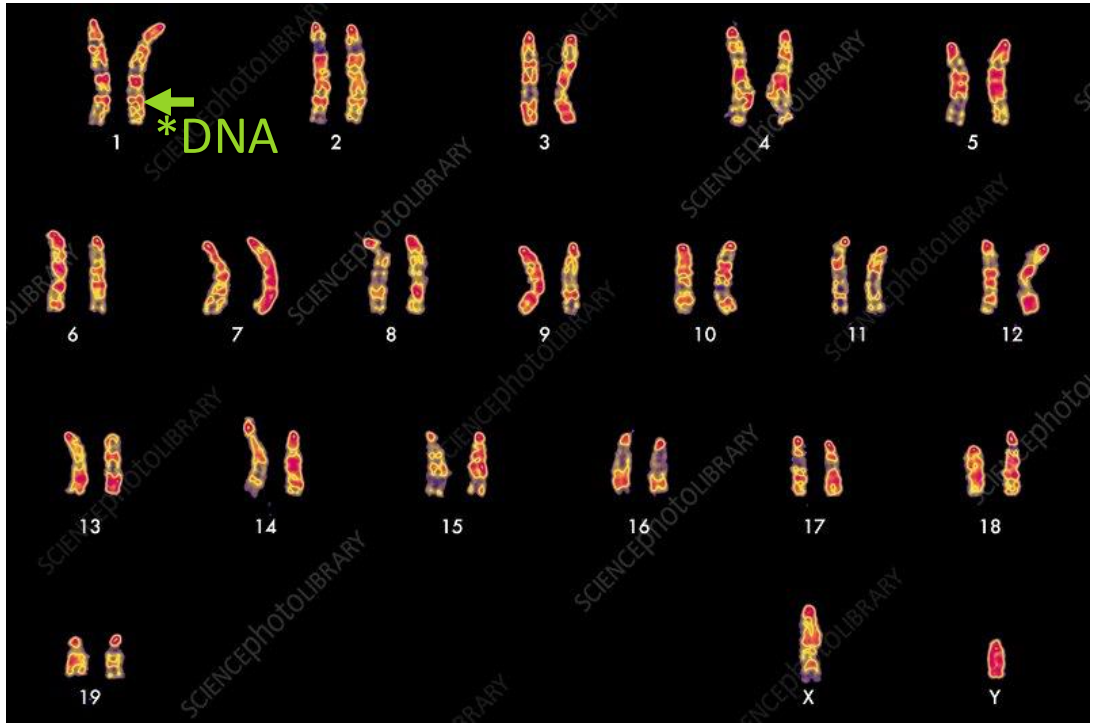


1. Genetic biocontrol (gene drives)
   -what are they?
   -how do they work (CRISPR)

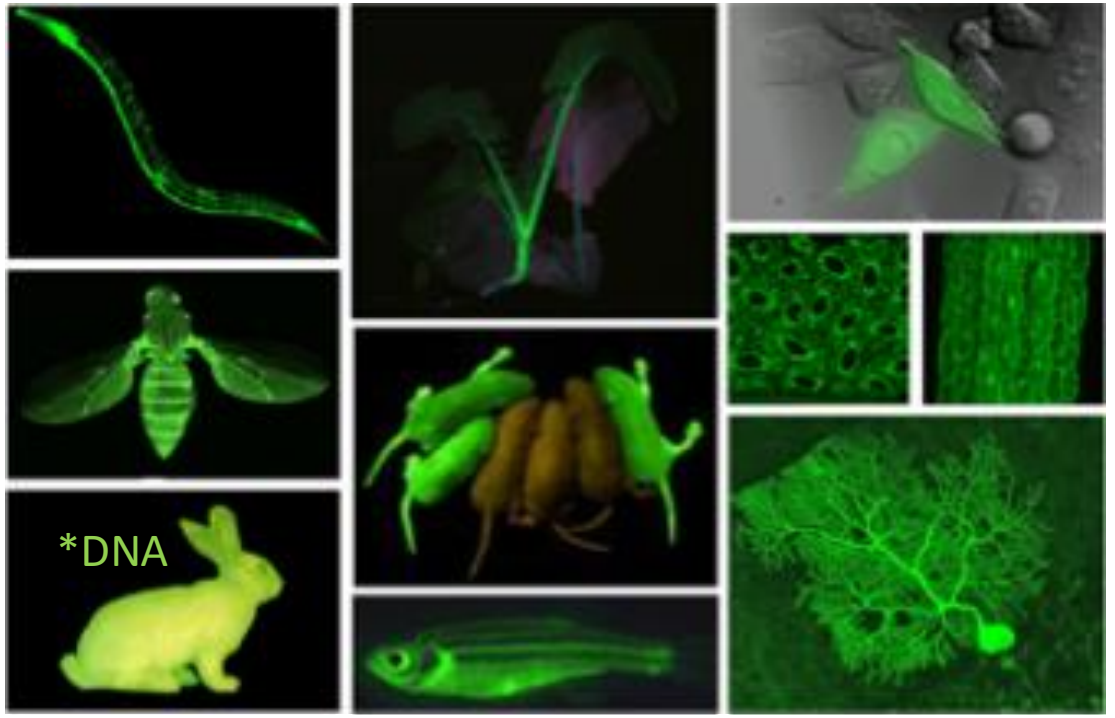
2. Could gene drives be developed in rabbits?
   -potential for suppression (modelling)
   -challenge/barriers

Genetics and transgenic animals 101

Mouse genome on 20 pairs of chromosomes (rabbits 22 pairs)



*DNA "Transgenic" mouse



(Chalfie PNAS 2009)

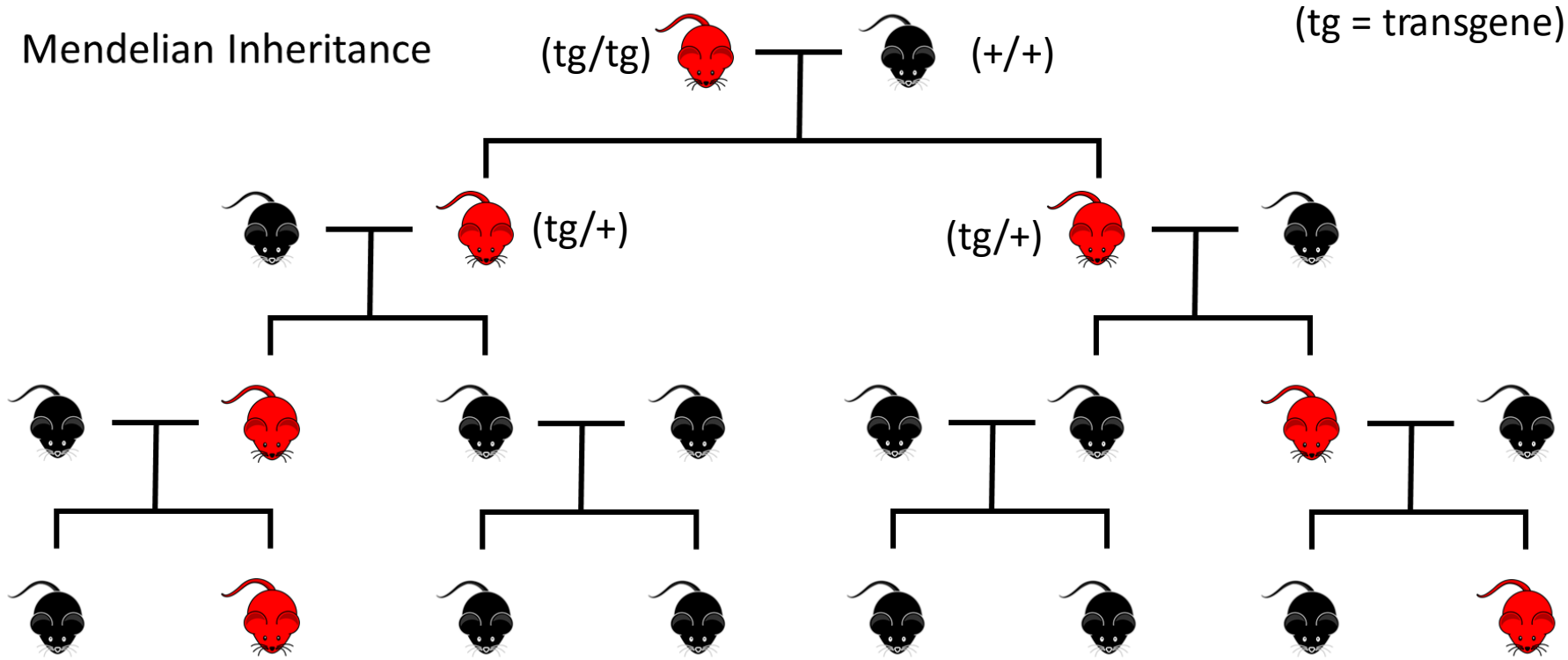
Every cell contains the blueprint for life…. (2.4) billions of DNA building blocks → 20,000 genes

Transgenesis is adding a "foreign" gene into the genome (*DNA) → new "phenotype"

(synthetic) gene drives are a type of transgenic animal which have **biased** inheritance

What is a Gene Drive?

- Genetic construct (transgene) that promotes its own inheritance at a rate greater than Mendelian inheritance
- Potentially spreads through entire population and allows population-level genetic engineering (modification or suppression (fertility or sex bias))



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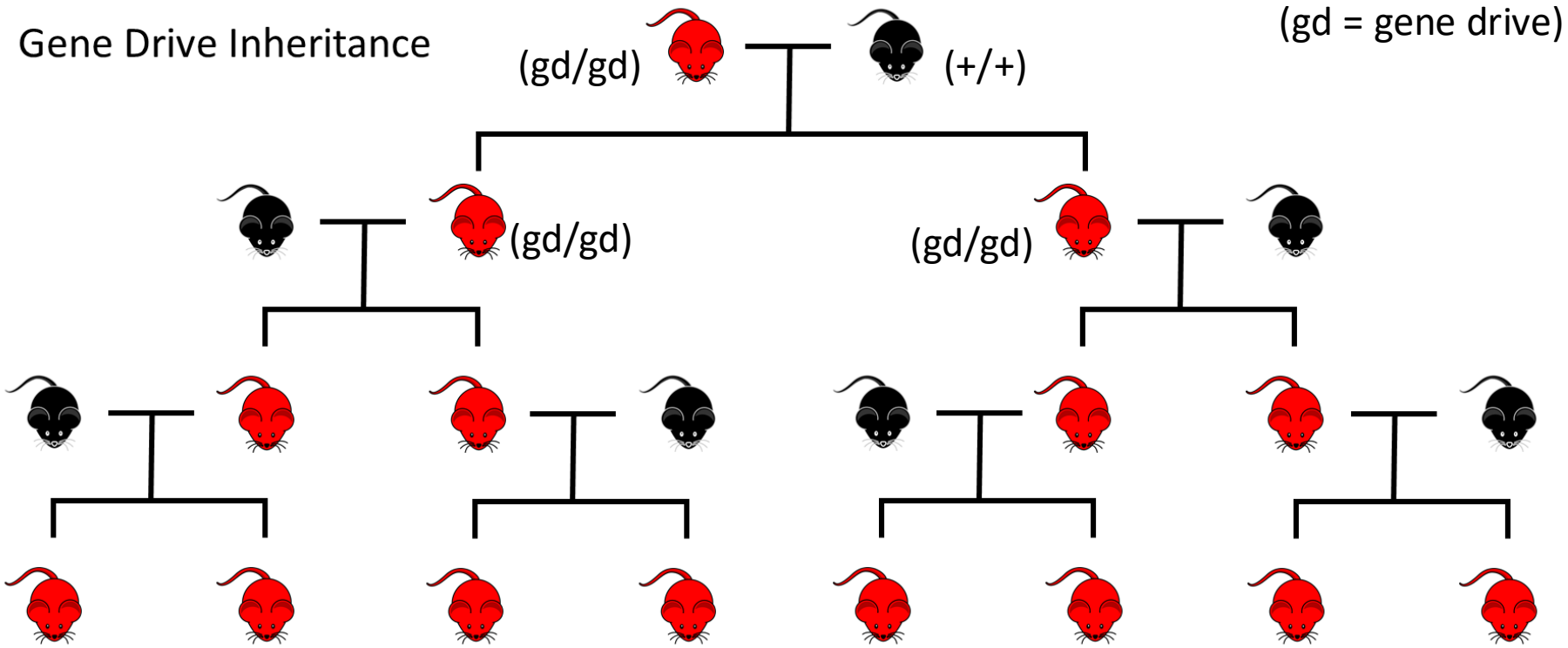

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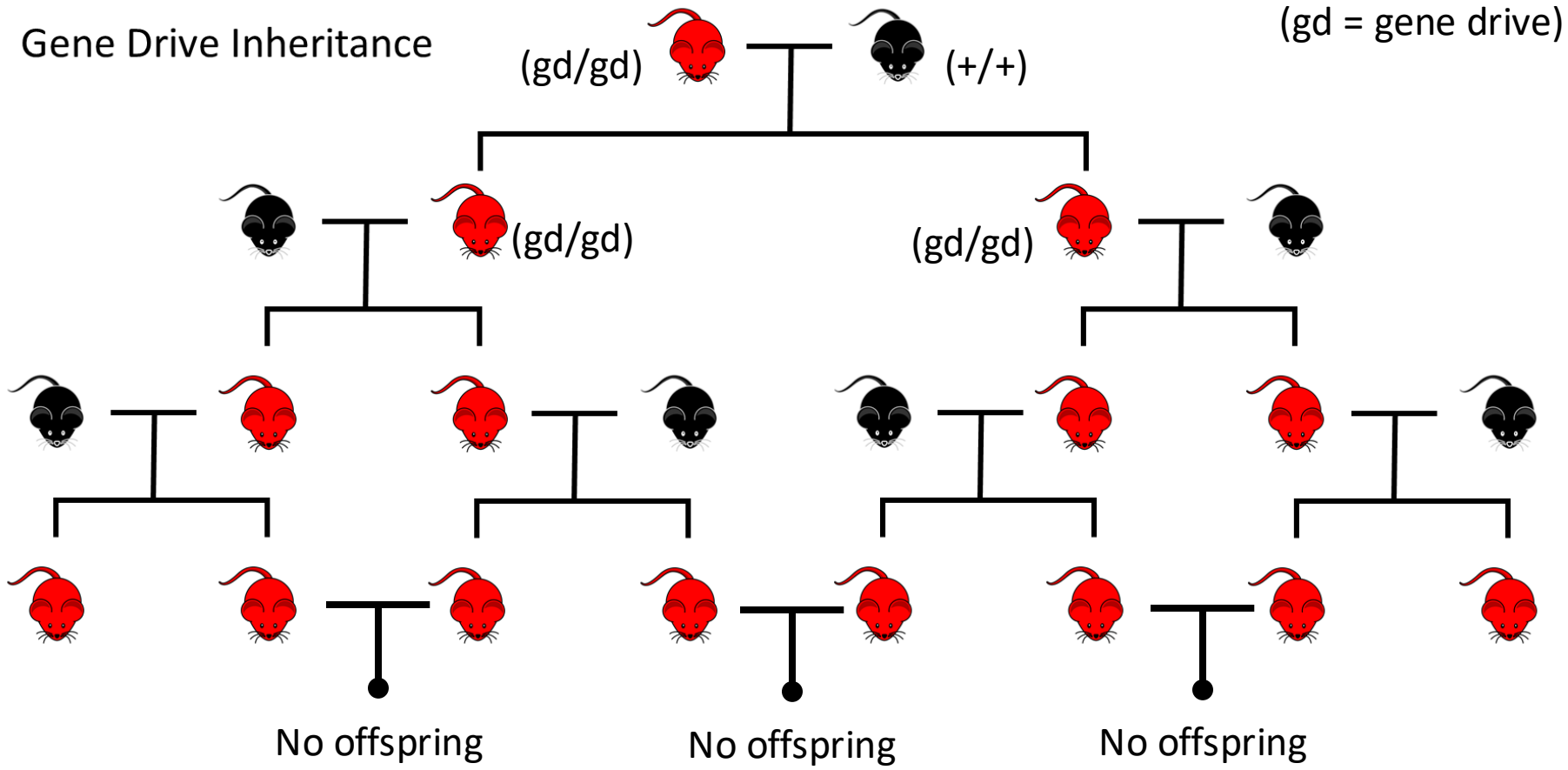

"Homing" female infertility drive

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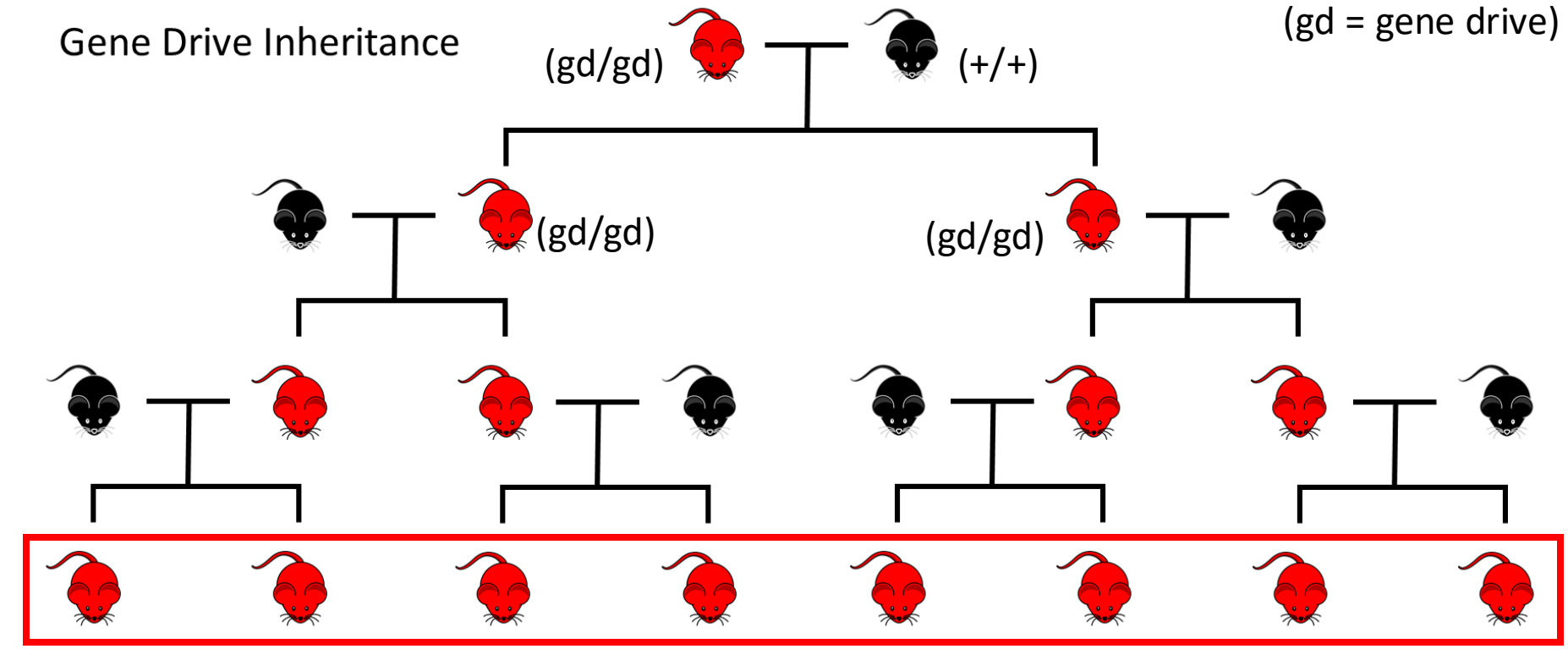

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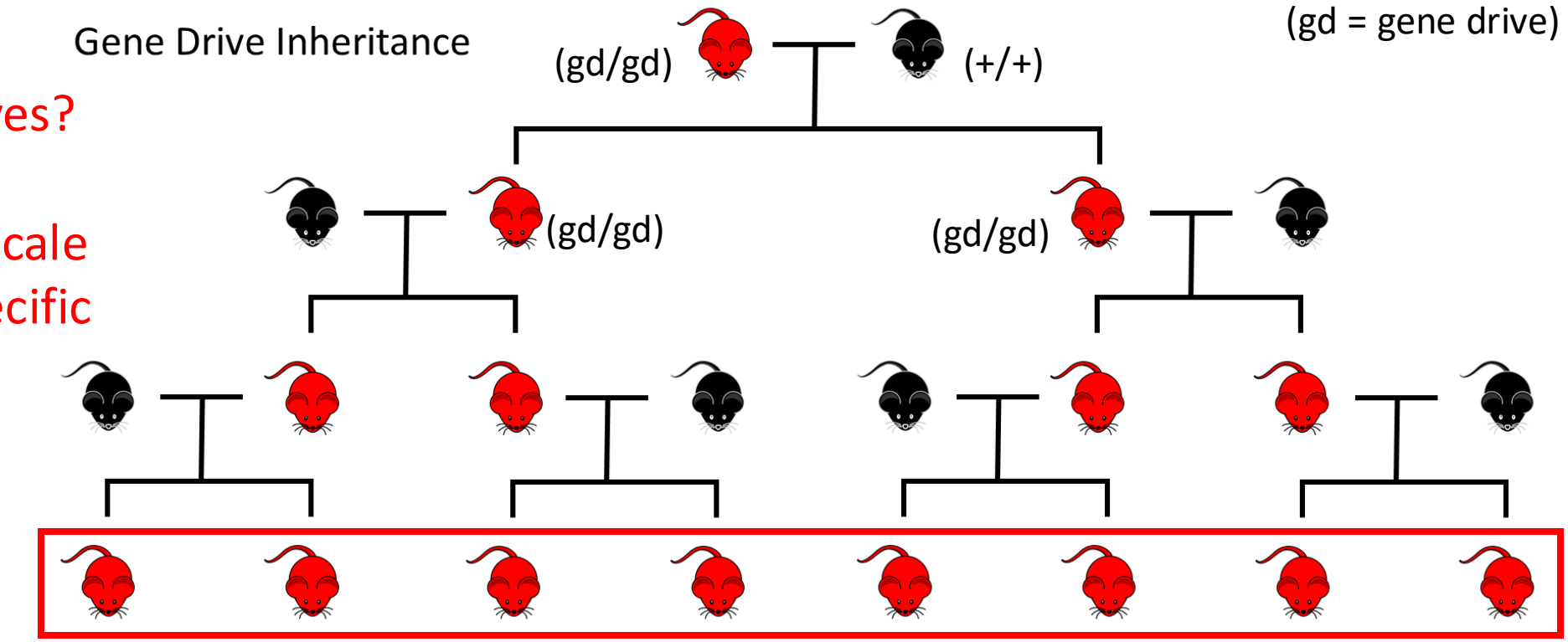
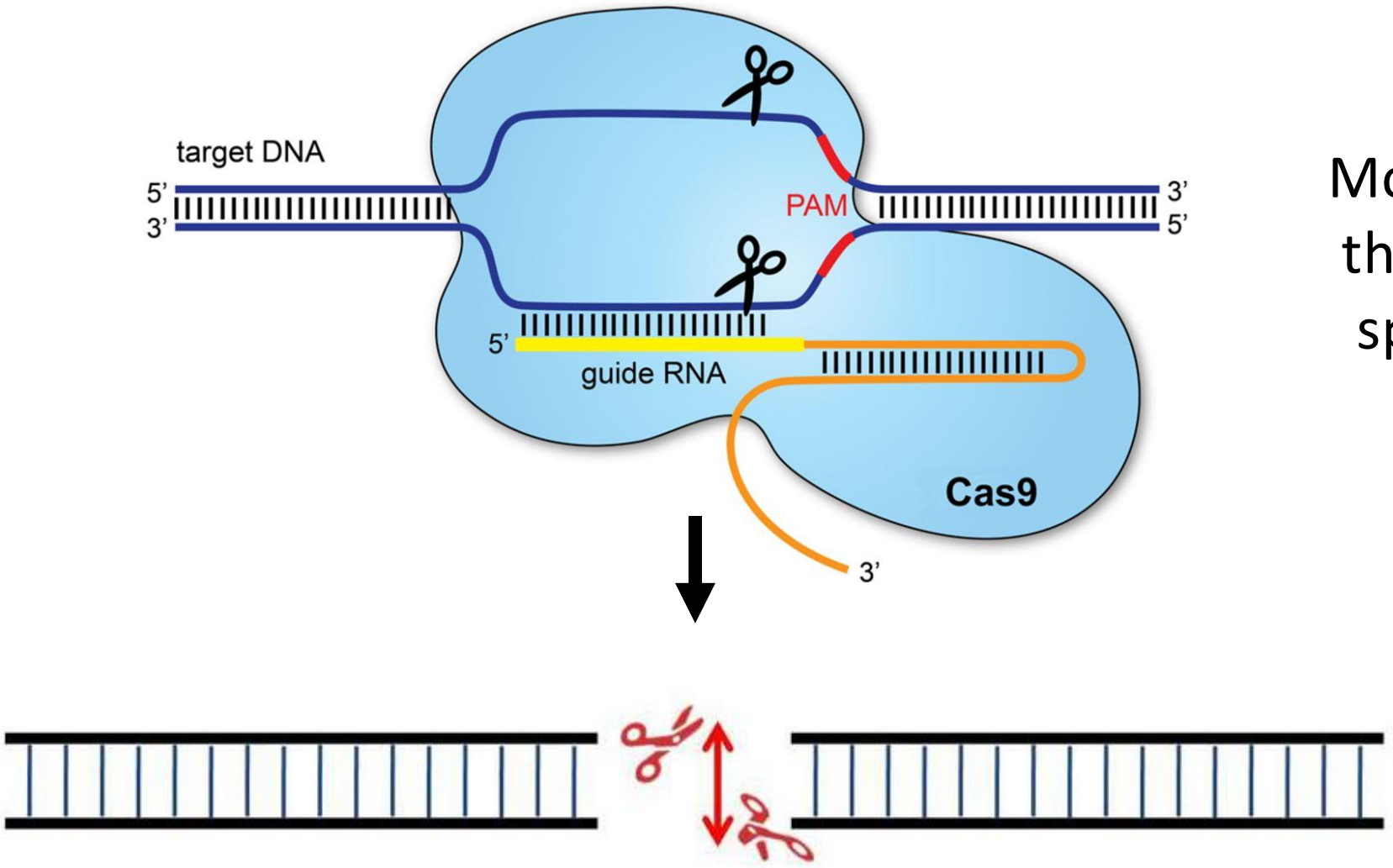


Why gene drives?

- Non-lethal
- landscape scale
- Species-specific

CRISPR/CAS9 Genome Editing



Molecular scissors that cut DNA at a specific location

CRISPR enables generation of gene drive (transgenic) animals and gene drive activity

Gene Drives

Gene Drive Strategies

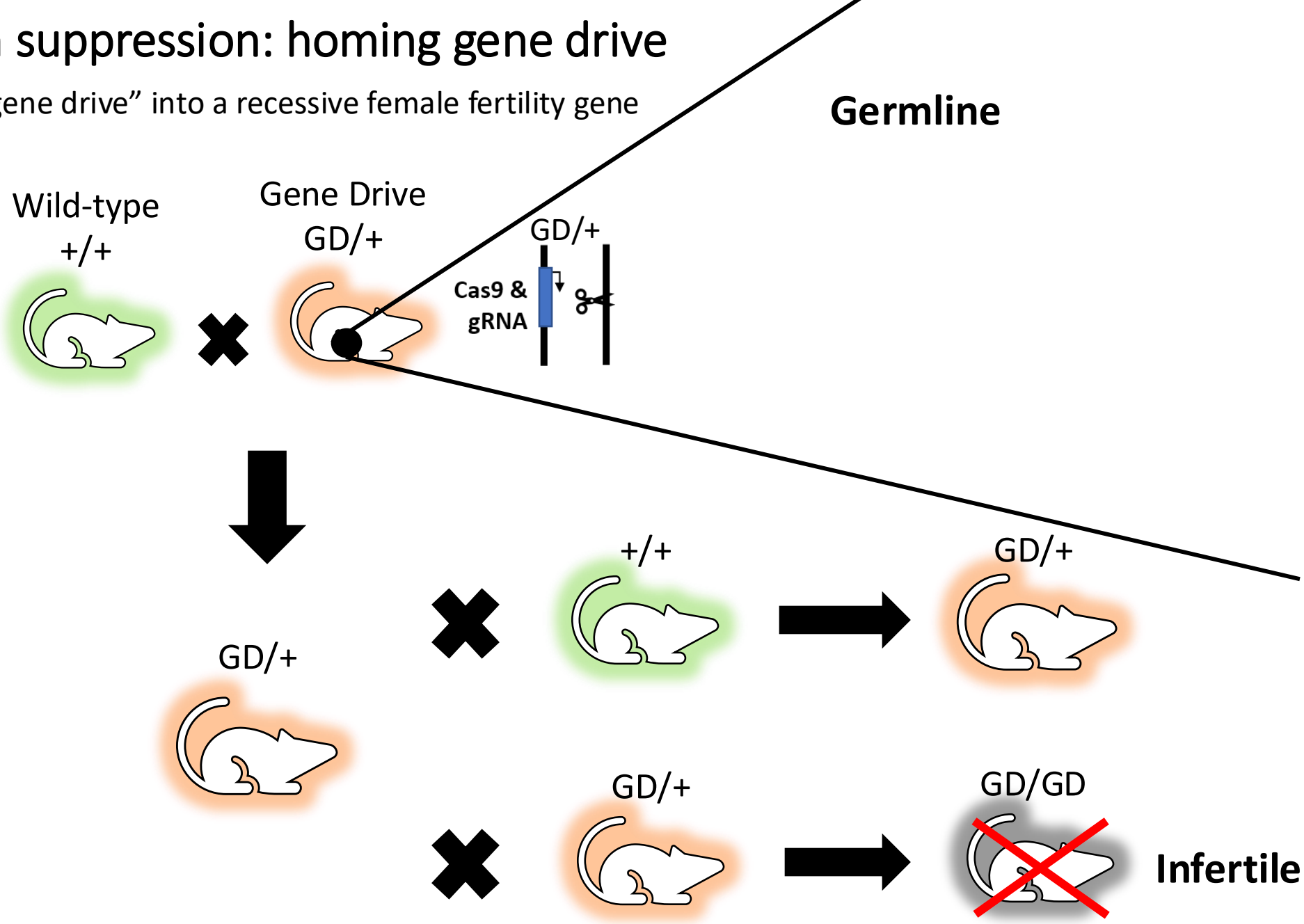
1. CRISPR ‘homing’ gene drive (female fertility)

2. X-shredder/driving Y (male bias)

3. *t*-allele + CRISPR = *t*-CRISPR (female fertility) (mouse-specific)

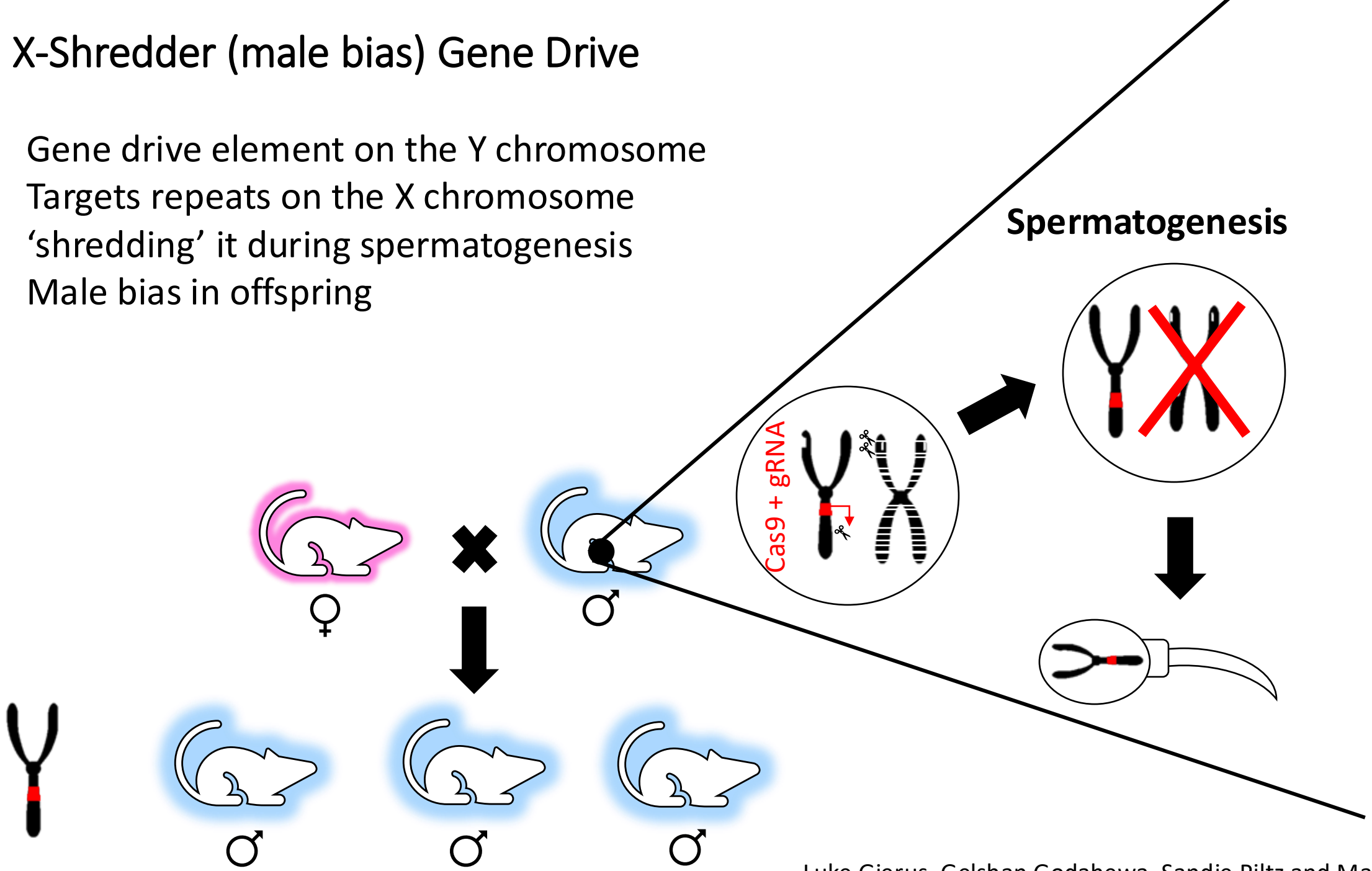
Population suppression: homing gene drive

- Insert the “gene drive” into a recessive female fertility gene



2. X-Shredder (male bias) Gene Drive

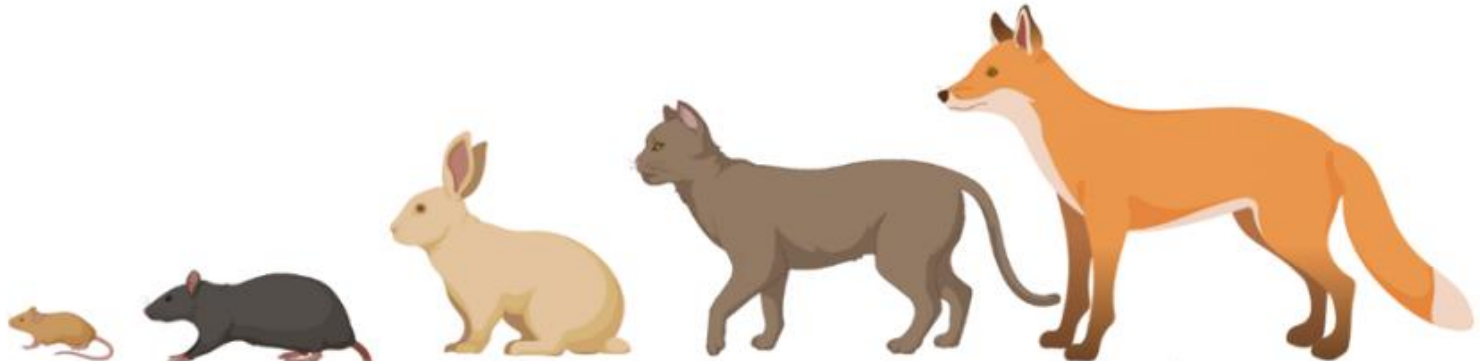
- Gene drive element on the Y chromosome
- Targets repeats on the X chromosome ‘shredding’ it during spermatogenesis
- Male bias in offspring

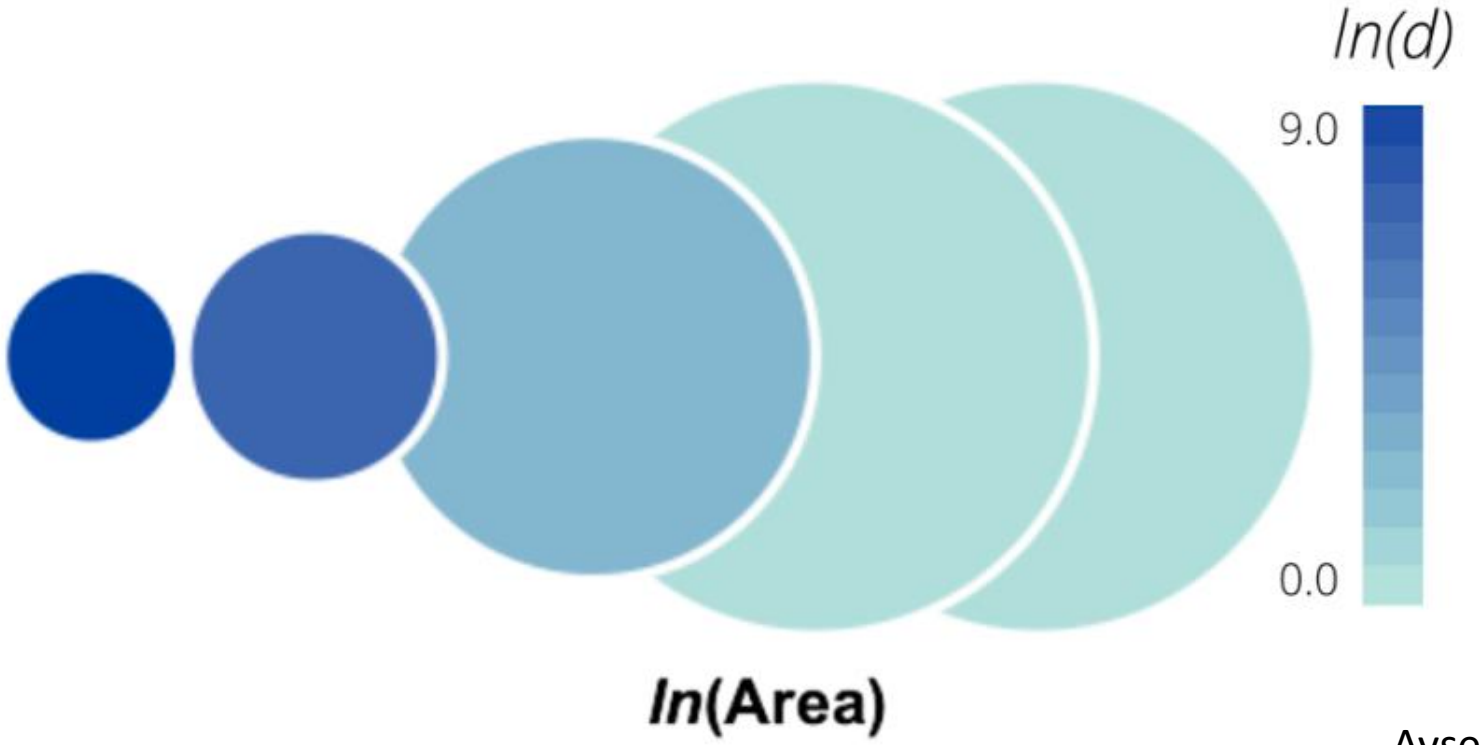


Luke Gierus, Gelshan Godahewa, Sandie Piltz and Mark Bunting

Modelling mammalian gene drives

N ~ 200,000





X-SHREDDER

Male biassing drive

HOMING

female infertility drive

Aysegul Birand

Life-history parameters

Survival probability

Probability of polyandry

Dispersal

Parameters:

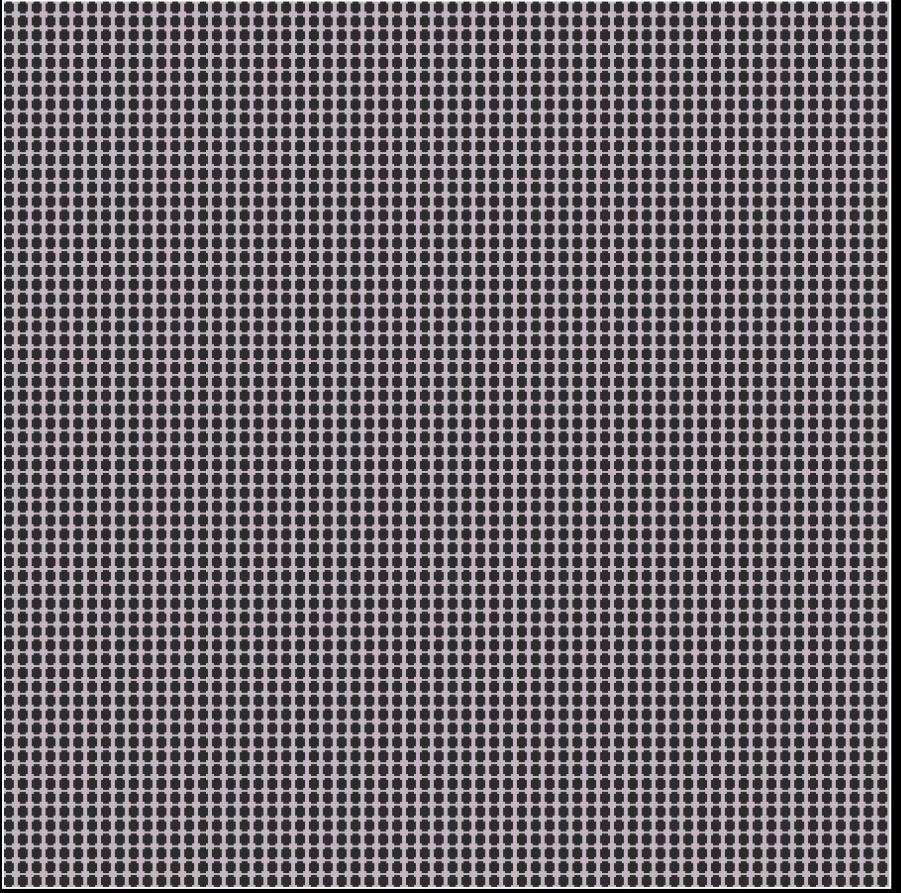
Species	b	n_c	age_m	ω	p_m	d	A	Δ_i	D
mouse	6	6	2	0.53	0.46	5000	40	0.4	3
black rat	4	6	2	0.62	0.68	1000	200	2	8
rabbit	4	4	3	0.82	0.20	25	8000	12.5	8
cat	4	2	5	0.85	0.25	2	100000	25	4
fox	4	2	5	0.88	0.76	2	100000	45	8

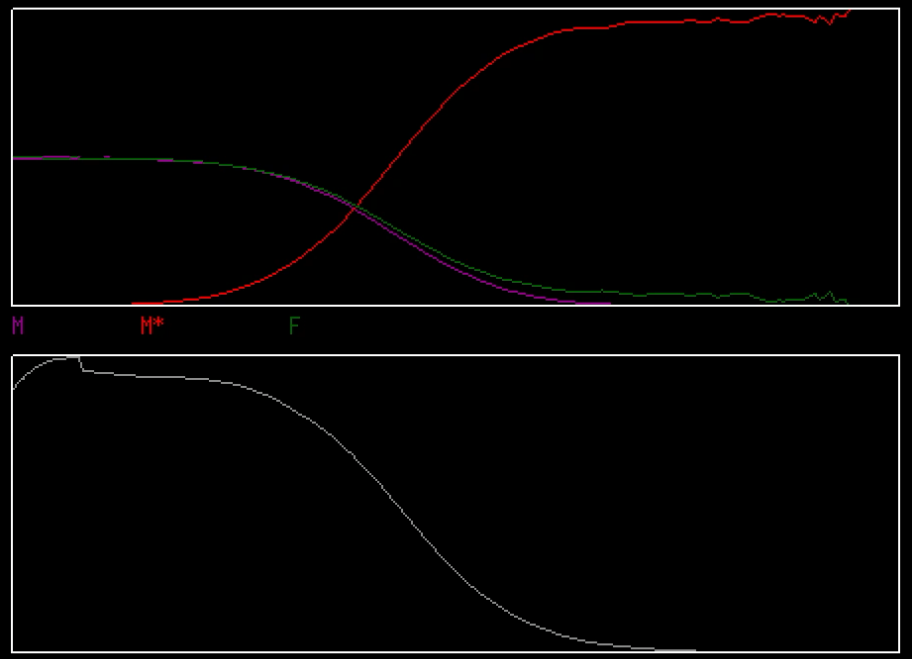
Aysegul Birand

Island population of 200,000 rabbits (about 2 x Kangaroo Island)

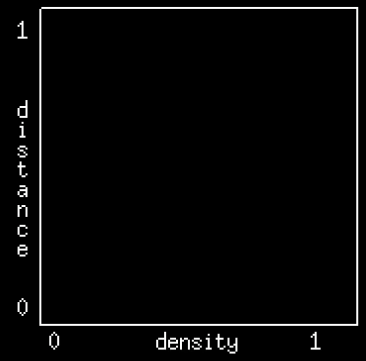
256 gene drive rabbits introduced

X-Shredder male biasing drive (same for homing drive)





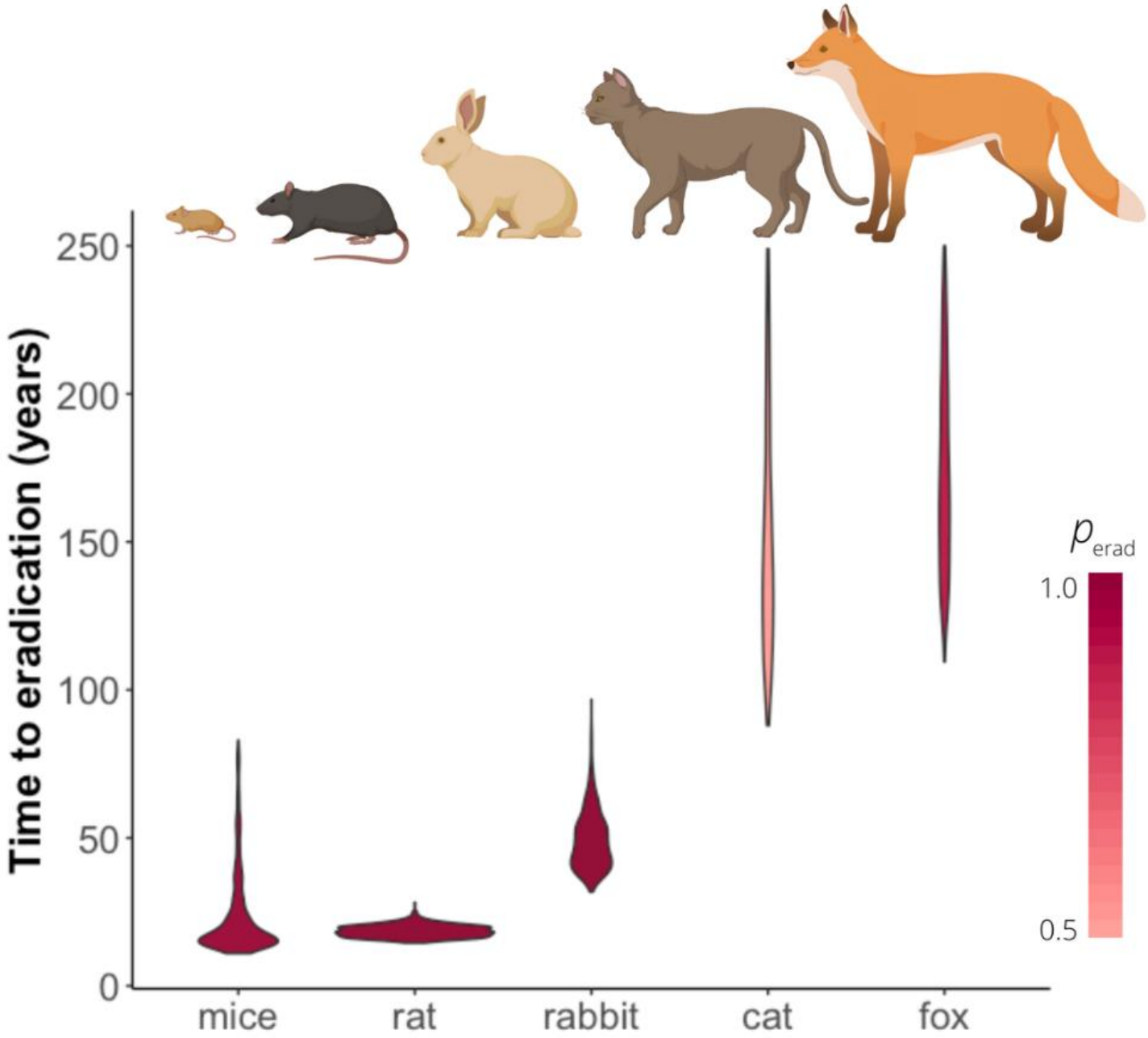
Speed:	0
Years:	-3.50 (0/176)
Mating cycles/year:	4
Male:	81920
Male*:	0
Female:	81920
N/T/P(inoc):	1/1/256
N(max):	184352
T(reduction):	29.25
Multiple Paternity:	nan



Aysegul Birand

Results

(1000 sim. per species)



Species	50%	90%	100%
Mouse	6.7	9.2	17.7
Black rat	9.0	11.7	18.5
Rabbit	16.8	24.1	48.0
Cat	71.0	92.0	143.2
Fox	74.0	103.5	169.0

Birand et al. 2022 NeoBiota 74: 93-103

Conclusions and Challenges

Genetic biocontrol (gene drive) technology is progressing in insects and mice – potential for disease control, conservation and agriculture

-stakeholder engagement, regulation, technical hurdles (inc. target population specificity)

Rabbit genetic biocontrol

-longer timeframes than rodents

-technical and financial challenges (transgenesis, facilities, genetics, reproductive technology)

- non-model animal

Stakeholder engagement (cf. CSIRO/Aditi Mankad stakeholder engagement survey) (hypothetical “cat gene drive” scenario)

Acknowledgements

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***t* mice**
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