Gene technology and its potential for pest control

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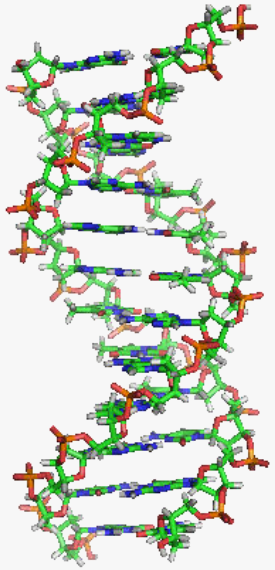
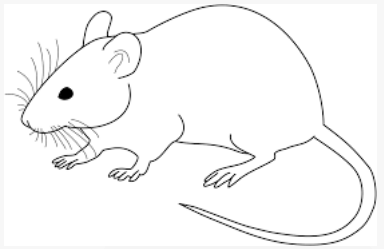
Overview



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

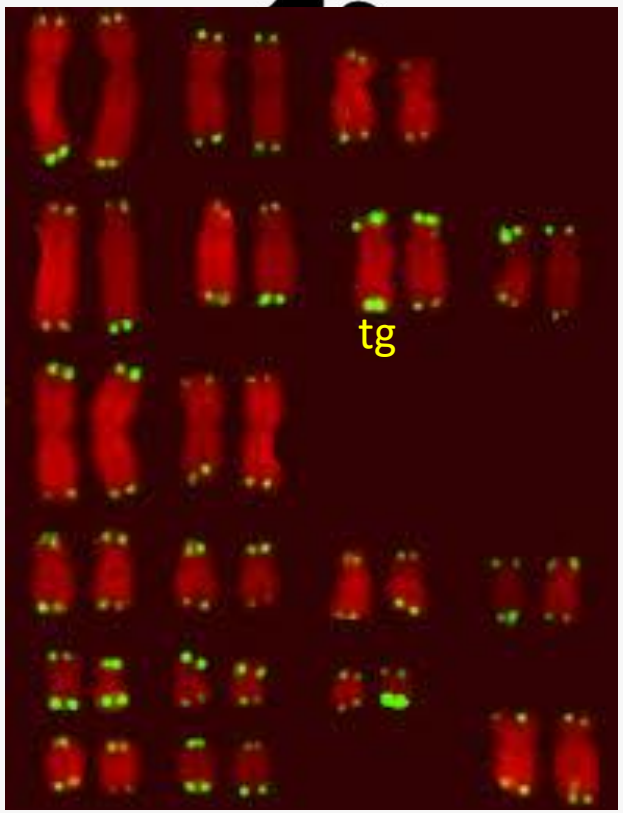
2. In what species have gene drives been developed?
   -invertebrates
   -mammals



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

Genetics and transgenic animals 101

Cat genome on 19 pairs of chromosomes



"Transgenic" cat

Bbc.com

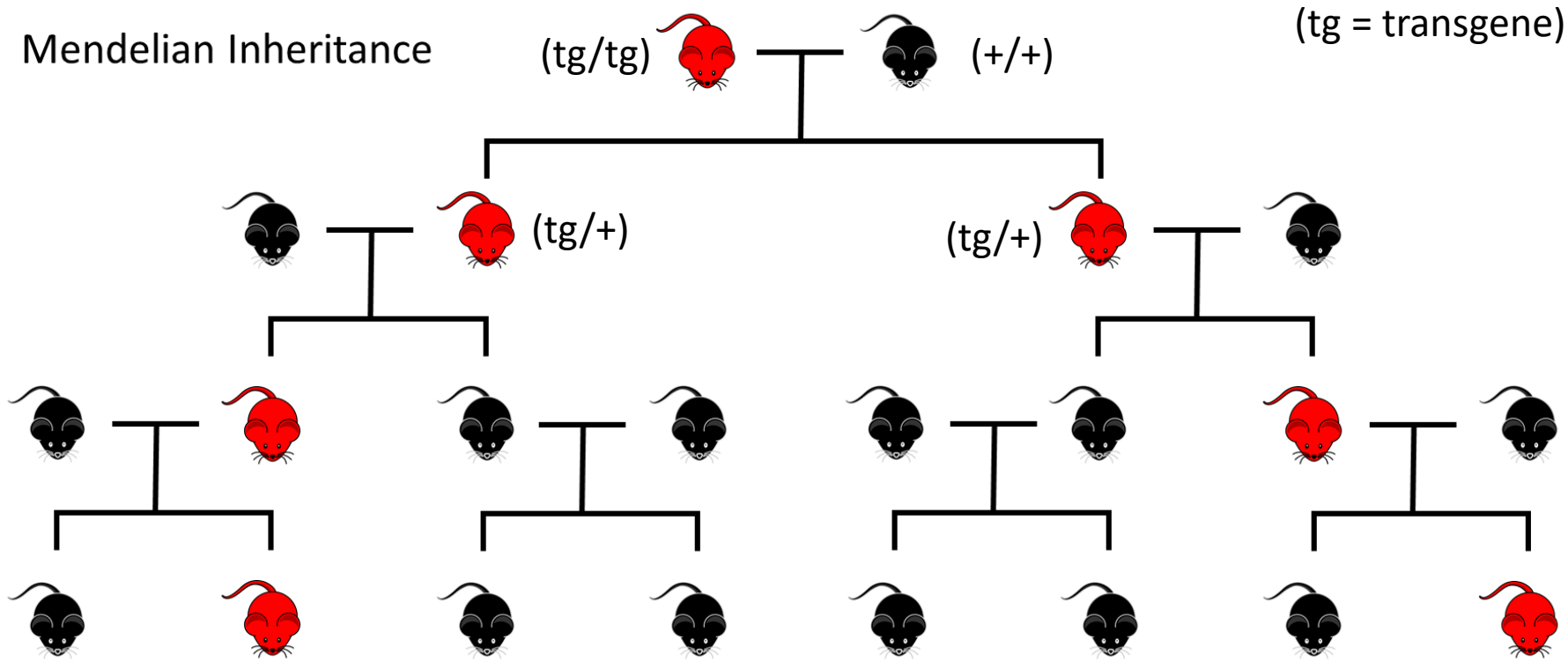
Every cell contains the blueprint for life…. (2.4) billions of DNA building blocks → 20,000 genes

Transgenesis is adding a "foreign" gene into the genome → 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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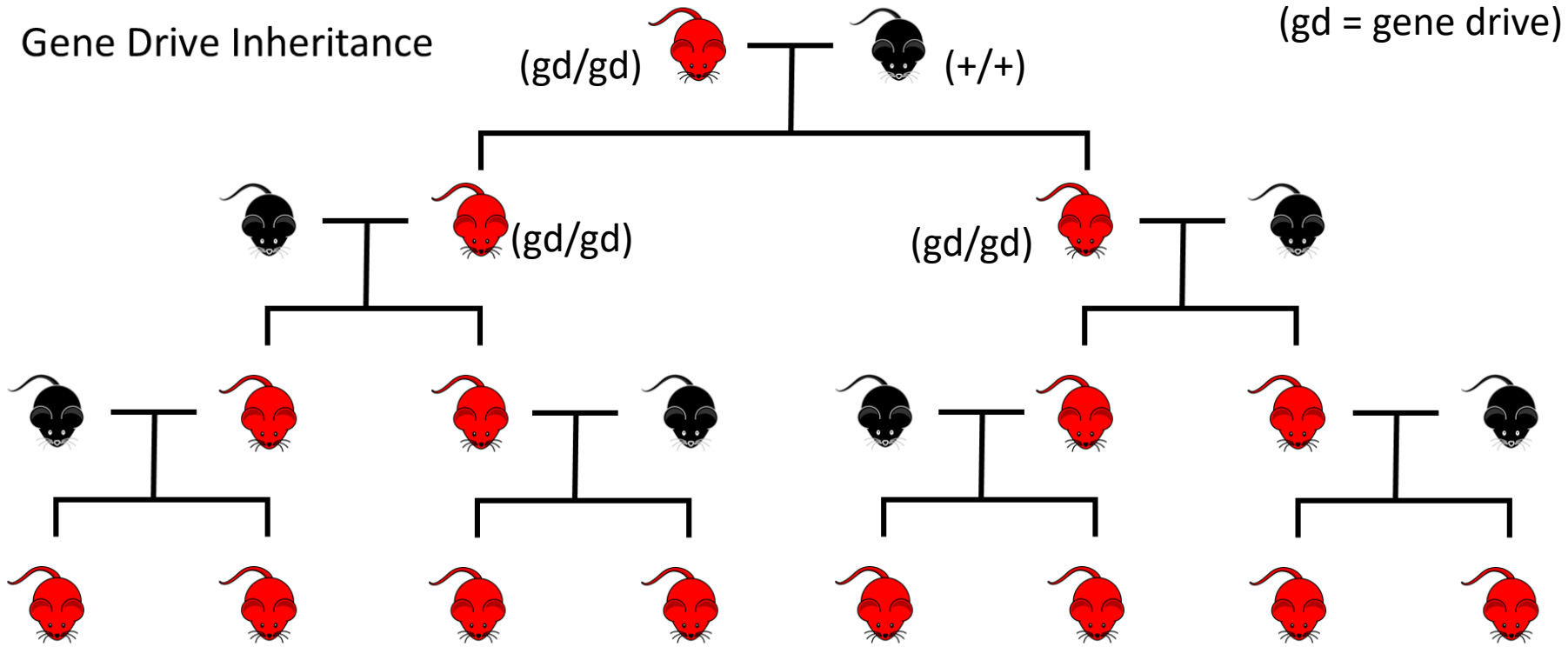

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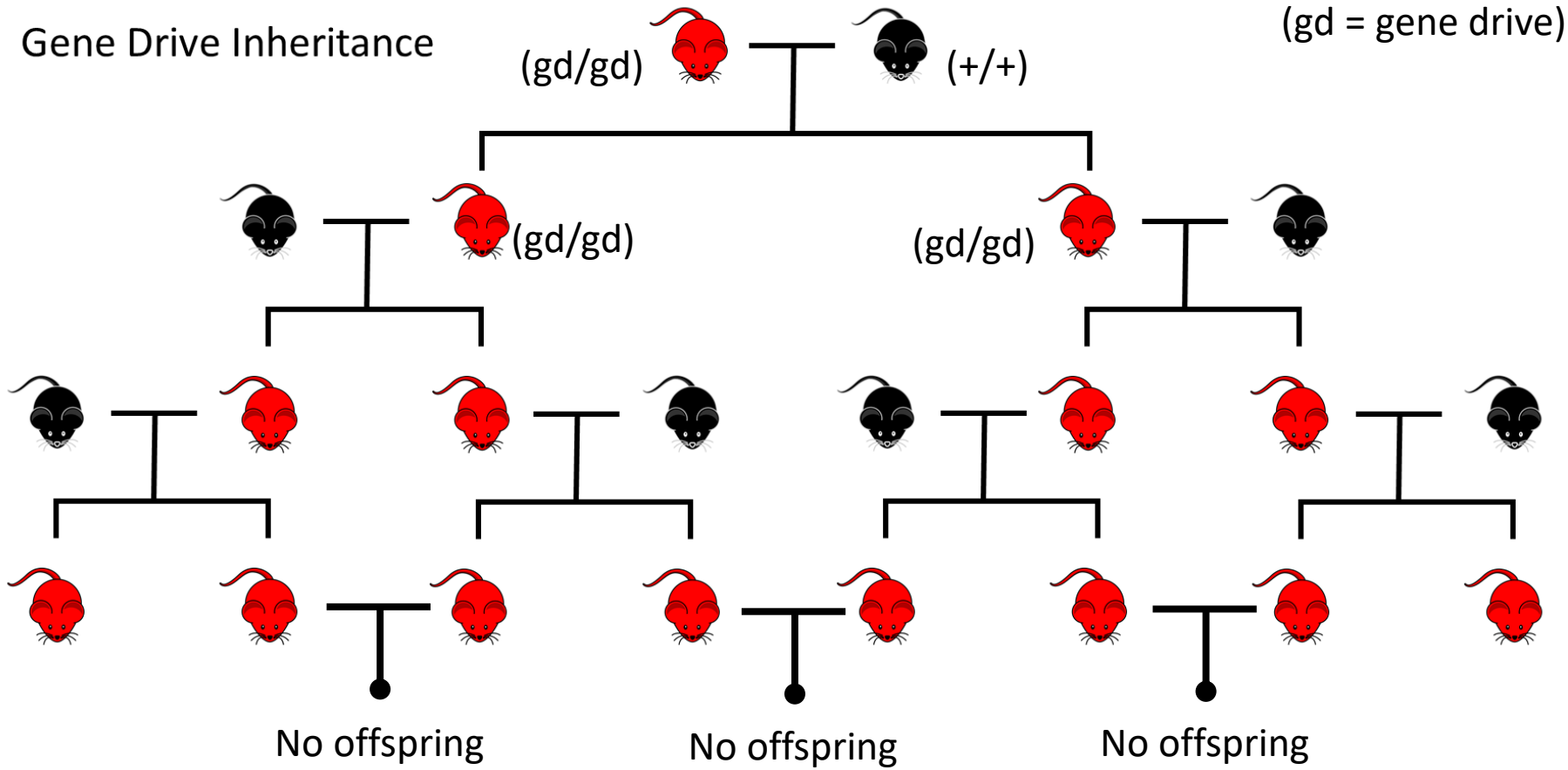

"Homing" female infertility drive

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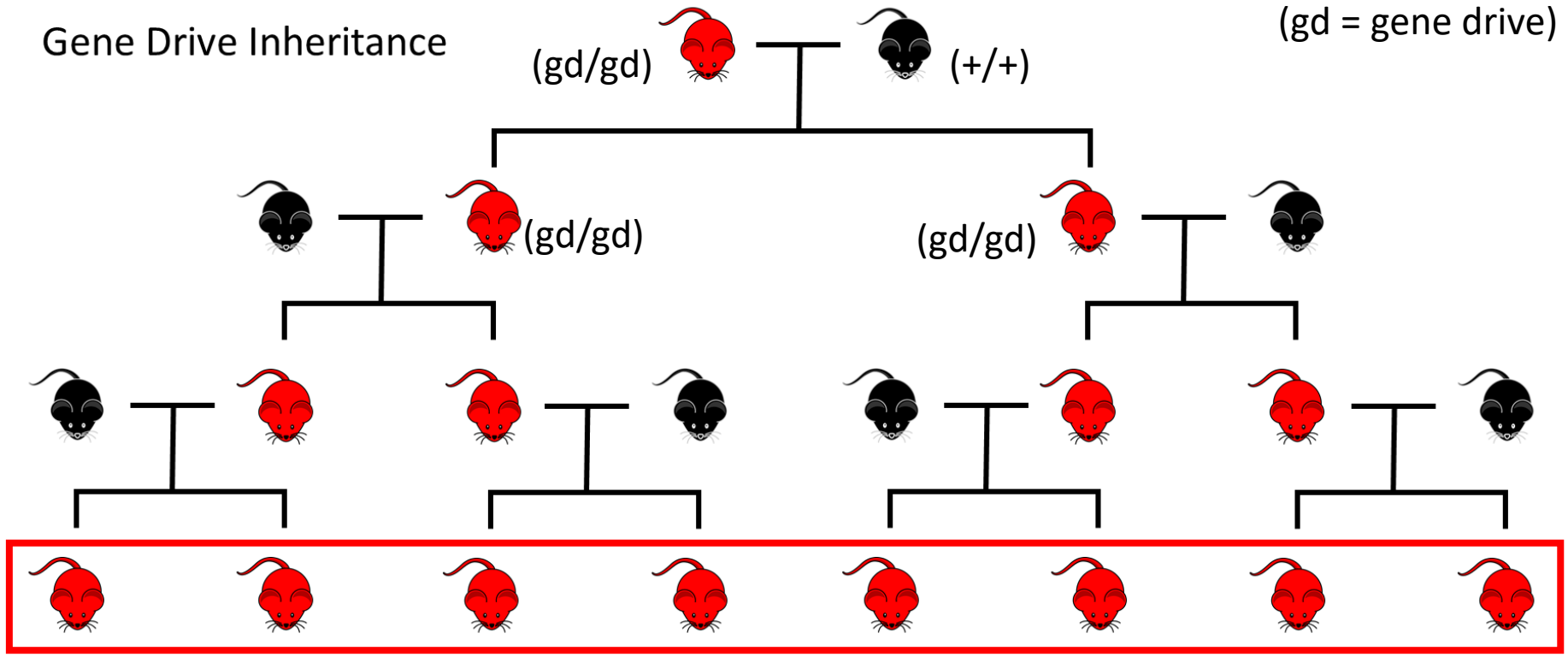
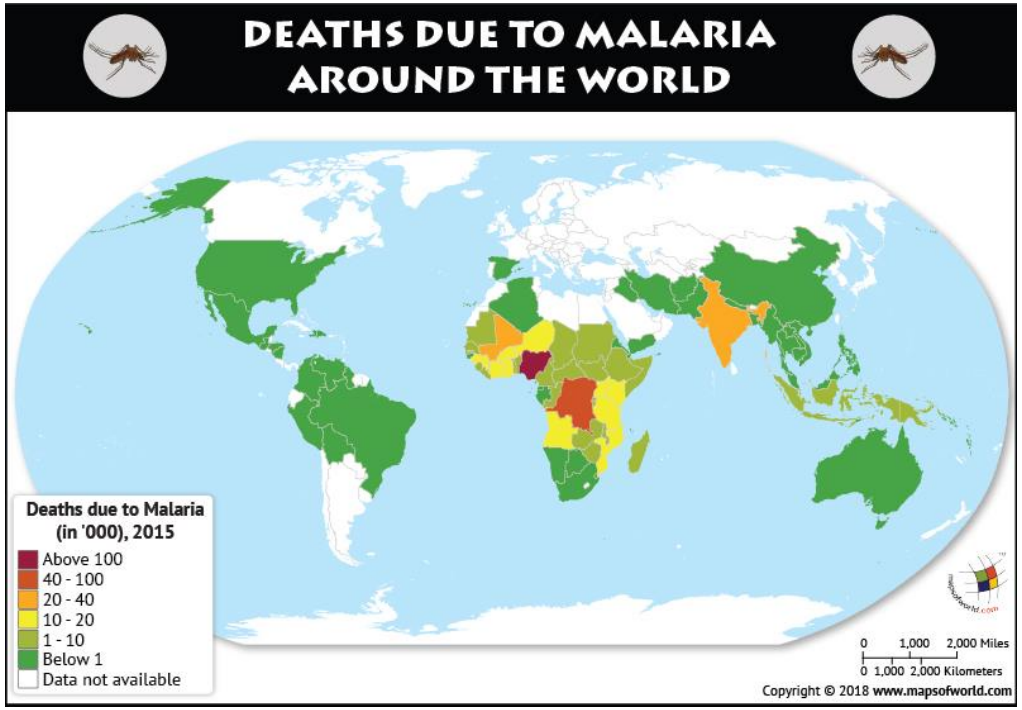


Why develop gene drives?

- Health, conservation & agriculture



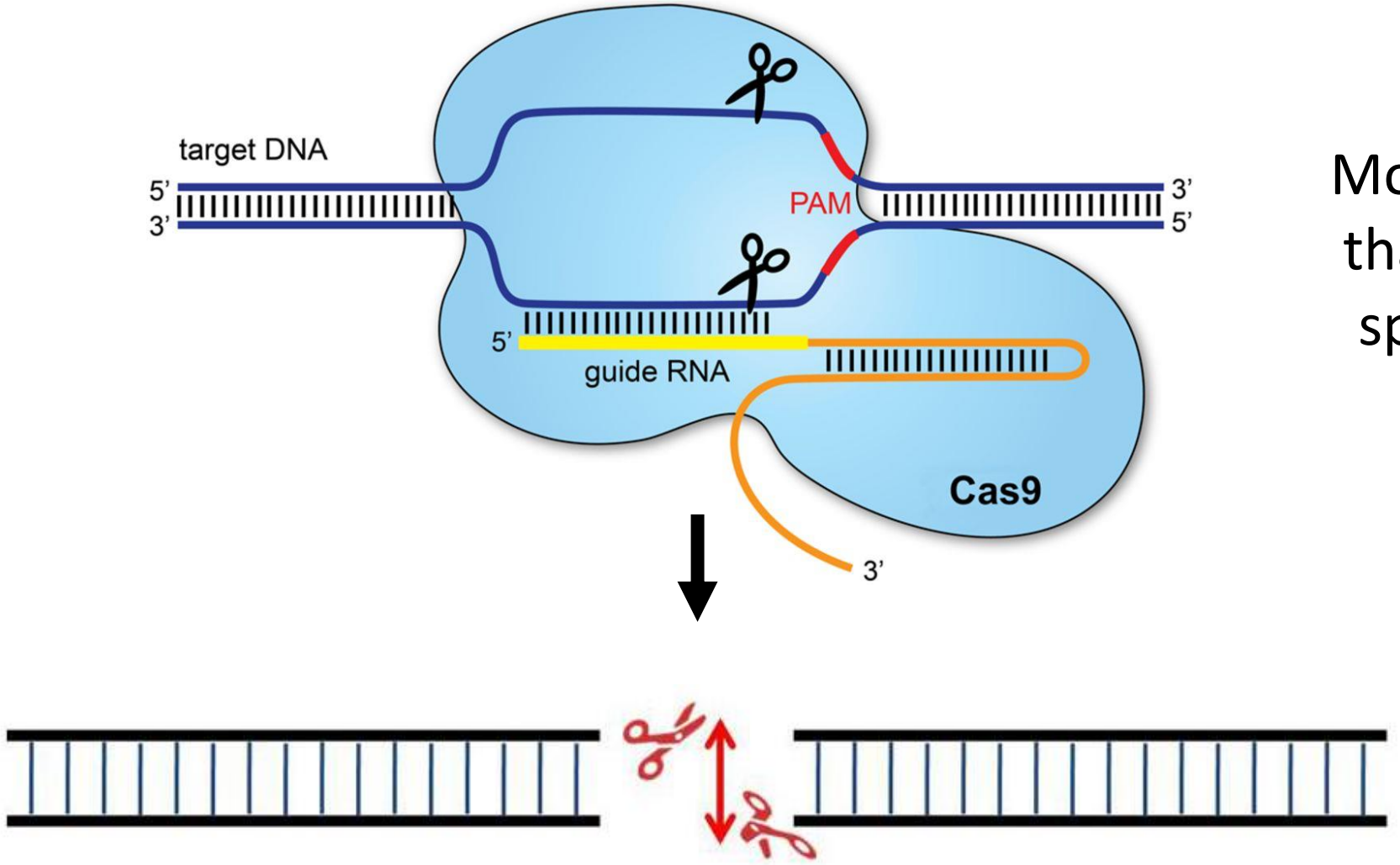
Malaria is responsible for >400,000 deaths per year

Hundreds of mice that have been trapped during the plague on Qld's Darling Downs. *(Supplied: Vicki Green)*

Environmental damage/loss of biodiversity

Agricultural loss of productivity/societal impact

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

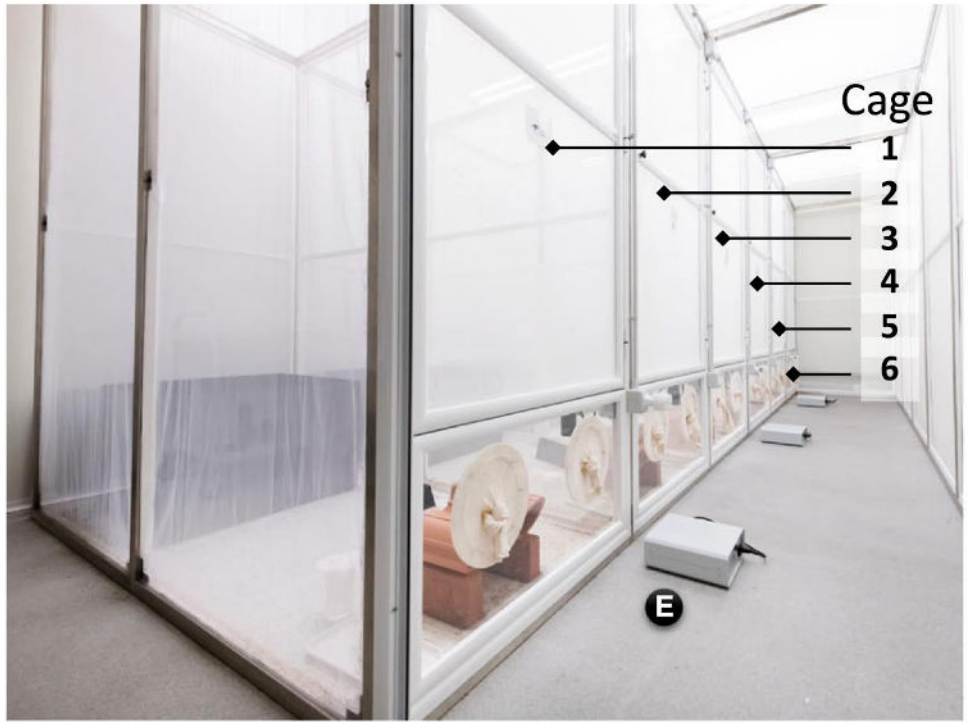
In 2021…

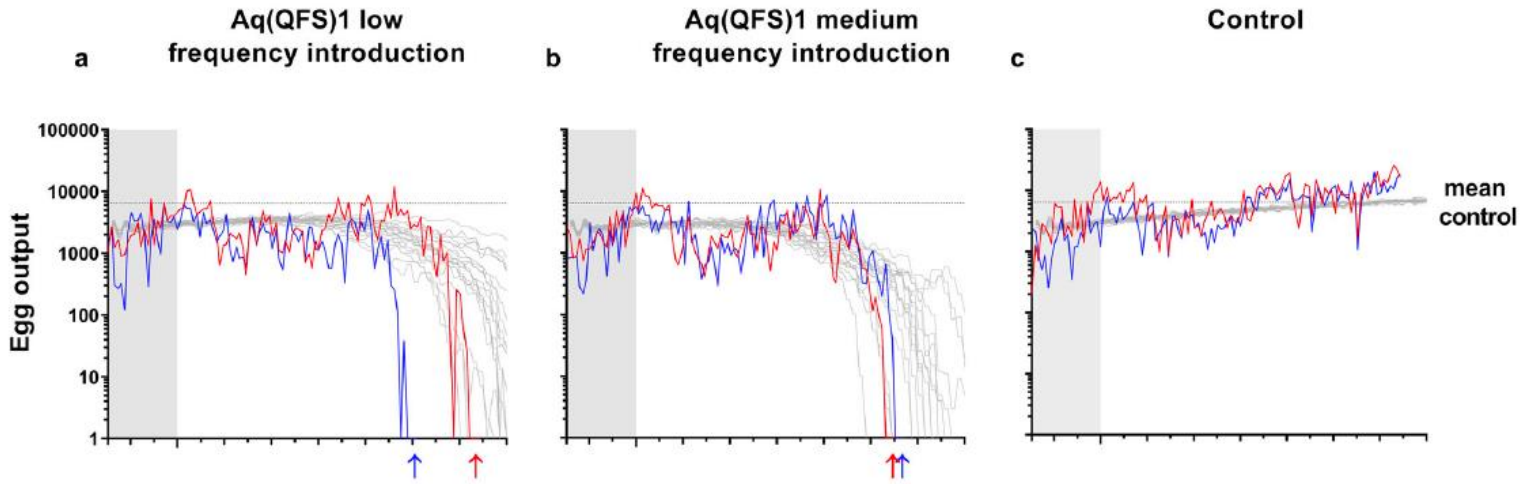
ARTICLE

https://doi.org/10.1038/s41467-021-24790-6 OPEN

Gene-drive suppression of mosquito populations in large cages as a bridge between lab and field

Andrew Hammond[1,2,9], Paola Pollegioni[3,4,9], Tania Persampieri[3,9], Ace North[5], Roxana Minuz[3], Alessandro Trusso[3], Alessandro Bucci[3], Kyros Kyrou[1], Ioanna Morianou[1], Alekos Simoni[1,3], Tony Nolan[1,6,10✉], Ruth Müller[3,7,8,10✉] & Andrea Crisanti[1,10✉]

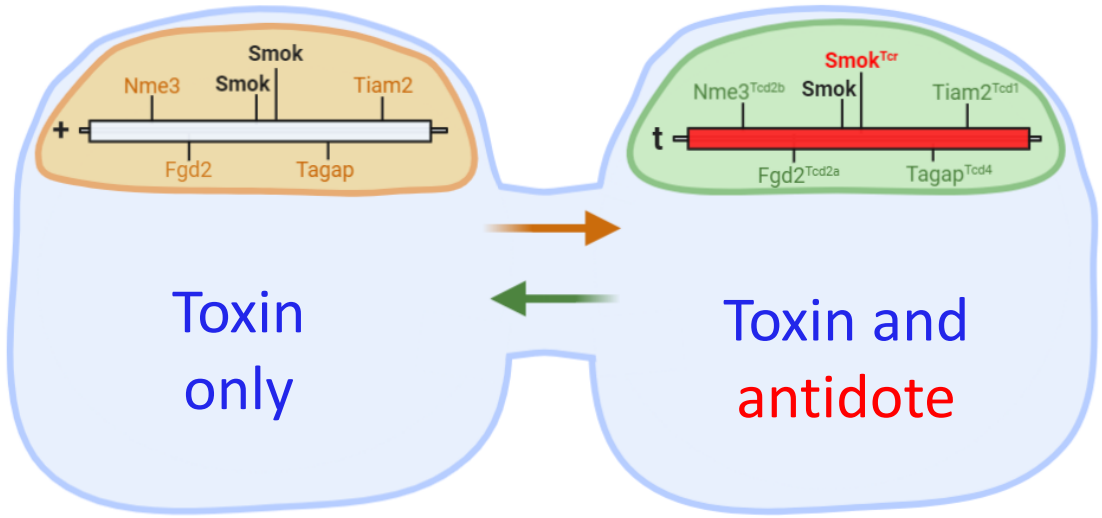


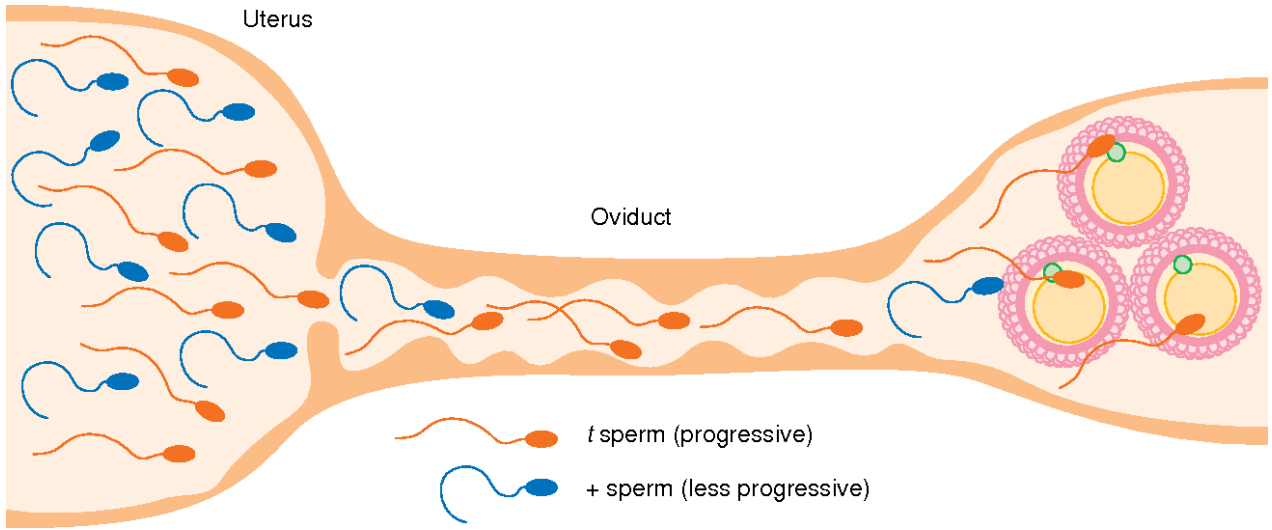


"homing drives" not efficient enough in mammals

The *t* haplotype – a natural gene drive in male mice

Developing sperm





Olds-Clarke et al 1997

Motility ☹ Motility ☺

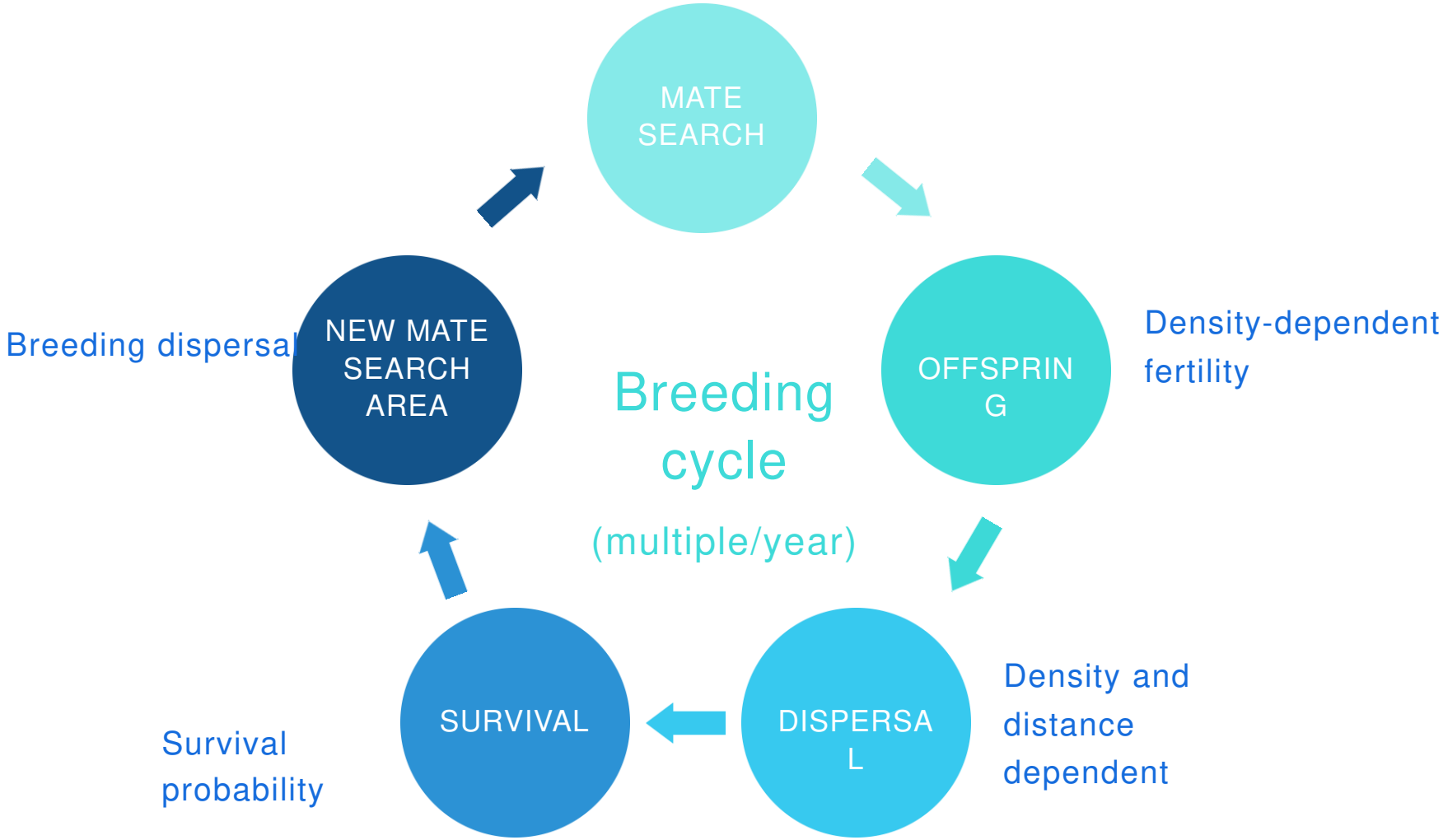
- Male heterozygotes pass on up to 95% (females 50%)
- Male homozygotes infertile (t^{w2})

Can we modify the *t* haplotype to create a suppression gene drive?

Model framework

Individual based,
spatially explicit,
stochastic

mate search distance (D)
polyandrous (sperm competition)
mate choice



Landscape

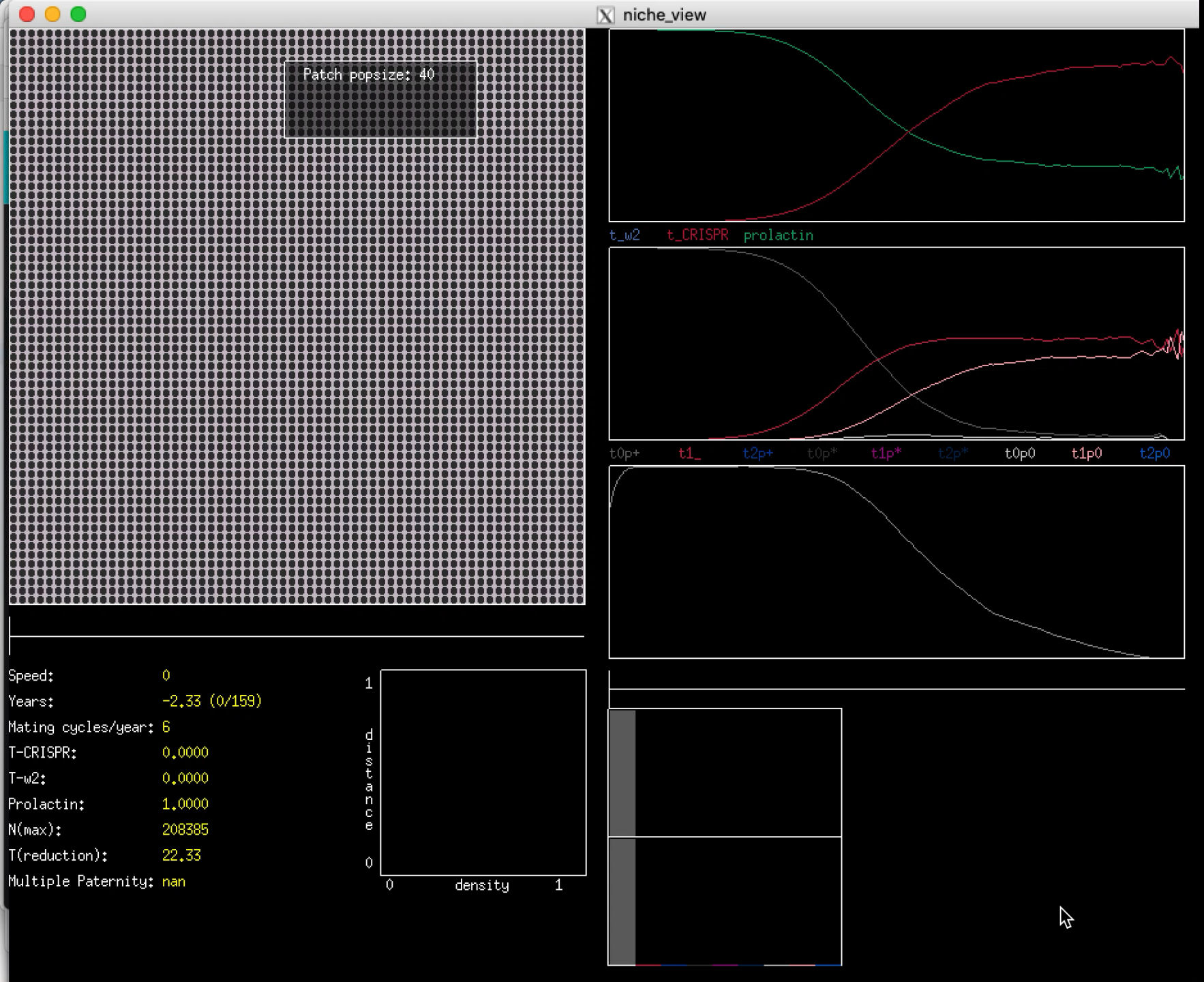
Array of patches
Individuals use multiple patches
N ~ 200,000

Individuals

Diploid
Discrete sexes (XX and XY)
Genetically controlled traits

Birand et al. 2022 Molecular Ecology 31:1907–1923.

Aysegul Birand



Stochastic individual-based modelling

Island population of 200,000 mice

Deploy 256 *t*-CRISPR mice (1/patch)

Proof of concept in lab mice

Aysegul Birand

Leveraging a natural murine meiotic drive to suppress invasive populations

Luke Gierus[a,b,1], Aysegul Birand[c,1], Mark D. Bunting[a,b], Gelshan I. Godahewa[b,d], Sandra G. Piltz[a,b], Kevin P. Oh[e,f], Antoinette J. Piaggio[g], David W. Threadgill[h], John Godwin[i], Owain Edwards[e,j], Phillip Cassey[c], Joshua V. Ross[k], Thomas A. A. Prowse[c] and Paul Q. Thomas[a,b,2]

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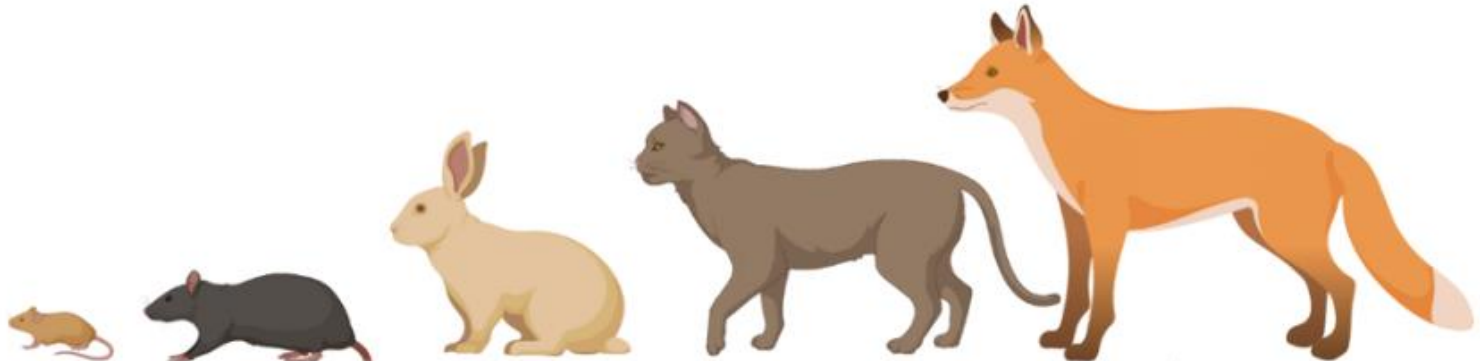
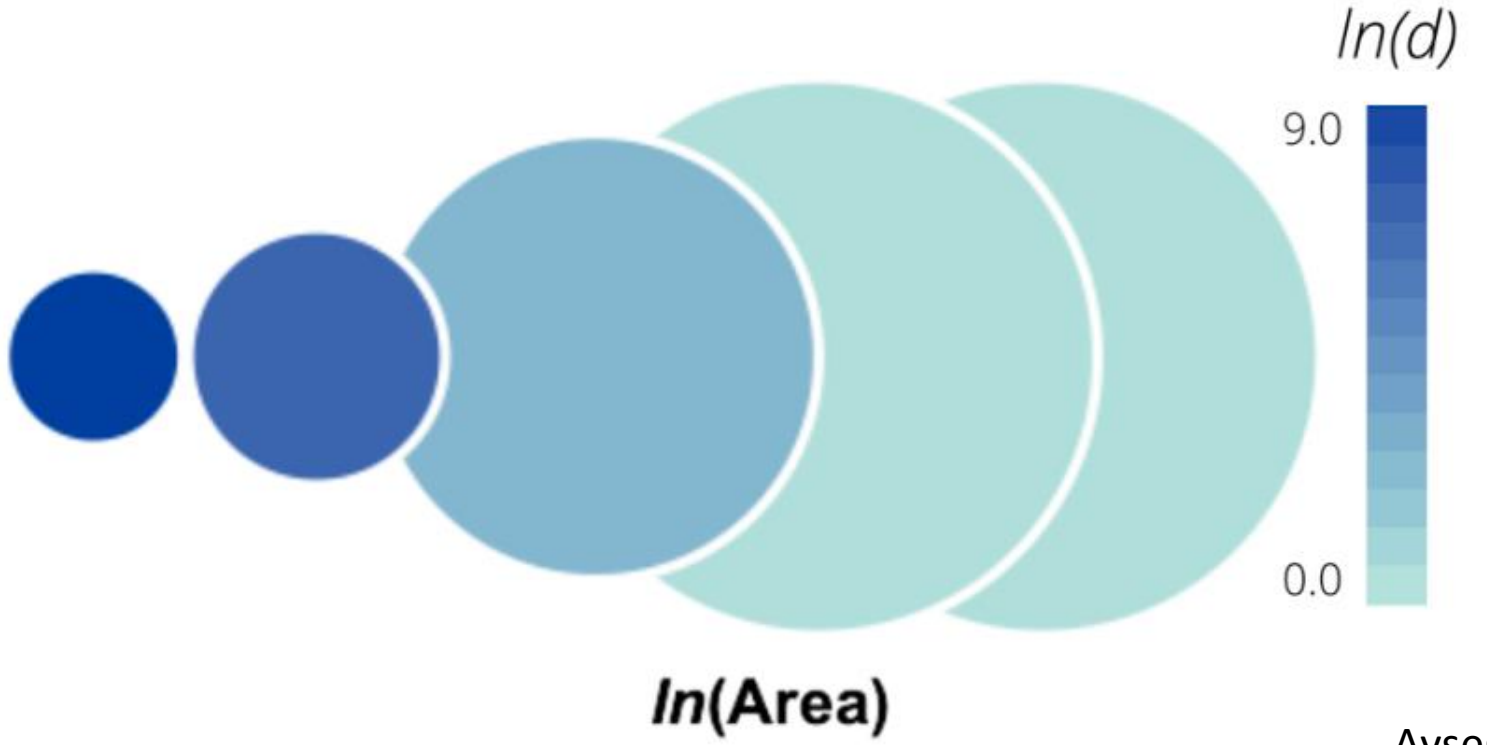
First proof of concept for a mammalian gene drive

What about cats (and other invasive pest mammals)?

What about other vertebrates?

N ~ 200,000





X-SHREDDER

Male biassing drive

HOMING

female infertility drive

Aysegul Birand

Life-history parameters

Survival probability

Probability of polyandry

Dispersal

Parameters:

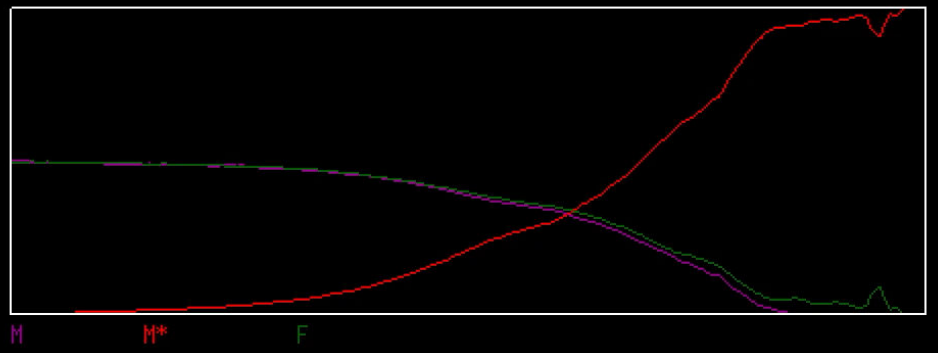
Species	b	n_c	age_m	ω	p_m	d	A	Δ_i	D
mouse	6	6	2	0.53	0.46	5000	40	0.4	3
black rat	4	6	2	0.62	0.68	1000	200	2	8
rabbit	4	4	3	0.82	0.20	25	8000	12.5	8
cat	4	2	5	0.85	0.25	2	100000	25	4
fox	4	2	5	0.88	0.76	2	100000	45	8

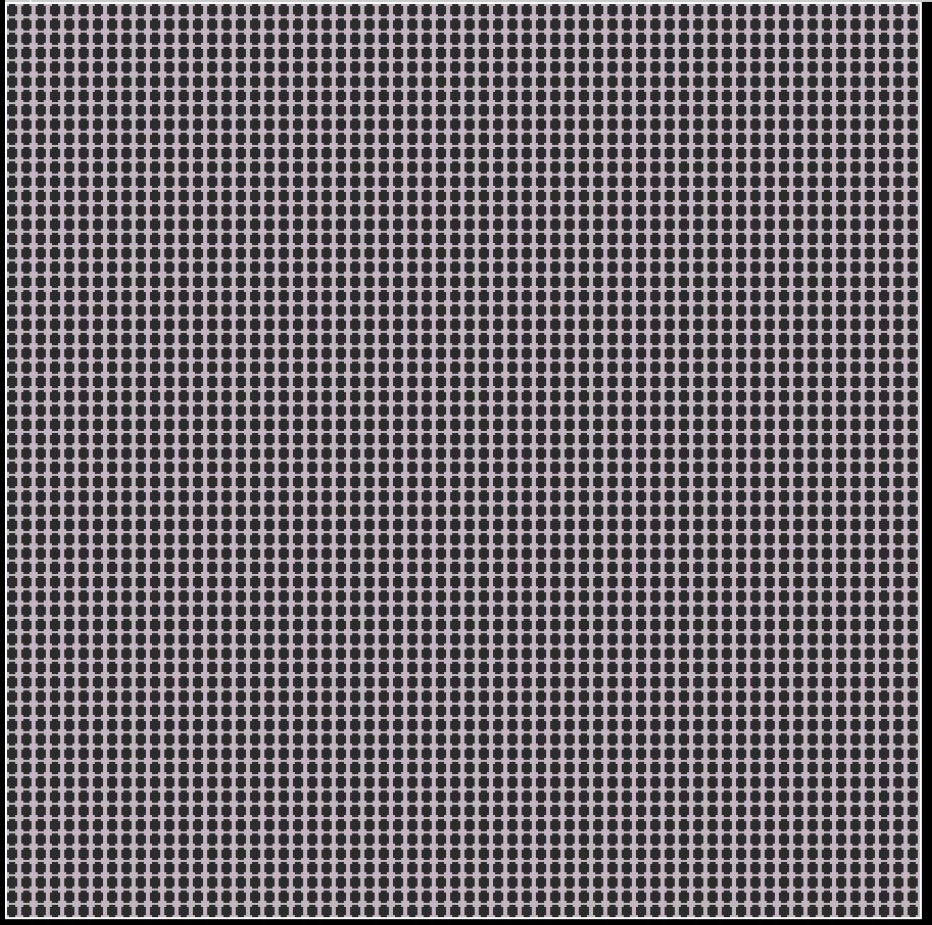
Aysegul Birand

Island population of 200,000 cats

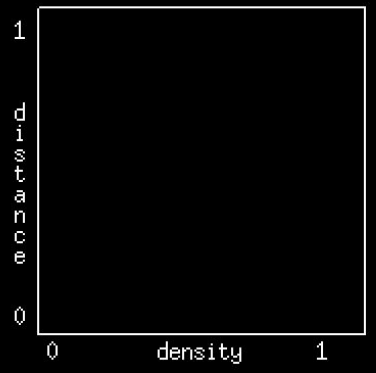
256 gene drive cats introduced

X-Shredder male biasing drive





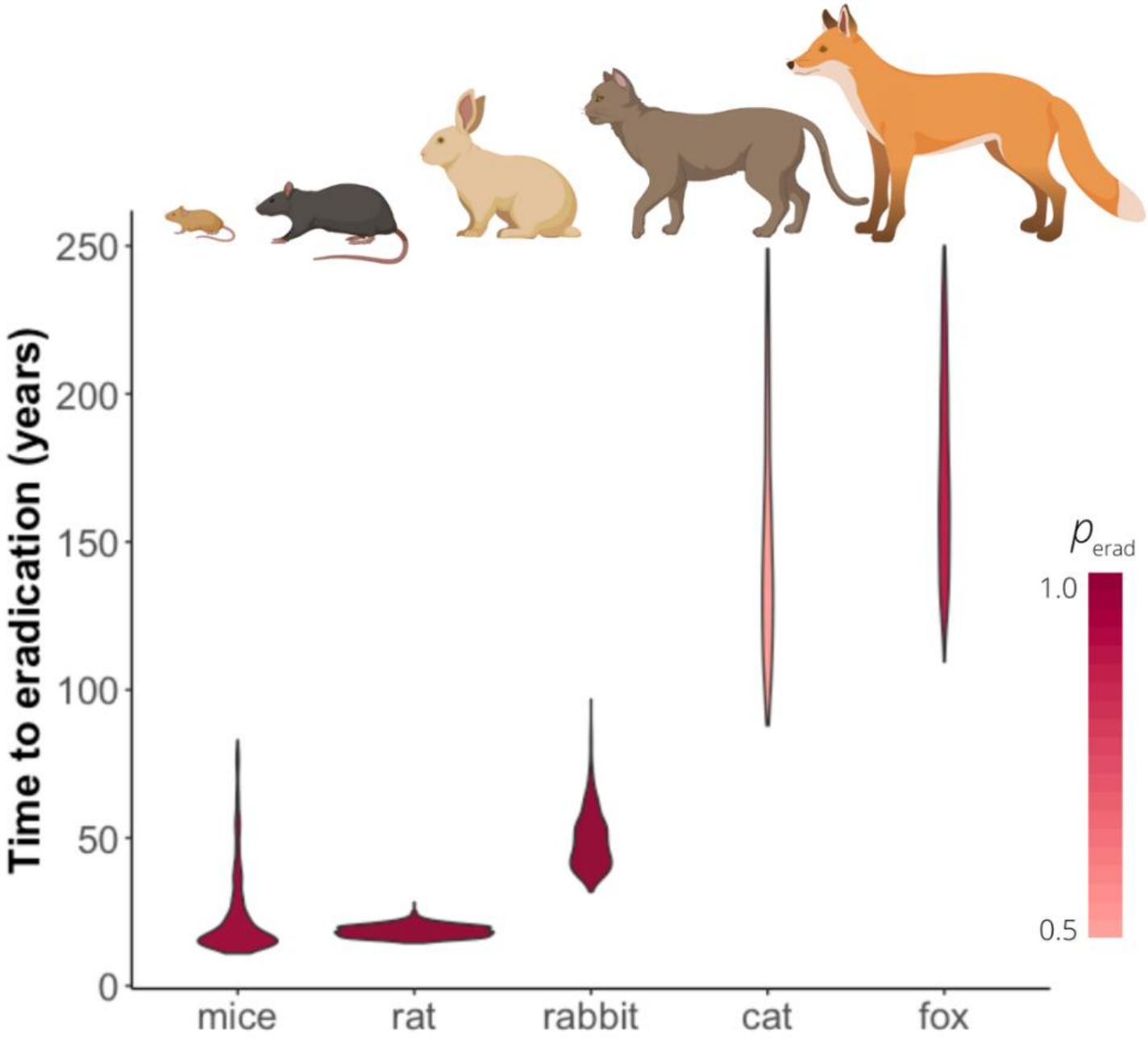
Speed: 0
Years: -7.00 (0/435)
Mating cycles/year: 2
Male: 81920
Male*: 0
Female: 81920
N/T/P(inoc): 1/1/256
N(max): 215466
T(reduction): 175.00
Multiple Paternity: nan



Eradication in ~200 years!

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)

Cat genetic biocontrol

-long timeframes

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

-domesticated non-model animal

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

Modelling informed by more accurate field data (CSIRO)

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THE UNIVERSITY of ADELAIDE

SAHMRI South Australian Health & Medical Research Institute

Thomas lab