

**Potential game changers: a spotlight on selected emerging technologies.**

**Gene drives and RNAi applications for rodent eradication.**



We can do this...

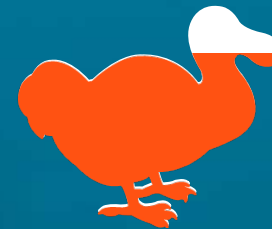
# Islands Represent



Less than 5% of land mass



40% of endangered species



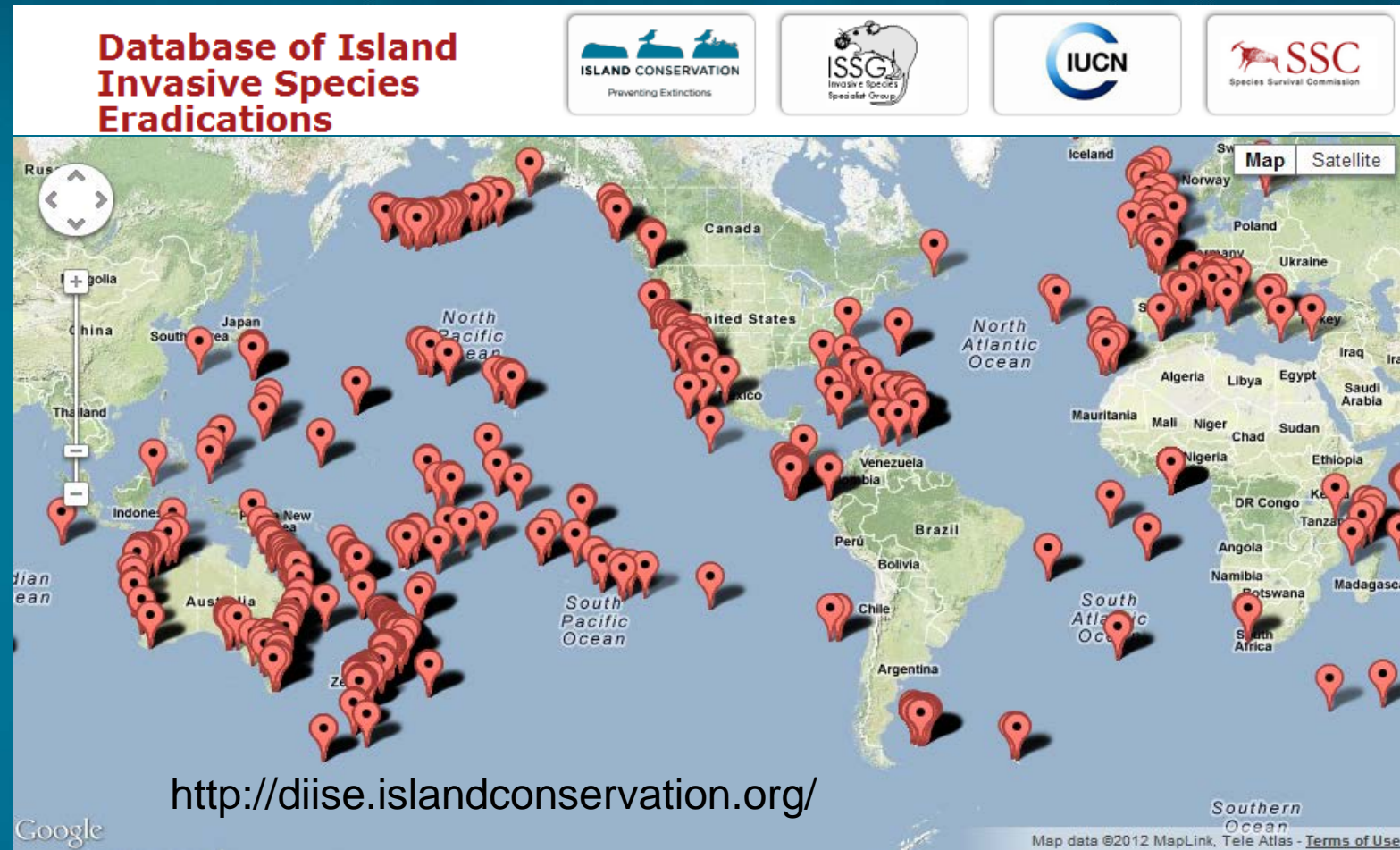
80% of extinctions since 1500

We can do this...

# Invasive alien mammal eradications

- 1100 successful
- Result in native species recovery

We can do this...



## Invasive mammal eradication on islands results in substantial conservation gains

Holly P. Jones<sup>a,b,1</sup>, Nick D. Holmes<sup>c</sup>, Stuart H. M. Butchart<sup>d</sup>, Bernie R. Tershy<sup>e</sup>, Peter J. Kappes<sup>f</sup>, Ilse Corkery<sup>g</sup>, Alfonso Aguirre-Muñoz<sup>h</sup>, Doug P. Armstrong<sup>i</sup>, Elsa Bonnaud<sup>j</sup>, Andrew A. Burbidge<sup>k</sup>, Karl Campbell<sup>c,l</sup>, Franck Courchamp<sup>j</sup>, Philip E. Cowan<sup>m</sup>, Richard J. Cuthbert<sup>n,o</sup>, Steve Ebbert<sup>p</sup>, Piero Genovesi<sup>q,r</sup>, Gregg R. Howald<sup>c</sup>, Bradford S. Keitt<sup>c</sup>, Stephen W. Kress<sup>s</sup>, Colin M. Miskelly<sup>t</sup>, Steffen Oppel<sup>n</sup>, Sally Poncet<sup>u</sup>, Mark J. Rauzon<sup>v</sup>, Gérard Rocamora<sup>w,x</sup>, James C. Russell<sup>y,z</sup>, Araceli Samaniego-Herrera<sup>h</sup>, Philip J. Seddon<sup>aa</sup>, Dena R. Spatz<sup>c,e</sup>, David R. Towns<sup>bb,cc</sup>, and Donald A. Croll<sup>e</sup>





ISLAND CONSERVATION



**Pinzon Giant Tortoise**

**Pinzon Island, Galapagos**

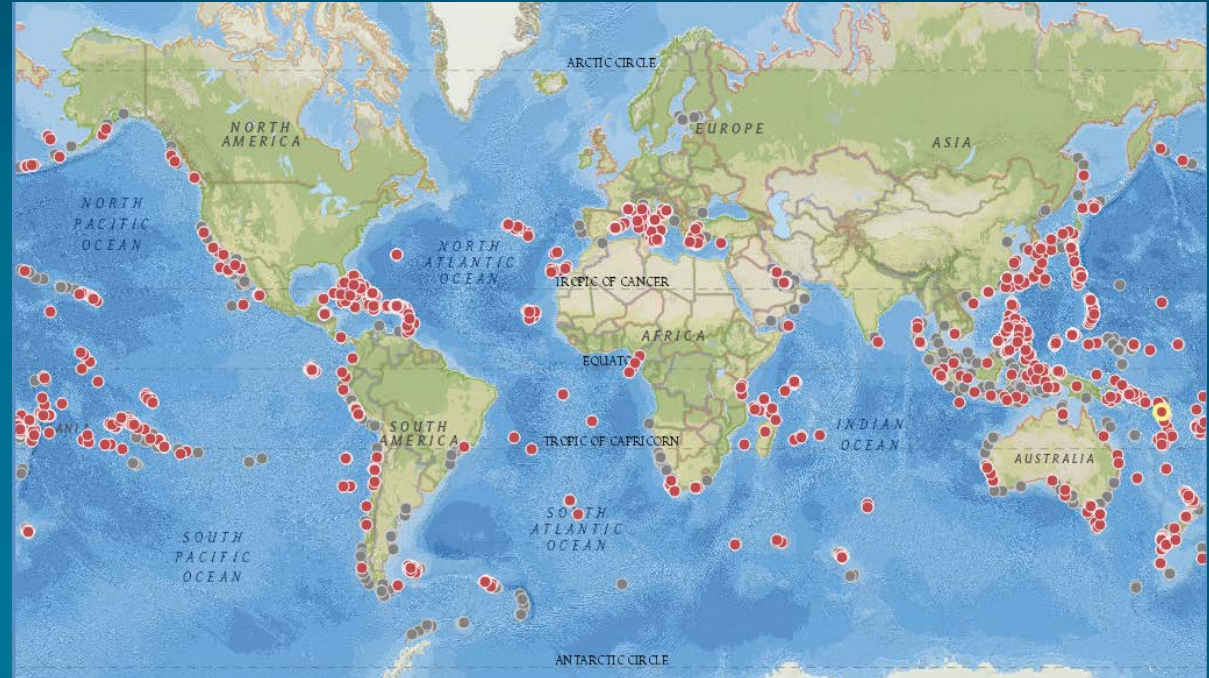
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**Four spp. invasive rodents  
impact 88% of CR/EN  
vertebrate spp. on islands**

**Current methods feasible  
for islands holding 15% of  
those CR/EN spp.**

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<http://tib.islandconservation.org>





# Innovation Strategy

Identify point of greatest impact

- Invasive rodents

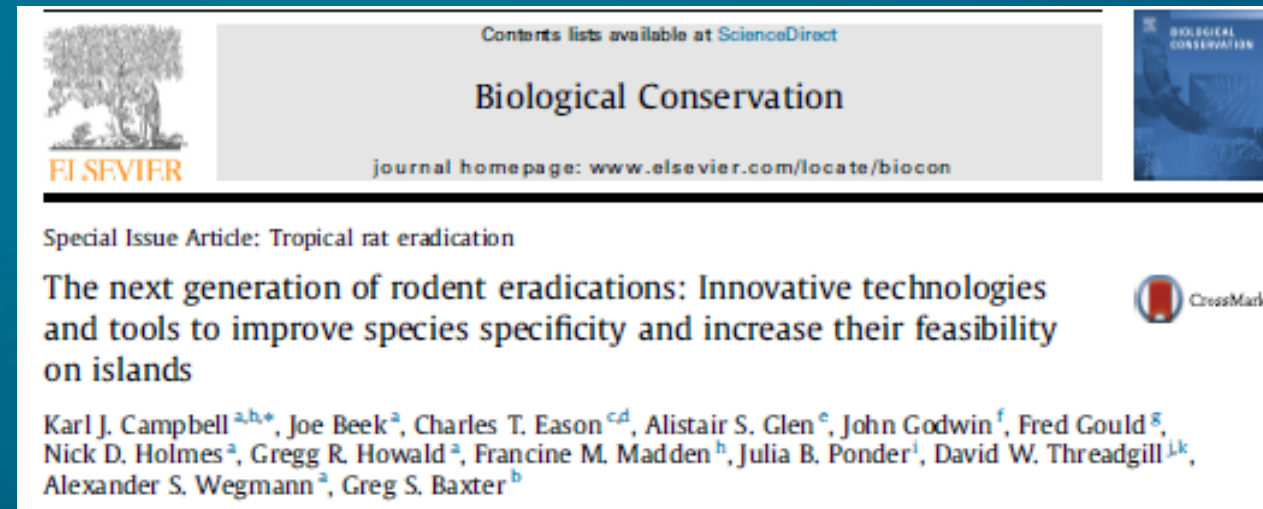
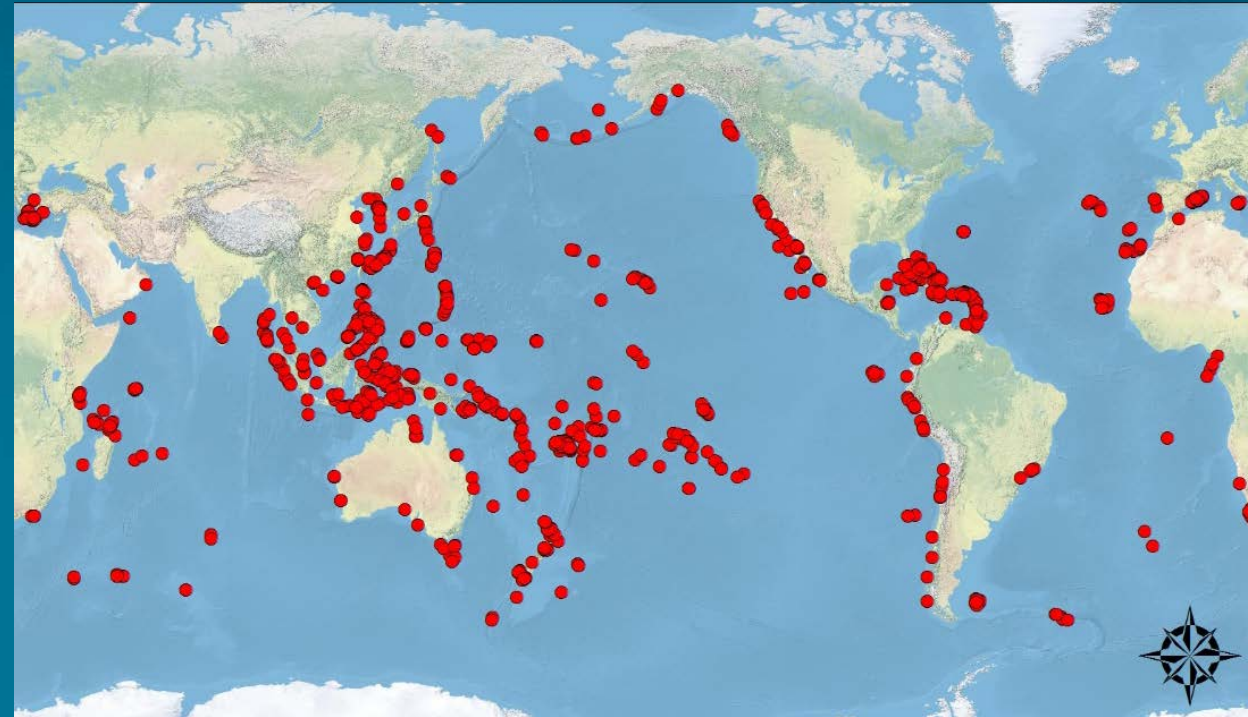
Match technology to the need

- Horizon scanning

Select investments

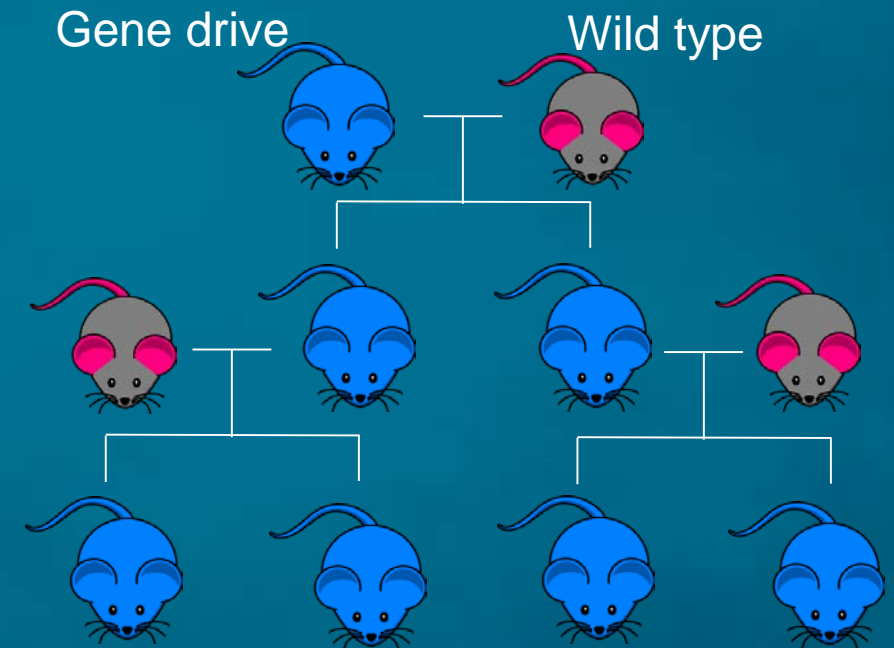
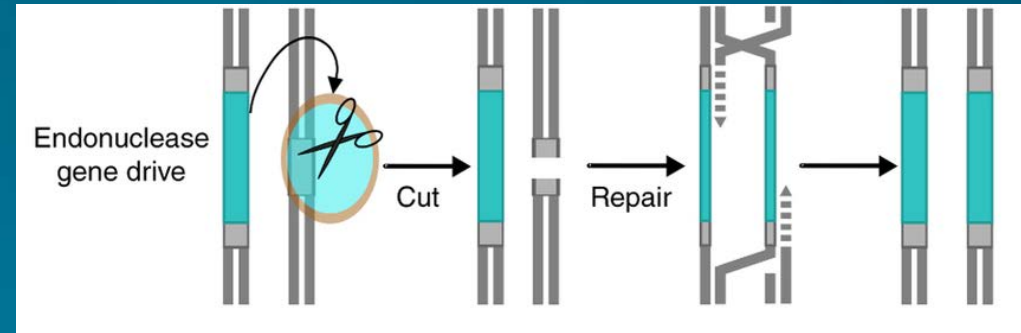
- Incremental
- Transformative

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# Gene drives

- Cause genes to be inherited more frequently than normal – up to 100%
- Sexual reproduction
- Ability to modify wild populations *by design*
  - Insert new, modify or delete genes
- CRISPR-Cas9

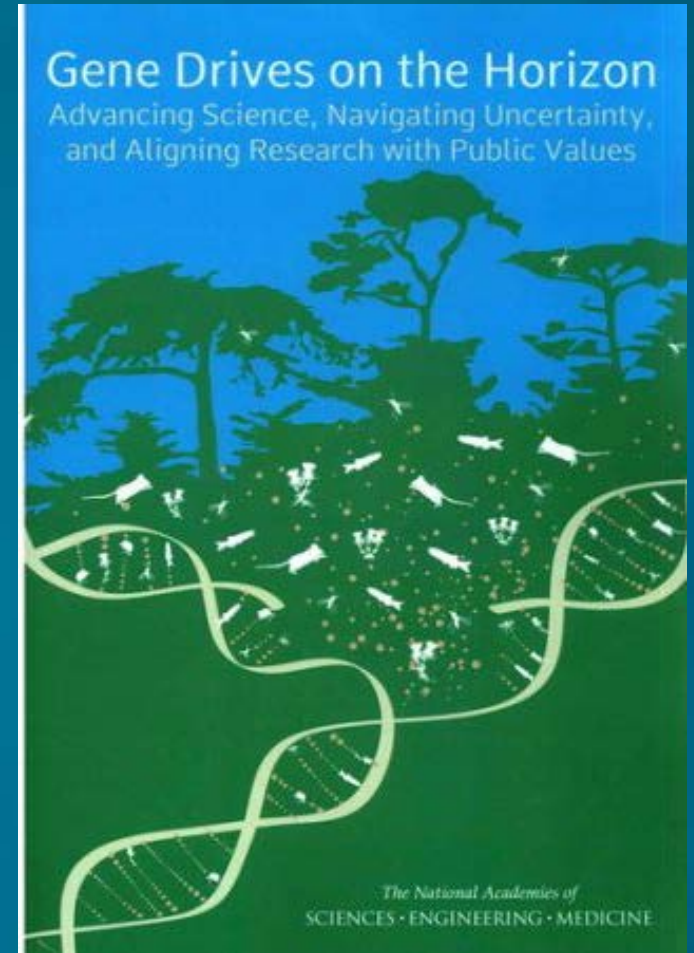


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# Gene drives

- Cause genes to be inherited more frequently than normal – up to 100%
- Sexual reproduction
- Ability to modify wild populations *by design*
  - Insert new, modify or delete genes
- CRISPR-Cas9
- Nascent fast-moving field
  - Pre-caution & phased approaches needed

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NASEM 2016; Kaebnick et al. 2016



# Genetic Biocontrol of Invasive Rodents program

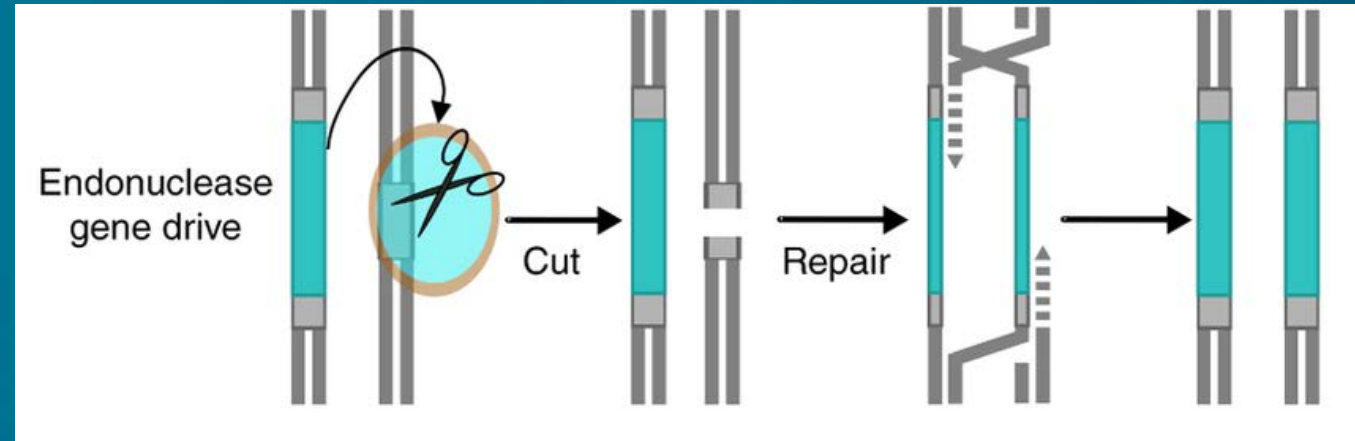
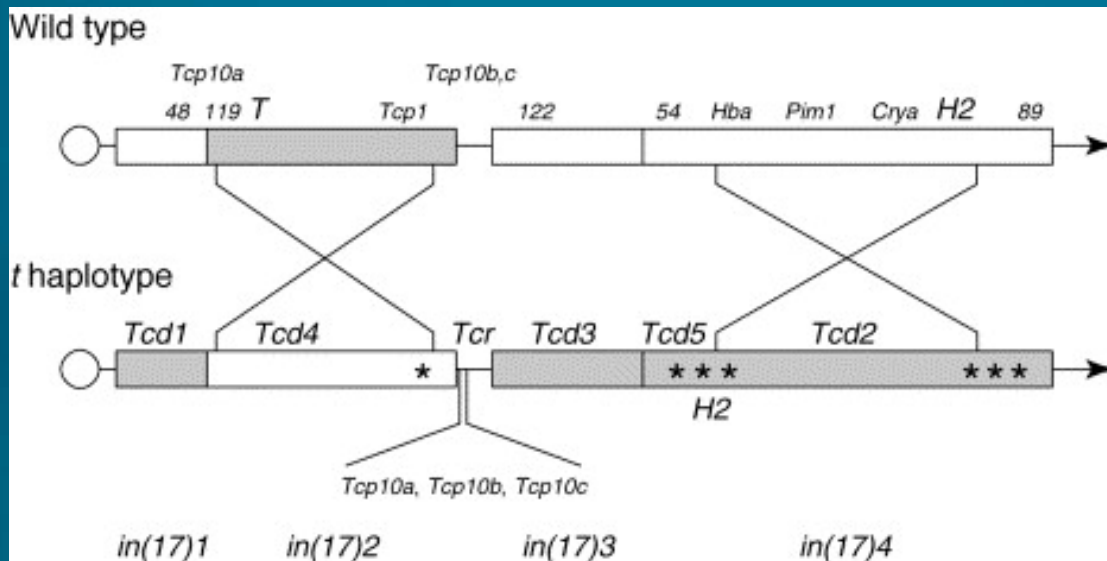


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# Gene Drive

T-Complex – natural

CRISPR/Cas9 - synthetic



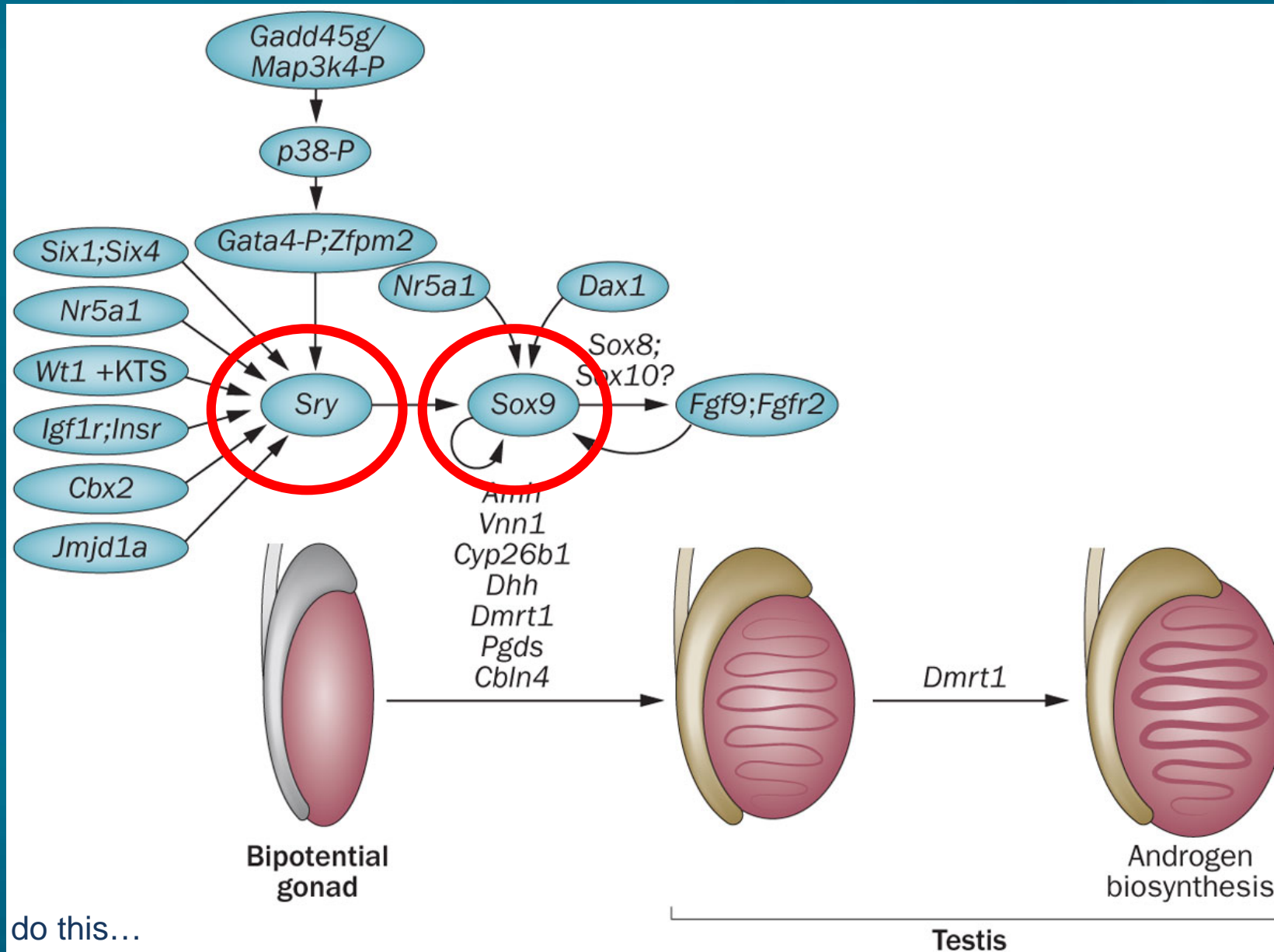
92%  $n = 691$



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of ADELAIDE

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# Mammalian Sex Determination



Bias sex ratio:

- Sry
- Sox9

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Eggers et al. 2014



# Genetic Biocontrol of Invasive Rodents

- *T-Complex/Sry*
- *CRISPR-Cas9/Sox9*
- Control mechanisms
- Risk assessment
- Mathematical models
- Breeding behavior
- Biocontainment
- Communications
- Island selection
- Genetic characterization of mouse populations & monitoring
- Regulatory (multi-national)
- Stakeholder/comm/public engagement
- Intellectual property
- Funding
- Program management
- Governance
  - Ethics committee
  - Advisory committee

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# Leverage biology

- Population ~1000 house mice
- Released 42 male & 35 female mice from Eday Island
- After 18 months, all mice trapped were hybrids (n=70)
- Males were disproportionately responsible for 'invasion'
- Leverage biology and promiscuity

Isle of May (57ha)



# RNA interference (RNAi)

## Ribonucleic acid (RNA)

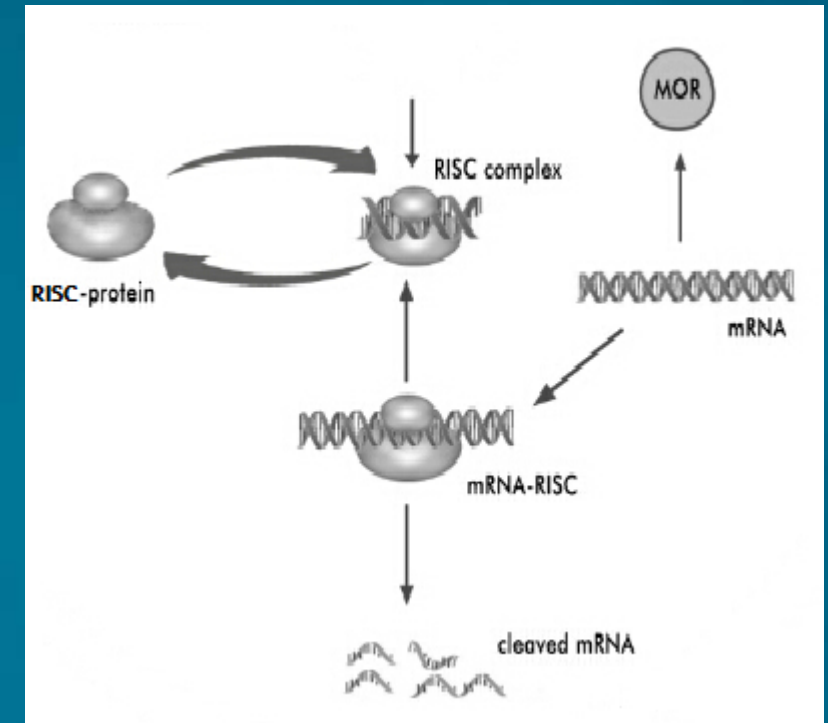
- Normally single stranded

## Double-stranded RNA

- Elicits immune response
  - Double-stranded RNA and matching single-stranded RNA destroyed

## Focus of a significant body of research:

- Invertebrate pest control
- Animal models (e.g. mice) as a potential cure for cancer and other diseases





# RNA interference (RNAi)

Double-stranded RNA can be synthesized chemically

- Use as taxa-specific bio-pesticides

Can be synthesized biologically (species can produce it)

- Plants & animals can be vectors

Vertebrates digest RNA

- Nanoparticles as carriers



# Gene drives & RNAi: Power-tools in the tool box?

Cautious investigation of opportunities  
required

Big picture

- Reduce risks
- Increase impact

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