ERADICATING INVASIVE RODENTS FROM ISLANDS: AN ASSESSMENT OF CURRENT AND FUTURE GENE DRIVE TECHNOLOGIES

Caroline Leitschuh, Dona Kanavy, Gregory Backus, David Threadgill, John Godwin

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Roadmap to Gene Drives: A Deliberative Workshop to Develop Frameworks for Research and Governance

PRESENTATION SUMMARY

Introduction

The Problem of Invasive Rodents

Current Invasive Rodent Control Technology

Gene Drive Technology for Invasive Rodent Control

- Options
- Ecological Factors
- Modeling
- Social and Ethical Questions

WHO AM I?

NCSU Doctoral Student

- PI John Godwin

GES Center

GES Cohort

- Gregory Backus, Dona Kanavy, Elizabeth Pitts, Megan Serr, Rene Valdez
- Rodents (mice) on Islands a focus
- https://research.ncsu.edu/islandmice

INTRODUCTION

Islands are 5% of Earth's landmass, but contain 20% of terrestrial animal species

Island ecosystems more vulnerable than mainland to invasive species

80% of 100,000+ islands have invasive rodents

- Known cause for 60+ vertebrates species

Current eradication methods limited, not always effective, difficult to use with human inhabitation

DIRECT THREATS OF RATS

Rattus rattus, Rattus norvegicus, Rattus exulans

Introduced by humans

- Cultural importance, deliberate introduction
- Accidental introduction

Omnivorous, eat native plants and animals

- Direct population reduction (Lord Howe Island)
- Reproductive cycle interruption (eg. eating plant seeds)

Human disease and agriculture impacts

DIRECT THREATS OF MICE

Mus musculus

Accidental human introduction

Similar ecological effects to rats

- Different behavior, more difficult to eradicate using current methods

Gough Island

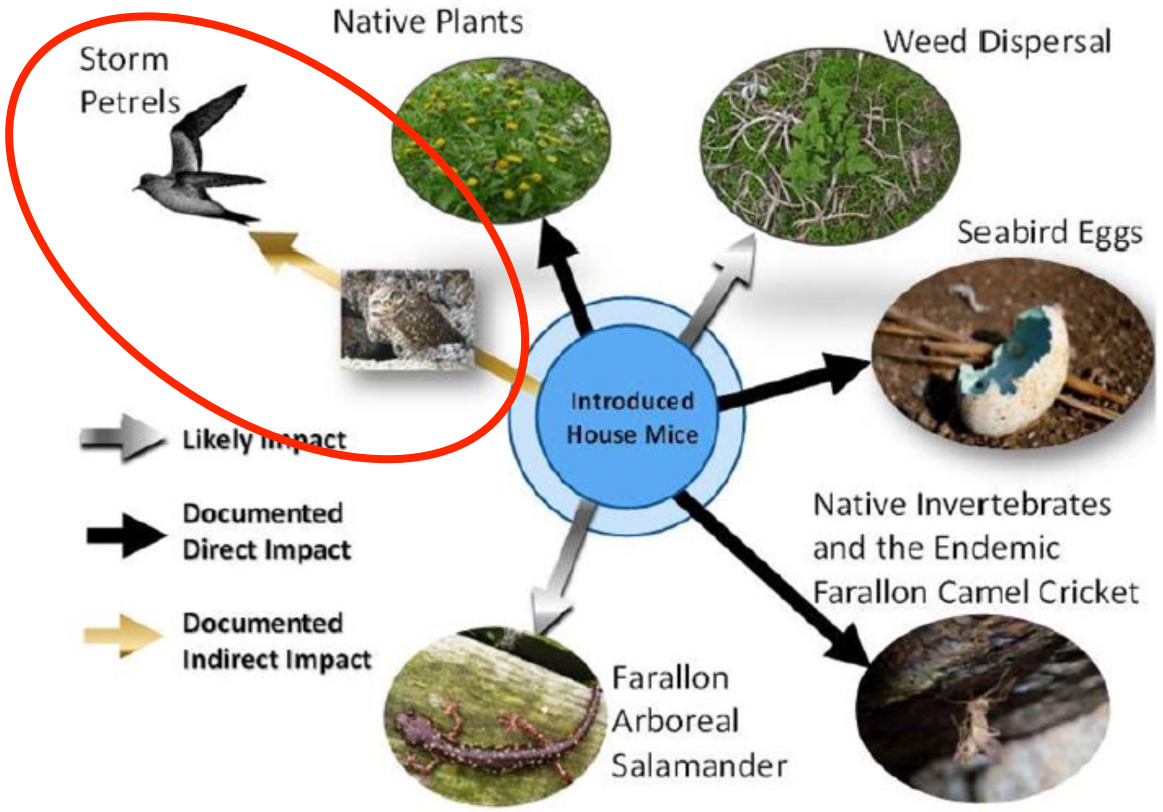
Human disease and agriculture impacts

INDIRECT RODENT THREATS

When both are present, rats suppress mouse populations

- Competitor release effect

Predator attraction



CURRENT ERADICATION METHOD

Toxicants only effective method

- Anticoagulants – brodifacoum most popular
- 5-10% failure for rats
- Up to 40% failure for mice

TOXICANT CONCERNS AND LIMITATIONS

Expensive

One chance to work

Difficult to assess immediate effects

- No long-term protection

Non-target species impact

- Rat Island

Threat to humans, livestock

Animal welfare concerns

GENE DRIVE OPTIONS FOR RODENT CONTROL

Not been applied in mammals yet

Farallon Islands EIA

Options limited

- Needs to be robust to be effective in the field

t-haplotype/*Sry*

- Currently being researched

CRISPR

NATURAL MEIOTIC DRIVE

t-haplotype: **Naturally** occurring genetic element with meiotic drive in wild house mice

- Impairs sperm without t-haplotype

t^{w2} variant has over 90% transmission rate

- No lethality

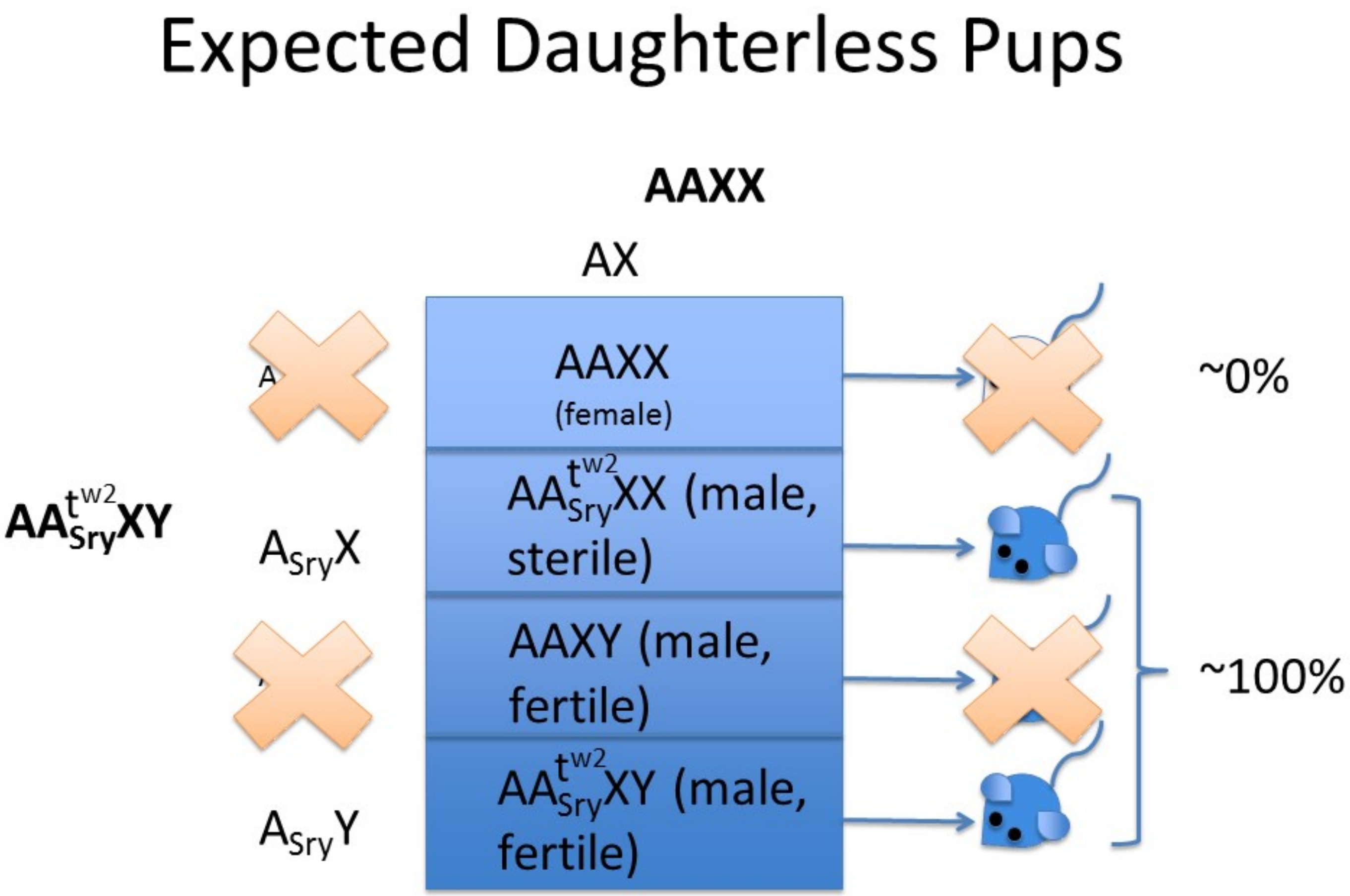
MALE DEVELOPMENT IN MICE

Sry gene: male-determining gene

- Found on Y-chromosome
- When moved to a non-sex chromosome, all offspring externally male

CREATING A MALE-BIASED POPULATION

Use t-haplotype to drive *Sry* gene into invasive mouse population



CONTAINMENT AND REVERSAL

Naturally occurring: t-haplotype cannot be contained

Inducible system

Fitness reduction – mice not as competitive

Release only on islands

Introduce wild type mice back into system

ECOLOGICAL FACTORS

Can engineered rodents survive in wild conditions?

- Background
- Fitness reduction
- Current research

Multiple releases necessary to drive gene into population

- Selection against construct

MATHEMATICAL MODELING

How many mice need to be released?

What happens to other species when mice are added or removed?

Planning when to release GE mice

What happens if a GE mouse were to escape?

CRISPR/CAS9

Clustered regularly-interspaced short palindromic repeats

Can be used for gene editing – used to insert material or silence genes

Can be used for gene drive

- Insert sequence for self-replication

CRISPR AS A MECHANISM FOR GENE DRIVE

Not naturally occurring in rodents

Applicable to other species

Use to insert *Sry* into autosome

Gene knockout

- *Foxl2* key in sex differentiation – knockout causes testes development

CONTAINMENT AND REVERSAL

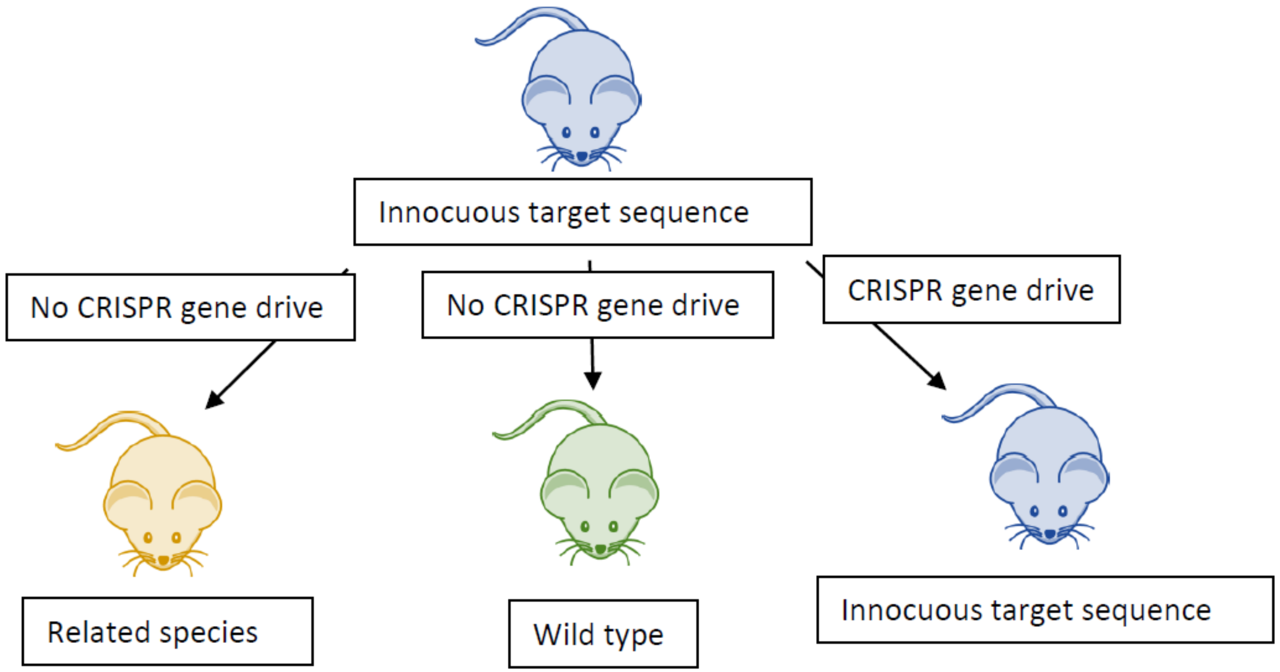
Target species-specific location in genome (synthetic drive)

- Insert innocuous target sequence

Regulated system

Introduce wild-type males and females

- Reversal drive



ECOLOGICAL FACTORS

Artificial genetic construct

- Not naturally occurring in rodents

Lower reduction in fitness?

Multiple releases necessary to drive gene into population

- Selection against construct

MATHEMATICAL MODELING

How quickly can a CRISPR system spread?

How easily can it be reversed?

Is global suppression or extinction a risk?

SOCIAL AND ETHICAL IMPLICATIONS

Using gene drive on islands with humans

- Cultural differences

Cis vs Trans

Human benefits

- Agriculture
- Disease

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U.S. FISH & WILDLIFE SERVICE

DEPARTMENT OF THE INTERIOR

prbo

PRBO Conservation Science

NSF

TEXAS A&M UNIVERSITY

RESEARCH UPDATES

Developing the *Sry* mouse

Mouse behavior

- Reproductive differences between wild and lab mice
- Differences in reactions to new environments

Mathematical modeling to understand the ecological consequences of eradicating invasive mice using gene drive techniques and the potential for the evolution of resistance to these techniques

Examining international differences in public media communication of rodent control efforts

Examining communication, governance, and organizational structure of new technologies