Preventing Tick-Borne Disease

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The Proposal

To prevent most human cases of tick-borne disease by heritably immunizing the local white-footed mice that infect most ticks.

Controlled releases of resistant mice would introduce immunity to most or all of the native mouse population.

Released mice would be genetically altered, but 100% mouse

Some of the Vineyard’s white-footed mice naturally express antibodies against the Lyme-causing spirochete; this would ensure that all of them do from birth.
Open, Community-Driven Science

- Clear benefits to citizens
- Discussions before experiments
- Safeguards agreed upon early
- Developed/run as a nonprofit
- Independent monitoring and analysis
- Open and responsive science

This project will only move forward if embraced by the community. It could supplement, not replace, existing control efforts.
Thoughtful,Measured Approach

Guiding principles:

• Rule 1: Make the smallest possible change capable of solving the problem
• Rule 2: Start local and only scale up if warranted

• The Steering Committee must secure federal, state and local approval
• All efforts will be guided and monitored by local and national ecologists
• Trials will be sequential: uninhabited islands first, then inhabited

Changes are **not** anticipated to spread beyond the island. **No gene drive!**
Tick-borne disease is an ecological problem

The spirochetes that cause Lyme disease persist by moving between mice and ticks
Tick-borne disease is an ecological problem

Ticks pass the spirochetes to humans, causing Lyme disease
Tick-borne disease is an ecological problem

What if white-footed mice could not become infected?
Breaking the Cycle

If *every mouse* produced antibodies conferring effective immunity from birth, the reservoir of *B. burgdorferi* would likely collapse.

No infected mice ➞ No infected ticks ➞ No infected people

**Important note:**
Some ticks could become infected from residual secondary reservoirs, but the rate should be *far* lower than today.
Relevant study #1

By-hand vaccination reduced *Borrelia* prevalence by
- 42% in mice
- 25% in ticks

This study did not control for unvaccinated mice migrating into the area.
Relevant study #2

An oral bait-delivered vaccine reduced tick infection rates by
• 25% when deployed for 2 years
• 76% when deployed for 5 years

This study did not control for unvaccinated mice migrating into the area.

The increase in mouse antibody levels was barely statistically significant.

The study had serious issues with proper controls, suggesting high site variability.
Our proposal: prevent the vast majority of human infections by *heritably* immunizing the mice

- Immunize mice against Lyme
  - Should not impact other species, but would not prevent other tick-borne diseases

- Immunize mice against ticks
  - Should prevent Lyme, babesiosis, anaplasmosis, ehrlichiosis, Powassan
  - Will also reduce the tick population
Heritable Ecological Vaccination

White-footed mice
Timeline

Build heritably immune mice

~2 years to engineer immune mice

~2-3 years to generate enough mice for a small island

Release on an uninhabited island

~2-3 years to evaluate effects and raise enough mice for a large island

Release on an inhabited island
Implementation on Martha’s Vineyard

• Release up to 100,000 resistant mice in early spring

• Introduced mice would increase the local mouse population to at most 300% of ‘normal’

• For context, mouse populations often fluctuate by >800% over the course of a year
Proposed Decision Points

1st Evaluation Point: After immune mice have been created in our lab
- Project go/no go recommendation by DSMB
  • Regulatory approval for next phase
  • Approval by decision-makers for uninhabited island(s)

2nd Evaluation Point: After uninhabited island field trial
- Project go/no go recommendation by DSMB
- If go, project must secure ...
  • Regulatory approval for next phase
  • Warrants proposed by the Boards of Health at Town Meetings
  • Warrants approved at Town Meetings
Project Management

**Steering Committee**
- 7-9 members
- Board of Health appointed

**Data Safety Monitoring Board**
- Independent of the Steering Committee, MIT, funding agencies or representative communities

**Project Manager**
- Joanna Buchthal
- Reports to the Steering Committee
Current Research & Ethics Team

**Key Collaborators**

Dr. Sam Telford  
Dr. Linden Hu  
Dr. Kevin Esvelt  
Dr. Jeantine Lunshof

**Research Team**

Dr. Ryan Kelly  
Dr. Aurelie Kern  
John Min  
Devora Najjar  
Joanna Buchthal
Funding

Laboratory Research
• MIT Media Lab
• Recommended for funding: Tick-Borne Disease Research award
• Rainwater Foundation

Field Trials
• Philanthropic funding

All project finances will be transparent
Project Status

Local Presentations
• Jun 2016: Nantucket Board of Health meeting
• Jul 2016: Martha’s Vineyard health agents meeting
• Jul 2016: Edgartown Library presentation with Professor Sam Telford and Dr. Michael Jacobs
• Oct 2016: Martha’s Vineyard All-island Board of Health meeting
• Jan 2017: Nantucket Board of Health and community meeting
• Mar 2017: Edgartown Board of Health

Project Management
• Jul 2016: Nantucket BOH agrees to jointly develop project management plan
• Dec 2016: Nantucket begins appointing Steering Committee members
• Mar 2017: 5/6 MV towns have agreed to send nominees to the Steering Committee

Project Milestones
• Our collaborators have finished vaccinating white-footed mice
• Dovetail Genomics has assembled the first white-footed mouse genome
• Initiated antibody library creation
Local, Open, Community-Responsive Science

- Focus on the most urgent needs
- Openly share proposals before experiments begin
- Actively invite concerns
- Request community guidance
- Arrange for independent assessment
- Nonprofit
- Start local and scale up

Esvelt KM (2016) Nature
Esvelt KM (2017) Science
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Questions?
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