Preventing Tick-Borne Disease

Joanna Buchthal & John Min
Whitehead Institute’s 2017-2018 Seminar Series for High School Teachers
Growing risk of tick-borne disease

Reported Cases of Lyme Disease in 2014

Centers for Disease Control and Prevention

Incidence Rates (per 100,000 population*) for Confirmed and Probable Lyme Disease in Massachusetts 2010-2014*

MA Special Commission Report
Tick-borne Disease is an ecological problem

The pathogens that cause Lyme and other diseases persist by moving between mice and ticks
Breaking the cycle

If *every mouse* produced antibodies conferring effective immunity from birth, the main reservoir of tick-borne pathogens would likely collapse.

No infected mice ➔ Few infected ticks ➔ Few infected people

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

To stably reduce the incidence of tick-borne disease by breaking the transmission cycle between white-footed mice (the primary reservoir) and 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

A percentage of the Nantucket’s white-footed mice naturally express antibodies against the Lyme-causing spirochete Borrelia burgdorferi
Two types of antibodies

**Anti-Lyme Antibody**

Protects mice from the Lyme spirochete only

Antibody target: *OspA*

*an outer surface protein on Borrelia burgdorferi*

**Anti-tick Antibody**

Protects mice from *all* pathogens carried by black-legged ticks

Antibody target: *subolesin*,

*a tick salivary protein*
How to make mice heritably Lyme resistant

**Step 1:** Inject white-footed mice with surface markers from *B. burgdorferi*

**Step 2:** Isolate B cells with antibodies that target the pathogen

**Step 3:** Sequence DNA from B cells

**Step 4:** Identify anti-Lyme antibody gene sequences

**Step 5:** Integrate antibodies into the mouse genome using CRISPR

*No gene drive!*
Timeline

Build heritably immune mice

~2 years to engineer immune mice

~2 years to generate enough mice for a small island

Release on an uninhabited island

Release on an inhabited island

2+ years to evaluate effects and raise enough mice for a large island
Implementation

Release immune mice in early spring

• Introduced mice would at most double the local mouse population for that time of year

• For context, mouse populations often fluctuate by >400% over the course of a year

• Bait stations could be used to reduce populations near commercial and residential areas

Local reductions will not impact the spread of resistance
Technical team

Dr. Kevin Esvelt  
MIT

Dr. Sam Telford  
Tufts

Dr. Duane Wesemann  
Harvard

Dr. Linden Hu  
Tufts

Dr. Teng Zuo  
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Dr. Neha Chaudhary  
Harvard

Dr. Jeantine Lunshof  
MIT/Harvard

Joanna Buchthal  
MIT

John Min  
MIT/Harvard

Plus: Dr. Tom Watson (Arc Bio) and Dr. Tanja Petnicki-Ocieja (Tufts)
Community-guided science

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 meeting
- Mar 2017: Edgartown Board of Health meeting
- May 2017: Aquinnah Board of Health meeting
- May 2017: Presentation at Martha’s Vineyard Regional High School
- August 2017: Nantucket Board of Health meeting
- Dec 2017: Steering Committee meeting on Martha’s Vineyard

Project Management Structure

- **Local Steering Committees**
  - Separate committees on Nantucket & MV, each with 6 BOH appointed representatives

- **Data Safety Monitoring Board**
  - Independent committee of national and local experts

- **Project Manager**
  - Reports to both Steering Committees
Responsive Science is a way of conducting research that invites openness and community involvement from the earliest stages of each project. Real-time interaction between scientists, citizens, and broader communities allows questions and concerns to be identified before experiments are performed, fosters open discussion, and encourages research studies and new technologies to be redesigned in response to societal feedback.