Heritably immunizing white-footed mice against tick-borne disease

Lay Abstract

At an estimated 300,000 cases per year, the Centers for Disease Control and Prevention ranks Lyme disease as the most commonly reported vector-borne illness in the United States. Unfortunately, Lyme is only the most common of a long list of tick-borne diseases, many posing more serious potential health risks and no near-term – let alone permanent – solutions. In the Northeast and upper Midwest, the risk of tick-borne disease has grown as a result of environmental changes that increased the number of white-footed mice, the primary reservoir of tick-borne pathogens, and black-legged ticks. Few areas are as afflicted as the islands of Martha’s Vineyard and Nantucket. Between 2010 and 2014, the town of Chilmark in Martha’s Vineyard and the island of Nantucket had the highest proportion of confirmed and probable Lyme disease cases in Massachusetts[4]. Our research project aims to reduce the incidence of tick-borne disease with a highly innovative solution that could safeguard these communities and one day prevent new cases across the United States.

In the Northeast, deer ticks typically become infected with the pathogens that cause Lyme disease when they feed on infected white-footed mice[1]. We propose to permanently break the ecological transmission cycle between white-footed mice and ticks in order to dramatically reduce the number of infected ticks and consequently prevent new human infections. In so doing, our project is directly relevant to the FY16 TBDRP Focus Area of Prevention.

Previous research has demonstrated that vaccinating even a fraction of a wild mouse population against Lyme disease can significantly reduce the number of infected ticks, even if immunity is weak[1, 2]. The aim of our Idea Award is to heritably alter white-footed mice to be immune to tick-borne disease. We plan to endow mice with naturally occurring mouse antibodies derived from the native mouse population. By inserting multiple copies of antibody-encoding genes into the genomes of mouse reproductive cells, we can ensure that immunity is passed on to subsequent generations. Releasing these resistant mice in large numbers would introduce inherited immunity to most of the native mouse population, interrupt the natural cycle of transmission and reduce the risk of tick-borne disease for many decades without any further intervention.

Pending approval by federal, state and local regulatory agencies, all of whom have already been consulted, we propose releasing large numbers of immune mice on a small uninhabited island. If our approach is deemed safe and effective by an independent safety monitoring board and broadly supported by the citizens of Nantucket and/or Martha’s Vineyard, we would follow a similar release schedule on these islands perhaps seven years after the project’s start. Since mice reproduce every 2.5 months, our solution could quickly transfer immunity to the entire island white-footed mouse population, deplete the local disease reservoir and dramatically reduce the population of infected ticks within a decade. Mainland populations could be similarly immunized using local or global gene drive technologies that we have devised [5, 6].

Given the growing rate of infections and the shortage of acceptable solutions, new approaches are urgently needed. Our proposal represents a highly innovative, long-lasting, safe and eco-friendly solution to a seemingly intractable problem. Unusually, we elected to approach local communities for guidance before initiating any experiments. We have been encouraged by strong initial support from both public health officials and local citizens at public meetings on Martha’s Vineyard[12] and Nantucket[3]. We will be guided by public feedback as we aim to make a lasting contribution to the field of tick-borne disease research by offering a novel ecological solution to this growing public health challenge.