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Researchers investigating the mystery of a tiny 'sin'

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Black-legged ticks, which carry Lyme disease, from the Cary Institute in Millbrook, NY. Credit: Michael Benjamin

When a strain of bacteria invades a human body, the immune system responds by generating antibodies to neutralize the threat. However, during subsequent infections by a similar bacterium, the immune system has a tendency to fall back on its memory, generating the same old antibodies again, even if they're not up to the task of the fighting the new invaders.

Therein lies the crack in the body's armor against certain recurring

infections, what has been called the original antigenic sin. It's a loophole in the immune system that Dustin Brisson, assistant professor of biology in the School of Arts and Sciences at the University of Pennsylvania, suspects certain pathogens may exploit by altering their structure just enough to fool the body into making useless antibodies.

Brisson studies the ecology and evolution of infectious diseases, in both natural and laboratory settings. He'll be able to delve deeper into microbe and human body interactions, especially the theory of original antigenic sin, now that the Burroughs Wellcome Fund has named him one of its 2013 Investigators in the Pathogenesis of Infectious Disease. The Fund supports scientists developing their early careers and helps advance basic biomedical science fields that are undervalued or in need of particular encouragement.

Brisson was awarded $500,000 of research support over five years after his nomination by Penn underwent peer review.

Most new investigators of infectious disease work in medical schools. Brisson is one of the few chosen from an arts-and-sciences department, Gregory M. Guild, biology professor and chair of the department, said.

"We hired him as a young guy right out of grad school without doing any postdoctoral studies –- a rarity these days," he said.

At Penn since 2007, Brisson teaches Introductory Biology and a seminar course, Humans in a Microbial World, aimed at non-biology majors.

He would like to examine the evolution of microbes in action against human antibodies. From the bacteria's point of view, there's an ideal structure, similar enough to a previous strain to evoke the same immune response but just different enough to slip past the immune system and overwhelm the host body.

"It is unclear if any bacteria have evolved to take advantage of original antigenic sin," he said. "Hopefully, this research will illuminate the evolutionary pressures on pathogens. It's a fundamental biological and medical issue with implications for recurring and chronic infectious diseases."

During a study published last year in the *New England Journal of Medicine*, Brisson and his colleagues learned that recurring cases of Lyme disease result from reinfection by different but related strains of the bacterium. Lyme disease is caused by the bacterium Borrelia burgdorferi, which hop aboard humans through the bite of infected black-legged ticks. Brisson has personally experienced the unpleasantness of Lyme disease, though that's not the reason he's studying it now.

"I'm interested in evolutionary biology, and Lyme disease is a very robust system to work on to answer fundamental questions in biology," he said.

If his work leads to breakthroughs in the fight against recurrent infectious disease, so much the better.

Provided by University of Pennsylvania