

# Multiplex Blood Test Being Developed to Differentiate Lyme, Seven Other Tick-Borne Diseases

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*Premium*



*Courtesy of Stuart Meek/Wikimedia Commons*

*Deer tick*

NEW YORK (360Dx) – A multiplex microarray under development could one day look at the body's immune response to effectively identify and distinguish between *Borrelia burgdorferi*, the Lyme disease pathogen, and seven other tick-borne pathogens.

The microarray scans 171,000 different peptide fragments in human blood that represent viruses, bacteria, and parasites that cause tick-borne diseases, and in a [study](#) published recently in *Nature Scientific Reports*, the authors said that their technology holds promise as a diagnostic test.

The developers consist of a broad collaboration among scientists at the Center for Infection and Immunity at Columbia University; the US Centers for Disease Control and Prevention; the National Institute of Allergy and Infectious Diseases; Roche Sequencing Solutions; Farmingdale State College; and Stony Brook University.

They are looking to collaborate with diagnostics industry companies to commercialize the test, and they intend to eventually conduct clinical trials and seek US Food and Drug Administration clearance, W. Ian Lipkin, one of the test's developers and director of the Center for Infection and Immunity at Columbia University, said in an interview.

According to researchers and clinicians, diagnosing tick-borne illness is tricky and can delay appropriate treatments for patients.

For Lyme disease, the recommended method for diagnosis is a two-tiered testing algorithm consisting of an ELISA test followed by western blots. The method is specific and sensitive in disseminated disease, but its utility in early-phase detection is limited, the researchers said. It accurately identifies less than 40 percent

of patients with early disease and can result in up to 28 percent of IgM western blots yielding false-positive results, they added. This traditional approach not only generates "a high rate of false negatives and false positives, it is expensive, laborious, and time consuming," Lipkin said.

The researchers' tick-borne disease Serochip, or TBD Serochip, promises to make diagnosis far easier and offers a replacement for current multistep testing that's subjective and lacking in sensitivity, he added.

From a new entrant's perspective, the market for tick-borne disease testing provides significant room for growth, Peter Wrighton-Smith, CEO of Oxford Immunotec, a firm developing tick-borne disease tests that target the immune system, said in January during a presentation at the 36th annual JP Morgan Healthcare Conference in San Francisco, California.

Existing testing technology in this market is "many decades old and it has a number of well-known limitations," he said, adding that there is increasing awareness of these limitations and greater "acceptance from physicians to be educated about new science in this area."

Such limitations have prompted not just Oxford Immunotec, but also other diagnostic companies and researchers to explore alternate diagnostic tools for tick-borne diseases.

A promising approach for resolving "the intrinsic lack of specificity associated with protein assays is the use of recombinant antigens or synthetic peptides that display immunodominant epitopes," the Serochip researchers said. This strategy improves assay specificity by eliminating non-specific and potentially cross-reactive epitopes and it is the approach employed in developing the TBD Serochip, they said.

The multiplex microarray would enable clinicians to do detection and confirmation with one test, Lipkin noted. "It is sensitive, specific, inexpensive, and not subjective, which are major advantages with respect to diagnosing Lyme disease, and it also allows us to simultaneously look at other infections that might be carried by ticks."

The researchers have not yet released sensitivity and specificity numbers for their test.

They said that TBD Serochip identified exposure to eight tick-borne pathogens present in the US — *Anaplasma phagocytophilum*, which is the agent of human granulocytic anaplasmosis; *Babesia microti*, the agent of babesiosis; *Borrelia burgdorferi*, the agent of Lyme disease; *Borrelia miyamotoi* and *Ehrlichia chaffeensis*, agents of human monocytic ehrlichiosis; *Rickettsia*, the agent of Rocky Mountain spotted fever; and the agents for Heartland virus and Powassan virus.

As new tick-borne infectious agents are discovered, the researchers can modify the TBD-Serochip to target them in less than four weeks. The microarray also identifies whether an individual is infected with more than one tick-borne pathogen, an important feature because individual ticks are frequently infected with more than one agent.

### **An expanding market**

The number of Americans diagnosed with tick-borne disease is steadily increasing as tick populations have expanded geographically.

Rafal Tokarz, the study's senior author, said in a statement that each year in the US alone, about 3 million clinical specimens are tested for tick-borne diseases. However, the true incidence of the disease is "greatly underestimated, as patients with presumed [diseases] are rarely tested for the full range of tick-borne agents," he said.

Tick-borne diseases are the principle vector-borne diseases in the US, eclipsing Zika, West Nile virus, and dengue that are transmitted by mosquitos, Wrighton-Smith said during his recent presentation. Citing CDC

statistics, the company's presentation noted that about 65 percent of tick-borne conditions are due to Lyme disease, 10 percent are due to mosquito-borne diseases, and the remainder, 21 percent, are due to other tick-borne diseases, such as anaplasmosis, ehrlichiosis, and babesiosis.

"All of these, if left unrecognized and untreated, can go on to have significant downstream morbidity," Wrighton-Smith said.

He noted that cases of Lyme have more than doubled over the past 15 years in the United States. These and other tick-borne disease cases are spreading across the country, causing growing concern among patients and physicians. Consequently, this is a "rapidly growing market" that is already worth about \$400 million to \$500 million annually in the US, he added.

In Q3 2017, currently the most recent quarter for which it has reported financial results, Oxford Immunotec said that its tick-borne disease-related revenue rose 45 percent to \$6.0 million from \$4.1 million in Q3 2016.

In June 2016, the firm [acquired](#) substantially all the assets of Lyme disease test company Imugen in a transaction worth \$22.2 million in cash, and in October 2106, it acquired Immunetics, a diagnostics company focused on developing specialized tests for infectious diseases, including Lyme disease, for \$6 million in cash and up to an additional \$6 million if certain conditions are met.

Oxford Immunotec offers testing with enzyme immunoassays and Western immunoblot for Lyme antibody analysis; an immunofluorescence test that uses fluorescent dyes to identify the presence of antibodies bound to specific antigens as part of its *Babesia microti* serology testing; and a microagglutination test used to determine the presence of antibodies in which *Frabcisella tularensis* antigen-coated latex particles are added to serial dilutions of a patient sample.

North Carolina-based Global Lyme Diagnostics has also [launched](#) a tick-borne diagnostic test service from a CLIA-certified laboratory. It uses proprietary chimeritopes in identifying variants of Lyme disease. And T2 Biosystems is developing the T2Lyme Panel through a partnership with Canon US Life Sciences, which would identify the bacteria that cause Lyme disease from a patient's blood.

In a research note this month, Leerink analyst Puneet Souda said that T2 expects a pivotal trial this spring in preparation for an application to the FDA for clearance to market its Lyme disease panel. The trial "could possibly extend into 2019," Souda said.

Columbia University's Lipkin noted that he and his colleagues have used multiplex PCR tests to conduct surveillance of tick diseases in New York, Connecticut, and elsewhere. However, using PCR for early tick-borne disease detection in clinical settings is not "particularly useful" because it requires circulating nucleic acids associated with the targeted pathogenic agent, and nucleic acid is not always present, he said.

Because the TBD Serochip measures the immune response, it does not present that concern, he said. Further, as new tick-borne disease agents are discovered, new targets can be added to arrays through *in situ* peptide synthesis, the researchers noted.

And the microarray can be employed to identify potential changes in reactive epitopes in individuals with persistent symptoms following antibiotic treatment.

However, they noted that a limitation of their platform is that it only displays linear peptides, so the test could miss non-protein epitopes important in pathogenesis.

The continued development of this test will require experimental comparisons to serologic assays, the researchers added.