

ChromaCode Tackling Tick-Borne Illness Testing With Multiplex Molecular Panel

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NEW YORK (GenomeWeb) – ChromaCode expects to fill an unmet need in the diagnostics market with a new molecular assay to test for common tick-borne pathogens. The firm launched a nine-target, research-use-only, qPCR panel test today that can detect a total of 12 species that are typically transmitted to humans by ticks in various regions of the US.

ChromaCode's core technology, called [HDPCR](#), enables standard thermal cyclers to run multiplexed panel tests.

Essentially, it modifies standard TaqMan chemistry to create unique curve signatures depending on the targets present, with specialized, user-friendly, cloud-based software to deconvolve and interpret the curves, Greg Gosch, the firm's CEO, said in an interview. ChromaCode's products, then, consist of reagents and software which can in turn be used in conjunction with a lab's existing real-time or digital PCR platforms.

A PCR-based test for tick-borne pathogens could have advantages in terms of ability to detect acute infections. Generally, these infections are detected using serology, but, "It takes a while for the immune system to respond to an infection, so early infections can go undiagnosed," Gosch said. On the other hand, PCR assays promise early detection, and ChromaCode's is the first comprehensive multiplex assay for these pathogens, he said.

ChromaCode's RUO panel represents a group of tick-borne pathogens commonly found in different regions of the US, including "the Upper Midwest, the Northeast, the Southeast, and a few things that cover tick-borne pathogens seen out West," said Scott Powell, ChromaCode's senior director of strategic marketing.

The test detects a total of nine DNA targets from bacteria and protozoa carried by ticks that bite people, but two of those targets can pick up multiple species.

The bacterial targets include *Anaplasma phagocytophilum*, which is the cause of [anaplasmosis](#), three species of Ehrlichia — *Ehrlichia chaffeensis*, *Ehrlichia ewingii*, *Ehrlichia muris eauclearensis* — and *Rickettsia* species that are known to cause [Rocky Mountain Spotted Fever](#).

The test also detects a few of the most common *Borrelia* species, a type of spirochete bacteria that is the cause of Lyme disease. Specifically, it detects *Borrelia miyamotoi*, as well as a target the firm calls Borrelia Group #1 — which includes *B. burgdorferi* and the [newly-discovered](#) *B. mayonii* — and a target called Borrelia Group #2 that detects *B. hermsii*, *B. parkeri*, and *B. turicatae*.

Finally, the test detects DNA of one tick-borne protozoa, *Babesia microti*, that is the cause of Babesiosis, an infection most common in the Northeast.

There are various algorithms to determine whether a patient should be tested using serological or molecular methods, said Blake Buchan, a pathologist at the Medical College

of Wisconsin who evaluated ChromaCode's test. An [algorithm](#) from the Mayo clinic labs advises PCR-based testing if a patient is acutely ill, with fever, chills, or sepsis, and has the appropriate exposure history.

A report to the US Congress by the Tick-Borne Diseases Working Group this year [recommended increased investment](#) in new technology or approaches for the diagnosis of Lyme disease and other tick-borne diseases. "A federal response that includes diagnostic test development and implementation would decrease the number of missed diagnoses of Lyme disease and other tick-borne infections, thereby reducing the number of people who have short- and long-term negative health effects due to untreated infections," the report said. Other researchers have also recently [emphasized](#) the need for new technologies, and overall the market for tickborne disease testing is reportedly [growing](#) due to increasing prevalence of infection.

Clinicians in different areas may typically only test for the pathogens common in their regions, but a panel-based approach could be beneficial given that the regional variability seems to be becoming less well-defined, according to Buchan.

Buchan noted that increasing travel and outdoor activities has led to patients presenting the same constellation of symptoms, but perhaps from different species of infection than are seen locally. Distribution of different tick species — and their animal hosts — is also changing due to climate change, urbanization, and other factors. Furthermore, although different species of tick tend to carry different pathogens, this also seems to be changing, according to a recent [study](#).

Thus, in practice, "It's very difficult for infectious disease doctors, currently, to figure out what's causing the illness," Buchan said.

Buchan presented the results of his lab's evaluation of the ChromaCode panel recently at Association for Molecular Pathology meeting. His lab used the panel to test 175 prospectively collected samples from patients suspected of having Lyme disease, as well as 20 retrospective samples from known positive cases, 93 simulated specimens, and samples collected locally as well as ones from a more rural part of Northern Wisconsin.

Overall, the evaluation found 19 clinical samples tested positive, and all had one of three targets, namely the *A. phagocytophilum*, *B. microti*, or *B. miyamotoi*. Compared to singleplex PCR testing, the latter two targets showed 100 percent sensitivity and specificity, while the former had 100 specificity and 91 percent sensitivity. There were two false-positive results — one for *E. muris eauclarensis* and one for the Rickettsia species target — that were retrospective clinical samples positive for *A. phagocytophilum*. The panel also uncovered two cases in which the pathogens that were detected were things the clinicians would not otherwise have tested for.

There may be future benefits to detecting and differentiating the species causing tick-borne illness, according to Buchan. It would help improve epidemiology, of course. Also, although most tick-borne illnesses will respond to the empiric antibiotic therapy that is used for Borrelia-induced Lyme disease, not every patient has Lyme.

Indeed, a study in [Molecular and Cellular Probes](#) last year also noted that, in order to elucidate which species are "exotic curiosities" and which are actually significant causes of morbidity, "We first need to recognize their presence through suitable diagnostic approaches."

And, from a prognostic standpoint, it may someday help clinicians confronted with patients experiencing post-Lyme syndrome — a condition for which the cause is unknown, according to the [US Centers for Disease Control and Prevention](#) — if they knew whether *Borrelia miyamotoi* is likely to cause the same post-Lyme symptoms as *B.*

burgdorferi, Buchan said. The relationship between species and prognosis is unknown at the moment, in part because there is no easy test to distinguish the pathogens.

"Right now we're really doing a disservice by not accurately identifying which tick-borne illnesses people have," Buchan said. And, it is possible that serology would detect Lyme in a patient that is actually an old, past infection, Buchan added. "We are potentially drawing false conclusions about future ailments — whether it's people who say they are relapsing or have the long term arthralgias — but it's difficult to connect the dots when you don't have a definitive diagnosis for the initial infection."

Buchan said his lab will now set about validating the commercially available test. He sees great interest in his hospital among infectious disease doctors, but still plans to help educate them about the test. He anticipates, if the lab does bring on the assay, that they will see an improved turnaround time compared to the send-out molecular testing they are currently using, as well as a substantial reduction in cost.

ChromaCode's Powell also noted that the firm is working on "flexible testing" to enable users to turn on and off different targets. The firm also has two panels in development for the near term — a multidrug resistance assay and a non-invasive prenatal testing application for use on digital PCR instruments. It is also utilizing a prototype respiratory panel the company has developed in discussions with potential instrument partners, Gosch said.

The firm plans to use a dual channel commercial strategy, selling directly using a small dedicated sales force. It is also actively engaged in partnership discussions with different qPCR and non-qPCR companies, Gosch said. "It's a pretty obvious fit for us to be able to partner with someone who's already got the instrumentation," he said, adding that commercialization is also part of those discussions.