Inside The Diagnostics Industry

T2 Biosystems Shifts Paradigm for Rapid Pathogen Identification Directly From Sample

John McDonough, CEO, T2 Biosystems

T2 Biosystems (Lexington, Mass.) is set to revolutionize diagnosis of sepsis infections. Within hours of sample receipt, the company's T2 Magnetic Resonance (T2MR) platform can identify the infection-causing pathogen, completely eliminating the need for blood cultures. Trimming time to results from days to hours has tremendous implications for patient care, antibiotic stewardship, and hospitals' bottom line. The company received U.S. Food and Drug Administration (FDA) clearance for the T2Dx instrument and its first panel (T2Candida) in September 2014 and earlier this year secured its initial customer contracts for the products.

The company is building a solid business case for the products with recently published studies showing not only great clinical performance in terms of the tests' significant impact on patient survival, but also that quicker definitive diagnosis of sepsis-causing infections can yield millions of dollars in savings per hospital. *DTET* recently spoke to T2 Biosystems' CEO John McDonough to learn more about the company's plans and how rapid pathogen identification will evolve.

What makes T2's T2MR platform unique?

T2MR is a novel and proprietary method of detection that uses a combination of magnetic resonance (four-inch diameter magnets) with advanced nanotechnology. We apply nanoparticles as part of our diagnostic reagents. The real power of the platform is that for the first time we have the ability to detect pathogens directly from clinical samples. The presence of a pathogen can be detected at extraordinarily low concentration levels—as little as a single cell per mL of blood, urine, or nasal swab. There are literally tens if not hundreds of applications that you can build on top of this detection method— similar to a computer's operating system on which you can develop different apps or software.

Where we have applied the technology early on is to address really large, unmet health care needs where we can quickly provide diagnostic results that cannot be delivered today. We can do this in a way that is meaningful for patients, offering, literally, the opportunity to save lives, while also taking significant costs out of the health care system. The first field for us is sepsis. We are the only FDA-approved technology in the market that can detect sepsis from a blood sample in three to five hours. The gold standard today for a suspected septic infection is a blood culture, which takes two to six days to identify the pathogen. As a result, the mortality rate for sepsis is above 30 percent. But, data shows if you put patients on the right drug within 12 hours you can cut mortality in half.

Many technologies including sequencing and mass spectroscopy are being applied to rapid pathogen identification. How will adoption of these technologies unfold?

There are use cases for most of the technologies in the marketplace. But in certain application areas where speed to results matters, I think T2 Biosystems is positioned to become the dominant diagnostic platform. Across sepsis—bacterial infections and fun-

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gal infections—a single cell puts you at serious risk of death and existing methods just can't detect down at that low level. That is why the other methods in the market require a blood culture—to grow the cells over several days until there are enough of them for the platform to detect. We are able to analyze directly from the sample, skip the blood culture, and provide the results in three to five hours. So, not only is our advantage in detecting pathogens quickly, but we detect more infected patients than blood culture. Typically, blood culture detects 50 percent to 60 percent of patients that have an infection. The sensitivity in our FDA clinical trial of over 1,800 patient samples was 91.1 percent. This is because sometimes the bug doesn't grow in the culture, like when patients are given drugs prophylactically or empirically and the drug impedes the growth in the culture even though there is an infection. But, that does not impact us.

President Obama recently unveiled a national initiative to combat antibiotic resistant bacteria, with a stated focus of improving rapid detection of infections. How will this initiative impact the diagnostic industry's efforts?

That the federal government is getting involved shows how big the problem really is. Sepsis affects more than 1.5 million Americans annually and sepsis is the single greatest cost to hospitals in the United States at over $20 billion. The President's initiative is really focused on supporting hospitals building anti-microbial stewardship programs where you get doctors, laboratorians, pharmacists, and administrators on stewardship committees to address two issues. The biggest issue is giving the right drug to the patient fast enough. But secondly, because you are waiting two to six days for blood culture results, doctors put many patients on drugs in advance of the correct diagnosis. For every one infected patient, 10 patients without infections are being treated, possibly with the wrong drug for that infection. All of that overuse has a cost, both monetarily and with increasing resistance. Many hospitals have already implemented antimicrobial stewardship programs, but the federal initiative really supports the use of those programs and puts more teeth behind the goal of reducing inappropriate use of these drugs.

T2 Biosystems By-the-Numbers

- Year Founded: 2006
- Number of employees: 150
- Patents Issued: 45 with 67 additional applications
- Time to T2Candida results: 3 to 5 hours
- T2Candida Performance: 91.1 percent sensitivity, 99.4 percent specificity
- T2MR Limit of Detection: As low as 1 CFU/mL

From T2 Biosystems' standpoint this is a very supportive initiative. Our products that are now getting adopted by hospitals are in large driven by these stewardship programs. These hospitals understand the importance of having a diagnostic that can provide rapid pathogen identification so the appropriate drug can be used first-line. This mandate raises awareness, drives changes in hospitals, and it addresses the missing piece of a real need for rapid identification and diagnosis.

Earlier this year you published a study on the economic case supporting adoption of T2 Biosystems Candida panel. Is demonstration of economic impact part of T2 Biosystems' strategic plan with all panels in the pipeline?

If you don't have a strong economic case, it is really tough to drive adoption in this health care environment. Candida fungal infections have a 40 percent mortality rate, a rate which has not changed in the last 20 years. Multiple independent publications show you can reduce that mortality

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to 11 percent if patients are treated with the right drug within 12 hours. The corollary to that is the economics. A typical patient with a candida infection is in the hospital for an average of 40 days with nine days in the intensive care unit (ICU). These are nasty, nasty infections. The average cost to treat a patient with a candida infection is $130,000. Data shows if you can treat patients with the right drug in the first 24 hours you can reduce the hospital stay by nine days and reduce the stay in the ICU by three. This translates into economic savings of between $25,000 and $30,000 to the hospital, when measuring just length of stay. There are other economic impacts like reducing treatment in patients who are negative that makes the economic picture even more compelling.

Mortality also affects economics. The patients who don't survive, end up costing 2.7 times more, on average, than patients who do survive. If you have a septic infection, you don't pass quickly. You struggle in the hospital or the ICU and in the last week you are put on all sort of drugs and interventions to gain survival and the cost is extraordinarily high. The good news is we can reduce mortality by as much as 50 to 75 percent, which translates into huge economic savings for the hospital.

"Over the next several years we will see that every symptomatic patient is given a rapid test because it would be inappropriate to not do so. The cost of the drugs avoided pays for the test."

—John McDonough, CEO, T2 Biosystems

At T2 Biosystems we have a simple mandate for everything we do. We want to develop and deliver diagnostic test results that will change therapeutic decisions in a way that is good for patients and will take significant costs out of the health care system. We must achieve both of those things before we embark on any development program. Economics studies are underway for the panels in our pipeline and we expect they will be published after the products receive FDA-clearance, much like they were with T2Candida.

How will rapid pathogen detection evolve in the next two to five years?

There will be a real paradigm shift. We are starting with sepsis as we are currently living in a world where millions of patients are aggressively treated with drugs that are not needed and it is taking too long to get patients on the right drugs. Over the next several years we will see that every symptomatic patient is given a rapid test because it would be inappropriate to not do so. The cost of the drugs avoided pays for the test. As soon as the market is aware of these diagnostics and their clinical performance, we will see the shift happen.

If we go out further in time we can take the technology to experiences you and I have had. Hopefully, you haven't had sepsis, but you have probably had a sore throat where they run a throat culture to see if it's bacterial or viral and you probably begged to be put on an antibiotic because you didn't want to wait to feel better. Ten years ago they would have given you the antibiotic—even though it will not treat a virus. Now this is done a little less often. In those cases you are not dealing with life or death, as with sepsis, but T2 Biosystems technology can address many, many applications including those that we are really familiar with, like throat infections.