Stroke Test Being Developed to Detect Cause, Enable Better Treatment

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NEW YORK (GenomeWeb) – Molecular diagnostics company Ischemia Care has developed a laboratory-developed test, the ISCDx, that it says can better determine the cause of strokes based on gene expression analysis, and help clinicians better treat patients.

The Oxford, Ohio-based firm is using a microarray-based platform leveraging technology licensed from the University of California to diagnose different types of stroke from blood samples, including ischemic strokes and transient strokes whose symptoms quickly abate.

The company is launching the new test as a CLIA-certified LDT through a company-owned laboratory in Dayton, Ohio, Jeff June, CEO of Ischemia Care, said in an interview.

The use of blood tests in the diagnosis of stroke is currently limited and takes a back seat to brain imaging, but their potential to enable a better understanding of how to treat stroke is driving research and development into new technologies.

Prompt and accurate acute treatment and identification of stroke etiology for secondary prevention are especially important to decrease the morbidity and mortality associated with cerebrovascular disease, Edward Jauch, a professor, neuroscientist, and director of research in the division of emergency medicine at Medical University of South Carolina, said in an interview. He also is the principal investigator of the Ischemia Care Biomarkers of Acute Stroke Etiology (BASE) clinical trial whose objective is to confirm the diagnostic accuracy of the Ischemia Care ISCDx test.

That's where the Ischemia Care blood-based biomarker test could make an impact, he said, adding that physicians treating ischemic attacks and more subtle transient ischemic attacks would benefit from understanding as soon as possible why a patient has had a stroke and initiate the correct therapies to prevent secondary strokes.

Although alternate technologies to blood tests are currently used for stroke diagnostics, "we still end up with about a third of all strokes having an unknown etiology," said Jauch, who is a joint author of the Guidelines for the Early Management of Patients with Acute Ischemic Stroke, published in 2013 in the journal *Stroke.*

The Ischemia Care test is based on research conducted by Frank Sharp, a professor of neurology at the University of California, Davis, who found that it may be possible to discriminate between various types of strokes by studying patients' genomic profiles derived from their white blood cells.

In combination with a clinical exam and results from other types of diagnostic testing, the ISCDx helps a physician identify the source of the stroke, Jauch said, adding that among the most important findings from BASE, the investigators were able "to discriminate well" between cardioembolic strokes, when the heart pumps unwanted materials into the brain circulation, and large artery strokes, which occurs due to interruption of blood flow in one of the main large arteries in the brain.

Clinicians do a better job of preventing second strokes when they know what has caused the first one. "The way you treat them with various medications and sometimes surgery vary greatly depending on the cause," Jauch said.

Investigators in the BASE trial are currently validating the clinical utility of the Ischemia Care blood-biomarker test to differentiate transient ischemic attacks from acute ischemic strokes, among other clinical objectives. So far, the test has demonstrated that it can explain more quickly the cause of a stroke, and according to Jauch, that information can be used by clinicians to better diagnose and treat patients.

About 1,700 patients from more than 20 US-based stroke treatment centers are participating in the study, which was described in the journal of *Translational Stroke Research*. The trial, ongoing since 2014, is expected to be completed by the end of this year.

Stroke numbers

In the US, about 800,000 people suffer an acute ischemic stroke each year. Additionally, hundreds of thousands more experience a transient ischemic attack — a momentary episode of neurologic dysfunction that often precedes a major stroke and serves as a warning for future ischemic events.

Currently, the diagnosis of stroke usually involves collecting a patient's clinical history, doing a clinical assessment, and conducting brain imaging.

Imaging has improved significantly over the years, but "the main value of blood tests is their potential for use in prognosis and planning rehabilitation strategies," James Meschia, chair of neurology at the Mayo Clinic in Jacksonville, Florida said in an interview. Meschia is not involved in the development of the ISCDx test and declined to speak about specific tests in the market, but said he sees the potential value that a blood test based on gene expression could have for stroke diagnostics. With colleagues, Meschia is leading a clinical trial that aims to prevent stroke in patients with asymptomatic carotid stenosis.

Blood-based tests could prove highly valuable, he said, in patient management and discharge planning, including deciding whether a patient requires nursing home rehabilitation or home-based physical therapy, for example.

They also have a place in helping diagnose silent, or transient, strokes that can outnumber symptomatic stroke 3-to-1, he noted.

Blood-based genetic testing also has value in contributing an understanding of the underlying mechanism of disease, he said. Patients are often diagnosed as being refractory to therapy when in reality they are receiving the wrong therapy and are sometimes endangered by the treatment, he said, adding that genetic tests have the potential to mitigate those risks and guide more precise treatments.

Quickly diagnosing and properly treating stroke also has implications for healthcare costs, Meschia said. In spite of the availability of advanced imaging, "there are many instances in which it's either impractical from a patient-care perspective or too costly overall to repeat imaging in

understanding how much damage has been done to a patient during a stroke," Meschia said.

Ischemia Care CEO June said that spending for stroke diagnostics and treatment costs the US health system about $65 billion per year.

Ischemia Care funded the BASE clinical trial and built its CLIA laboratory with about $9 million in seed funding. June said that its lab-developed test is reimbursed under an existing diagnostic related grouping, or DRG, which is how the US Centers for Medicare & Medicaid Services and some health insurance companies categorize hospitalization costs and determine how much to pay for a patient's hospital stay.

The addressable market for its first test, which clinicians will use to stratify patients at various points in the care continuum, is about $200 million dollars per year, he said, adding that in the US each year there are about two million emergency room visits associated with suspected stroke.

A point-of-care version of the test for use in the emergency department is under development. "We anticipate covering the full stroke-care continuum, from point of care through hospitalization and secondary prevention," he said.

Going forward, the company also plans to introduce a PCR kit for stroke diagnostics for sale to hospital labs. Ischemia Care will use information from the BASE clinical trial and post-launch information as part of a submission to obtain US Food and Drug Administration clearance, but the timing of a submission is unclear, June said.

Josh Goldsmith, the firm's director of sales and marketing, said that for sales it is looking to collaborate with companies competing in the interventional stroke market. "Our test can be used to stratify 250,000 patients that may or may not need a product from an implantable cardiac monitoring company," he said.

While Ischemia Care is working with five hospitals to begin processing samples this summer, a number of entities are pursuing new technologies to improve stroke diagnosis, including Cerebrotech Medical Systems.

Additionally, Roche Diagnostics has launched a bleeding-risk test to benefit patients at risk of stroke who need to decide whether to take oral anticoagulants for atrial fibrillation, and Abbott this week announced that researchers have found that elevated troponin-I levels using its High Sensitive Troponin-I blood test are associated with having future cardiac events, including stroke and heart attack.

A University of Edinburgh-led team has also developed a model that combines computed tomography scans and genotyping to predict whether someone who has had a stroke is more likely to have another one.

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