

Stopping stroke before it strikes

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J Clin Invest. 2005;115(8):1968-1968. <https://doi.org/10.1172/JCI26116>.

News

The most common type of stroke, ischemic stroke, affects nearly 700,000 people per year, or 1 person every 45 seconds. Because stroke is notoriously difficult to treat, a sought-after approach is to find ways to avoid stroke before it can happen. To this end, the FDA recently approved the first blood test designed to predict a patient's risk of ischemic stroke. The new test, called the PLAC test, can help identify at-risk patients so that preventative measures, such as lifestyle modification and treatment with daily aspirin and statins, can be taken. The ability to forecast stroke is critical but has been challenging. The vascular changes that precede it develop stealthily and are not evident for a long time. "Stroke is by nature unpredictable," says Mark Fisher, chair of the Department of Neurology at University of California, Irvine. And despite years of intense research, treatment for a person who has had a stroke is extremely limited. "Stroke is hard to treat because we don't have any treatment," says Patrick Lyden, director of the Stroke Center at University of California, San Diego. "The other issue is that too few patients recognize stroke." The only approved therapy for stroke is tissue plasminogen activator (tPA), which must be administered within a few hours and is considered controversial since it increases the risk of neuronal [...]

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and roll. In my spare time, what little there is, I play guitar and harmonica in a group called *the Transactivators* with friends from my department. Inspired by the Willie Nelson Professorship, we are working on a new tune called “Mama, don’t let your stem

cells grow up to be cowboys”.

JCI: At the end of your career, what do you hope to have accomplished?

Olson: My long-term goals are to create a blueprint for development of cardiac, skeletal, and smooth muscle cells and to use

that knowledge to improve human health. Along the way, I hope to populate the field with outstanding, independent trainees and the next generation of scientific leaders.

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The only approved therapy for stroke is tissue plasminogen activator (tPA), which must be administered within a few hours and is considered controversial since it increases the risk of neuronal toxicity and bleeding in the brain when given improperly. Patients often don’t get to the hospital in time for the currently recommended 3-hour window for tPA. The need for prompt treatment, Fisher notes, has led to the phrase “time is brain.”

In fact, tPA only reaches 3% of stroke patients and is successful in only 10% of those recipients.

The PLAC blood test measures levels of an enzyme called lipoprotein-associated phospholipase A2 (Lp-PLA2), previously found to be predictive of coronary

artery disease, which is associated with artery hardening and atherosclerosis and causes blockage of blood vessels, which can lead to stroke. Results from a large study by the National Heart Lung and Blood Institute, Atherosclerosis Risk in Communities, showed that people with elevated levels of Lp-PLA2 have twice the risk of ischemic stroke over 6 to 8 years.

Traditional risk factors for stroke include diabetes, high blood pressure, smoking, atherosclerosis, and age. All of these can facilitate clot production in the blood vessels or support the growing thrombus once it is logged in the brain artery, says Berislav Zlokovic, associate chair of the Department of Neurological Surgery at the University of Rochester. Lp-PLA2 predicts stroke independently of these factors.

Some question the utility of the test in light of previous findings showing that levels of C-reactive protein (CRP), which increase upon inflammation of blood vessels, are elevated many years before stroke. A test for CRP levels has already been shown to predict stroke risk independently of other traditional risk factors.

Eng Lo, director of the Neuroprotection Research Laboratory at Harvard, points out that basic biochemistry suggests that CRP and Lp-PLA2 are independent risk factors indicative of different arms of the inflammatory cascade. Despite lack of overlap, both tests would lead to the same outcome, he says, in terms of modifying behavior or taking pills. “So is there really a lot of added value with PLAC? How does the test relate to non-hemodynamic embolic strokes or hemorrhagic strokes?” Lo asks.

“There are not that many studies that have looked at Lp-PLA2 in stroke,” Fisher says, and this is another limiting factor in the PLAC test. As for clinical utility, it is still too soon to tell.

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The new PLAC blood test can now predict a person’s risk of stroke. Photo courtesy of Centers for Disease Control.