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Mayo Clinic Develops First Genomic-Based Test To Predict Stroke From Ruptured Brain Aneurysm

ScienceDaily (Mar. 21, 2005) — ROCHESTER, Minn. -- Mayo Clinic researchers have discovered a genetic marker that may pave the way for a fast, inexpensive blood test to predict one type of deadly stroke that strikes 30,000 people in the United States annually.

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neurosurgical researcher who led the study. "There has been a search for a marker that would identify patients with rupture-prone aneurysms for a very long time because this disease can strike like lightning. Rupture typically happens suddenly and completely unexpectedly -- and when it does at least half of patients die or suffer long-term disability. That's why our results suggesting that we may have found such a marker are so exciting: there is an urgent public health need for it."

Significance of the Mayo Clinic Research

The Mayo Clinic researchers conclude that they have found the first genetic marker to help doctors identify which cases of a condition known as sporadic brain aneurysm are at highest risk for death and disability due to rupturing and subsequent bleeding into the brain. Sporadic brain aneurysm is a different medical condition from familial aneurysm, for which genetic markers are already known. However, approximately 90 percent of all cases of aneurysm -- a dangerous thinning of blood vessel walls in the brain -- fall into the "sporadic" category. While development of sporadic brain aneurysm is relatively common (as autopsies have shown) many people have them and have no symptoms or warning signs that they could be at risk of catastrophic rupture that is imminently life endangering.

The Key Finding

The Mayo researchers are the first to identify specific genetic variations or "polymorphisms" associated with an approximately 10-fold increased risk of a ruptured aneurysm. If further studies validate these findings, screening for these polymorphisms could be done with a fast, inexpensive blood test to predict which patients with aneurysms are at risk. The experimental blood test researchers developed detects specific variations in the gene that encodes an important

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Dr. Khurana notes that the Mayo Clinic group's effort is just the beginning of their research. Their hope is that a large, multicenter and international clinical trial will test their results. "But our initial results are really very powerful," he adds. "Our findings have very strong implications for brain aneurysm research. I think from a public health point of view, if you consider the millions and millions of dollars that go to sorting out this lightning-like, catastrophic disease, every year in the United States alone there are potentially 30,000 people who could be affected by this."

Background Biology

Physicians and researchers have long been puzzled by the discrepancy between the large numbers of people with brain aneurysms -- 10 to 15 million people in the U.S. -- and the incidence of aneurysms rupturing in a relatively small fraction of those people. Doctors knew some aneurysms were more prone to rupture, but didn't know why. They suspected genes played a role, but lacked convincing studies supporting this hypothesis.

The Mayo Clinic research team had previously done extensive work with a molecule (nitric oxide synthase) known to play a pivotal role in the endothelium. The endothelium is the lining of the blood vessels that is very important to maintaining smooth blood flow. Disrupted blood flow in brain arteries is associated with increased risk of stroke. The Mayo team's previous work showed that when the amount of this molecule is increased using a gene therapy approach, the arteries relax and maintain smooth, healthy flow.

The Investigation

To determine the role of nitric oxide synthase gene variations in ruptured brain aneurysms, the Mayo Clinic team screened the genetic variants of 49 patients who had unruptured brain aneurysms, and compared them with the genetic variants of 58 emergency room patients with ruptured aneurysms.

Blood samples were taken from all, and DNA analysis performed. There was no significant difference between the two groups in terms of age, race, gender, health history, family history, and smoking habits. Despite these similarities, the genetic differences were striking. Says Dr. Khurana: "Our findings are the first to present strong evidence that the reason for sporadic brain aneurysm rupture may be genetic."

Collaborators and Support

In addition to Dr. Khurana, other Mayo Clinic collaborators include: Irene Meissner, M.D.; Youvraj Sohni, Ph.D.; William Bamlet; Robyn McClelland, Ph.D.; Julie Cunningham, Ph.D.; and Fredric Meyer, M.D. Their work was supported by the Departments of Neurologic Surgery and Neurology, Mayo Clinic and Mayo Foundation.

Adapted from materials provided by [Mayo Clinic](#).

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