Biomarker points to Alzheimer's risk

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(Medical Xpress)—A study involving Rochester-area seniors has yielded the first accurate blood test that can predict who is at risk for developing Alzheimer's disease. This discovery – which appears today in the journal *Nature Medicine* – could be the key to unlocking a new generation of treatments that seek to head off the disease before neurological damage becomes irreversible.

The biomarker – which consists of 10 specific lipids found in blood plasma – predicted with greater than 90 percent accuracy which individuals would go on to develop Alzheimer's disease or a precursor condition known as amnestic mild cognitive impairment (aMCI). The cost of the simple blood test required to detect these lipids is a fraction

of other techniques and, unlike alternatives, it identifies risk early in the disease process before cognitive symptoms appears.

"The ability to identify individuals who are at risk of developing Alzheimer's before the clinical manifestation of cognitive impairment has long been a Holy Grail of the neuromedicine community," said Mark Mapstone, Ph.D., a neuropsychologist with the University of Rochester School of Medicine and Dentistry and lead author of the study. "Current efforts to develop a treatment for this disease are coming up short because they are probably being used too late. Biomarkers that can allow us to intervene early in the course of the disease could be a game-changer."

Alzheimer's research is at an impasse with many once promising experimental therapies failing in late stage clinical trials. These setbacks have led all but a few major pharmaceutical companies to pull back from their research and development in the disease.

The absence of an effective treatment for Alzheimer's, and the dwindling options in the drug development pipeline, mean that the nation – and the world – are woefully unprepared for the coming "Silver Tsunami" of aging baby boomers who will develop the disease in the coming years. By 2050, an estimated 14 million Americans will have Alzheimer's, consuming an estimated $1.2 trillion in health care costs per year.

There is an emerging scientific consensus that once the cognitive symptoms of the Alzheimer's have emerged, it may be too late to slow or reverse the neurological damage caused by the disease. Researchers speculate that if treatments could be initiated early in the disease cycle, they may stand more of a chance of being effective. In fact, many of the same experimental treatments that have failed in recent clinical studies may ultimately prove to be successful if they are given to patients

sooner. The challenge is there currently exists no way to identify which people are at risk of developing Alzheimer's.

There are several screening methods that can detect Alzheimer's disease. These include spinal taps which measure the presence of the proteins beta amyloid and tau and advanced imaging systems such as MRIs, PET scans, and functional MRIs that spot changes in the brain. But these techniques have significant limitations. First, they have only been shown to be effective in confirming the diagnosing of the diseases after the cognitive symptoms have surfaced. And second, the high cost associated with these technologies is a significant barrier to widespread use in clinical practice.

The Rochester Aging Study, which was launched in 2007, is a community-wide collaboration that involves physicians and researchers from the University of Rochester School of Medicine and Dentistry, Unity Health, and Rochester General Health System.

In total, 425 seniors from the Rochester area participated in the study. The volunteers underwent a comprehensive cognitive assessment and a blood draw once a year over a five-year period. An additional 100 individuals from Irvine, CA were enrolled in the study.

Researchers at the University of Rochester and Georgetown University used a technique called mass spectrometry to screen for lipid levels in blood plasma. Lipids are a class of naturally occurring molecules found in the body that play a role in energy storage, signaling, and form the structural components of cell membranes. The scientists identified 10 specific lipids that, if present in lower than normal levels, could predict with more than 90 percent accuracy whether an individual would go on to develop either Alzheimer's or aMCI.

The scientists are not entirely sure why this particular set of lipids is

indicative of Alzheimer's. All ten represent a class of lipids called phospholipids, molecules that are important cellular building blocks. The researchers speculate that the lower lipid levels could be an early indication that the brain cells lost in the disease are beginning to lose their integrity and break down.

Once commercialized, a blood test required to detect these lipids would likely cost less than $200 – compared to thousands of dollars for a spinal tap or MRI – and could be ordered as a part of a routine exam by an individual's primary care physician.

"Having a tool that is able to identify, with a high degree of accuracy and at a low cost, which individuals will convert to Alzheimer's could transform how we care for this devastating disease," said Mapstone.

Provided by University of Rochester Medical Center