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A blood marker may indicate Alzheimer's risk

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A simple blood test capable of predicting if a person might develop Alzheimer's disease is within sight, and could eventually be used to help scientists reverse onset of the disease in those most at risk.

According to new research by Rockefeller University scientists and their colleagues at Columbia University, which followed a large population of elderly people for more than four years, blood levels of a protein called Amyloid-β 42 (Aβ42) may allow doctors to detect an individual's predisposition to developing the disease. The findings, published online in the Proceedings of the National Academy of Sciences, have the potential to change the way that the disease is treated and, one day, perhaps even prevent it from taking hold.

The study — a collaboration between Jeffrey Ravetch, Theresa and Eugene M. Lang Professor and head of the Leonard Wagner Laboratory of Molecular Genetics and Immunology, and scientists at the Columbia University Medical Center — showed that plasma levels of Aβ42 increase before the onset of Alzheimer's disease and decline shortly after the onset of dementia. The researchers found that people with elevated levels of Aβ42 in their blood appear to be at increased risk of developing Alzheimer's, especially when those levels then begin to decrease over time.

The research built on a study that began 20 years ago with an elderly population in New York who were at risk of, or had already begun to develop Alzheimer's. The scientists tested 1,125 people over the course

of 4.6 years and found that plasma levels of Aβ42 appeared to increase before the onset of disease and decline shortly after the first signs of dementia. They believe that Aβ42 may become trapped in the brain in a "traffic jam" of sorts, which would account for the decrease in post-dementia levels. The study's coauthor, Richard Mayeux, codirector of Columbia's Taub Institute of Research on Alzheimer's Disease and the Aging Brain, likens the finding to a similar pattern seen in heart attack patients, who typically have elevated lipid levels in their bloodstream prior to a heart attack but, after the event, may see those levels decrease.

In a subset of 402 participants, Ravetch and Mayeux honed in on the most detrimental variant of Aβ42, a specific form of the amyloid protein called protofibrillar Aβ42. Using an antibody that Ravetch created — the first ever capable of detecting the protofibrillar form of Aβ42 — the researchers were able to identify the compound in 34 percent of their subjects. Strikingly, those people with the highest levels of Aβ42 also had the highest detectable levels of protofibrillar Aβ42, Ravetch says, "and the decline of the protofibrillar form was associated with conversion to mild Alzheimer's and cognitive impairment."

While the cognitive impairments of Alzheimer's can be monitored as the disease runs its course, clinicians have had no reliable way to monitor its pathologic progression. But Ravetch's assay to uncover blood levels of this previously undetectable protein is critical, Mayeux says. "It strongly supports the use of protofibrillar Aβ42 as a biomarker of risk."

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Provided by Rockefeller University