Preliminary new blood test to detect Alzheimer's disease uncovered

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UT Southwestern Medical Center scientists have helped develop a novel technology to diagnose Alzheimer's disease from blood samples long before symptoms appear.

This preliminary technology, which uses synthetic molecules to seek out and identify disease-specific antibodies, also could be used eventually in the development of specific biomarkers for a range of other hard-to-diagnose diseases and conditions, including Parkinson's disease and immune system-related diseases like multiple sclerosis and lupus, the researchers predict.

"One of the great challenges in treating patients with Alzheimer's disease is that once symptoms appear, it's too late. You can't un-ring the bell," said Dr. Dwight German, professor of psychiatry and an author of the paper published in the Jan. 7 edition of *Cell*. "If we can find a way to detect the disease in its earliest stages – before cognitive impairment begins – we might be able to stop it in its tracks by developing new treatment strategies."

Because patients with Alzheimer's disease (AD) exhibit immune system activation and neurodegeneration in several brain regions, researchers in the study hypothesized that there may be numerous antibodies in the serum of affected patients that are specific to the disease and can serve as a biomarker.

Antigens – substances such as protein from a virus or bacteria that

triggers an immune response – traditionally have been necessary for the discovery of antibody biomarkers. It has been impossible previously to identify an antibody (a type of targeted immune molecule) without first knowing the antigen that triggers its production.

The new study, however, challenges conventional wisdom and uses synthetic molecules (peptoids) rather than antigens to successfully detect signs of disease in patients' blood samples. These peptoids have many advantages; they can be modified easily and can be produced quickly in relatively large amounts at lower cost.

The adaptive immune system is thought to be a rich source of protein biomarkers, but diagnostically useful antibodies remain undiscovered for a large number of diseases, Dr. German said. This is, in part, because the antigens that trigger an immune response in many diseases are unknown. The technology behind this discovery is essentially an immune-system reader, which is designed to pick out antibodies without knowing in advance which ones to look for.

The researchers used a combination library of several thousand peptoids to screen serum samples from mice with multiple sclerosis-like symptoms as well as from healthy control mice. The particular peptoids that retained more antibodies from the blood samples of the diseased animals were identified as potential agents for capturing diagnostically useful molecules.

The investigators then examined serum samples from six AD patients, six healthy patients and six patients with Parkinson's. Three peptoids were identified that captured six times the IgG antibody levels in all of the Alzheimer's patients when compared to the control group or to the Parkinson's patients. Two of the peptoids were found to bind the same IgG antibody, while the third was shown to bind to different antibodies – meaning there are at least two candidate biomarkers for AD. Using an

additional set of 16 normal control subjects and 10 subjects at the very early state of AD, the three candidate biomarkers identified AD with 90 percent accuracy.

"The results of this study, though preliminary, show great potential for becoming a landmark," said Dr. German.

Provided by UT Southwestern Medical Center