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A blood test for Alzheimer's disease?

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Scientists from the Florida campus of The Scripps Research Institute, have developed a novel technology that is able to detect the presence of immune molecules specific to Alzheimer's disease in patients' blood samples. While still preliminary, the findings offer clear proof that this breakthrough technology could be used in the development of biomarkers for a range of human diseases.

The study, led by Scripps Research Professor Thomas Kodadek, Ph.D., was published in the January 7, 2011 edition of the journal *Cell*.

Traditionally, antigens—a substance such as a protein from a virus or bacteria that stimulates an immune response—have been necessary for the discovery of antibody biomarkers. There has previously been no way 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 rather than antigens to successfully detect signs of disease in patients' blood samples.

These synthetic compounds have many advantages – they can be modified easily and can be produced quickly in relatively large amounts at lower cost.

"Dr. Kodadek has conceived of a new approach for identifying antibody biomarkers of human disease that bypasses the conventional, but difficult, step of identifying the natural antigens or antigen mimics," said James M. Anderson, M.D., Ph.D., director of the National Institutes of

Health (NIH) Division of Program Coordination, Planning, and Strategic Initiatives, who helps oversee the NIH Common Fund's Pioneer Award Program. "The results in the paper suggest great potential for using this approach to rapidly develop diagnostic biomarkers for a variety of significant human diseases. Such boldness to challenge conventional paradigms to achieve important scientific advances is a hallmark of the NIH Director's Pioneer Award Program, which supported much of this research."

"This study essentially puts an end to the notion that the only way to pull a potentially useful antibody from blood samples is with a specific antigen," said Kodadek. "Because the antigen identification problem has proven to be so difficult, we decided to take it out of the equation."

A Focus on the Immune System

To test the concept, Kodadek and his colleagues used comparative screening of combinatorial libraries of synthetic molecules – peptoids – against serum samples obtained from mice with a multiple-sclerosis-like condition or healthy controls. Those synthetic molecules that retained more immunoglobulin (IgG), a major type of antibody, from the blood samples of the diseased animals were identified as potential agents for capturing diagnostically useful molecules. This worked well.

The team next turned to serum samples from six Alzheimer's patients, six healthy individuals, and six Parkinson's disease patients. Three peptoids were identified that captured at least three-fold higher levels of IgG antibodies from all six of the Alzheimer's patients than any of the control or Parkinson's patients. The results showed that two of the peptoids bind the same IgG antibodies; a third binds different antibodies, resulting in at least two candidate biomarkers for the disease.

"We use these peptoids as a lure to capture the IgG antibodies," Kodadek

said. "Some of these synthetic molecules recognize the antigen-binding sites of disease-specific antibodies well enough to pull them from blood samples, although they almost certainly don't bind as well as the native antigens. This ability should make it possible to short circuit the discovery of the natural antigens."

More information: "Identification of Candidate IgG Antibody Biomarkers for Alzheimer's Disease through Screening of Synthetic Combinatorial Libraries," by M. Muralidhar Reddy et al.

Provided by The Scripps Research Institute