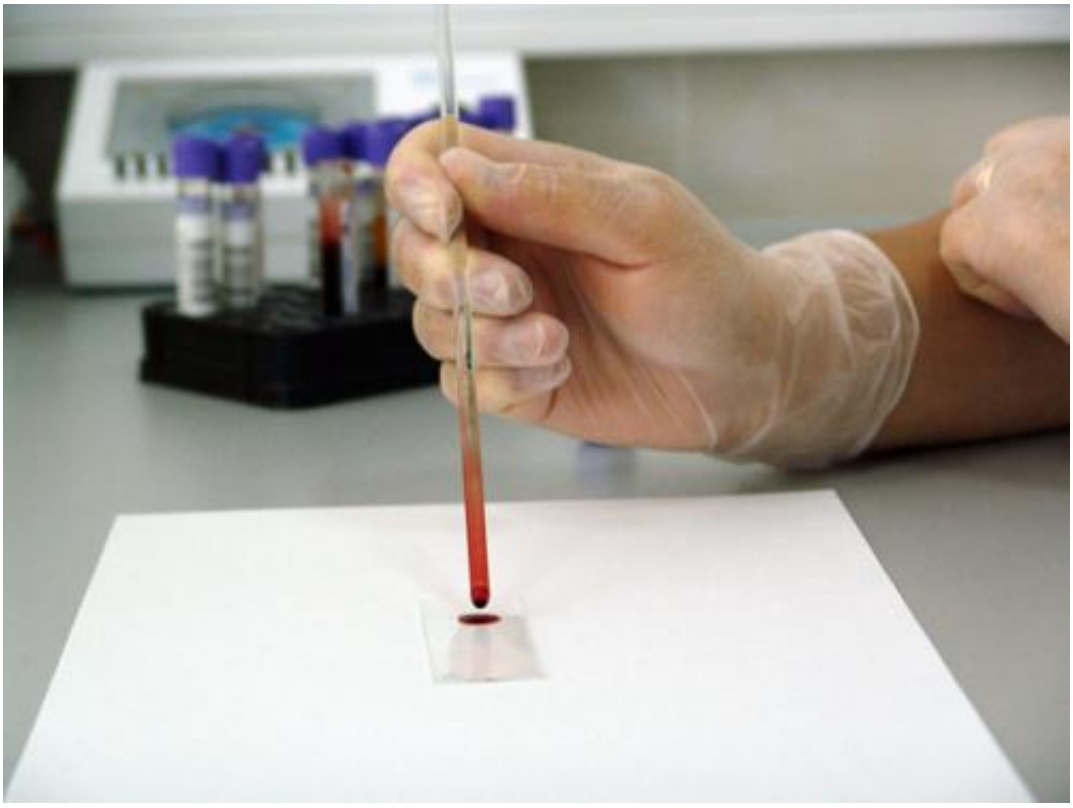
MedicalXpress

Test holds potential to diagnose myriad conditions with drop of blood

June 9 2016



Credit: public domain

Researchers at the University of Pittsburgh have developed a unique method for detecting antibodies in the blood of patients in a proof-of-principle study that opens the door to development of simple diagnostic tests for diseases for which no microbial cause is known, including auto-immune diseases, cancers and other conditions.

The results, reported in the *Journal of Immunological Methods* and funded by the Bill & Melinda Gates Foundation, are the first evidence that it is possible to develop blood tests for any infectious disease by screening random libraries of non-biological molecular shapes.

"This 'needle-in-a-molecular haystack' approach is a new way to develop diagnostic assays," said senior author Donald S. Burke, M.D., Pitt Graduate School of Public Health dean and director of Pitt's Center for Vaccine Research. "The method does not rely on starting with known viral components. This is important because there are conditions for which there isn't a known antigen, such as newly emerged epidemics, autoimmune diseases or even responses to traumatic injury."

When a person's immune system is faced with an antigen or foreign invader, such as an infectious disease, or even an injury with tissue damage, it responds by producing antibodies. Like puzzle pieces, specific parts of the surface of these antibodies fit to the shape of the molecules on the invader or the damaged tissue.

The Pitt researchers used a technique pioneered by co-author Thomas Kodadek, Ph.D., of the Scripps Research Institute, that synthesizes random molecular shapes called "peptoids" hooked onto microscopic plastic beads. The technique can produce millions of molecular shapes. The peptoids are not organic, but if they match to the corresponding shape on an antibody, that antibody will connect to them, allowing the scientist to pull out that bead and examine that peptoid and its corresponding antibody.

Using this technique, Dr. Burke's team chemically generated a huge library of random molecular shapes. Then, using blood from HIV-infected patients and from non-infected people, the researchers screened a million of these random molecular shapes to find the ones that bound only to antibodies present in the blood of HIV-infected patients, but not

the healthy controls. No HIV proteins or structures were used to construct or select the peptoids, but the approach, nonetheless, successfully led to selection of the best molecular shapes to use in screening for HIV antibodies.

The team then resynthesized that HIV-antibody-targeting peptoid in mass and tested it by screening hundreds of samples from the Multicenter AIDS Cohort Study (MACS), a confidential research study of the natural history of treated and untreated HIV/AIDS in men who have sex with men (supported by the National Institutes of Health). Study co-author Charles Rinaldo, Ph.D., chair of Pitt Public Health's Department of Infectious Diseases and Microbiology and director of the Pittsburgh arm of the MACS, selected the samples, but blinded the testers to which samples were HIV-positive or -negative. The test distinguished between the samples of HIV-positive blood and HIV-negative blood with a high degree of accuracy.

"This technology means that we may be able to take a single drop of blood from a patient and detect antibodies to all manner of infections, cancers or other conditions they may be carrying or been exposed to. We hope that this is the first step toward development of an 'Epi-chip' that can be used to reconstruct a person's entire exposure history," said Dr. Burke, who also holds the UPMC-Jonas Salk Chair of Global Health at Pitt.

Provided by University of Pittsburgh Schools of the Health Sciences