A new test to rapidly identify worldwide tuberculosis infections

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An animation depicting an active TB infection targeting the lungs. Credit: Jason Drees, Biodesign Institute at Arizona State University

Tuberculosis (TB), once better known as consumption for the way its victims wasted away, has a long and deadly history, with estimates indicating it may have killed more people than any other bacterial pathogen.

Studies have discovered evidence of its human impact going back to as early as 8,000 BCE, and estimates suggest that it has killed a billion people over the past two centuries.

Now, a group of scientists from Arizona, Texas and Washington DC has teamed up to develop the first rapid blood test to diagnose and quantitate the severity of active TB cases.

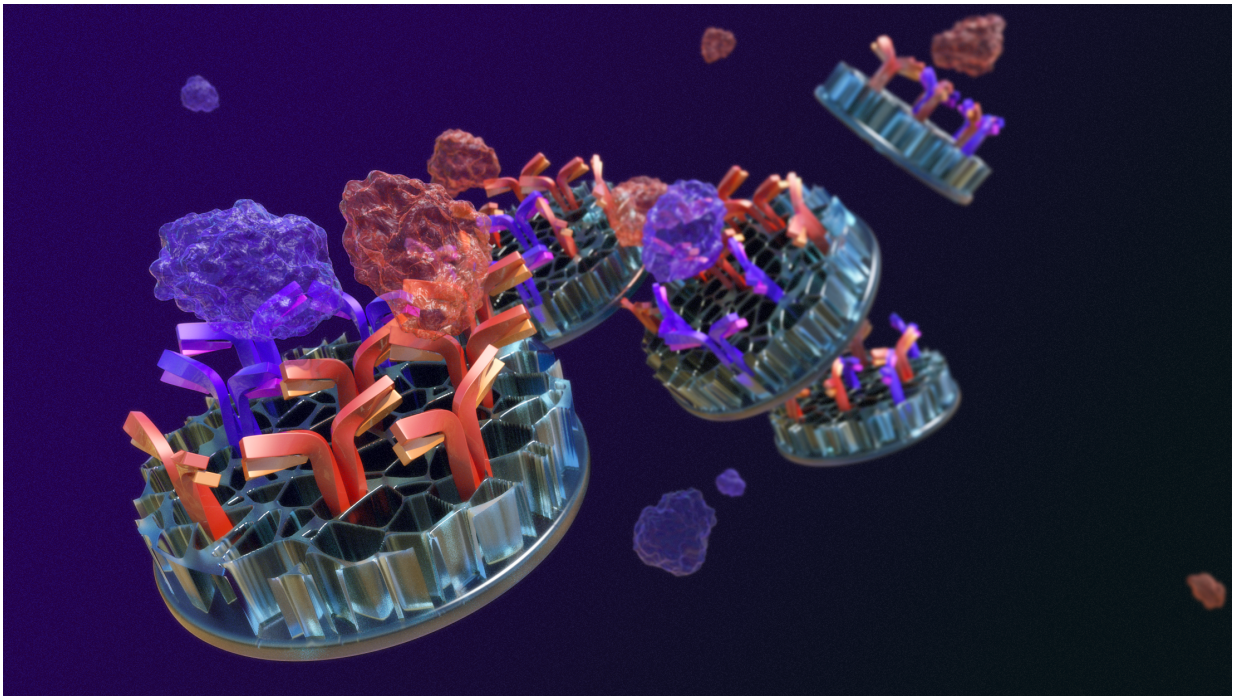
Led by Tony Hu, a researcher at Arizona State University's Biodesign Institute, eight research groups, including the Houston Methodist Research Institute and scientists at the National Institutes of Health, are harnessing the new field of nanomedicine to improve worldwide TB control.

"In the current frontlines of TB testing, coughed-up sputum, blood culture tests, invasive lung and lymph biopsies, or spinal taps are the only way to diagnose TB," said Hu, a scientist in the Biodesign Institute's Virginia G. Piper Center for Personalized Diagnostics. "The results can give false negatives, and these tests are further constrained because they can take days to weeks to get the results."

Despite $6.6 billion spent for international TB care and prevention efforts, TB remains a major risk to human health, particularly for the developing world and people with HIV infections.

Making matters worse, TB bacteria can lurk dormant in a person's lung tissue, often for decades, before spontaneously producing full-blown TB disease that can then spread to others. Currently, the World Health Organization (WHO) estimates that up to one-third of the world's population may have such dormant TB infections.

In 2016, an estimated 10 million people worldwide still develop TB each year according to the WHO's most recent report, resulting in almost two million deaths. TB treatment has prevented almost 50 million deaths between 2000 and 2015, but TB remains a worldwide epidemic due to the lack of an effective TB vaccine, the rise in drug-resistant strains and the relatively poor performance of available TB diagnostics.



The research team's newly developed NanoDisk-MS assay (see infographic), could significantly improve TB diagnosis and management because it is the first test that can measure the severity of active TB infections. It does so by accurately detecting minute blood levels of two proteins (CFP-10 and ESAT-6) that TB bacteria release only during active infections. Credit: Jason Drees, Biodesign Institute at Arizona State University

A new and easy way to rapidly screen those susceptible to TB infections was recognized by WHO and other public health officials as the major technological hurdle needed to overcome the disease.

The team's newly developed blood-based TB test not only outperforms all others currently on the market but also takes just hours to complete. This is critical since effective TB control requires that patients start treatment as soon as possible to reduce the risk of spreading TB.

This test also holds promise for rapid assessment of TB treatment, an important factor in reducing the development and spread of drug-resistant TB strains.

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"We are particularly excited about the ability of our high-throughput assay to provide rapid quantitative results that can be used to monitor treatment effects, which will give physicians the ability to better treat worldwide TB infections," said Hu. "Furthermore, our technology can be

used with standard clinical instruments found in hospitals worldwide."

Current TB assays often demonstrate reduced performance with HIV-positive TB patients or those with TB infections in non-lung tissues, and these patients can require tissue biopsies for diagnosis. The NanoDisk-MS assay, however, detected lung- and non-lung-resident TB cases with similar sensitivity (about 92 percent) regardless of patient HIV status, and revealed good specificity to distinguish patients with related disease cases (latent TB and nontuberculous mycobacterial infections; 87 and 91 percent, respectively) and healthy subjects (100 percent).

The strategy used to generate this assay may also be adaptable to other infectious diseases. Hu is now developing the current TB assay for clinical approval in the fight against TB.

The study was published in the Early Edition of the journal *Proceedings of the National Academy of Sciences*.

More information: Quantification of circulating Mycobacterium tuberculosis antigen peptides allows rapid diagnosis of active disease and treatment monitoring, *PNAS*, www.pnas.org/cgi/doi/10.1073/pnas.1621360114

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