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Cheap test slashes time taken to diagnose TB

Enzyme-based method could become the fastest tuberculosis test yet.

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Sputum samples containing tuberculosis bacteria (bottom two rows) fluoresce in the presence of CDG-3, the basis for a rapid test under development.

An inexpensive portable diagnosis system can cut the time it takes to spot tuberculosis (TB) bacteria from weeks or months to less than half an hour, potentially helping doctors to catch infections before patients have time to unknowingly infect others.

The bacteria that cause TB, *Mycobacterium tuberculosis*, grow extremely slowly in the lab, so clinicians have few options for diagnosing the disease, says epidemiologist Jason Andrews at Stanford University in California. They can either try to grow the bacteria from a sample — which can take up to two months — or look for them in a sputum sample smeared across a slide, a technique that can miss an infection 50% of the time. A method called GeneXpert, made by Cepheid in Sunnyvale, California, and endorsed by the World Health Organization since 2010, can accurately detect *M. tuberculosis* DNA within a couple of hours, but it requires specialized equipment and trained personnel, making it impractical for rural areas or developing countries.

To speed up the process, chemist Jianghong Rao of Stanford and microbiologist Jeffrey Cirillo of Texas A&M Health Science Center in Bryan developed a chemical called CDG-3, which glows when it is broken down by an *M. tuberculosis* enzyme called BlaC. The researchers found that they could detect as few as ten bacteria in a millilitre sample.

They then tested the method on 50 sputum samples from people in Texas. It correctly identified all the samples that contained *M. tuberculosis* visible under a microscope, and 80% of those in which infections were not visible. When tested in people without TB, the CDG-3 probe diagnosed them correctly 73% of the time. The results are published online today in *Angewandte Chemie*[1].

Front-line testing

David Alland, an infectious disease specialist at Rutgers University in Newark, New Jersey, says that although the test is impressively sensitive, the fact that it said healthy people had TB 27% of the time means that it will be most useful as a triage method. It could be used in a remote village, for instance, to weed out people who do not need treatment and send the rest to a clinic for further testing with a more expensive and accurate method such as GeneXpert. In a study published last year[2], Alland and his colleagues calculated

that a hypothetical triage system could cut costs by 30–40%.

Rao and Cirillo are now working with diagnostics company GBDbio in Temple, Texas, to develop a portable, battery-powered device that measures the fluorescence coming from CDG-3 as it is broken down. Chief executive Michael Norman says that the company hopes to have the device completed and on the market in 2015. He expects that a single test will cost about US$5, and will take less than 30 minutes to deliver a diagnosis.

“There's a lot of space for more rapid triage tests,” says Graham Timmins, a toxicologist at the University of New Mexico in Albuquerque. He points out that from a health perspective, false negatives that result in infected people being sent home are more worrying than false positives, in which healthy people are treated unnecessarily — though overuse of antibiotics can foster drug resistance. He praises the paper for making a “quantum leap” from the lab to the clinic, but says that the technology needs to be tested in a much larger number of people.

Rao and Cirillo say that they are validating the CDG-3 test and the reading device in larger groups, including some in developing countries. They are also developing similar tests that will flag up enzymes that allow *M. tuberculosis* to resist antibiotics. Such diagnostics could eventually tell physicians how best to treat a particular infection.

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References

1. Cheng, Y. *et al*. *Angew. Chem. Int. Edn Engl.* http://dx.doi.org/10.1002/anie.201405243 (2014).
2. van't Hoog, A. H. *et al*. *PLoS ONE* **8**, e82786 (2013).