RNA signatures from suspected TB patients could form the basis of a diagnostic test

October 22 2013

A set of RNA transcriptional signatures expressed in the blood of patients might provide the basis of a diagnostic test that can distinguish active tuberculosis (TB) from latent TB and also from other diseases that have similar clinical symptoms and signs according to research published in this week's *PLOS Medicine*.

Even though TB is both curable and preventable, approximately 1.4 million people died because of TB in 2011 according to the World Health Organization, and TB infections remain one of the leading causes of death in people infected with HIV. One of the challenges for clinicians is correctly diagnosing TB because the signs and symptoms of TB may be similar to those of other diseases and current TB diagnostics have substantial limitations.

New research by an international team led by Michael Levin from Imperial College London, UK, aimed to identify a host blood RNA transcriptional signature that could form the basis of a simple diagnostic test. The researchers recruited 584 adult patients with suspected TB in South Africa and Malawi who were eventually diagnosed with either TB, latent TB infection or another disease (where TB was considered in the differential diagnosis but then excluded). The researchers took blood samples from these patients and analysed their blood transcriptional profiles to identify signatures that could be used to calculate a disease risk score capable of differentiating TB from other conditions prevalent in HIV-infected and -uninfected African adults.

In the test cohorts, the disease risk score had a high sensitivity (95%) and specificity (90%) for distinguishing TB from latent TB (sensitivity is a measure of true positives, correctly identified as such and specificity is a measure of true negatives, correctly identified as such) and for distinguishing TB from other diseases (sensitivity 93% and specificity 88%). In the independent validation cohort, the researchers found that patients with TB could be distinguished from patients with latent TB (sensitivity 95% and specificity 94%) and also from patients with other diseases (sensitivity 100% and specificity 96%).

While the results are promising, the authors acknowledge that further work is required before the findings can be used in the clinic. They note, "from a clinical perspective a simple transcriptome-based test that reliably diagnoses or excludes TB in the majority of patients undergoing investigation for suspected TB, using a single blood sample, would be of great value, allowing scarce hospital resources to be focused on the small proportion of patients where the result was indeterminate. The challenge for the academic research community and for industry is to develop innovative methods to translate multi-transcript signatures into simple, cheap tests for TB suitable for use in African health facilities."

In a related Perspective article Adithya Cattamanchi (uninvolved in the study) from the University of California San Francisco, and colleagues reflect on the research noting, "Levin and colleagues have provided compelling proof of the concept that a blood transcriptional signature can distinguish between TB and clinical mimics in high-incidence settings. The field can now move on to asking more practical questions to determine the feasibility and optimal use for an RNA expression-based biomarker for TB in clinical settings."

  More information: Kaforou M, Wright VJ, Oni T, French N, Anderson ST, et al. (2013) Detection of Tuberculosis in HIV-Infected and -Uninfected African Adults Using Whole Blood RNA Expression

Signatures: A Case-Control Study. PLoS Med 10(10): e1001538.

Perspective Article: Cattamanchi A, Walter ND, Metcalfe JZ, Davis JL (2013) A Transcriptional Signature for Active TB: Have We Found the Needle in the Haystack? PLoS Med 10(10): e1001539.