Docket #: S15-057

Gene Set for the Diagnosis of Active Pulmonary Tuberculosis

Stanford researchers have identified a small set of genes that can be used to diagnose active tuberculosis (TB), distinguish active TB from latent TB or other diseases, and predict progression from latent to active TB months before conventional tests. TB is a worldwide public health problem. It is hard to accurately diagnose, which leads to difficulties in selecting appropriate treatment. Traditional diagnostic methods cannot distinguish between latent and active TB and have lower sensitivity in HIV-positive patients. To overcome these limitations the inventors have identified this set of genes that provides a robust diagnostic for active TB. The gene set not only detects active TB; it can also distinguish active TB from latent TB and other diseases, predict who will develop active TB up to 6 months before sputum conversion, and correlate with lung inflammation severity. In addition, it can be used to track treatment response as expression of the gene set falls with successful treatment. This gene set has broad applications for TB diagnosis, progression prediction, and treatment response monitoring.

Stage of Research
The inventors have extensively validated the gene set in external datasets and demonstrated it is a robust diagnostic for active TB. The technology has now been prospectively validated in three independent cohorts across different clinical settings and meets WHO target product profile criteria for TB diagnostics.

Applications

- Diagnostic for Tuberculosis (TB) testing and bulk screening
- Prognostic for predicting progression from latent to active TB
- Biomarkers for monitoring TB treatment response

Advantages

- Can distinguish active TB from latent TB and other diseases
- Predicts TB progression 6 months before sputum conversion (86% sensitivity, 84% specificity)
- Meets WHO target product profile for non-sputum-based triage test (90% sensitivity, 70% specificity)
- Blood-based: does not require complex procedures or patient sputum
- High negative predictive value (99.3%) for ruling out disease
- Can be used to diagnose TB in children
- Unaffected by clinical confounders such as HIV status or BCG vaccine status
- Small gene set: reduces cost and complexity
- Validated across multiple platforms (microarray, RNA-seq, RT-qPCR)
- Allows for quantitative monitoring of TB treatment response: can identify non-responders earlier
- May be used to improve TB drug clinical trials
- Can be used as a stand-alone diagnostic or as an adjunct to existing diagnostics

Publications

- Warsinske, H. C., Rao, A. M., Moreira, F. M., Santos, P. C. P., Liu, A. B., Scott, M., ... & Khatri, P. (2018). "Assessment of validity of a blood-based 3-gene signature score for progression and diagnosis of tuberculosis, disease severity, and treatment response. JAMA network open, 1(6), e183779-e183779.
- Timothy E. Sweeney, MD, Lindsay Braviak, Cristina M. Tato, PhD, Purvesh Khatri, PhD, (2016)"Genome-Wide Expression for Diagnosis of Pulmonary Tuberculosis: a multicohort analysis." Lancet Respiratory Medicine, Volume 4, Issue (213-224), March 2016.

Patents

- Published Application: WO2017066641
- Published Application: 20180291452
- Published Application: 20210348233
- Issued: 10,920,275 (USA)

Innovators

- Purvesh Khatri
- Timothy Sweeney

Licensing Contact

Mona Wan

Senior Licensing Manager for Special Projects

Email