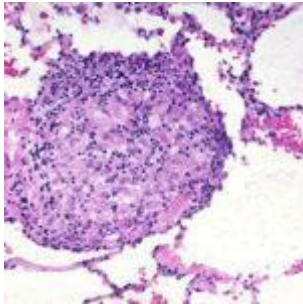# TB biomarker based on anti-Ag85B and 4 inflammatory molecules.

Tuberculosis (TB) is the leading cause of death due to an infectious agent. Of the approximate 10 million incident cases, 30% of these individuals had no access to quality care and were untreated (2019 Global TB Report). One of the potential reasons for this is the inability to diagnose TB in one visit [in high burden and low income settings]. As a result the world health organisation (WHO) emphasises the need for improved diagnostics among other interventions under the "WHO Flagship Initiative*:"Find. Treat. All. #EndTB"*. In this article we report findings from a recently published article : ["A rapid triage test for active pulmonary tuberculosis in adult patients with persistent cough"(Ahmed *et al.,* 2019).](#)

Ahmed et al., *"hypothesized that a blood protein-based host response signature for ATB could distinguish it from other TB-like disease (OTD) in adult patients with persistent cough and provide the foundation for a community-based triage test for ATB."* To test this they measured 47 inflammatory markers* using luminex. Using machine learning algorithms they were able to develop a host based protein signature for ATB based on 4 molecules: IL-6, IL-8, IL-18 and VEGF, *"with an accuracy [receiver operator characteristic—area under the curve (ROC-AUC)] of 0.87, sensitivity of 86% and specificity of 65%."*

One caveat of Luminex is low analytical sensitivity (ability to detect low concentrations), which often meant that some analytes were undetectable in some of the samples. To improve the analytical sensitivity of detection, researchers utilised the Simoa platform to detect IL-6, IL-8, IL-18 and VEGF. Simoa (see video below) is an ultra-sensitive immunoassay which has a better analytical sensitivity than Luminex and can be used with small sample volumes.

Researchers then optimised their assay for use with the Simoa platform, and included the measurement of anti-Ag85B antibody with the hope of improving the performance of the test. They then validated this 4 protein and 1 antibody based biomarker in plasma samples from Africa, Asia and South America, where they observed an improved sensitivity and specificity of 86% and 69% respectively.

In summary Ahmed *et al.*, have developed a biomarker based on detection of 4 inflammatory molecules and an anti-Ag8B Ab which can output results in 30 minutes. Though highly specific, the sensitivity does not meet the WHO criteria, and would have to be improved or used in combination with symptom based screening or diagnostics.

Journal Article: Ahmed *et al.,* 2019. [A rapid triage test for active pulmonary tuberculosis in adult patients with persistent cough.](#) Science Translational Medicine.

There's a large unmet need for accurate, fast, and inexpensive tests to identify patients who have active tuberculosis (ATB), which claims the lives over a million people per year. A team of researchers from the Wyss Institute and several collaborating institutions has created a fast, ultrasensitive, multiplexed triage test for ATB that could be used in low-resource settings to identify patients who are at high risk for ATB and need immediate medical attention. Credit: Wyss Institute at Harvard

** Some of the 47 molecules measured using Luminex are matrix metalloproteinases (2,3 & 9), MIP-1α, MIP 1β, TNF molecules (α & β), C-reactive protein, interleukins (IL-1α, IL-1β, IL-2, IL-3, IL-4, IL-5, IL-6, IL-7, IL-8, IL-10, IL-12p40, IL-12p70, IL-15, IL-17, IL-18, IL-23) and VEGF etc. All these markers have been shown to be either downregulated or upregulated during TB pathogenesis.