

BIOMARKERS FOR TB DETECTION



WHAT ARE TB BIOMARKERS AND WHY DO THEY MATTER?

Tuberculosis (TB) is caused by bacteria (*Mycobacterium tuberculosis*, or 'Mtb') and it most often affects the lungs. TB is spread through the air when people with lung TB cough, sneeze, or spit. A person can become infected after inhaling only a few germs.

It's estimated that one-quarter of the world's population is infected by Mtb, 10 million of whom fall ill with active TB disease each year. The rest may have TB infection but are not sick, or have cleared the bacteria, and cannot transmit the disease.

WHY IS IT DIFFICULT TO DIAGNOSE TB?

- ✔ **Current methods of diagnosing active TB mainly rely on detecting the presence of Mtb bacteria itself**
- ✔ For example, culture requires isolating Mtb bacteria from a patient specimen and then trying to grow it; smear microscopy involves examining a patient specimen under a microscope and looking for Mtb bacteria; PCR-based methods like Xpert MTB/RIF look for Mtb-specific DNA
- ✔ For people living with HIV (PLHIV), people with TB outside the lungs, people with smear-negative TB, or children, the common methods often fail to detect TB. This is due to the low numbers of Mtb bacteria found in their specimens

WHAT IS A BIOMARKER?

- ✔ **A measurable host or pathogen characteristic that indicates normal or pathogenic state**
- ✔ A helpful biomarker for active TB would be necessary and specific to the TB disease process – this way, it would always be present during TB, but would be absent in healthy individuals

WHY DO BIOMARKERS MATTER FOR TB DIAGNOSTICS?

- ✔ **Detecting biomarkers provide a promising alternative to current TB testing methods, especially for cases with low Mtb counts**, because their presence does not directly depend on the number of Mtb bacteria in a specimen
- ✔ Some biomarkers are easier to measure than Mtb itself, which may allow for the use of simpler and cheaper detection assays. Additionally, many biomarkers may be measurable in specimens that are simple to collect, such as urine or blood

WHAT BIOMARKERS ARE CURRENTLY USED FOR TB DIAGNOSIS?

- ✔ Besides Mtb DNA, the only biomarker-based TB test currently on the market is Abbott's (formerly Alere) Determine TB LAM. LAM forms part of Mtb bacteria cell walls and it is found in urine
- ✔ **We need to scale-up Determine TB LAM because it can be life-saving for people living with HIV (PLHIV)**
- ✔ The accuracy of another LAM-based test, Fujifilm SILVAMP TB LAM, is currently being studied across multiple continents
- ✔ Many other biomarkers are under research, including cytokines, CRP, anti-Mtb antibodies, RNA signatures, and breath-based compounds

WHY DO WE NEED TO INVEST IN TB BIOMARKER RESEARCH?

- ✔ **Current TB tests are expensive, require sophisticated infrastructure, or do not work well in all TB patients**
- ✔ Diagnostic tests that are cheap and deployable close to where patients first present with TB-like symptoms are urgently needed. Biomarker-based tests have the potential to meet these criteria, and have the added benefit of being measurable in TB cases with low Mtb burden
- ✔ Many TB-associated biomarkers have been identified, but few make it further in the development pipeline. We need to invest in validation studies to understand the usefulness and application of these biomarkers