**HIGHLIGHTS**

* We evaluated the accuracy of host markers elicited after overnight stimulation of whole blood with ESAT-6/CFP-10, Rv0081, Rv1284 and Rv2034, for the diagnosis of TB disease in presumed TB patients
* Our study identified a six-analyte biosignature that allowed promise in the diagnosis of active TB
* The identified host markers could play a role as adjunctive markers in improving the sensitivity of immunodiagnostic assays for TB disease
* The most useful analytes were detected in unstimulated culture supernatants, indicating there may be no added accuracy obtained through stimulation with *Mtb* antigens