Potential immunological biomarkers for the detection of *Mycobacterium tuberculosis* infection in an endemic setting, Ethiopia

Takele Teklu, Kwon Keehwan, Biniam Wondale, Milkessa HaileMariam, Mengistu Legesse, Girmay Medhin, Aboma Zewude, Rembert Pieper and Gobena Ameni

University of Gondar, Ethiopia

A ccurate diagnosis and early treatment of tuberculosis (TB) and latent TB infection (LTBI) are vital to prevent and control TB. The lack of specific biomarkers hinders these efforts. This study's purpose was to screen immunological markers that discriminate against *M. tuberculosis* (Mt) infection outcomes in an endemic setting of Ethiopia. Whole blood from 90 participants was stimulated using the ESAT-6/CFP-10 antigen cocktail. The interferon-γ (IFN-γ)-based QuantiFERON diagnostic test was used to distinguish between LTBI and uninfected control cases. Forty cytokines/chemokines were detected from antigen-stimulated plasma supernatants (SPS) and unstimulated plasma samples (UPSs) using human cytokine/chemokine antibody microarrays. Statistical tests allowed us to identify potential biomarkers that distinguish the TB, LTBI, and healthy control groups. As expected, the levels of IFN-γ in SPSs returned a high receiver operating characteristic curve (AUC) value comparing healthy controls and LTBI cases (Z=0.911; P<0.001). The SPS data also indicated that IL-17 abundance discriminates LTBI from healthy controls (Z=0.763; P=0.001). RANTES and MIP-1β were significantly elevated in SPSs of TB-infected compared to healthy controls (P<0.05), while IL-12p40 and sTNF-RII were significantly increased in active TB cases compared to the combined LTBI and control groups (P<0.05). Interestingly, quantitative changes for RANTES were observed using both SPSs and UPSs with P-values of 0.013 and 0.012, respectively, in active TB versus LTBI cases and 0.001 and 0.002, respectively, in active TB versus healthy controls. These results encourage biomarker verification studies for IL-17 and RANTES. Combinations of these cytokines may compliment IFN-γ measurements to diagnose LTBI and distinguish active TB from LTBI cases.

takeleteklu@gmail.com