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# Discriminative expression of whole blood genes in HIV patients with latent and active TB in Ethiopia

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**Background:** Transcriptomic host biomarkers could assist to develop effective diagnostics and therapeutics for tuberculosis (TB). However, different gene biomarkers may be discriminatory in different populations depending on the host and bacilli genetics, and host immune reactivity due to HIV infection, which need to be addressed.

**Methods:** The expression levels of 45 genes that are known to be involved in or affected by TB pathogenesis were analyzed using Reverse Transcriptase Multiplex Ligation Probe Amplification (RT-MLPA) assay in whole blood of 106 HIV positive individuals including active TB patients ($TB^+HIV^+$, n=29), and non TB patients that are tuberculin skin test positive (TST+) ($TST^+HIV^+$, n=26), or TST negative ($TST^-HIV^+$, n=51).

**Results:** Between the two clinical groups ($TB^+HIV^+$ vs. TST-$HIV^+$) 8 genes were differently expressed (CCL19, CD14, CD8A, FPR1, IL7R, CCL22, TNFRSF1A, and FCGR1A); between $TB^+HIV^+$ vs. $TST^+HIV^+$, 6 genes (CD14, IL7R, TIMP2, CCL22, TNFRSF1A, and FCGR1A) were differently expressed. Since no difference in gene expression was revealed between $TST^+HIV^+$ vs. TST-$HIV^+$, we clustered both the $TST^+HIV^+$ and TST-$HIV^+$ individuals as one group ($TST^{+/-}HIV^+$) and compared gene expression with $TB^+HIV^+$ patients. Thus, the results revealed that the levels of five genes (CD8A, TIMP2, CCL22, FCGR1A and TNFRSF1A) were the most accurate single gene markers for differentiation between $TB^+HIV^+$ and $TST^{+/-}HIV^+$, with AUCs of 0.71, 0.71, 0.79, 0.83 and 0.73, respectively. However, the combination of two genes (CCL22 +FCGR1A) and FCGR1A alone was the most accurate marker for differentiation between the two groups ($TB^+HIV^+$ and $TST^{+/-}HIV^+$) with AUC of 0.85 and 0.83, respectively.

**Conclusions:** We showed that five genes (CD8A, TIMP2, CCL22, FCGR1A and TNFRSF1A), specifically FCGR1A and CCL22 have the potential to discriminate active TB from non-active TB in HIV patients in Ethiopia and could be used to improve diagnostic tools for active TB in HIV patients, and to understand the pathogenesis of TB/HIV confection

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