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# Evaluation of the Diagnostic Potential of IL-2 after Specific Antigen Stimulation with PE35 (Rv3872) and PPE68 (Rv3873) for the Discrimination of Active and Latent Tuberculosis

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**Abstract :** Although cytokine analysis has greatly contributed to the understanding of tuberculosis (TB) pathogenesis, data on cytokine profiles that might distinguish progression from latency of TB infection are scarce. Since PE/PPE proteins are known to induce strong humoral and cellular immune responses, the aim of this study was to evaluate the diagnostic potential of interleukin-2 (IL-2) as biomarker after specific antigen stimulation with PE35 and PPE68 for the discrimination of active and latent tuberculosis infection (LTBI). The production of IL-2 was measured in the antigen-stimulated whole-blood supernatants following stimulation with recombinant PE35 and PPE68. All the patients with active TB and LTBI had positive QuantiFERON-TB Gold in Tube test. The level of IL-2 following stimulation with recombinant PE35 and PPE68 were significantly higher in LTBI group than in patients with active TB infection or control group. The discrimination performance (assessed by the area under ROC curve) for IL-2 following stimulation with recombinant PE35 and PPE68 between LTBI and patients with active TB were 0.837 (95%CI: 0.72-0.97) and 0.75 (95%CI: 0.63-0.89), respectively. Applying the 12.4 pg/mL cut-off for IL-2 induced by PE35 in the present study population resulted in sensitivity of 78%, specificity of 78%, PPV of 78% and NPV of 100%. In addition, a sensitivity of 81%, specificity of 70%, PPV of 67% and 87% of NPV was reported based on the 4.4 pg/mL cut-off for IL-2 induced by PPE68. In conclusion, peptides of the antigen PE35 and PPE68, absent from commonly used BCG strains, stimulated strong IL-2- positive T cell responses in patients with LTBI. This study confirms IL-2 induced by PE35 and PPE68 as a sensitive and specific biomarker and highlights IL-2 as new promising adjunct markers for discriminating of LTBI and Active TB infection.

**Keywords :** IL-2, PE35, PPE68, tuberculosis
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