



# Regulation network of serum cytokines induced by tuberculosis-specific antigens reveals biomarkers for tuberculosis diagnosis

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**ABSTRACT.** In this study, we identified potential serum biomarkers for the diagnosis of active tuberculosis (TB) and screening for latent TB infections (LTBIs). Peripheral blood samples from 40 healthy individuals, 40 patients with TB, and 40 LTBI individuals were stimulated with the TB-specific antigens ESAT-6 and CFP-10. Human inflammatory cytokine arrays were used to detect the expression of inflammatory cytokines. Cytokines with significant changes were screened to construct a cytokine regulation network. The levels of the cytokines CCL1 (I-309), CXCL9 (MIG), IL-10, IL-6, CSF2, CSF3, IL-8, IL-1 $\alpha$ , IL-7, TGF- $\beta$ 1, CCL2, IL-2, IL-13, and TNF $\alpha$  were significantly upregulated in the active TB group. The levels of CCL3, IL-1 $\beta$ , CCL8, IFN $\gamma$ , and CXCL10 were significantly increased in the TB groups compared to those in the healthy control group. sTNF RII was upregulated in the LTBI group. CCL4 and MIP1d were significantly increased in all groups. The upregulated cytokines were mainly found in the

IFN $\gamma$  and IL-1 $\alpha$  regulatory networks. Importantly, we found that CXCL10 (IP-10), CCL3, CCL8, and IL-1 $\beta$  may be more suitable than IFN $\gamma$  for active or latent TB infection screening. Furthermore, we found that levels of CCL1 (I-309), CXCL9 (MIG), IL-10, IL-6, CSF2, CSF3, IL-8, IL-1 $\alpha$ , IL-7, TGF- $\beta$ 1, CCL2, IL-2, and IL-13 after TB antigen stimulation may help distinguish between active and latent TB.

**Key words:** Cytokine regulation network; Inflammatory cytokines; Interferon-gamma; Tuberculosis