



Biomarkers to identify *Mycobacterium tuberculosis* infection among borderline QuantiFERON results

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Additional laboratory testing of IP-10/CXCL10 and MIG/CXCL9 in individuals at increased risk of reactivation TB with a borderline QuantiFERON-TB Gold Plus result just below the formal cut-off helps to identify those with *M. tuberculosis* infection <https://bit.ly/3t8zR7r>

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Abstract

Background Screening for tuberculosis (TB) infection often includes QuantiFERON-TB Gold Plus (QFT) testing. Previous studies showed that two-thirds of patients with negative QFT results just below the cut-off, so-called borderline test results, nevertheless had other evidence of TB infection. This study aimed to identify a biomarker profile by which borderline QFT results due to TB infection can be distinguished from random test variation.

Methods QFT supernatants of patients with a borderline (≥ 0.15 and < 0.35 IU·mL⁻¹), low-negative (< 0.15 IU·mL⁻¹) or positive (≥ 0.35 IU·mL⁻¹) QFT result were collected in three hospitals. Bead-based multiplex assays were used to analyse 48 different cytokines, chemokines and growth factors. A prediction model was derived using LASSO regression and applied further to discriminate QFT-positive *Mycobacterium tuberculosis*-infected patients from borderline QFT patients and QFT-negative patients

Results QFT samples of 195 patients were collected and analysed. Global testing revealed that the levels of 10 kDa interferon (IFN)- γ -induced protein (IP-10/CXCL10), monokine induced by IFN- γ (MIG/CXCL9) and interleukin-1 receptor antagonist in the antigen-stimulated tubes were each significantly higher in patients with a positive QFT result compared with low-negative QFT individuals ($p < 0.001$). A prediction model based on IP-10 and MIG proved highly accurate in discriminating patients with a positive QFT (TB infection) from uninfected individuals with a low-negative QFT (sensitivity 1.00 (95% CI 0.79–1.00) and specificity 0.95 (95% CI 0.74–1.00)). This same model predicted TB infection in 68% of 87 patients with a borderline QFT result.

Conclusions This study was able to classify borderline QFT results as likely infection-related or random. These findings support additional laboratory testing for either IP-10 or MIG following a borderline QFT result for individuals at increased risk of reactivation TB.

