Enhancing TB Detection: The Role of CD8 T-cell Responses in QFT-Plus

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Latent tuberculosis infection (LTBI) is a critical reservoir for future tuberculosis (TB) disease. In South Korea, TB incidence has fallen sharply in recent years, yet cases now cluster in older adults, making targeted LTBI detection and treatment central to elimination efforts. Traditional tools have important limits: the tuberculin skin test (TST) lacks specificity in BCG-vaccinated populations and carries operational drawbacks—two visits and reader variability—as well as frequent false negatives in the immunosuppressed and the elderly.

QuantiFERON-TB Gold Plus (QFT-Plus) advances IGRA performance by adding a second antigen tube (TB2) with short ESAT-6/CFP-10 peptides that elicit CD8 as well as CD4 responses. Across studies, QFT-Plus preserves high specificity (~96% in low-risk groups) and shows pooled sensitivity near ~94% in active TB, modestly exceeding its predecessor. Notably, the additional CD8+ signal appears to enhance detection in several clinically important contexts. In TB contacts, higher TB2–TB1 interferon-gamma differences have been associated with recent infection, suggesting a potential role for risk stratification. In patients with active TB, particularly those with greater bacterial burden, “TB2-only” responses have been observed, indicating CD8 dominance. In immunocompromised populations, including people living with HIV and patients on prolonged immunosuppressive therapy, TB2 responses have captured infections missed by CD4-only stimulation. Similarly, in elderly populations where CD4 responses may wane, CD8 detection appears to sustain test sensitivity.

QFT-Plus offers clinicians and public health programs a more comprehensive immunological readout than prior assays. By incorporating CD8 T-cell responses, QFT-Plus strengthens diagnostic confidence, reduces false negatives in vulnerable groups, and supports targeted preventive therapy. In the global effort to eliminate TB, CD8 T-cell detection within QFT-Plus represents a pivotal advance in accurate, safe, and scalable LTBI testing.