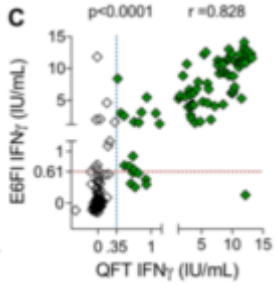
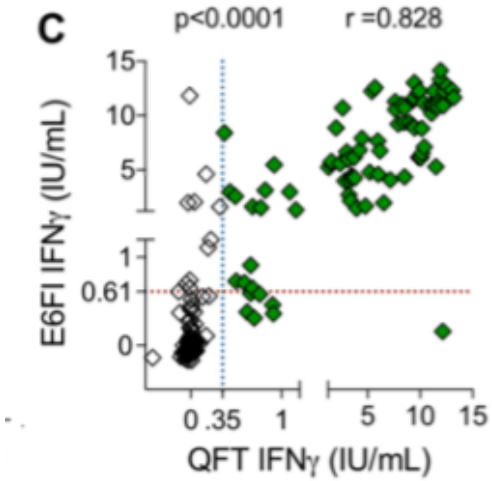
Have you heard of the ESAT-6 free IGRA ?





Correlation between IFN-γ values obtained by QFT and E6FI in all participants was assessed by Spearman test. The dotted lines denote assay cut-offs: 0.35 IU/mL for QFT (vertical line) and 0.61 IU/mL for E6FI (horizontal line).(Source: Nemes *et al.*, 2019)

One of the proposed strategies to combat the tuberculosis (TB) epidemic is the development of pre-exposure vaccines that prevent *Mycobacterium tuberculosis* (M.tb) infection. In

theory, such a vaccine would induce protective memory responses that would prevent M.tb growth and clear bacteria before sustained M.tb infection is established, by so doing prevent development of TB disease.

There is currently no gold standard to measure M.tb sensitisation (exposure or infection). However, the world health organisation recommends the use of either interferon-gamma release assays (IGRA) and/or tuberculin skin test (TST). Unlike TST which measure immune responses to mycobacterial antigens some of which are also found in the BCG vaccine, IGRAs only measure immune responses specific for M.tb antigens CFP10-ESAT6, ESAT-6 and/or TB7.7. As such can be used to determine new M.tb infections in prevention of M.tb infection efficacy trials.

Of the various TB vaccines currently in the TB vaccine pipeline some contain ESAT-6 as one the vaccine antigens. This makes the utility of using current IGRAs such as the QuantiFERON®-TB Gold (QFT®) limited, as both the vaccine (if the vaccine contains ESAT-6) and M.tb infection can induce ESAT-6 specific immune responses. To combat this the ESAT-6 free IGRA was developed (Ruhwald *et al.*, 2017) as a companion diagnostic for TB vaccines that contain ESAT-6. The ESAT-6 free IGRA measures immune responses to CFP-10 as well other immunodominant antigens (EspC, EspF and Rv2348).

A study conducted in South Africa aimed to qualify the ESAT-6 free IGRA in adolescents from a TB endemic region, as well assess its diagnostic performance in comparison to the QFT®. Using M.tb uninfected (QFT negative) individuals and TB patients from South Africa as controls , they were able to define an assay cut-off of 0.61IU/ml. Based on this cutoff, they showed that results from the ESAT-6 free IGRA and QFT are highly correlated with 91% concordance. Theses results demonstrate the suitability of the ESAT-6-free IGRA as diagnostic to determine recent M.bt infection in clinical TB vaccines trials for vaccines that contain ESAT-6.

Article: Nemes *et al.*, 2019. Diagnostic accuracy of ESAT-6 free IGRA compared to QuantiFERON-TB Gold In-tube. Clinical Infectious Diseases.

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