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## BLOOD BASED METHODS OF IDENTIFYING TUBERCULOSIS INFECTIONS IN HIGH HIV/TB INCIDENCE AREAS

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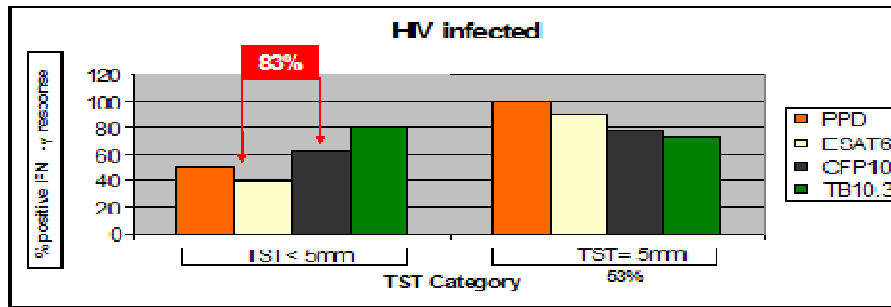
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**BACKGROUND:** TB infection in the HIV-infected presents unique diagnostic challenges. The aim of this study was to determine *in vitro* reactivity to *Mycobacterium tuberculosis* antigens in healthy people with and without HIV infection as well as to compare *in vitro* reactivity with PPD TST (mantoux).

**METHODS:** In a cross-sectional design, 80 people, similar numbers being HIV-infected and uninfected, were recruited for a study that has 80% power to detect a 25% difference (or > 99% power to detect a 40% difference) in RD1 positivity at 5% significance level. The study was conducted at Ubuntu Clinic in Khayelitsha, Cape Town. VCT was the entry point for recruitment. Active TB was exclusory. Skin testing and phlebotomy for laboratory assays were done on the first visit. Skin reactions were measured 48-72 hours later. Diluted whole blood was cultured for 72 hours in the presence of various antigens of *M. tuberculosis*. The Interferon-gamma content of supernatants was determined by ELISA. HIV-infected participants with reactions >5mm were offered isoniazid.

**RESULTS:**

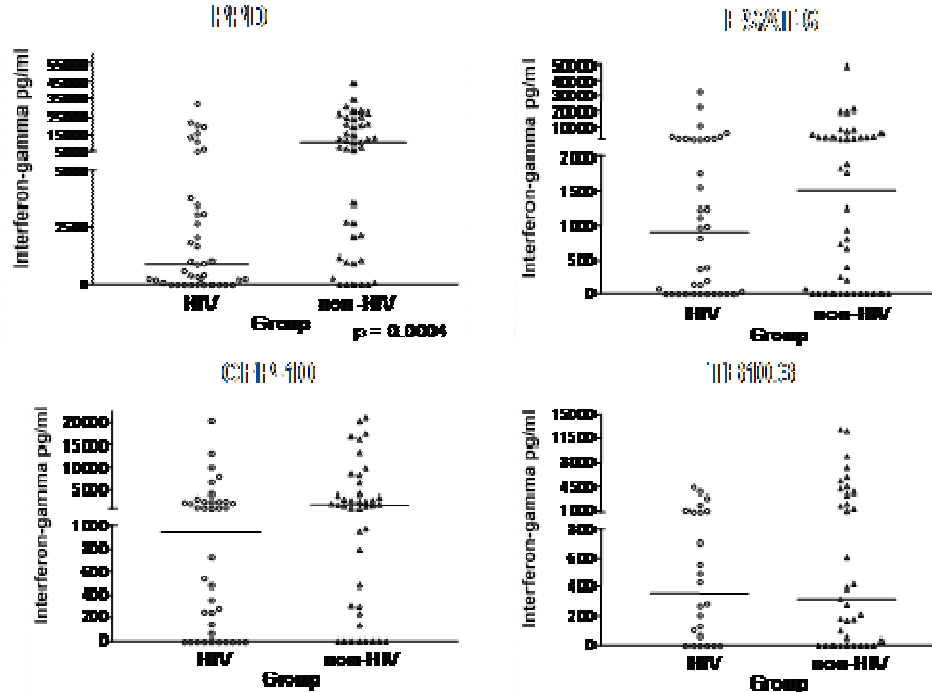
**Figure 1 Showing Percentage of individuals with positive IFN-gamma responses to ESAT6 family of antigens by TST cut off point**



**53% were positive by skin test and the high rate of in vitro reactivity to *M. tuberculosis* antigens accords well with likely latent infection in this group. In the skin test negative group, 83% HIV infected persons reacted to either ESAT-6 or CFP-10, a similar rate to that found in the HIV uninfected group.**

[Percentage with positive responses by TST]

**Figure 2: Interferon-gamma secretion in response to PPD and to three antigens secreted by replicating *Mycobacterium tuberculosis*.**



**The results show that whilst the in vitro response to PPD is clearly depressed in HIV infected people, the response to antigens actively secreted by replicating *M. tb.* is less affected**

[Median IFN-gamma responses]

**CONCLUSIONS:** Compared to HIV uninfected, the recall response to PPD in HIV-infected people is impaired. By contrast, the responses to antigens secreted by dividing *M. tuberculosis* are well preserved. This has implications for immunodiagnosis: There is a role for RD1 assays in the HIV context and these tests may identify more people for TB prophylaxis. HIV may not quite be the Achilles' heel of T cell based assays!

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