

INTRODUCING IP-10 AS A SPECIFIC DIAGNOSTIC MARKER FOR INFECTION WITH *M.TUBERCULOSIS*

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Introduction: IFN- γ responses to *M.Tuberculosis* specific antigens (ESAT-6, CFP10 and TB7.7) are used in the *in vitro* diagnostic tests for tuberculosis. The *in vitro* tests have proven both sensitive and specific for latent and active tuberculosis disease, but may lead to false positive or negative diagnostic results as they rely on measurements of IFN- γ produced at very low levels.

We have screened a panel of 25 biomarkers as alternatives to IFN- γ as diagnostic markers of TB infection. This screening led to the discovery of one potentially highly interesting marker, the chemokine IP-10 (CXCL10). We here present data from a small scale study in patients with active TB.

Material and methods: Twelve patients with active TB and positive IFN- γ test (Quantiferon); seven patients with active TB and negative IFN- γ test (of which five were immunosuppressed due to HIV+) and eleven healthy TB unexposed controls were included. Whole blood from each patient was set up in 3 cultures and stimulated with saline, TB specific antigens (ESAT-6, CFP10, TB7.7) and mitogen (PHA) respectively. Plasma was analysed by Luminex for IP-10, IL-2 and IFN- γ production and compared to IFN- γ measurement by Quantiferon ELISA.

Results: Concentration of IP-10 in plasma of whole blood was significantly higher in patients with active TB than in un-exposed healthy individuals after *in vitro* stimulation with *M.tuberculosis* specific antigens. IP-10 was released in significantly higher amounts compared to IFN- γ and IL-2.

Of the seven patients with active TB but negative IFN- γ test, four produced strong IP-10 responses.

Discussion: We have identified a novel specific *in vitro* diagnostic marker for infection with *M.tuberculosis* which appears more sensitive than IFN- γ . As IP-10 is produced in significantly higher amounts compared to IFN- γ , a new highly sensitive test for the use in immunocompromised individuals, or a simple dipstick method for use in a resource poor setting may be developed.