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Genetic susceptibility and resistance to tuberculosis

This study investigated possible biomarkers of susceptibility and resistance to *Mycobacterium tuberculosis*, identifying gene expression profiles associated with active tuberculosis (TB). Among a South African cohort, genome-wide transcription profiles of whole blood were obtained from 33 TB patients, 34 healthy donors latently infected with *M tuberculosis* (LTBI) and 9 healthy non-infected donors (NIDs). Cluster analysis of genes demonstrated pronounced differences among TB patients compared with the LBTI and NID groups, with no significant difference in clustering between the LBTI and NID groups.

Reverse transcriptase PCR identified Fc γ receptor 1B (FCGR1B) as the most strongly differentially expressed gene in the TB group compared to LBTI. This gene, combined with four other most prominently differentiated genes—CD64, Lactoferrin, guanylate binding protein 5 and Granzyme A—allowed discrimination between TB and LTBI groups with a sensitivity of 94% (30/32 patients) and specificity of 97% (33/34 patients). Functional annotation clustering demonstrated distinct differences between TB and LBTI groups with increased expression of macrophage-associated genes and reduced expression of natural killer-associated genes as well as reduced apoptosis in TB patients compared to the LBTI group.

This research demonstrates the importance of genetic control over the innate immune system in the development of active TB. Defining a genetic biosignature of resistance or susceptibility to *M tuberculosis* identifies targets for future drugs and vaccines, an approach critically important in reducing the significant burden of TB disease worldwide.

► **Maertzdorf J**, Repsilber D, Parida SK, *et al*. Human gene expression profiles of susceptibility and resistance in tuberculosis. *Genes Immun* 2011;**12**:15–22.

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