TNF-308 and DDX39B-22/-348 polymorphisms in individuals with latent versus active tuberculosis in Salvador, Bahia, Brazil

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Polymorphisms in genes that regulate the immune response can influence the progression of tuberculosis (TB) from latent infection to disease. TNF is a cytokine that influences many aspects of TB disease, including granuloma formation and maintenance, cytotoxicity and death of infected cells. We addressed three polymorphisms in the short arm of human chromosome 6 that influence the TNF production: the polymorphism TNF-308G>A, in the promoter region of the TNF gene, and the polymorphisms DDX39B-22C/G and -348C/T. The DDX39B gene encodes a nuclear protein called HLA-B-associated transcript 1 (BAT1) that also influences the production of other pro-inflammatory cytokines. We describe the genotypic and allelic frequencies of TNF-308G>A, DDX39B-22C/G and -348C/T in active tuberculosis patients compared with latently infected individuals. Individuals of both sexes aged 18-60 years recently diagnosed with active TB (confirmed by positive BAAR and/or culture) or with latent TB (confirmed by tuberculin skin test induration equal or above 10mm within 48-72h of application) were recruited in a reference TB hospital. Volunteers were excluded if they refused HIV test or had an indeterminate HIV result, or if no PCR product could be amplified from blood collected in EDTA vacuum tubes after 3 attempts of DNA extraction from 2 independent aliquots. The polymorphisms were assessed using PCR restriction fragment-length polymorphism analysis in agreement with previous work. We observed significant association of TNF -308A with active TB disease in our population. Individuals with active TB had 4.8 times higher odds of presenting the GA/AA genotype. The DDX39B -22 GG genotype and the DDX39B -22 G allele were also associated with active TB. The allelic combinations TNF-308G/DDX39B-22C/DDX39B-348T and TNF-308A/DDX39B-22G/DDX39B-348C were associated with active disease.

Key-words: tuberculosis; genetic variants; immune modulation; human.

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