

Tuberculosis in Association with Human Leukocyte Antigen

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Commentary

Currently, association between human leukocyte antigen (HLA) and the development of tuberculosis (TB) is still not widely well-known. Tuberculosis is still a global threatening disease in this century, particularly in the developing countries like Asian and African countries. Excellent knowledge in TB-related HLA is substantially needed for the development of novel strategic measures against TB, particularly multidrug-resistant TB around the world, such as the development of novel adult TB vaccines. The articles selected and cited in this review are mostly related to the developing countries, particularly Asian countries, where TB is a threatening public health problem.

HLA studies conducted in India revealed that there was association of *HLA-DQ 1* and *-DR 2* antigens with susceptibility of pulmonary TB [1]. A study in North Indian patients demonstrated that the allele *DRB 1*1501* of *HLA-DR 2* was higher compared with *DRB 1*1502* [1] whereas *HLA-DQB 1*0601* (a subtype of *HLA-DQ 1*), *-DRB 1*1501* and *DPB 1*02* were demonstrated to be positively associated with pulmonary susceptibility among South Indian patients [1]. Antigen processing gene 2 and mannose-binding protein (MBP) genes along with *HLA-DR2* have been associated with pulmonary TB [1]. Mannose-binding lectin-54 heterozygotes may be associated with protection against TB meningitis [1]. *HLA-DQB 1*0601* and *HLA-DRB 1*0803* were associated with TB disease progression in Korean populations [2]. The frequencies of *HLA-DQB 1*0402* and antigens DR4 and DR8 were significantly decreased in patients with pulmonary TB but the frequencies of *HLA-DQA 1*0101*, *-DQB 1*0501* and *-DRB 1*1501* were significantly increased in immunocompetent patients with pulmonary TB [3]. An increased frequency of *HLA-B*27* in the Greeks, *HLA-A*2* and *-B*5* in the Egyptians, *HLA-B*5*, *-B*15* and *-DR*5* in the North American blacks, *HLA-B*8* in the Canadians was observed [1] whereas *HLA-DQB 1*0502* and *-DQB 1*0503* alleles were demonstrated among the Thai and Vietnamese TB patients, respectively [1,4]. *HLA-B*17-tumor-necrosis-factor- α -238/A*, *-tumor-necrosis-factor- α -308/2* and *-tumor-necrosis-factor- β -2* have been shown to be associated with TB bacteriological relapse among Indian population [5]. Recently, a novel *HLA-DR*-restricted peptide E7 from the ESAT-6 protein of *Mycobacterium tuberculosis* before and during TB treatment was used to prepare modified *HLA-DR*08032/E7* and

*HLA-DR*0818/E7* tetramers to monitor tetramer-positive CD4+ T-cells in direct staining of single specimen and flow cytometric analyses and resulted in 0.1 to 8.8% in the initial pulmonary TB patients' blood, 0.1 to 10.7% in pleural fluid of the initial tuberculous pleuritis patients, 0.02 to 2.2% in non-TB patients' blood, 0.02 to 0.48% in healthy donors' blood and mostly resulted in 0 to 0.2% in umbilical cord blood [6]. After 90-120 days of initial TB symptoms, levels of tetramer-positive CD4+-T cells in tetramer-positive CD4+-T cells reached and kept at low even normal at 0.03 to 0.3% [6]. Tetramer-positive, interferon- γ -producing and/or tumor-necrosis-factor- α -producing CD4+-T cells in pulmonary granuloma, lymph node and cavernous tissues of TB patients could be detected by in situ staining [6]. Sensitivity and specificity of tetramer molecules should be confirmed in the future in order to develop possible diagnostic reagents and research [6].

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