International Journal of Mycobacteriology xxx (2016) xxx–xxx

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Susceptibility to pulmonary tuberculosis: host genetic deficiency in tumor necrosis factor alpha (TNF-α) gene and tumor necrosis factor receptor 2 (TNFR2)

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ARTICLE INFO

Article history:
Received 13 September 2016
Accepted 14 September 2016
Available online xxxx

Keywords:
Single nucleotide polymorphisms
TNF-α gene
TNF Receptor 2 (TNFR2)
Tuberculosis

ABSTRACT

Objective/Background: The susceptibility to tuberculosis (TB) depends upon different factors, and the risk of developing diseases after infection with *Mycobacterium tuberculosis* ranges from 5% to 10%. This suggests that besides the mycobacterial itself, the host genetic factors may determine the differences in host susceptibility to TB. Among the important risk factors, cytokines and especially tumor necrosis factor alpha (TNF-α) genes, are thought to be responsible for regulating the protective immune responses. The TNF-α gene that encodes the cytokines TNF-α is located within the class III region of the major histocompatibility complex (MHC). The TNF-α gene and its receptors have significant suppressive effects on bacterial growth into macrophages. Tumor necrosis factor receptor 1 (TNFR1) is more responsible when apoptosis is needed but tumor necrosis factor receptor 2 (TNFR2) is involved in cell survival. TNF-α conducts its replicative effects on immune cells via the latter. Up to now, several polymorphisms within the promoter region of the TNF-α gene have been shown to be associated with susceptibility or resistance to TB in different ethnic groups. By contrast, the correlation of TNF-α gene with their receptors such as TNFR2 in susceptibility to TB has not been resolved yet. In this study, we aimed to analyze the single nucleotide polymorphisms (SNPs) in the TNF-α gene at the –238, –308, –857, and –863 positions, and compare the susceptibility to TB with polymorphisms at TNFR2 (T587G).

Methods: One hundred fifty-one tuberculosis patients ($n = 151$) and 83 control subjects ($n = 83$) were included in this study. Polymorphisms in the TNF promoter region, namely TNF (SNP), –238, –308, –857, and –863 were studied using polymerase chain reaction–restriction fragment length polymorphism (PCR–RFLP). For TNFR2 polymorphisms at 587 positions, the following primers were used to amplify a 242 base pair (bp) product: 5′-TTCTGGAGTTGGCTGCGTGT-3′ and ACTCTCCTATCCTGCCTGCT-3′. PCR products of TNFR2 digested with 2 U enzymes of NLA III.

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Peer review under responsibility of Asian African Society for Mycobacteriology.
http://dx.doi.org/10.1016/j.ijmyco.2016.09.038

Results: The current study found a strong correlation between two polymorphisms in different loci of TNF-α gene including 857 C/C (85; 56.2%) and TNF 238 A/A 127 (84.1%). However, there were no associations between polymorphisms of the TNF-α gene and its receptor, that is, TNFR2.

Conclusion: Concerning our current study, screening assessments for TNF-α-857 and A238GSNPs in Iran would be important in order to make future decisions for preventive treatments before getting the disease among individuals who are at high risk considering their genotyping.

Conflicts of interest

All authors have no conflicts of interest to declare.

Please cite this article in press as: E Ghamari et al. Susceptibility to pulmonary tuberculosis: host genetic deficiency in tumor necrosis factor alpha (TNF-a) gene and tumor necrosis factor receptor 2 (TNFR2). Int. J. Mycobacteriol. (2016), http://dx.doi.org/10.1016/j.ijmyco.2016.09.038