

Genetics of Inflammatory bowel disease: Role of cytokine genes polymorphisms

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Background: Inflammatory bowel disease (IBD) comprising of ulcerative colitis (UC) and Crohn's disease (CD), is a chronic inflammatory disorder of gastrointestinal tract with global medical importance. It is a multifactorial disease in which immune dysregulation caused by genetic and/or environmental factors plays an important role. An active inflammatory response is an important feature of IBD. Both UC and CD are characterized by activation of macrophages and T lymphocytes; pro-inflammatory cytokine, chemokine, and adhesion molecule expression; and an inability to adequately down-regulate immune activation. IBD, particularly CD, is characterized by a predominantly T helper (Th) 1 type profile, involving the up-regulation of pro-inflammatory cytokines. Interleukins (IL) , Tumor necrosis factor (TNF) and transforming growth factor (TGF)- β 1 are key cytokines in the initiation and propagation of IBD. The objective of this study was to evaluate the role of these cytokines genes polymorphisms in the etiology of IBD in Saudi patients.

Methods: A total of 379 Saudi subjects including 179 IBD patients and 200 age and sex matched healthy controls were recruited. IL-10, IL-6, TGF- β 1 genes were amplified using an amplification refractory mutation systems PCR methodology to evaluate the IL-10 (-1082G/A), (-819C/T), (-592C/A), IL-6 (174G/C) and TGF- β 1 (509C/T) polymorphisms in patients and control groups.

Results: The frequencies of alleles and genotype of IL-10 (-1082G/A), (-819C/T), and (-592C/A) polymorphisms differed between IBD patients and controls however the difference was statistically significant only for IL-10 (-1082G/A) polymorphism. Moreover the distribution of alleles and genotypes of IL-6 (174G/C) and TGF- β 1 (509C/T) polymorphisms was not significantly different in patients than controls. Our study clearly indicated that the IL-10 (-1082 G/A) polymorphism is associated with the risk of IBD susceptibility, while IL-10-819C/T, IL-

10-592C/A, IL-6 (174G/C) and TGF- β 1 (509C/T) polymorphisms are not associated with IBD in Saudis.

Conclusion: IL-10 (-1082G/A), polymorphism is associated with risk of developing IBD in Saudi patients. However, well-designed epidemiological as well as genetic association studies with large sample size among different ethnicities should be performed in order to have better understanding of this relationship.