FOXP3 Gene Polymorphism among Egyptian patient with Behcet's *Disease*

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SUMMARY

Behçet's disease (BD) is a chronic relapsing multisystemic inflammatory disorder characterized by four major symptoms (oral aphthous ulcers, genital ulcers, skin lesions, and ocular lesions) and occasionally by five minor symptoms (arthritis, gastrointestinal ulcers, epididymitis, vascular lesions, and central nervous system) **(Cho *et al.,* 2012b)**. Patients with BD may manifest all or only some of these clinical features **(Schwartz *et al*., 2000; Harmouche *et al*., 2007; Wallace *et al*., 2007).**

BD has a worldwide distribution, but it is more prevalent in the regions along the ancient trading route known as "Silk Road," extending from Mediterranean countries such as Turkey and Iran to the Far East including Korea and Japan. The prevalence of BD in Turkey is particularly high 80–420⁄100,000 **(Azizlerli *et al*., 2003)**. In Egypt the prevalence is at 7.6/100,000 **(Assaad-Khalil *et al*., 1997)**.

Although its etiopathogenesis remains elusive, the most widely accepted hypothesis is that the excessive inflammatory response is triggered by an infectious agent in a genetically susceptible host. Human leukocyte antigen (HLA)–B51 has been identified as the genetic marker most strongly associated with BD, but it has also been reported that the highest contribution made by the HLA-B locus to overall genetic susceptibility to BD is 19%. This is why other susceptibility genes have been extensively

investigated **(Gül 2001; Gül *et al*., 2001)**.It is now well known that cytokines play critical roles in the pathogenesis of BD, because they mediate many of the effectors and regulatory functions of immune and inflammatory responses (**Yazici, 2004; Imamura *et al*., 2005; Ahn *et al*., 2006**).

T regulatory (T reg) cell is one of the immune system cells involved in the pathogenesis of BD , defined by the expression of CD4, CD25 and the transcription factor forkhead box (**FOXP3**) which is master regulator for the development and function of Treg cells **(Fontenot *et al.* 2003;Hori *et al.* 2003; Khattri *et al.* 2003)** The FOXP3 gene provides instructions for producing the forkhead box P3 (FOXP3) protein. Which bind to specific regions of DNA and helps control the activity of genes that are involved in regulating the immune system.

The aim of this study was to investigate the potential associations of two SNPs at Foxp3 (–3499 A/G) and (–3279 C/A) with the susceptibility or clinical manifestations of BD in the Egyptian population.

Blood samples, collected in (EDTA) sterile tubes, from 69 BD patients (52 men and 17 women) recruited from the Department of Rheumatology at El-Kasr El-Aini hospital. All patients were diagnosed according to **(ISG) for Behcet's Disease, 1990)**. At time of blood sampling, patients with two or more lesions in the previous 4 weeks were regarded to have active disease **(Aydintug *et al*., 1995)**. A control group composed of eighty four age and gender matched healthy control unrelated to each other or to the patients were recruited.

Genomic DNA was extracted from blood samples by using Wizard® Genomic DNA Purification Kit (Promega ,USA) according to the

manufacturer's instructions. We genotyped Foxp3 (-3499 A/G) and (-3279 C/A) using (PCR- RFLP) .

No association between any genotype of Foxp3 (-3499 A/G) and (-3279 C/A) polymorphism and the susceptibility to BD .

It was found that male patients with BD had significantly lower frequency of -3279 C allele ($P < 0.05$) than healthy control. Also BD patient totally have lower frequency of total C allele . C allele is negatively correlated with BD patient ($r = 0.495$; $P < 0.05$) , it might be protective allele .

Also we found Significant association between Foxp3 (-3279 C/A) A allele and neural involvement in BD was found that patients with neural involvement had significantly heigher frequency of -3279 A allele ($P = 0.048$) than patients without and neural involvement is positively correlated with -3279 A allele ($r = 2.31$).

CONCLUSION.

1- There is no association between any genotype of Foxp3 (-3499 A/G) and (-3279 C/A) polymorphism and the susceptibility to BD .

2- The C allele (-3279 C/A) is negatively correlated with suceptability to Behcet's Disease.

3- The neural involvement is positively correlated with A allele (-3279 C/A).