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SNPs in the promoter region of FOX P3 gene: A critical analysis of association with Graves's disease and Hashimoto's thyroiditis in terms of Th1/Th2 responses

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Abstract

The forkhead box P3 (FOX P3) is a major transcriptional regulatory factor required for the development and functioning of T –regulatory cells (CD4+, CD25+, T-cells). Through interaction with the nuclear factor of the activated T-cells (NFAT) , the FOX P3 molecule controls the functioning of the regulatory T-cells. In this presentation we analyze the association of two Single Nucleotide Polymorphisms (SNPs) in the promoter region of the FOX P3 gene -3279C/A and -2383C/T with Graves disease and Hashimoto's thyroiditis respectively. An important feature of these two autoimmune diseases is that a predominant Th2 type of immune response to thyroid antigens (eg. Anti-TSHR antibodies) is reported in Graves disease contrary to a predominant Th1 response in Hashimoto's thyroiditis. This indicates a profound influence of the genotypes of -3279C/A and -2383C/T SNPs of FOX P3 gene in determining the pattern of immune response (Th1 / Th2). The role of the above mentioned polymorphisms in affecting clonal expansion / functional efficiency of T regulatory cells and thus resulting in diverse patterns of immune response in autoimmune thyroid disorders will be discussed in combination with genotypes of certain pro- and anti-inflammatory cytokines. Ethnic differences in the association of genotypes of these SNPs and variations in the frequencies of their genotypes / alleles will also be discussed.