Introduction

Graves' disease is a thyroid-specific autoimmune disorder in which the body makes antibodies to the thyroid-stimulating hormone receptor (TSHR). It is the most common cause of hyperthyroidism, causing a wide range of symptoms from anxiety and restlessness to insomnia and weight loss. In addition, the eyeballs may begin to stick out, causing eye irritation and tearing ***(Saitoh and Nagayama, 2006)***.

To function properly, the immune system must discriminate between self and non-self. When self/non-self discrimination fails, the immune system destroys cells and tissues of the body and as a result causes autoimmune diseases. Regulatory T cells actively suppress activation of the immune system and prevent pathological self-reactivity, i.e. autoimmune disease. $CD4^+CD25^+$ regulatory T cells (Treg) play a central role in the prevention of autoimmunity and in the control of immune responses by down-regulating the function of effectors $CD4^+$ or $CD8^+$ T cells. The critical role regulatory T cells play within the immune system is evidenced by the severe autoimmune syndrome that results from a genetic deficiency in regulatory T cells ***(Shevach, 2002; Chen et al., 2007).***

The development of T cell-mediated autoimmune diseases [such as thyroiditis, gastritis and insulin-dependent diabetes mellitus (IDDM)] can be prevented in various animal models by inoculating $CD25^+CD4^+$ T cells prepared from histocompatible normal animals. Furthermore, various autoimmune diseases including thyroiditis, gastritis and IDDM can be *de novo* produced in normal rodents by simply removing a $CD25^+$

subpopulation of $CD4^+$ T cells without exogenous immunization with self-antigens, and reconstitution of the removed cell population prevented the development of these autoimmune diseases , so regulatory T cells play important roles in immune system homeostasis, and may also be involved in tumor immunotolerance by suppressing Th1 immune response which is involved in anti-tumor immunity ***(Cao et al.,2007).***

Two major classes of regulatory T cells have been described, including the naturally occurring Treg cells and the adaptive or induced Treg cells. Naturally occurring Treg cells (also known as $CD4^+CD25^+FoxP3^+$ Treg cells) arise in the thymus, whereas the adaptive Treg cells [also known as Type 1 T regulatory (Tr1) cells or T helper-3 (Th3) cells] may originate during a normal immune response in the periphery. Naturally occurring Treg cells can be distinguished from other T cells by the presence of an intracellular molecule called FoxP3 ***(Hong et al., 2006)***.

Apoptosis is a form of programmed cell death that is characterized by specific morphologic and biochemical properties. Morphologically, apoptosis is characterized by a series of structural changes in dying cells: blebbing of the plasma membrane, condensation of the cytoplasm and nucleus, and cellular fragmentation into membrane apoptotic bodies ***(Steller, 1995***).

Apoptosis plays a critical role in the development and homeostasis of multicellular organisms. An increased rate of apoptosis is involved in the pathogenesis of several diseases ***(Mihara et al., 1999)***.

Besides autoantibodies to the thyroid-stimulating hormone receptor, autoantibodies to thyroglobulin (Tg) and thyroid peroxidase (TPO) are characteristic serum markers of thyroid autoimmunity in Graves' disease. Moreover, Ab to both autoantigens are frequently present in the same patient. One explanation for their concurrence is that they arise independently in response to the release of their respective autoantigens (***Latrofa et al., 2004).***