B. IMMUNE TOLERANCE SECTION
HEAD: PANOS VERGINIS, PhD

BACKGROUND

Autoimmune diseases develop as a consequence of failure in central and/or peripheral tolerance. Therefore, by using animal models of autoimmune inflammatory rheumatic diseases we would aim in the development of strategies that could result not only in prevention but also in the cure of the unwanted autoimmune response.

Two important mechanisms account for self-nonself discrimination by the immune system, which permits immunity while maintaining tolerance to self: clonal deletion of potentially hazardous self-reactive lymphocytes within the thymus represents one important mechanism. Despite its high efficiency, it is well known that thymic deletion does not eliminate all autoreactive T cells and that healthy individuals harbor an autoimmune repertoire. Accumulating evidence suggests that autoreactive T cells in the periphery, are kept in check by regulatory T cells (Tregs) that actively suppress both their activation as well as their effector function, thereby preventing the development of autoimmune disease. The discovery of the transcription factor Foxp3 as a specific marker for Tregs has been very useful to distinguish Tregs from other T cells. These findings as well as the elucidation of pathways that govern Treg generation raise hope to clinically use these cells to suppress undesirable immune responses to autoantigens or foreign antigens.

RESEARCH

1. Induction of antigen-specific Tregs. We have recently showed, in an animal model, that infusion of an alloantigen by osmotic mini-pumps, results in transplantation tolerance, through the induction of alloantigen-specific Treg cells. According to our hypothesis, pump infusion of a given autoantigen will convert naïve CD4+ T cell to autoantigen-specific Tregs that will suppress the autoimmune response. This hypothesis will be addressed by using mouse models of SLE and RA.

2. Role of PD-1 on Treg development and function. Several lines of evidence suggest that the PD-1/PD-L1 pathway plays an important role as a negative regulator of autoimmune response. PD-1 is expressed on activated B, T, myeloid cells as well as Tregs. Since PD-1 gene disruption in mice results in a lupus-like glomerulonephritis and destructive arthritis, it is of great interest to assess how Treg development and function is affected.

REPRESENTATIVE PUBLICATIONS

1. Guy C., Wang J., Verginis P., Kolypetri P., Carayanniotis G. Suppression of thyroiditis in mice expressing a transgenic TcR specific for a thyroglobulin peptide may reflect involvement of regulatory T cells. Manuscript in Preparation. 2007

2. Verginis P., McLaughlin KA., Wucherpfennig KW., Von Boehmer H., Apostolou I. Induction and visualization of antigen-specific regulatory T cells in wild-type mice: implications for transplantation tolerance. Blood, 2007 Submitted

3. H. S. Li, P. Verginis and G. Carayanniotis. Maturation of dendritic cells by necrotic thyrocytes facilitates induction of experimental autoimmune thyroiditis. Clinical and Experimental Immunology, 2006 144 (3), 467-474.

4. Verginis P., Li S.H., Carayanniotis G. Tolerogenic semi-mature dendritic cells suppress experimental autoimmune thyroiditis by activation of thyroglobulin-specific CD4+CD25+ T cells. The Journal of Immunology, 2005, Jun 1; 174(11): 7433-7439

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