Controlling Inflammation: Inducing and Maintaining Regulatory T cells in Tissues

ABBAS, Abul K.

Professor and Chair, Department of Pathology, University of California San Francisco, USA

E-mail: abul.abbas@ucsf.edu

ABSTRACT

The immune system exists in a balance between the generation of effector and memory lymphocytes to protect against pathogens and the generation of $Foxp3^+$ regulatory T cells (Tregs) to prevent or limit inflammatory reactions. Failure of control mechanisms is the fundamental cause of many inflammatory disorders. We have exploited transgenic mouse models to examine T cell responses to systemic and tissue-restricted self antigens and how these responses are controlled. Exposure of naive CD4 T cells to systemic or tissue antigens under various conditions leads to the development of pathogenic effector cells, and inflammatory disease. The disease resolves spontaneously, associated with the generation and activation of Tregs. Tregs that encounter tissue antigen acquire increased suppressive activity, and a fraction of these Tregs persists as a memory population that continues to control subsequent inflammatory reactions in the tissue. Thus, Tregs go through a sequence of development in the thymus, activation in the periphery to perform their function, and survival as memory cells, which is fundamentally similar to the life history of all lymphocyte populations. The generation and maintenance of pathogenic effector T cells vs protective Tregs are determined by: i) the duration of antigen exposure, with persistent antigen reducing effectors and preserving Tregs, and ii) cytokines, especially IL-2, which, at low concentrations, preferentially expands and maintains Tregs.

Elucidating the stimuli that generate and maintain functional Tregs in tissues will likely be valuable for manipulating immune responses in inflammatory diseases and for optimal vaccination and cancer immunotherapy.