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SEMINAR

Gene signature of regulatory cells: adaptive Tr1 cells and tolerogenic DC-10

Speaker

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Abstract

Regulatory cells are critically involved in promoting and maintaining immune tolerance via their ability to control responses to self and foreign antigens. Over the years, several types of regulatory cells have been identified but, to date, the best characterized are the CD4+ regulatory T cells (Tregs) and tolerogenic dendritic cells (DC). The latter play a key role in limiting immunity and in promoting tolerance primarily via the induction of Tregs. Previous and current work from our laboratory aims at elucidating the mechanisms underlying the induction of Tregs via tolerogenic DC.

Among CD4+ Tregs we studied the CD4+ IL-10-producing Tr1 cells, which are induced in the periphery upon chronic Ag stimulation in the presence of IL-10, and suppress T cell responses mainly via cytokine-dependent mechanism and of the killing of myeloid antigen-presenting cells through the release of Granzyme B. Moreover, our group identified and characterized a new subset of human tolerogenic DC, termed DC-10, present in vivo and inducible in vitro from monocytes in the presence of IL-10. DC-10 secrete high amounts of IL-10, express high levels of membrane-bound (mb)HLA-G1 and the tolerogenic immunoglobulin-like transcript (ILT)4, and potently induce antigen-specific Tr1 cells.

Our work is currently focusing on defining the molecular signature of Tr1 cells and identifying a pattern of DC-10-specific markers and further defining their tolerogenic role in vivo. To this end, we performed a gene expression profile of Tr1 cell clones and of DC-10 and we identified a number of gene up- and down-regulated in both Tr1 and DC-10.

Results will provide the basis for a deep understanding of Tr1 cells and of DC-10 role in tolerance and for elucidating the molecular mechanisms governing their induction and functions.

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