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The Important Role of TH1/TH2 Balance in Immune Disease: its Regulation by Interleukin-12

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Recently, it has been demonstrated that antigen-specific naive Th cells are differentiated into two types of functional Th cell subsets, Th1 and Th2 cells. Th1 cells producing IFN-γ, IL-2 and TNF-β are involved in the regulation of cellular immunity. On the other hand, Th2 cells producing IL-4, IL-5 and IL-6 are important in humoral immunity. Thus, Th1/Th2 balance plays an important role in immunoregulation. In this paper, we investigated the role of Th1/Th2 balances in various immune disease models including tumor and infectious diseases, Moreover, we addressed what factors are involved in genetically-controlled Th1/Th2 balance in vivo.

In vivo administration of IL-12 caused the inhibition of both transplantable and primary tumor growth in concomitant with the augmentation of serum IFN-γ levels and the generation of tumor-specific protective immunity. Such activation of Th1-dominant immunity was also demonstrated to be effective on *Trypanosoma cruzi* infection models and Th2-dependent autoimmune model.

Reversely, IL-12 accelerated the onset of some immune diseases such as Th1-dependent liver injury and graft versus host diseases (GVHD). In such diseases, in vivo administration of anti-IL-12 mAb showed a strong therapeutic effect. Thus, it seems to be true that Th1/Th2 balance plays an important role in various immune diseases and it is possible to regulate their balance by IL-12 or its antagonist.

In mice, predisposition toward differentiation to pathogenic Th1 or Th2 effector cells in immune disease models appeared to be genetically controlled. We found that the strain different skewing to Th2 immunity was closely correlated with their distinct ability to produce IL-4 or IL-10, which is controlled by non-MHC gene-encoded unknown factors. The determination of these factors involving the regulation of Th1/Th2 balance will provide a new strategy for the development of diagnosis and immunotherapy for immune diseases.

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