T-BET EXPRESSION IN REGULATORY B CELLS

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T-bet (Tbx21) was originally described as a T cell specific transcription factor that plays a central role in Th1 development. It was recently discovered that T-bet has an important function in B cells too; T-bet regulates immunoglobulin class switching and contributes to the production of pathologic IgG2a. From our results, we have learned that in B cells, T-bet is regulated by signals mediated through the B cell antigen receptor and Toll-like receptor 9, the same receptor-mediated cascades that have a well known impact on the function of so-called regulatory B cells. Regulatory B cells are an inducible B cell population, characterized by cell surface phenotypes and IL-10 production and by the suppressive role they show during the remission phase of autoimmune diseases.

Based on these knowledge, we were very interested in to characterize the population of regulatory B cells and find out more about their suppressive function on autoimmune processes. For this purpose we generated the CIA mice (Collage-Induced-Arthritis in mice; an inducible animal model of human rheumatoid arthritis) and followed the changes in regulatory B cell numbers during the disease progression. Isolated regulatory B cells from the acute and remission phases of CIA were analysed for T-bet and IL-10 expressions in order to find out if there was any connection between T-bet expression and the suppressive function of IL-10 on isotype switching and autoimmune IgG2a antibody production.

For the induction of CIA, female DBA/1J mice at 10 weeks of age were immunized with bovine type II collagen in complete Freund's adjuvant. During the disease progression mice were observed and scored weekly for clinical signs of arthritis. Spleens were removed during the acute and remission phases of arthritis and regulatory B cells were sorted by their cell surface characteristics. For the analysis of T-bet and IL-10 mRNA expressions RNA was isolated from sorted cells, converted to cDNA and analysed by real-time RT-PCR.

From our experiments we found that in correlation with the elevated serum IgG2a levels the absolute number of regulatory B cells increased during the disease progression, moreover gene expression experiments showed inducible upregulation of IL-10 expression by signals important for regulatory B cells.

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