the context of MHC class II molecules and (2) co-stimulation. Using myelin oligodendrocyte glycoprotein (MOG)-induced experimental autoimmune encephalomyelitis (EAE) as a prototypical model of T cell-driven autoimmune disease, the authors and others demonstrated previously that autoimmune B cells are crucial in T cell activation by acting as potent antigen-presenting cells. Although the importance of the second signal, co-stimulation, is demonstrated by the clinical efficacy of CTLA4-Ig in different autoimmune diseases, it remains unknown whether this signal can be efficiently provided by B cells and the relative contribution of autoantigen presentation versus co-stimulation. To address experimentally if exaggerated co-stimulation without cognate antigen presentation by B cells is sufficient to activate pathogenic T cells, the authors studied the development of spontaneous EAE in the presence of MOG-specific T cells and non-antigen-specific B cells which constitutively express the co-stimulatory molecule CD70.

Materials and Methods 2D2 mice (in which 95% of T cells are MOG-specific) were crossed with CD70 mice (with transgenic expression of the co-stimulatory molecule CD70 under the CD19 promotor, leading to constitutive expression by B cells). Mice were scored for signs of spontaneous EAE on a 4-point scale over a 20-week period. Brains, spinal cords, optical nerves, blood and lymphoid organs were harvested for histological and functional analysis.

Results 4% of the mice in the single transgenic group developed signs of EAE. In contrast, 24% of 2D2 CD70 mice developed spontaneous EAE ($p=0.06$, mean maximal clinical score 2.8; mean age of onset 73 days). Histological analysis revealed inflammatory foci in the spinal cord of sick double transgenic animals. Moreover, infiltrating lymphocytes were detected in the optical nerves of both sick and healthy double transgenic mice. Phenotypic analysis of lymphocytes in 2D2+CD70 mice relative to the single transgenic 2D2 revealed an increase in CD4 T cells, the corresponding decrease in B cells and a decrease in FoxP3+ regulatory T cells.

Conclusions The constitutive expression of the co-stimulatory molecule CD70 B cells is sufficient to activate pathogenic T cells and induce autoimmune disease in this model. The functional profile of these activated T cells is currently under investigation.

A180 CONSTITUTIVE CO-STIMULATION BY B CELLS IS SUFFICIENT TO TRIGGER T CELL-DRIVEN AUTOIMMUNE DISEASE

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Objective At least two distinct signals are required for classical T cell activation: (1) the cognate antigen presented in