

6 B LYMPHOCYTES CAN REGULATE THE MATURATION AND FUNCTION OF HUMAN DENDRITIC CELLS BUT ARE PARTIALLY INEFFICIENT IN SYSTEMIC LUPUS ERYTHEMATOSUS

Ahsen Morva,¹ Sébastien Lemoine,¹ Achouak Achour,¹ Alain Saraux,² Jacques-Olivier Pers,¹ Pierre Youinou,¹ Christophe Jamin¹ ¹Laboratory of Immunology, Université de Brest and Université Européenne de Bretagne, Brittany, France; ²Department of Rheumatology, Université de Brest and Université Européenne de Bretagne, Brittany, France

10.1136/annrheumdis-2011-201234.6

Background and objectives Mature dendritic cells (DCs) are stimulators of T cell immune response, whereas immature DCs support T cell tolerance. Murine B cells can inhibit the production of interleukin 12 (IL-12) by DCs, and thereby, hinder the inflammatory response. Notwithstanding the importance of this modulation, only a few studies are available in humans.

The current study was aimed at determining the regulatory capacity of human B cells on DC maturation and function, and at evaluating their efficiency in autoimmune disorder.

Materials and methods Peripheral blood B cells from six healthy donors (HDs) and six systemic lupus erythematosus (SLE) patients were stimulated by CD40 and TLR9. Peripheral blood monocytes were differentiated into immature DCs and then into mature DCs. Activated B cells were co-cultured with DCs and HLA-DR, CD80, CD86 expressions and IL-12 production by the DCs evaluated by flow cytometry. Variations of expressions were used to determine the B cell regulatory effects on maturation. CFSE-labelled T cells were cultured with mature DCs and the DC-dependent proliferative response evaluated in the presence of activated B cells to determine their influence on the function of DCs.

Results Activated B cells restrained the development of monocytes into immature DCs and their differentiation into mature DCs. They decreased the density of HLA-DR from mature DCs, the expression of CD80 and CD86 co-activation molecules, the production of IL-12p70 required for antigen presentation and Th1 differentiation. They also inhibited the DC-induced T cell proliferation. These modulations were mediated by CD19+IgD^{low}CD38+CD24^{low}CD27⁻ B cells and needed CD62L interaction for the control of CD80 and CD86 expression, and a soluble factor for the control of IL-12 production. Finally, mature DCs from SLE patients displayed insensitivity to the regulation of IL-12 by both normal and SLE B cells.

Conclusions Human B cells can regulate DC maturation and function. However, they are inefficient in SLE due to refractory DCs. This may influence an improper balance between an effector inflammatory response triggered by mature DCs, and tolerance induction favoured by immature DCs, and thereby, may contribute to the pathogenesis of SLE.