

INTERVIEW about

CD25 positive B cells
with

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How many subsets of B cells are known?

Mikael Brisslert: It depends on how "subset" is defined, but B cell subsets are usually classified depending on their surface molecule expression. In man there are several types of B cells including memory B cells, plasma cells, and germinal center B cells. Naïve B cells, which has not encountered any antigen specific for their B cell receptor and are generated in the bone marrow, express CD20, IgD and low amounts of CD38 (1). In addition, the naïve B cells have just recently been found to express ATP-binding cassette (ABG)B1 transporter and can be used to distinguish these B cells from other subtypes (2). Memory B cells express CD20, CD27 and IgM/IgG/IgA but lack CD38 (3-5). Plasma cells (the B cell type that secretes the majority of all immunoglobulins) lack the B cell marker

CD20 and surface Ig's but express CD138 and have a high expression of CD27 and CD38 (3,6). Germinal center B cells express CD20, Ig's and high levels of CD38 (1,3). Recently, regulatory B cells has also been suggested as a subset of the B cell family based on their production of the immunosuppressive cytokine IL-10 (7).

Our suggestion is that naturally CD25 expressing B cells is a unique population of B cells, different from CD25 negative B cells stimulated to express CD25 (8). Whether the naturally occurring CD25 positive B cells belong to the regulatory B cell subset remains to be elucidated. However, it seems that CD25 positive B cells rather activate the immune response in contrast to the "regulatory" B cells, which dampen the response.

Are CD25 positive B cells phenotypically different from other B cell subsets?

Mikael Brisslert: They share some of the commonly expressed markers with other B cell subsets. We have shown that CD25 positive B cells co-express IgG, IgM, or IgA, the memory marker CD27, and the costimulatory molecule CD80 at significantly higher frequencies than CD25 negative B cells (8). In addition, on the cell surface of

CD25 positive B cells, CD122 and CD132 are found at significantly higher levels (8). In contrast, the CD25 positive B cells express less HLA class II as compared to CD25 negative B cells (8). Our recent unpublished data suggest that the CD25 positive B cell phenotype falls within the memory B cell subpopulation.

Have CD25 positive B cells a functional IL-2receptor?

Mikael Brisslert: Yes they have. We have recently published data where we compare stimulation of CD25 positive B cells versus CD25 negative B cells with recombinant IL-2 finding significant differences in proliferation (8). This

result and the fact that we can detect significantly higher levels of the other two IL-2 receptor subunits, CD122 and CD132, suggest that the CD25 positive B cells have a fully functional high affinity IL-2 receptor.

Can CD25 expression be modulated on B cells?

Mikael Brisslert: Yes! It can be readily upregulated on CD25 negative B cells using selected TLR-ligands including CpG-ODN (TLR9), Pam3Cys (TLR2/6) (8), as well as the cytokine IL-4 (unpublished data).

However, not all stimuli upregulate CD25 expression on CD25 negative B cells. TLR-3 ligand PolyIC and Epstein-Barr virus lack any modulatory effect on human CD25 expression by B cells (8).

Why do you believe that CD25 positive B cells performed better antigen-presentation?

Mikael Brisslert: When performing a mixed lymphocyte reaction, the peptide presented in the MHC class II cleft of CD25 positive B cells induce significantly higher proliferation of the responder T cells as compared to CD25 negative B cells (8). This finding is puzzling since CD25 positive B cells have lower expression of MHC class II on their surface. How-

ever, this may be compensated by the fact that CD25 positive B cells have instead significantly higher levels of co-stimulatory molecules on their surface. This antigen presenting capacity can be of importance in autoimmune diseases such as rheumatoid arthritis and systemic lupus erythematosus where autoreactive B cells are involved in disease pathogenesis.

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