The expression and function of CD25 B cells in man and in mice

Akademisk avhandling

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av
Sylvie Amu

Fakultetsopponent:
Professor Birgitta Heyman
Rudbecklaboratoriet
Uppsala universitet, Uppsala

Avhandlingen baseras på följande arbeten:

1. **Sylvie Amu**, **Katrina Strömberg, Maria Bokarewa, Andrej Tarkowski, and Mikael Brisslert**.
   CD25-expressing B-lymphocytes in rheumatics diseases.
   Scandinavian Journal of Immunology. 2007; 64:182-91

2. **Sylvie Amu, Andrej Tarkowski, Thomas Dorner, Maria Bokarewa, and Mikael Brisslert**
   The human immunomodulatory $CD25^{+}$ B cell population belongs to the memory B cell pool.
   Scandinavian Journal of Immunology. 2007;66:77-86

3. **Sylvie Amu, Inger Gjertsson, Andrej Tarkowski, and Mikael Brisslert**.
   B cell CD25 expression in murine primary and secondary lymphoid tissue.
   Scandinavian Journal of Immunology. 2006; 64:482-92

4. **Sylvie Amu, Mikael Brisslert, and Andrej Tarkowski**
   Functional characterization of CD25 expressing B cells in mice
   Manuscript

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Sylvie Amu, Department of Rheumatology and Inflammation Research
University of Gothenburg, Sweden, 2008

ABSTRACT

B cells play an important role both in the physiology and pathology of immune responses by production of antibodies, cytokines and by presentation of antigens. It has been shown that human CD25 expressing B cells display a mature phenotype, perform better as antigen presenting cells but secrete less immunoglobulins.

The aim of this thesis was to investigate human CD25 expressing B cells phenotypically, not only in healthy individuals but also in patients with rheumatoid arthritis (RA) and systemic lupus erythematosus (SLE). Further, we have also studied the phenotype and function of CD25 expressing B cells in mice. Our results from human studies show that $CD25^+$ B cells display a highly mature and activated phenotype. These cells show high expression of IgA, IgG and CD80, and low expression of IgD and IgM both in healthy individuals and in RA patients when compared to $CD25^-$ B cells. $CD25^+$ B cells from SLE patients did not show any difference in IgA and IgG expression but did expressed higher levels of the costimulatory molecule CD80 when compared to $CD25^-$ B cells. Furthermore, we have shown that 60% of $CD27^+$ B cells in healthy controls, 51% in RA and 48% in SLE patients coexpress CD25, suggesting that $CD25^+$ B cells belong to the memory B cell population. Finally, $CD25^+$ B cells were able to produce IL-10 in much higher levels than $CD25^-$ B cells.

In mice, CD25 expressing B cells from secondary lymphoid organs showed a mature and activated phenotype, high expression of the costimulatory molecules CD80 and CD86, in addition to IgA, IgG, and the early activation marker CD69. Functionally these B cells were efficient alloantigen presenting cells, they spontaneously secreted high levels of immunoglobulins of the IgA, IgG and IgM classes, were able to become antigen specific antibody secreting cells and produced high levels of different cytokines including IL-4, IL-6, IL-10, and IFN-γ.

In conclusion, we have shown that human CD25 expressing B cells display a highly mature and activated phenotype and belong to memory B cell subset. Also, in mice there was a clear difference both phenotypically and functionally between the $CD25^+$ versus $CD25^-$ B cells. These data suggest that CD25 expressing B cells play a major role not just in the physiology of the immune system but also may participate in the pathogenesis of autoimmunity.

Key words: *B cell, CD25, rheumatoid arthritis, systemic lupus erythematosus, mice*

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