

The role of chemokine receptors in B-cell migration in response to a thymus-independent antigen

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Research Project:

Introduction:

The chemokine system is essentially involved in the migration of immune cells during inflammatory responses as well as during homeostatic circulation of immune cells. CXCL13 is the only chemokine that binds the chemokine receptor CXCR5. CXCL13 and CXCR5 are both required for B cell migration into the follicles (1). The chemokine CCL25 specifically binds to CCR9 and guides IgA secreting plasma cells to the small intestine (2). B1-cells are the most abundant B cell population in coelomic cavities and can be subdivided into B1a and B1b subsets (3,4). Antibodies produced by B1a cells are the first-line defense against encapsulated bacteria. The exposure to this type of thymus-independent antigen does not elicit memory (5). B1b B cells can confer T cell-independent long lasting unmutated IgM memory to pathogens such as *Borrelia* (6).

Patients, who have undergone removal of spleen for clinical reasons, very often suffer from life-threatening repetitive pneumococcal infections. Similarly, immunocompromised patients are also very susceptible to infections with this microorganism. To protect them from life-threatening consequences of this infectious disease, Pneumovax vaccine is administered subcutaneously. Pneumovax is a polysaccharide vaccine that mainly stimulates a protective IgM T-cell independent response. As expected Pneumovax vaccine stimulates an IgM response after intraperitoneal injection administration in mice and subcutaneous injection in human (7,8).

Research objective:

To determine the role of the chemokine receptors CXCR5 and CCR9 as well as of b2-integrin in the migration of plasma cells differentiating from peritoneal cavity B-cells to the spleen in response to a thymus-independent type 2 antigen.

Hypothesis:

Splenectomized patients are prone to suffer from repetitive pneumococcal infections, but they respond remarkably well to a thymus-independent unconjugated polysaccharide vaccine elaborated from a mixture of capsular polysaccharides of 23 different serotypes of *Streptococcus pneumoniae*, when the antigen is administered subcutaneously. Curiously, splenectomized mice do not mount an immune response when they are challenged intraperitoneally with the same antigen. This indicates that the route of antigen administration and delivery, that is, draining lymph node versus peritoneal cavity is critical to achieve a productive humoral immune response and formation of plasma cells. Chemokine receptors are involved in the trafficking of immune cells and our proposal is aiming at tracking down the migration of plasma cells in response to a thymus independent type 2 antigen from the peritoneal cavity to the spleen and bone marrow in splenectomized and non-splenectomized WT mice after adoptive transfer of peritoneal cavity B cells from CXCR5-, CCR9- and b2-integrin deficient mice.

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