

## Is the Spleen Really Important?

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### Short Communication

The spleen is a mysterious organ located in the left side of the abdominal cavity and is linked to the blood and lymphatic circulation. It is a secondary lymphoid organ and its micro architecture is divided by a trabecular connective tissue which is composed by a red and white pulp. The red pulp (RP) is specialized in the removal of old cells from the blood stream with the help of reticular fibers, fibroblasts and macrophages. The white pulp (WP) is the splenic lymphoid component and it is structured around a central arteriole where is possible to identify the periarteriolar lymphoid sheath (PALS), the marginal zone (MZ) and the lymphoid follicles (LF). The macrophages from MZ are important antigen processing cells; they express receptor such as SIGNR1 and SINGLEC1 (CD169). There are also B cells in the MZ that are also antigen present cells (APC). The CD4+ T lymphocytes are found in the PALS, whereas IgD+ IgM+ B cells are located in the germinal centers. The spleen anatomy is important for the development of immune responses to different types of antigens as well as to maintain the memory B cell repertoire [1].

Various genes are responsible for the development of the spleen during embryonic fase. The Pbx1, the Bapx1 and the Nkx3.2 are responsible for the expression of homeobox 11 (Hox 11). These genes code for structural components of the spleen. Hox11 knockout (KO) mice do not bear spleens and they are more susceptible to infections. The lymphoid and myeloid colonization of spleen is not well defined yet. The presence of cytokines from lymphotoxin family is fundamental to the cellular arrange of the organ. The chemokine CXCL13 is important for B cell migration to the WP [2,3]. On the other hand, CCL19 and CCL21 are fundamental for the entry of T cells into the spleen. Some selectins are also important; L-selectine, for example, is required for the migration of naïve lymphocytes into the organ [4]. The correct formation of the spleen anatomy is critical for the establishment of interactions between APC and effectors cells leading to fully mature immunological responses.

Despite of the many immunological functions attributed to the spleen, splenectomy is a frequent medical practice in different situations. Clinical studies have reported evidences of uncontrolled infection, and increase incidence of sepsis in patients submitted to splenectomy. Because of the spleen complexity and location, it is a key organ for the development of innate and acquired immune responses. Splenic macrophages and dendritic cells are constantly activated because of the blood influx that brings along many antigens from the circulation. This constantly activation of APC is important for T cell stimulation, proliferation and cytokine production. After splenectomy, IFN-gamma levels are usually decreased [5], and this can be one of the reasons for the increased susceptibility to some infections. The spleen integrity is necessary to preserve B cell repertoire, reactive oxygen species (ROS) production, and maintenance of memory B cells [6].

The production of inflammatory cytokines by lymph nodes is decreased after splenectomy in mice models of Trypanosomacruzi [7], Listeria monocytogenes and of gram negative bacterial infection. In some animal and clinical studies, there is clear evidence showing that the spleen absence increases host mortality [8,9].

The spleen is a neglected organ even in the immunological studies, and this mysterious organ should be better investigated. How lymphoid cells migrate into the spleen, how cells are activated and how they are driven to other lymphoid organs still to be clarified. The importance of the spleen in the development of systemic immune response requires a scientific effort to be described.

The absence of spleen can cause some immunological disorders and increase mortality, especially in the case of some infections. Splenectomy is a common clinical practice although asplenic individuals bear several hematological and immunological disorders.

Regardless of these facts, I would like to invite the immunologists and related researches to go deeper into the scientific questions about the role of spleen in physiological and pathological responses in each specific field.

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