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New Parallels in Understanding the Spleen as a Hematopoietic Organ

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Abstract: A brief review presents the latest literature data on the structural and functional zones and cellular components of the organ and the functions they perform.

Key words: pipeline system; extracellular matrix; fibroblastic reticular cells; lymph node; secondary lymphoid organ; stromal cell, BMSC, immune system, aging, P21/PCNA, oxidative stress.

The spleen is a mysterious organ a peripheral organ of the immune system involved in hematopoiesis and is a graveyard for old red blood cells . The functions of the spleen are not yet fully understood. For a long time it was considered an endocrine (without excretory ducts) gland. Since there is no reliable data on the secretory activity of the spleen, this theory had to be abandoned, although recently it has to some extent received a second life.

The spleen is the largest peripheral lymphoid organ, which contributes to the formation of the immune response, the quantitative and qualitative composition of immunocompetent blood and lymph cells. It is known that, starting from early postnatal ontogenesis, together with the mother's mammary gland and other organs of the newborn's immune system, the spleen is involved in protecting the baby's body. [Arpan Haldar 2021]

The spleen, in its main function, is a blood filter. It quickly reacts to antigens and damaged cells contained in it, changing the structure and cytoarchitectonics both in a normal body and in the event of pathological conditions. [BB.Khasanov 2022]. In the spleen, the process of further development of a subpopulation of lymphocytes and cells of the mononuclear phagocyte system occurs, their cooperative interaction during the immune reaction with the subsequent formation of clones of active immunocompetent cells.

Currently, the spleen is also responsible for the hormonal regulation of bone marrow function . The article [Z Wang·2020] describes bone marrow mesenchymal stem cells (BMSCs), which are considered an important regulator of immune function. Specific markers of BMSCs (bone marrow mesenchymal stem cells) were identified using flow cytometry, and successful induction of BMSCs into steatoblasts and osteoblasts was observed. Compared with the aging model, BMSCs significantly increased the spleen and thymus index and improved the histological changes in spleen and thymus tissue. BMSCs significantly reduce tissue damage in the aging spleen and thymus, BMSCs (bone marrow mesenchymal stem cells) can improve organ aging by influencing cytokines, oxidative stress and P21/PCNA.

The spleen is the primary filter for blood-borne pathogens and antigens and a key organ for iron metabolism and red blood cell homeostasis. [D Zheng·2022·] However, the immune and

hematopoietic functions of the mouse spleen have recently been discovered, indicating an additional role for this secondary lymphoid organ. The spleen contains all major types of mononuclear phagocytes, including macrophages, DCs, and monocytes. [D. _ Tarlinton . 2013] These cells are key defenders of the body as they identify pathogens and cellular stress, remove dying cells and foreign materials, regulate tissue homeostasis and inflammatory responses, and shape adaptive immunity. [S Im.· 2022·] Recent research has shown that the immune system does more than just control pathogens. Even without infection, the immune system can produce sterile inflammatory responses. This non-canonical function is currently the subject of much debate. These discussions assume that the classical role of the immune system in killing pathogens is only part of the overall function of the immune system. Efforts are being made in this direction to understand the role of the immune system comprehensively from the point of view of physiological homeostasis [Medzhitov R 2021]

This organ is now believed to play a central role in the regulation of the immune system, is a metabolic asset, and is involved in endocrine function in relation to non-alcoholic fatty liver disease. [G Tarantino 2019] In recent years, after in-depth studies of the organization and structure of the spleen, cell function, secretion and innervation, a better understanding of the function of the spleen has been achieved. It was originally believed that the spleen not only filters the blood, but is also an important center for regulating the body's immune, metabolic and endocrine systems. However, a number of questions have arisen: is the spleen a player or a bystander and what is the role of certain cytokines, adipokines/growth factors and neurotransmitters in this complex mechanism? Adipokines have pro- and anti-inflammatory properties and play a critical role in the integration of systemic metabolism with immune function. [P Mancuso 2016] In other words, what is the contribution of the spleen to the development of non-alcoholic fatty liver disease, is it a further manifestation of metabolic syndrome [G Tarantino 2019]. The spleen, being the largest secondary lymphoid organ in the body, performs a wide range of immunological functions along with its role in hematopoiesis and red blood cell clearance. [SM Lewis 2019]

The physical organization of the spleen allows it to filter the blood from pathogens and abnormal cells and facilitate unlikely interactions between antigen-presenting cells (APCs) and related lymphocytes. Spleen-specific APCs regulate T and B cell responses to these antigenic targets in the blood. There are cell types, cellular organizations, and immunological functions that are specific to the spleen, influencing the initiation of adaptive immunity and to systemic blood-borne antigens. The article [SE Acton·2021] reviews fibroblastic reticular cells (FRCs), which are an important part of the stromal cell infrastructure of secondary lymphoid organs (SLOs). With their help, fibroblasts of lymphoid organs are formed. Specialized niches for the interaction of immune cells and thereby control lymphocyte activation and differentiation. Moreover, FRCs create and cover a network of extracellular matrix (ECM) microfibers called the channel system. Channels generated by the FRC promote fluid and immune cell control by funneling fluids containing antigens and inflammatory mediators through the SLO. Functions and interactions of immune cells, complex relationships between the cellular FRC and fibrillar conduction networks that together provide the basis for efficient communication between immune cells and tissues. The physical organization of the spleen allows it to filter the blood from pathogens and abnormal cells and facilitate unlikely interactions between antigen-presenting cells and lymphocyte-related APCs (antigen-presenting cells), which are unique to the spleen because they regulate the response of T and B cells to these antigen targets in the blood The spleen is the primary TLS arising in association with adaptive immunity in early jawed vertebrates. The spleen, especially its lymphoid compartment, the white pulp (WP), has undergone numerous modifications during evolution. [HR

Neely·2016]. The spleen also contains about one-quarter of the body's lymphocytes and initiates the immune response to blood antigens. [P Kubes 2018] This function is assigned to the white pulp surrounding the central arterioles. The white pulp is composed of three subcompartments: the periarteriolar lymphoid membrane (PALS), follicles, and marginal zone. [MA Fares 2023] Histocytometric study Kage et al . [M Kage 2019] and Almenari others. [S Almenar 2019] showed that the spleen is surrounded by a capsule consisting of dense fibrous tissue, elastic fibers and smooth muscle, the outer layer of the capsule. The spleen consists of mesothelial cells, irregularly distributed trabeculae of smooth muscle and elastic fibers of tissue extending from the capsule into the splenic parenchyma. [Rahman N. _ 2016, Shringi N. _ 2017]. On the other hand, Rahmouni et al. [DE Rahmoun 2020] showed that these trabeculae also contain blood vessels, lymphatic vessels and nerves.

A capsule surrounded by dense fibrous tissue, elastic fibers and smooth muscle - this is what the spleen is, it is a large lymphoid organ without the structure of the cortex-medullary layer, surrounded by a dense connective tissue capsule extending inward. [P Kaewmong 2023]

The outer layer of the spleen capsule consists of mesothelial cells, which may not be visible on histological sections. Irregularly distributed trabeculae of smooth muscle and fibroelastic tissue extend from the capsule into the splenic parenchyma. The complex vascular system of the spleen plays a central role in the successful filtration of blood and recycling of red blood cells. Blood enters the spleen at the hilum and flows sequentially as follows: splenic artery → trabecular arteries → small arterioles → red pulp → central arterioles → small arterioles → capillary beds of the white pulp ending in the marginal sinus, marginal zone, or red pulp. [MA Fares·2023] Penincillary arteries and small arterioles move blood through the MH (marginal zone) and either into the venous sinuses (90%) or into the reticular network. According to modern concepts, the spleen of mammals is considered as a segmented organ. Each segment includes white pulp, which is divided into lymphoid nodules (follicles) (B-dependent zones) and periarterial lymphoid sheaths (T-dependent zones).

The red pulp of the segment consists of venous sinuses (sinusoidal homocapillaries), splenic cords and a marginal zone located on the border of the red and white pulp. A number of researchers also classify the splenic cords and marginal zone as the white pulp of the spleen, since the cell population of these zones contains almost all types of immunocompetent cells and microenvironmental cells that are characteristic of lymphatic follicles. [BB.Khasanov 2022, KM Boes 2017] The functions of the spleen are concentrated on the systemic circulation. Thus, it lacks afferent lymphatic vessels. It consists of two functionally and morphologically distinct sections: the red pulp and the white pulp. [I Udroiu·2017] The red pulp is a blood filter that removes foreign material, damaged and dying red blood cells. The spleen is the primary filter of blood-borne pathogens and antigens and a key organ for iron metabolism and red blood cell homeostasis. However, immune and hematopoietic functions of the mouse spleen have recently been discovered, suggesting an additional role for this secondary lymphoid organ. [Bronte 2013]

White pulp: ALS and lymphoid follicles.

The lymphoid compartments of the white pulp include the periarteriolar lymphoid membranes [PALS], primary and secondary follicles, marginal zone, and mantle, which vary among species. [MER Hermida·2018]. Identification and characterization of each compartment of the spleen, including assessment of the relative size and cellularity of the periarteriolar lymphoid sheaths (PALS), the size and maturation of lymphoid follicles, the presence or absence of marginal zone cells, and the relative abundance of smaller lymphoid aggregates . , are key to accurately assessing the immunological effects on the spleen.

Trabeculae also contain blood and lymphatic vessels and nerves. Lymphatic vessels are efferent vessels through which lymphocytes migrate to the splenic lymph nodes.

It follows that the spleen is a blood filter and is a highly vascular organ. [I Udroiu·2017·] Blood flow through the spleen is a rather complex but important and sometimes controversial concept. Blood enters the spleen at the hilum through the splenic artery. The splenic artery is divided into trabecular arteries, located inside the trabeculae, which flow into the splenic parenchyma. Small arterioles arise from the trabecular arteries and enter the red pulp, where they become central arterioles surrounded by lymphoid tissue. [Birte S. Steiniger 2022]

Conclusions- The data we have reviewed in this article clearly indicates that due to its anatomical features, such as high blood flow and loose capillaries, the spleen is highly susceptible to and influenced by the immune system, and a wide range of immunological functions along with its role in hematopoiesis and erythrocyte clearance represents an important site for the clearance of exosomes and nanoparticles and can direct immune responses against their PEG secrecy. In conclusion, the spleen, that little, forgotten organ, continues to amaze us with unexpected physiological functions: After recently being linked to the pathophysiology of non-alcoholic fatty liver disease in the spleen, hematopoietic functions have a new role emerging, and this little, forgotten organ is certainly , deserves closer attention from pharmacologists in the future.

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