IMMUNE ORGANS AND CELLS

The function of the immune system of fish is equivalent to that of other vertebrates: diseases resistance. However, in teleost fish the absence of bone marrow and lymph nodes is one of the main characteristics of their immune system. The primary and secondary processes that protect fish against various pathogens are known as innate immunity and specific or adaptive immunity.

Immune organs and tissues

The immune system of fish consists of primary lymphoid organs, thymus and head kidney, and secondary lymphoid organs, comprising the spleen, trunk kidney, and mucosa-associated lymphoid tissues (MALT) present in peripheral immune tissues.

MALT can be subdivided into four main lymphoid tissues: skin-associated lymphoid tissue (SALT), gill-associated lymphoid tissue (GIALT), gut-associated lymphoid tissue (GALT), and nasal-associated lymphoid tissue (NALT).

Recently, a secondary lymphoid tissue similar to bursa of Fabricius of birds, called salmonid bursa, has been described, but more knowledge is still required to understand its immunobiological function (**Figure 1**).

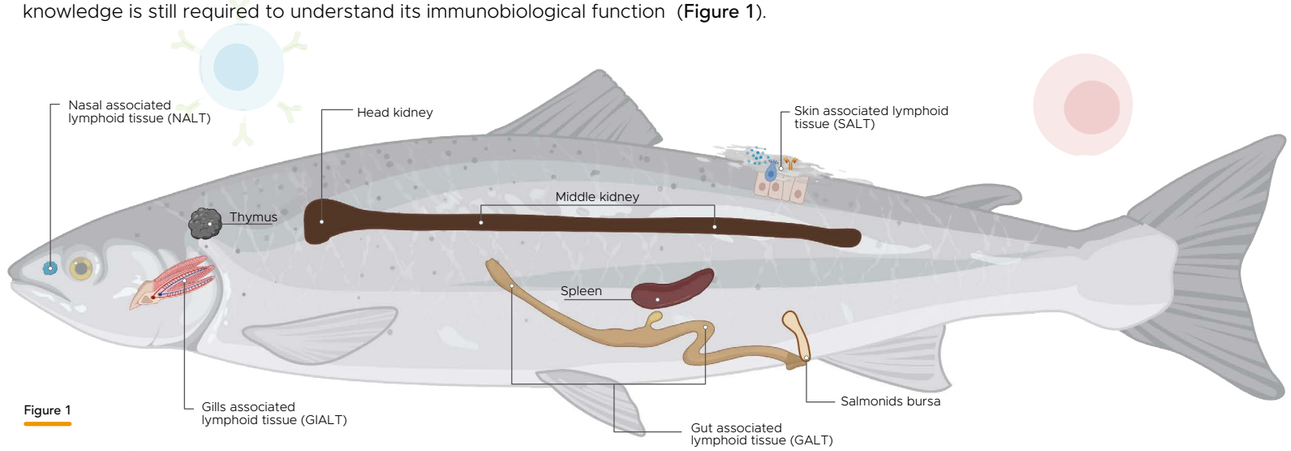

Figure 1

Thymus: It is an organ of differentiation and selection of T lymphocytes.

Head kidney: It contains a large number of macrophages and B lymphocytes, and due to its great hematopoietic capacity it is considered as an analog of mammals' bone marrow.

Spleen: Has similar functions to those of head kidney with emphasis on antigens presentation and adaptive immune response induction.

Mucosa-associated lymphoid tissue: The mucosal surfaces of skin, gills, gut and olfactory organ provide fishes' first line of defense against threats that present in the immediate environment.

Mucosal surfaces involve concerted action of physical barriers that orchestrate the first line defense by directly trapping and eliminating pathogens.

If pathogen manages to infiltrate, the recognition pattern receptors of immune cells detect pathogens through their pathogen-associated molecular patterns, activating the innate immune system.

Antigen uptake can have different pathways:

A. Initiation of inflammatory process caused by release of cytokine mediators and attractants corresponding to specific cell type.

B. Antigen presentation that activates antigen-specific action of lymphocytes that contain receptors that recognize specific molecules. This triggers secondary responses, including processes involved in adaptive immunity.

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Immune cells

Leukocytes are divided into granulocytes (neutrophils, eosinophils) and agranulocytes (lymphocytes and monocytes), which are distinguished by their functional and morphological characteristics (**Figure 2**).

Eosinophils: In fish they are usually found in low concentrations, some studies indicate that these cells participate together with neutrophils and macrophages in the inflammatory response. In circulating blood they are in less than 5% proportion.

Monocytes: They are large cells that make up between 1 and 5% of leukocytes in salmonids. Monocytes are actively phagocytic cells that specialize to macrophages in tissues. Monocytosis occurs in similar conditions to neutrophilia, and can be present in both acute and chronic inflammatory responses and associated with an infectious agent, foreign body and/or post-vaccination reactions.

Dendritic cells (DCs): Along with macrophages and B lymphocytes, DCs belong to to the family of antigen presenting cells. Because they express various pattern recognition receptors, they are able to rapidly detect invading microbes on mucosal surfaces, internalize them, and present them via major histocompatibility complex (MHC) type I (intracellular antigens) or MHC type II (extracellular antigens) to T cells, witch induce their activation and proliferation, triggering CD4+ and CD8+ T cell responses.

Neutrophils: Correspond to around 20% of circulating leukocytes population and have high capacity for phagocytosis, chemotaxis and bactericidal functions.

Lymphocytes: Corresponding 70 to 80% of cells in circulating blood of fish, they are the predominant leukocytes. Functionally, they are divided into B and T lymphocytes, being responsible for humoral adaptive and cell-mediated immune response, respectively.

Two classes of T cells are present in teleost fish, both of which display T-cell receptors (TcR) on their surface, **αβ-TcR and γδ-TcR**, along with TcR coreceptors, and express gene patterns that indicate the presence of T-cell subpopulations such as they are known in mammals: cytotoxic (CD8), auxiliary (CD4) and regulatory (Treg, Th17).

Recent research has shown that fish have B cells that express three classes of immunoglobulins (IgM, IgT, and IgD). The main characteristics of fish B cells are: (i) high natural serum IgM content in non-immunized fish; (ii) little increase in affinity for IgM after secondary immunization; (iii) presence of memory B cells; (iv) spontaneous phagocytosis; (v) pathogen-induced mucosal secretory IgT production; (vi) presence of kidney lymphocyte precursors similar to mouse spleen B1-B cells; and (vii) presence of proliferating B cells in peritoneal cavity.

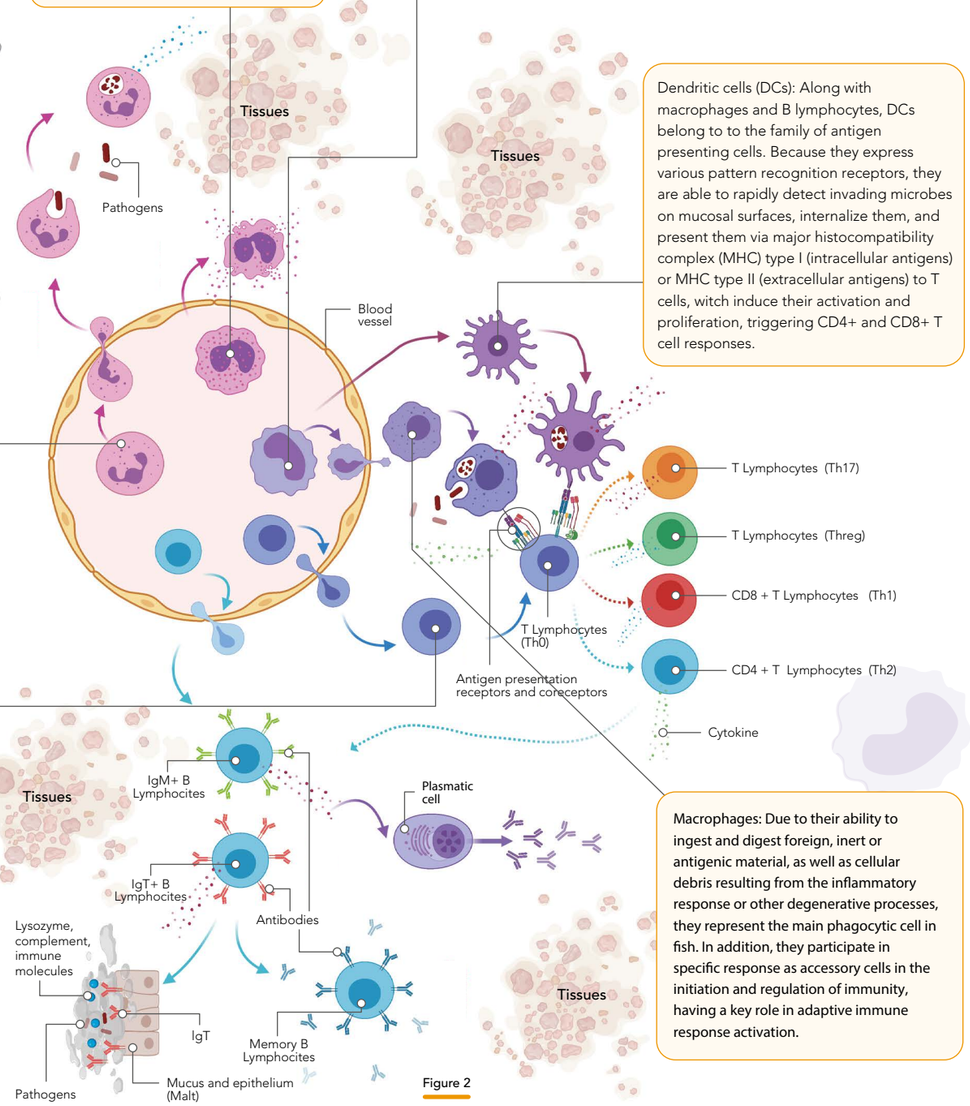

Figure 2

Macrophages: Due to their ability to ingest and digest foreign, inert or antigenic material, as well as cellular debris resulting from the inflammatory response or other degenerative processes, they represent the main phagocytic cell in fish. In addition, they participate in specific response as accessory cells in the initiation and regulation of immunity, having a key role in adaptive immune response activation.