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Comparative histology of the human and teleost fish thymus

Histologia Comparativa de timo de humanos e peixes teleósteos

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ABSTRACT
Thymus is considered a key component of the vertebrates' immune system. It is an organ that is only found in these animals whose development may be accompanied through the evolutionary scale, being considered as a facilitator and regulator in the interaction of lymphoid cells and lymphoid organs. In this study not only a morphological but also functional homology were demonstrated, in that it affects the immune system, of the humans and teleost fish thymus. The material of study was composed of the thymus tissue samples of humans who were donated by the Department of Pathology of Hospital Parmenio Piñero, Buenos Aires Argentina belonging to two patients with ages between 6 and 8 years, as well as specimens of fish from different origins. The thymic tissue samples were submitted to histological analysis, immunohistochemistry and transmission electron microscopy. Through the data shown here it is possible to consider that, both in fish as in humans, there are two tracks in the modulation of the immune response, an afferent pathway that begins with the presentation of the antigen and an efferent pathway through which the result of the lymphocytes, antibodies stimulation or other effector mechanisms are canalized. In these two phases both in humans and in fish, a mixed population of lymphocytes, the differentiation of lymphocytes in the thymus and the T4 lymphocytes production, play a fundamental role in the success of the immune response.

Keywords: Histology, thymus, lymphocytes

RESUMO
O timo é considerado um órgão-chave do sistema imunológico dos vertebrados. É um órgão que só é encontrado nestes animais cujo desenvolvimento pode ser acompanhado através da escala evolutiva, sendo considerado um facilitador e regulador na interação de células e órgãos linfóides. Neste estudo, não apenas foi demonstrada uma homologia morfológica, mas também funcional, que afeta o sistema imunológico, timo de humanos e peixes teleósteos. O material de estudo foi composto por amostras de tecido do timo humano que foram doadas pelo Departamento de Patologia do Hospital Parmenio Piñero, Buenos Aires Argentina pertencentes a dois pacientes com idades entre 6 e 8 anos, como também exemplares de peixes de diferentes origens. As amostras de tecido tímico foram submetidas à análise histológica, imunohistoquímica e de Microscopia Eletrônica de Transmissão. Através dos dados aqui expostos podemos considerar que, tanto em peixes como em humanos, existem duas vias na modulação da resposta imune, uma via aferente que começa com a apresentação do antígeno e uma via eferente por onde se canaliza o resultado da estimulação de linfócitos, anticorpos ou outros mecanismos efetores. Nestas duas fases tanto em humanos como em peixes, a população mista de linfócitos, a diferenciação de linfócitos no timo e a produção de linfócitos T4, desempenham um papel fundamental no êxito da resposta imune.

Palavras-chave: Histologia, timo, linfócitos.

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1 INTRODUCTION

The word thymus comes from the Latin derivation from the Greek word "thymus", which means "warty aspect". Due to thymus also mean "soul" or "spirit", the thymus was appointed as the seat of the soul by the ancient Greeks (Skinner, 1961; Jacobs, Frush, Donnelly, 1999). It was Gaenen Pergamum (130 - 200 AD) who realized for the first time that thymus was proportionally greater during the childhood (May, 1968), referring to the thymus as a "mysterious organ", a concept that has remained quite appropriate for nearly two millennia.

Stannius identified the thymus in teleost fish in 1850. Since then, this gland has been described in many teleosts belonging to approximately 28 different families. Hamxar examined the greatest part of this literature in 1909, and since then has been studied as a fundamental organ of the fish immune system.

The lack of bone marrow and lymph nodes, is one of the main differences between the immune system in teleost fish and superior vertebrates. Fish possess a bone marrow equivalent, which is the anterior kidney pronephros and the interstice of the definitive (posterior) kidney (Zapata et al.,1996). That is why in these animals it is difficult to distinguish clearly between organs and primary and secondary lymphoid organs. Consequently, it has been given the title of lympho-hematopoietic organs, those which blood cells and lymphocytes generate and mature, with their different populations. The three main components organs related to immune system are the anterior kidney (pronephros), the spleen, thymus and the mucosa-associated lymphoid tissue (MALT) (Romano, 2010).

Thymus is considered a key component of the vertebrates' immune system. It is an organ that is only found in these animals whose development may be accompanied through the evolutionary scale, begins in the first species of fish as a thickening in the epithelium of the branchial chamber (Manley, 2000). In general, it is considered that the thymus facilitates and regulates the interaction of lymphoid cells and lymphoid organs (Boehm, 2003). Miller in 1961 describes some functions of the thymus in mammals and identifies two types of lymphocytes, T lymphocytes and B lymphocytes, as well as their functions.

In humans thymus is composed of two identical lobes, which are located anatomically in the anterior superior mediastinum, in front of the heart and behind the sternum. The thymus reaches its greatest weight in relation to the end of fetal life, but its absolute weight continues to rise, reaching 30 to 40 g at the time of puberty. The, it begins to suffer an involution until when, in adults, the component is replaced in large part by adipose tissue (Moore and Persaud, 1993).

Thymus is the first lymphoid organ that develops during the ontogeny. In humans, the

beginnings of the thymic tissue appear at the end of the fifth week of embryonic life. The pair of epithelial rudiments originates bilaterally from the endoderm, the third pair of pharyngeal pouches, in the anterior portion of the digestive tube that is in the mesoderm and is surrounded by resident mesenchymal cells derived from the neural crest (Nishino et al., 2006; Rodewald, 2008). Mesenchyme gives rise to thymic structures, such as capsule, septa and perivascular cells. The interaction between epithelial and mesenchymal cells is essential for the success of the thymus development and function (Owen, McLoughlin, Suniara, Jenkinson, 2000).

In fish, the thymus appears for the first time as an individual component in Chondrichthyes and Osteichthyes fish (Rasmussen and Arnason, 1999). This excludes the class Cyclostomata (agnatha), which includes lampreys and hagfish. The lampreys and the hagfish have a notochord and a modified olfactory and pituitary system. Both characteristics may be significant in the thymus development, once that the thymus develops near the cartilage and respond to pituitary hormones (Hirokawa, Utsuyama, Kobayashi, 1998). Hagfish and lamprey are the first vertebrates to appear in the fossil record, and although they have morphologically identifiable lymphocytes in peripheral blood and in lympho-hematopoietic tissues l, both in the kidney and in the lamina propria of the internal intestine, they do not have true lymphoid organs and, presumably, only have a nonspecific immune response similar to aquatic invertebrates and different from most complex responses of the vertebrates 'specific or adaptive immune system (Zapata, Chiba, Varas, 1996).

Anatomically, in the fish, thymus is a paired organ, bilateral, located under the lateral pharyngeal epithelium, laterals dorsum and housed on the internal superior part of the branchial chambers. The main cellular components are the lymphocytes in maturation. As in other vertebrates, it is considered as a primary lymphoid organ which produces the pool of lymphocytes that migrate to join with the peripheral lymphocytes in the circulation and in other lymphoid organs. They can also be present in epithelioid cells or macrophages type cells the macrophage itself and eosinophilic granular cells (Fergusson, 1989). As in mammals, the involution of this organ is observed in greater age specimens. In young salmonids, the thymus is completely different and separate from the external environment by a layer of simple epithelial cells. Its superficial location suggests a certain vulnerability to severe fungal and bacterial infections (Zapata et al., 1996). Regarding the embryonic development of the thymus in fish, it has been studied and established in some species, for example, that the thymus appears between 14 and 16 days after hatching in *Rachycentron canadum* (Klosterhoff et al., 2015).

Aiming at a comparative approach of thymus between humans and fish, here is a comprehensive study of the organ, using the histology by light microscopy, the

immunohistochemistry with monoclonal anti-CD3 and anti-CD4 antibodies and ultrastructural analysis by transmission electron microscopy. Therefore, it is possible to evaluate the organ behavior and functionality in the different studied species.

2 MATERIAL AND METHODS

Study material composed of tissue samples from human thymus were donated by the Department of Pathology of Hospital Parmenio Piñero, Buenos Aires Argentina belonging to two patients with ages between 6 and 8 years old who died by accident submitted to an autopsy operation, with the thymic parties weighing 22 and 24 g, respectively.

The studied fish species, as well as their origin, are shown in Table 1. The fish were euthanized with a bath in M-222 100 ppm (Western Chemical, USA), were subsequently dissected and the pharyngeal region of the branchial chamber was removed; in smaller fish the cephalic region was cut and used in its entirety. Both the human and the fish thymic tissue were fixed in 10% buffered formalin. After fixation, the tissues were dehydrated through ascending concentrations of ethanol, diaphanized in xylol and embedded in paraffin. Afterwards, they were cut in the microtome (LEICA RM2245) in 30 micrometer thickness. The tissue was stained with hematoxylin and eosin (HE), with dual and triple argentic impregnation of Del Rio-Hortega (Rio-Hortega, 1942). After being stained, the slides were observed under a microscope Primo Star Zess with digital camera AxioCam ERc5S.

2.1 IMMUNOHISTOCHEMISTRY

The histological sections were stained using a modified technique of avidin–biotin-peroxidase complex previously used by one of the authors (Hsu, Raine, Fanger, 1981). After the deparaffinization and hydration, the sections were washed in water for 5 minutes, exposed to a solution of hydrogen peroxide to 1% in methanol for 30 minutes to block the endogenous peroxidase activity and rinsed in phosphate buffered saline (PBS), pH 7.2, for 20 minutes. Then, they were incubated with bovine serum albumin at 3% in PBS (BSA, type V Sigma Brazil) for 40 minutes.

The sections were incubated for 90 minutes with an anti-CD3 and anti-CD4 monoclonal antibody (Dako Argentina) at a dilution of 1:2500 in PBS, then washed in PBS and exposed for 45 minutes to avidin-biotin-peroxidase complex (Vectastain ABC kit, Vector). The sections were exposed for 7 minutes in a solution of 0.1% Diaminobenzidine (Dako Argentina) to which oxygenated water 0.2% in 50 mM Tris, pH 8 was added before use.

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As a positive control the studied human thymus was considered. As a negative control, sections in which the primary antibody was replaced by normal rabbit serum were used in a similar dilution.

2.2 TRANSMISSION ELECTRONIC MICROSCOPY

Small fragments of tissue were cut into 1 mm blocks and immediately fixed in phosphate buffered glutaraldehyde (pH 6.9 at 4°C), washed in Millonig's solution, and postfixed in 1% osmium tetroxide; the tissue blocks were then dehydrated in a graded series of ethanol-acetone, immersed in propylene oxide, and embedded in Durcupan ACNI (Fluka Chemie A.G., Switzerland). Thin sections were cut with an LKB ultramicrotome and double stained with uranyl acetate and lead citrate before examination in a Jeol JEM-8T electron microscope (Jeol, Tokyo, Japan).

3 RESULTS

3.1 OPTICAL MICROSCOPY OF THE HUMAN THYMUS

The thymus was observed as a component essentially lymphoepithelial composed mainly of lymphocytes, epithelial cells and other mesenchymal cells. A thin fibrous capsule covers the organ and from this capsule fibroconnective septa depart that penetrate the parenchyma and divides it into lobes, these lobes appear as the organ histological unit.

The limit between the two zones is quite distinct. The medullary portions are continuous from lobe to lobe and have a highly ramified wooded setting. The thymus epithelial cells form the framework of the organ, the epithelium is continuous, but has large intercellular spaces which make it an open mesh infiltrated by lymphocytes. The thymus epithelial cells surround the organ. A characteristic trait of the thymic medulla is the presence of Hassall corpuscles. These are formed by a mass of mature epithelial cells that arise on top of each other concentrically and keratinize. Calcifications in these corpuscles were not visualized, being observed in general a well keratinized corpuscle and occasionally, in place of keratin, the central space contains a proteinaceous, amorphous eosinophilic material (Figure 1).

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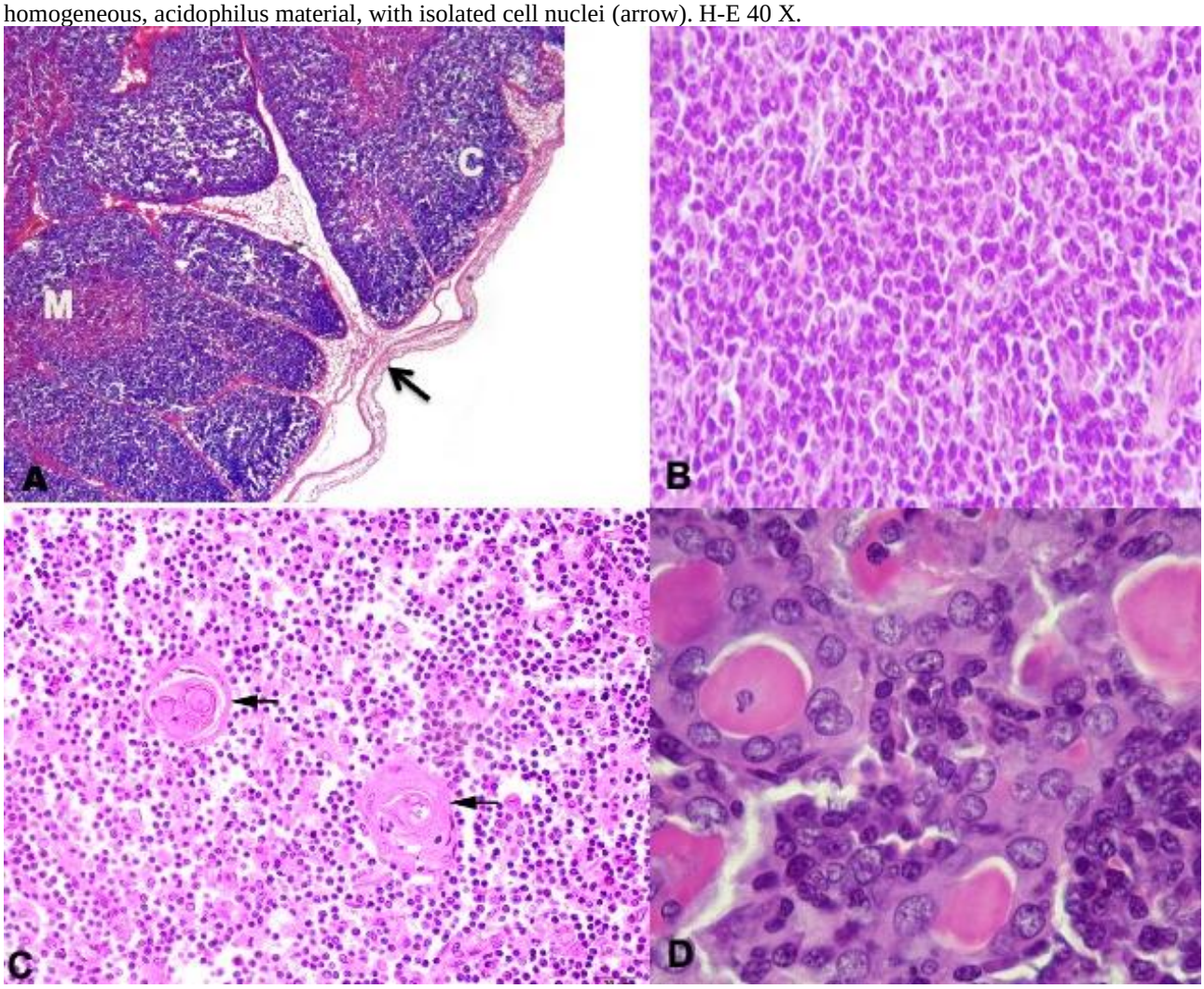
FIGURE 1-A. Human thymus where there is a clear difference between the cortex (C) and the bone marrow (M). The cortex has abundant lymphocytes and the bone marrow is vascularized. The thymus is surrounded by a capsule which emits septa to its interior (arrow). H-E 10 X.
FIGURE 1-B. Human thymus where Hassall' corpuscles are observed in the bone marrow. These bodies are composed of well-united epithelial reticular cells and arranged concentrically (arrow). H-E 20 X.
FIGURE 1-C. Hassall' corpuscles looking like onion layers (arrow). H-E 40 X.
FIGURE 1-D. Human thymus where Hassall' corpuscles are observed. In this case the bodies are composed of denser, homogeneous, acidophilus material, with isolated cell nuclei (arrow). H-E 40 X.



3.2 OPTICAL MICROSCOPY OF THE FISH THYMUS

In all the studied species the thymus is an organ anatomically symmetrical located in the dorsal region of each branchial cavity. A thin capsule was observed that covers the lymphoid population that is trapped between the capsule and the branchial chamber epithelium. In *R. canadum*, there is no such capsule but rather an epithelium of vacuolated cells.

In *C. auratus*, *A. ocellaris* and *H. reidi* the thymus shape is oval, but both in *O. mykiss*, *E. figaro* and *O. argentinensis* the thymus is elongated, extending over the branchial chamber epithelium. In none of the studied fish a differentiation between cortex and medulla was observed, as observed in humans. Regarding the Hassall's corpuscles, it was only clearly observed in the

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thymus of *R. Canadum*. Through argentic techniques an important development can be observed of the capillary vascular system in the stroma and macrophages with phagocytosed argentaffin material (Figures 2, 3).

FIGURE 2-A. *Elacatinus figaro* thymus where it is observed that this organ is symmetrical bilateral and is located in the inner part of the branchial chamber (arrows) H-E 4X.
FIGURE 2-B. Thymus of *Carasius auratus* constituted by lymphocytes without differentiation between cortex and marrow (arrow). The lymphocytes are in a single mass (*) H-E 10X.
FIGURE 2-C. Thymus of *Amphiprion ocellaris* constituted by lymphocytes without differentiation between cortex and marrow (arrow). The lymphocytes are arranged in a single mass without any differentiation (*) H-E 10X.
FIGURE 2-D. Thymus of *Rachycentron canadum*, it is observed that it is bilateral organ (arrows) located in the inner part of the branchial chamber. It can be observed that the thymus is surrounded by a cubic mucosecretant epithelium. E: Encephalon. H-E 4X.
FIGURE 2-E. Thymus of *Rachycentron canadum*, the thymus in the branchial chamber, coated by a mucosecretant epithelium (arrow). G: Gills. H-E 10X.
FIGURE 2-F. *Hippocampus reidi*, the thymus (*), presents no differentiation in the cortex and marrow and has a mucosecretant aspect epithelium coating (arrow). G: Gills. H-E 20X.
FIGURE 2-G. *Odontesthes argentinensis*, the thymus (*) shows no differentiation in the cortex and the marrow is inserted in the branchial chamber. H-E 10X.
FIGURE 2-H. *Odontesthes argentinensis*, the thymus (*) detaches from the epithelium which covers the branchial chamber (arrow). H-E 10X.
FIGURE 2-I. *Oncorhynchus mykiss*, the thymus (*) is elongated

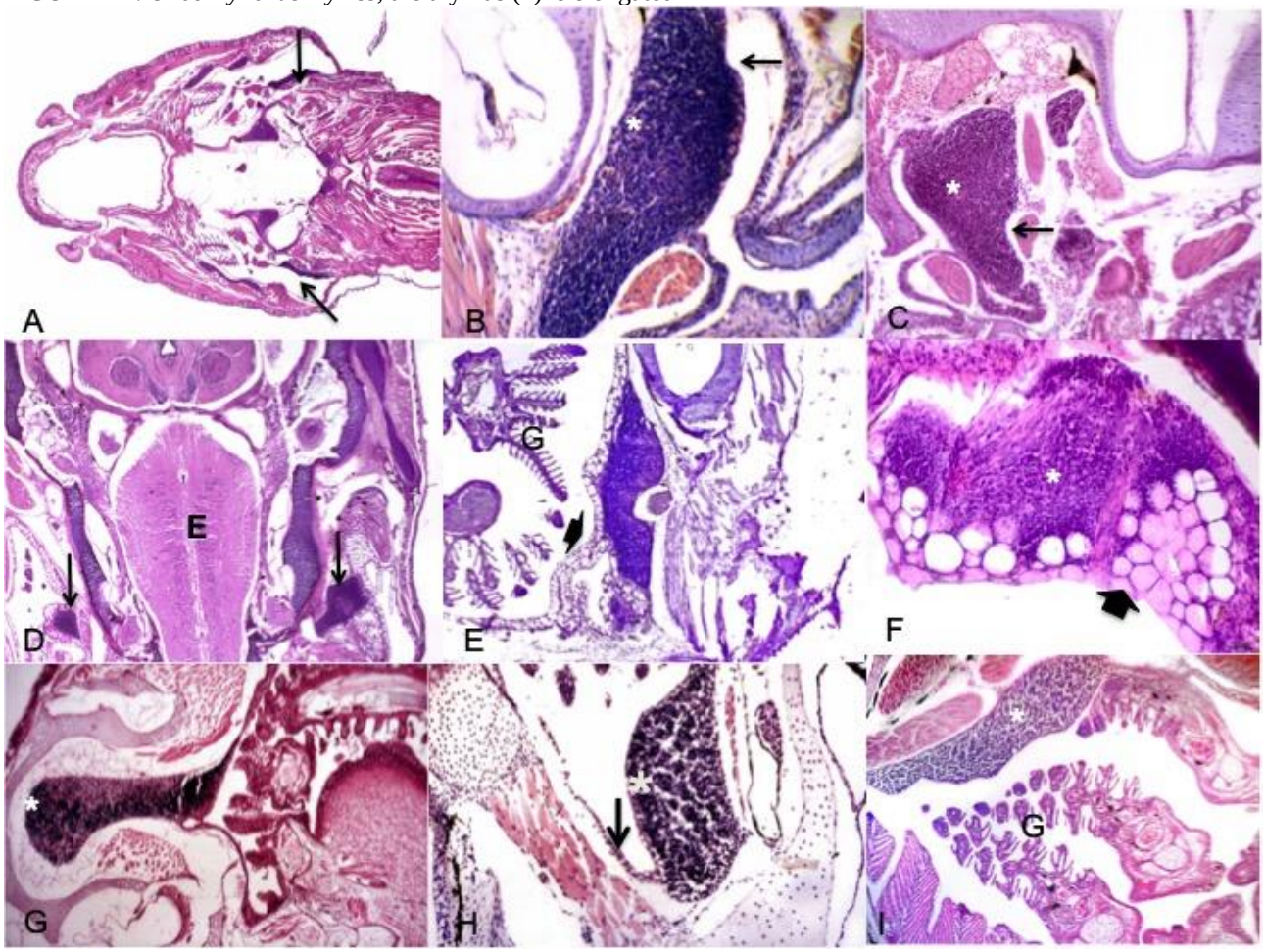

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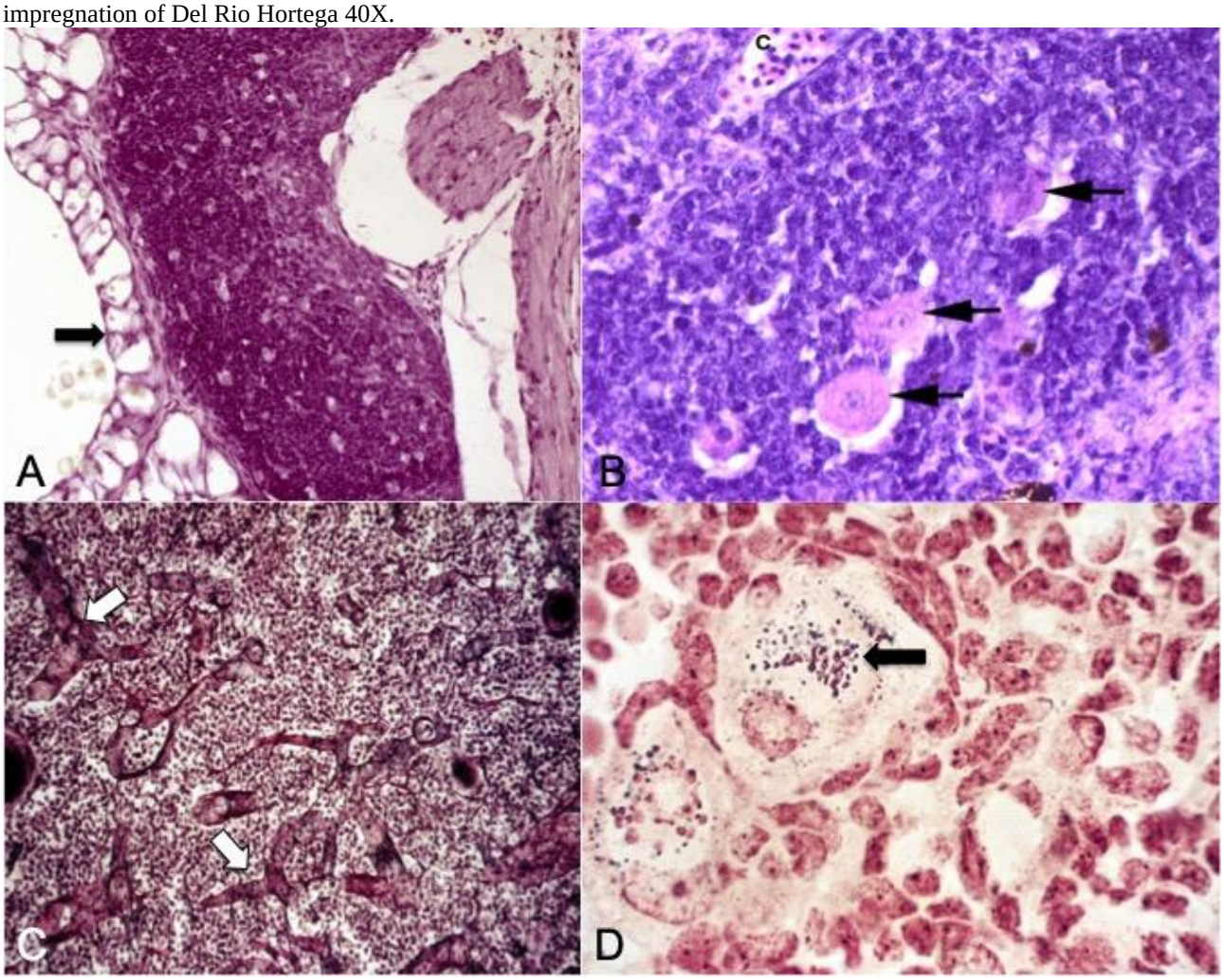
FIGURE 3-A. Thymus of *Rachycentron canadum*, the thymus shows lymphocytes and several eosinophils structures that correspond to the Hassall's corpuscles. The thymus is lined by a mucosecretant aspect epithelium (arrow). G: Gills. H-E 10X.
FIGURE 3-B. Thymus of *Rachycentron canadum*, the thymus shows lymphocytes and Hassall's corpuscles (arrows). C: capillary. H-E 40X.
FIGURE 3-C. Thymus of *Rachycentron canadum*, lymphocytes and macrophages with phagocytosed material are observed (arrow). Double impregnation of Del Rio Hortega 40X.
FIGURE 3-D. Thymus of *Rachycentron canadum*, a well-developed vascular network is observed (arrows). Triple impregnation of Del Rio Hortega 40X.



3.3 IMMUNOHISTOCHEMISTRY

Not only in the human thymus but also in the fish thymus, the staining to the CD3 receptor was positive, and even though the immunostaining is stronger in the humans thymus that in fish, the staining was diffused throughout the thymic parenchyma.

Concerning the CD4 receptor staining, this was positive both in the human and in the fish thymus. In both cases, the immunostaining is not diffuse as in the case of CD3, only in some groups of lymphocytes distributed in the thymic parenchyma (Figure 4).

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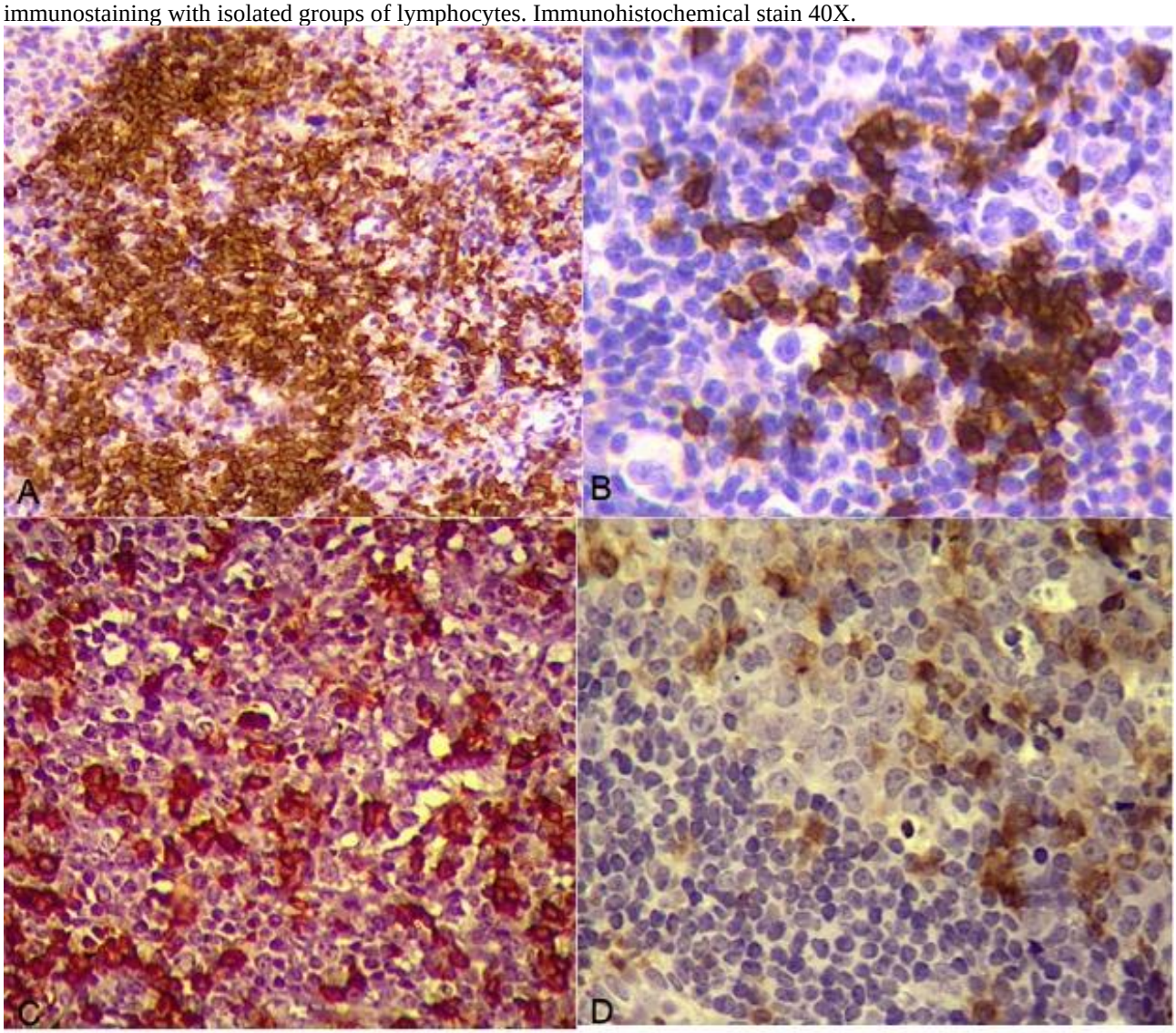
FIGURE 4-A. Immunostaining of human thymus with anti-CD3, it is possible to observe the positive diffuse immunostaining. Immunohistochemical stain 20X.
FIGURE 4-B. Immunostaining of human thymus with anti-CD4, it is possible to observe the immunostaining restricted to a group of lymphocytes. Immunohistochemical stain 40X.
FIGURE 4-C. Immunostaining of *Rachycentron canadum* thymus with anti-CD3, it is possible to observe the positive peripherical non-diffuse immunostaining. Immunohistochemical stain 40X.
FIGURE 4-D. Immunostaining of *Rachycentron canadum* thymus with anti-CD4, it is possible to observe the immunostaining with isolated groups of lymphocytes. Immunohistochemical stain 40X.



3.4 ELECTRONIC MICROSCOPY OF HUMAN AND FISH THYMUS

Ultrastructurally it was found that the thymus basic architecture is similar in humans and in the studied fish. This consists of epithelial cells or better called epithelial- reticulum with very elongated processes among which the lymphocytes are observed. The term epithelial-reticulum cell is acceptable, since it denotes the tendency of these cells to have long process and also indicates its epithelial nature. This epithelial nature can be deduced ultrastructurally from the formation of

typical adherent macules (desmosomes) and branching of cytoplasmic tonofilaments, being many of these filaments inserted in the desmosomes.

The processes of attenuated epithelial cells cover the thymus surface. In human thymus separate the cortical lymphocytes from the capsule of collagen. A basal lamina is present on the surface of epithelial cells and is also evident where the epithelium is supported in the connective tissue, such as around the blood vessels.

In humans, the epithelial cells have been subdivided into several categories that tend to emphasize the corticomedullary differences. Those that are located in the cortex have more elongated and slenderer processes, while that of the spinal have shorter processes and a more abundant cytoplasm.

The epithelial cells within the Hassall's corpuscles may have a marked villous surface configuration. In several animal species, spaces have been described in the form of glands, which villous epithelial cells connected by desmosomes around the lumen of the gland are formed. These coating cells may contain dense granules and are sometimes ciliated. Although such structures have been described in human fetuses and neonates, they have not been reported in the postnatal thymus.

The thymic lymphocytes are not morphologically different from other lymphoid tissues. Many have typical appearance of inactive ells; that is, they have abundant nuclear heterochromatin, a ringed nucleus, and very scarce cytoplasmic polyribosomes. In addition to the epithelium and the lymphocytes, a small quantity of other cells can be found ultrastructurally in the normal thymus (Figures 5, 6).

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FIGURE 5-A. Transmission electron micrograph shows a filament-containing epithelial cell with a long process that encloses basal lamina at one point (arrow). Two smooth surfaced lymphocytes are present. Uranyl acetate-lead citrate stain. X7200.
FIGURE 5-B. This irregularly rounded epithelial cell is rich in tonofilaments (arrow). Uranyl acetate-lead citrate stain. X16.500.
FIGURE 5-C. A gland like space in a thymoma contains amorphous material (*). Lining cells have surface microvilli (arrow), contain tonofilaments, and are connected by well-defined desmosomes. Uranyl acetate-lead citrate stain. X5800. Inset: X16.500.
FIGURE 5-D. The surface is covered by attenuated epithelial cell processes distinguished by tonofilaments and a desmosome attachment. A 450-angstrom basal lamina separates the epithelial cells from the collagen capsule. Uranyl acetate-lead citrate stain X30.000.

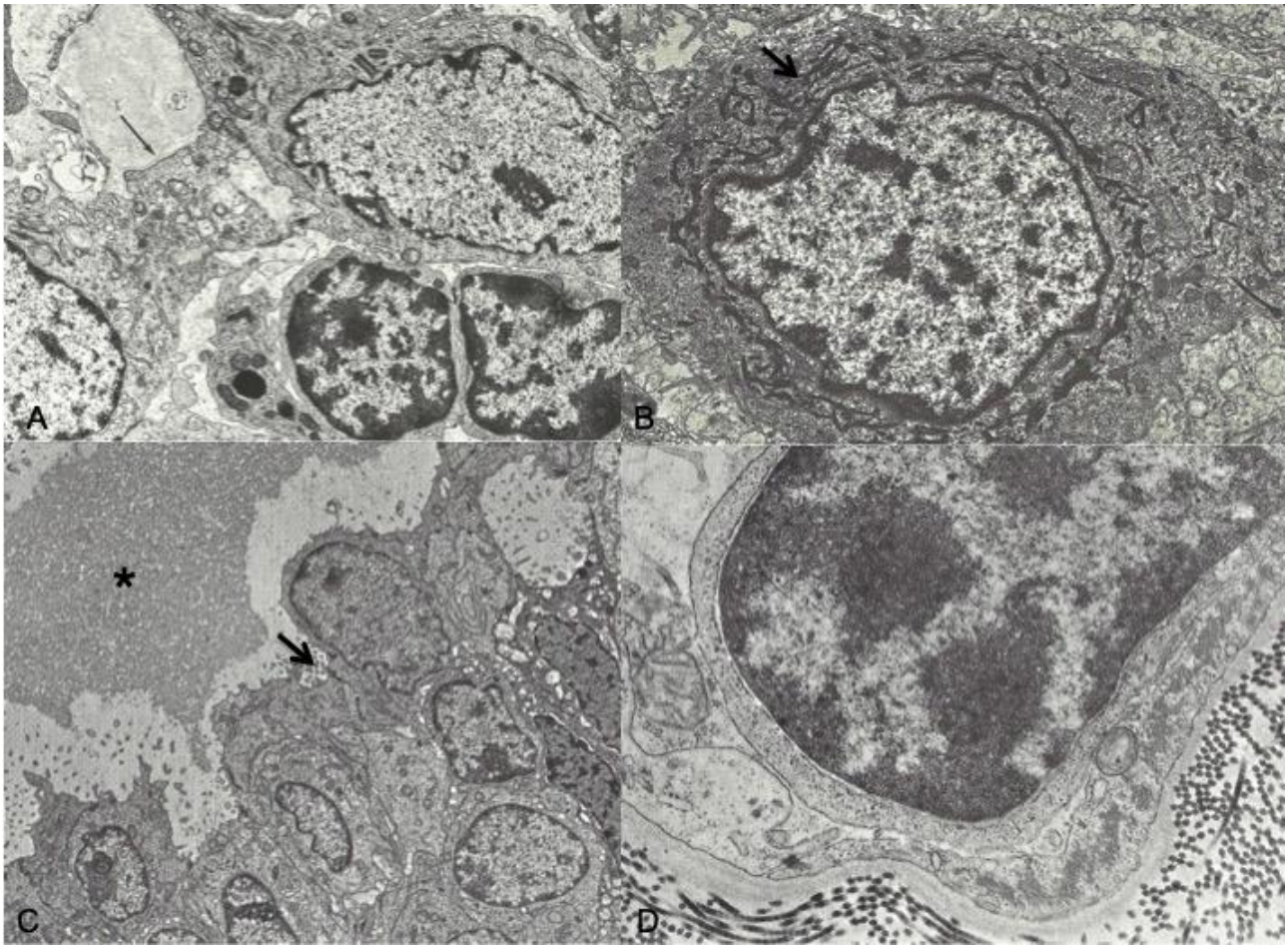

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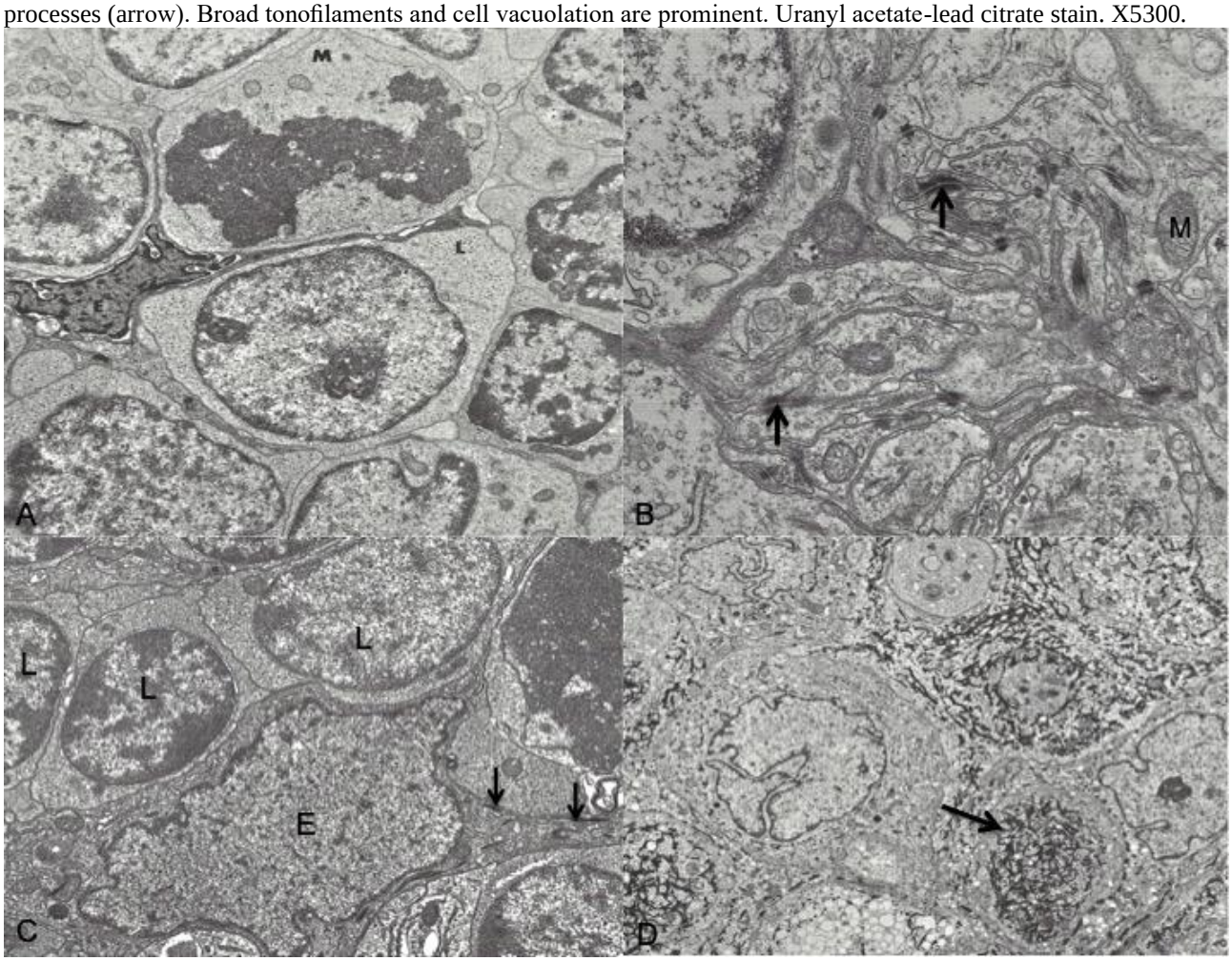
FIGURE 6-A. An epithelial cell (E) is shown with attenuated processes, an electron dense nucleus, and cytoplasm. Lymphocyte activation is manifested by scant heterochromatin, and nucleolar prominence (L). One of the lymphocytes is in mitosis (M). Inactive lymphocytes are also present. Uranyl acetate-lead citrate stain. X8000.
FIGURE 6-B. Complex cellular interdigitations, many desmosomes (arrow), and basal laminae. Uranyl acetate-lead citrate stain. X20.000.
FIGURE 6-C. This epithelial cell (E) has elongated cell processes and tonofilaments (arrow). A lymphocyte mitosis is seen (L). Uranyl acetate-lead citrate stain. X8000.
FIGURE 6-D. This normal human thymus shows the early formation of a Hassall's corpuscle with intertwining cell processes (arrow). Broad tonofilaments and cell vacuolation are prominent. Uranyl acetate-lead citrate stain. X5300.



4 DISCUSSION

Thymus is the immune system organ that is found in all vertebrates. In humans it is a small gland, whose main function is to produce T lymphocytes, participates actively in the immune response, being involuted since sexual maturity, before participating the "sowing" of lymphocytes in other tissues as pronephros, bone marrow, lymph nodes, spleen, lymph tissue and the mucosa-associated lymphoid tissue (MALT) (Uribe et al., 2011). In some fish the also involute soon after the sexual maturity (Zapata et al., 1996).

The fact of being found in all the vertebrate phylum, considering the evolutionary time, it is expected that the thymus be not very different among the vertebrates species. The differences in the

thymus among the species include the number per animal, the anatomical position, the structure of the thymic lobes and the development processes. For example, many species of teleost fish have a thymus composed of only one or two bilateral lobes, although the anuran amphibians and mammals, birds and cold-blooded eutheria vertebrates have multiple thymuses (Rodewald, 2008). Anatomically the human thymus is a mediastinal central and unique organ (Gideon and Mackay, 1969; Lele, Lele, Anderson, 2001). Histologically differences are observed, being observed in humans a clear differentiation between cortex and medulla, characteristic not observed in the studied fish (Roberts, 2012; Mokhtar, 2017). The presence Hassall's corpuscles are also discussed, with such corpuscles related to aging and the thymic involution, being for several authors nonexistent in fish and for others are present (Zhu et al., 2013; Klosterhoff et al., 2015). In this study Hassall's corpuscles were found very evident in *Rachycentron canadum*.

The electronic microscopy showed no difference between the human thymus and of the different species studied herein. They were found in both epithelial cells with long processes, among which are the lymphocytes. Thymus is a lymphoepithelial organ and this is demonstrated by the ultrastructure, the formation of typical desmosomes and large cytoplasmic branched tonofilaments. Most of these filaments are inserted into the desmosomes. In humans, this is more significant in the Hassall's corpuscles.

The immunohistochemistry showed the CD3 evolutionary conservation (Clone: F7.2.38. Isotype: IgG1, kappa) and CD4 (Clone: 4B12. Isotype: IgG1, kappa), once both were immunostained with antibodies made for humans. In other studies, the affinity of such antibodies has been demonstrated by thymic fish lymphocytes (Romano, Marozzi, Zenobi, 2004). Some physiological phenomena in fish alter both the phenotypic and the genotypic expression of these receptors (Batista et al., 2014, 2015).

In vertebrates, the CD3 complex and CD4 and CD8 co-receptors are essential for the transduction of signals during the T cells activation. The presence of these receptors in the initial phase of ontogenic development has a fundamental role in the immune system efficiency (Klosterhoff et al., 2015).

The nonspecific immunity (antigen-independent) makes a bridge with the specific immune response (dependent antigen). As it is already known that the premise for the existence of a specific immunity is the presence of mixed lymphocytic populations, T lymphocytes (thymus dependent) and B lymphocytes (bursa dependent), being such populations already described in fish (Arkoosh, 1991).

To understand the importance of T4 lymphocyte in specific immune response one should

remember that both fish and humans have a Major Histocompatibility Complex (MHC). MHC is a set of genes that encode the proteins of the cell surface essential so that the acquired immune system recognizes foreign molecules in vertebrates, which in turn determines the histocompatibility. In a cell, the protein molecules of the host's phenotype itself or other biological entities synthesize and degrade continuously. Each MHC molecule on the cell surface shows a molecular fraction of a protein called epitope (Dixon and Stet, 2001). This glycoprotein complex accounts with three types of glycoprotein, the type I, Type II and type III, the antigen presenting cells (APC) have the type I and II of MHC and these are in charge of separating the epitopes (antigenic determinants) of the antigen and pass these epitopes to the T4 lymphocyte.

The antigen presented can be own or not, thus avoiding the immune system of a body point its own cells. In its entirety, the MHC population is as a mediator that indicates the proteins equilibrium inside the cell.

In both fish and mammals, the antigen presenting cells (APC) constitute a heterogeneous population with a delicate immunostimulant capacity (Roitt, Brostoff, Male, 2001). In mammals, the skin Langerhans cells, interdigitating and follicular dendritic cells of the lymph nodes, the B lymphocytes and some macrophages, among others, represent the population of cells capable of presenting antigens. In teleost fish there are similar cells included in the mononuclear phagocytic system and are distributed throughout the body, especially in the gills, spleen, thymus and sectors of the intestinal mucosa, B lymphocytes, dendritic cells, and the melanomacrophages centers are considered APCs (Angius, 1985; Aghaallaei et al., 2012; Bassity and Clark, 2012). Most of these cells are fixed or circulating macrophages, but other mesenchymal cells as gills pillar cells, B lymphocytes, endothelial cells, as well as some epithelial cells, are capable of presenting antigens (Anderson, 1974, 1990). These cells have a key role in the induction of functional activity of T4 cooperating lymphocytes. The antigen presentation is accompanied by the production of molecules that intervene in the T4 lymphocytes activation; the most characteristic of all these molecules is interleukin- 1 (IL-1), a molecule that stimulates the lymphocytes proliferation and induces the production of other cytokines (Kato et al., 2013). Both the T and B lymphocytes have at rest receptors for IL-1. The occupation of these receptors, when the specifics of antigen are activated, leads to induction of both classes of cells. Then T cells express receptors for interleukin-2 (IL-2) (known as growth factors of T lymphocytes), and begin to produce IL-2; thus, the growth of a clone of T4 lymphocytes specific for the presented antigen begins, as shown in Figures 7, 8 (Holland and Lambris, 2002; Ashfaq et al., 2019).

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FIGURE 7. Schematic where one can observe the central role that the T4 lymphocyte occupies starting the specific immune system both humoral and cellular.

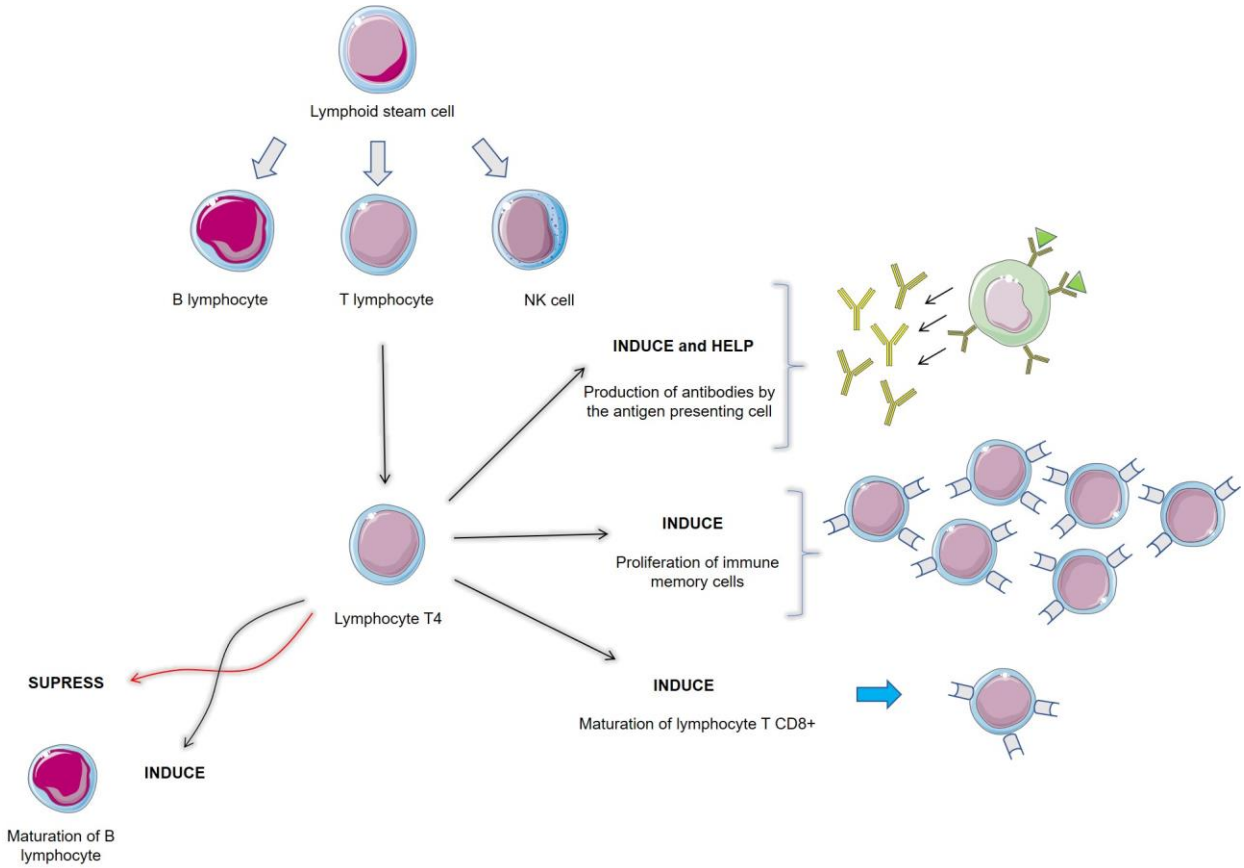

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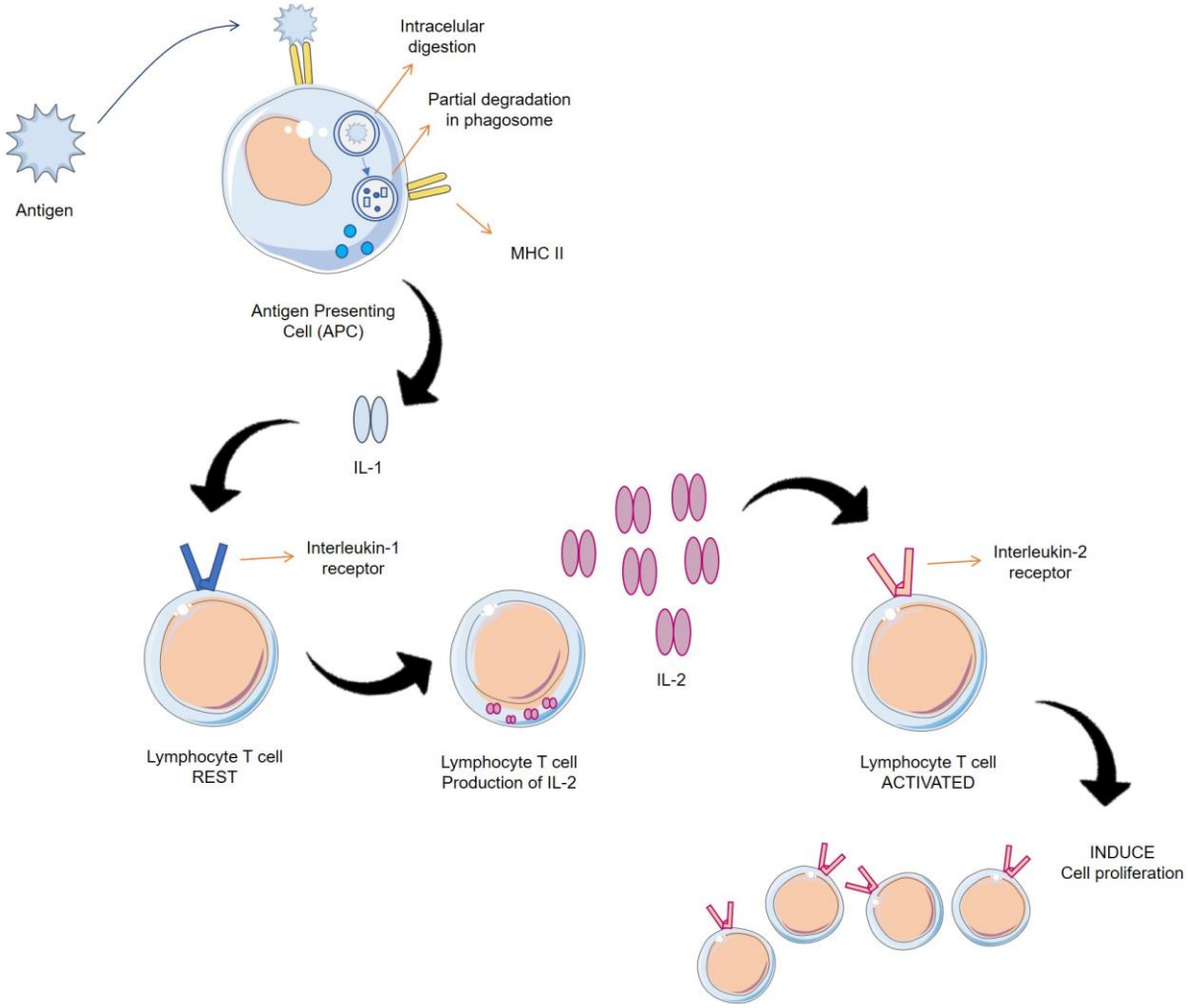
FIGURE 8. APC, this cell has type II glycoproteins of histocompatibility what determines all actions for the transfer of the epitope extracted from processed antigen to T4 lymphocytes and releases interleukins (IL-1 and IL2) which ensure the monoclonal proliferation of the cell line that will trigger a specific reaction on this epitope.



In this study not only a morphological but also functional homology were demonstrated, in that it affects the immune system, of the humans and teleost fish thymus. Regarding its involution that varies according to the species, Lele in 1932 conducted a comparative study of the thymus in teleosts and discovered that its lifespan was distinct in different species, being in the **lower teleosts** before sexual maturity, but survived and even grew, during several years after maturity in **higher teleosts**.

Definitely, both in fish as in humans, it is possible to consider the existence of two tracks in the modulation of the immune response, an afferent pathway that begins with the presentation of the antigen and an efferent pathway through which the result of the T8 lymphocytes (cytotoxic), antibodies or other effector mechanisms are canalized. In these two phases both in humans and in fish, a mixed population of lymphocytes, the differentiation of lymphocytes in the thymus and the T4 lymphocytes production, play a fundamental role in the success of the immune response.

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TABLES

Table 1. Fish species studied.

Species	Number of individuals	Weight in grams	Total length in millimeters.	Origin
Amphiprion ocellaris	2	3/ 2	40.3/ 30.8	EMA[1]
Rachycentron canadum	2	300/ 280	300/ 245	EMA[1]
Odontesthes argentinensis	2	60/ 87	250/ 280	EMA[1]
Hippocampus reidi	2	3/ 2.6	90/ 56	EMA[1]
Elacatinus figaro	2	1.1/ 0.8	20/ 18	EMA[1]
Carasius auratus	2	16/ 21	15/ 18	Commercial Aquarium
Oncorhynchus mykiss	2	150/ 170	200/ 230	Commercial Property

[1]Marine Station of Aquaculture, Institute of Oceanography, Federal University of Rio Grande (FURG) - RS, Brazil.