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IMMUNOLOGICAL POTENTIAL OF PLATELETS – A META-ANALYSIS

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ABSTRACT

Innate cells are crucial for the initial stages of pathogenic invasion because they express different pattern recognition receptors (PRRs). By identifying dangerous substances generated by the host body through danger-associated molecular patterns (DAMPs) and pathogen-associated molecular patterns (PAMPs), PRRs aid in recognizing microbial invasion. The innate immune system's cells react to danger by releasing or producing molecules for effector function, which involves organising the recruitment and activity of several specialised cell populations that use phagocytosis and lytic functions to combat invasive pathogens. Examples of these molecules include defensins, cytokines, and chemokines. Innate cells' PRRs play a crucial role in starting some cells' ability to convey antigens to lymphocytes. Adaptive immune cells, known as lymphocytes (T and B cells), offer an additional layer of defence to a host. Thrombocytes can be round, oval, spindle, or spiking cells with long cell processes. They are sized similarly to lymphocytes. A surface-connected canalicular structure appears to exist in the cytoplasm of thrombocytes. A wide range of bioactive proteins, including those that are antibacterial, inflammatory, and immune-modulating compounds, can also be produced and released by thrombocytes.

KEYWORDS: Adaptive immune cells, known as lymphocytes (T and B cells), offer an additional layer of defence to a host.

1. INTRODUCTION

Innate and adaptive immunity, which has both cellular and non-cellular (or humoral) components, make up the immune systems of fish and birds. Various cells, including macrophages, granulocytes (polymorphonuclear cells like neutrophils), thrombocytes, basophils, eosinophils, and natural killer cells, are components of the non-specific, innate immune response. Innate cells are crucial for the initial stages of pathogenic invasion because they express different pattern recognition receptors (PRRs). By identifying dangerous substances generated by the host body through danger-associated molecular patterns (DAMPs) and pathogen-associated molecular patterns (PAMPs), PRRs aid in recognizing microbial invasion. The innate immune system's cells react to danger by releasing or producing molecules for effector function, which involves organising the recruitment and activity of several specialised cell populations that use phagocytosis and lytic functions to combat invasive pathogens. Examples of these molecules include defensins, cytokines, and chemokines. Innate cells' PRRs play a crucial role in starting some cells' ability to convey antigens to lymphocytes. Adaptive immune cells, known as lymphocytes (T and B cells), offer an additional layer of defence to a host. It is known that certain cells, such as dendritic and macrophages, digest pathogenic peptides and present antigens to lymphocytes in the context of the major histocompatibility complex (MHC) to trigger a more focused adaptive immune response to eradicate infection. The function of thrombocytes in fish and birds' immunological responses is the primary focus of this paper. Fish, amphibians, birds, and reptiles all include thrombocytes that are analogous to enucleated platelets found in humans.[1] Similar to thrombocytes or platelets, nucleated haemocytes are present in the hemolymph of invertebrate species.[2,3] Thrombocytes are the second most common blood cell after erythrocytes in the majority of vertebrate circulation.[4-6] Depending on the species and vertebrate group, adult animals undergo thrombopoiesis in various tissues. Megakaryocytes are the precursor cells of platelets in mammals.[7] Bird thrombocytes are generated in the area where the earliest intraembryonic hematopoietic cells emerge, from cells that resemble multipotent hematopoietic progenitors.[8] Fish liver, kidney, and spleen are examples of lymphomyeloid and lymphoid organs where thrombopoiesis is observed.[9, 10] Thrombocytes can be round, oval, spindle, or spiking cells with long cell processes. They are sized similarly to

lymphocytes.[1,5,6,11–14] A surface-connected canalicular structure appears to exist in the cytoplasm of thrombocytes.[15] A wide range of bioactive proteins, including those that are antibacterial, inflammatory, and immune-modulating compounds, can also be produced and released by thrombocytes.[16–23] Depending on the species and vertebrate group, adult animals undergo thrombopoiesis in various tissues. Megakaryocytes are the precursor cells of platelets in mammals.[7] Bird thrombocytes are generated in the area where the earliest intraembryonic hematopoietic cells emerge, from cells that resemble multipotent hematopoietic progenitors.[8] Fish liver, kidney, and spleen are examples of lymphomyeloid and lymphoid organs where thrombopoiesis is observed.[9, 10] Thrombocytes can be round, oval, spindle, or spiking cells with long cell processes. They are sized similarly to lymphocytes.[1,5,6,11–14] A surface-connected canalicular structure appears to exist in the cytoplasm of thrombocytes.[15] A wide range of bioactive proteins, including those that are antibacterial, inflammatory, and immune-modulating compounds, can also be produced and released by thrombocytes.[16–23] Furthermore, avian thrombocytes have been shown to have massive, acid phosphatase-positive granules that resemble mammalian lysosomal granules.[24] Activated thrombocytes have the ability to discharge a variety of intracellular secretory granules (such as granules, dense granules, and lysosomes) into the bloodstream.

2. Immune Receptors

Though their primary roles in thrombosis and haemostasis have been established, research over the past 20 years has shown that platelets and thrombocytes also play a part in infection, inflammation, and the immune system as a whole. The identification of thrombocytes as carriers of PRRs, such as toll-like receptors (TLRs), has provided insight into the function of these cells in a range of innate immune responses. The TLR1, 2, 3, 4, 5, 7, and 21 for birds have been found[25,26], and the functional TRL1, 2, 4, 5, 7, 8, 9, 20, and 21[23, 27] are for ichthyoid thrombocytes. While TLRs 3 and 7–9 recognise double-stranded and single-stranded RNA frequently associated with viruses in fish and chicken, TLRs 1, 2, 4, and 5 are typically linked to the identification of patterns associated with bacteria.[28, 29] The identification of mycoplasma and fungal particles is likewise linked to TLR 1 and 2 subtypes.[30] TLR 20 is exclusively found in fish and is linked to the identification of protozoan parasites.[31] The ability to recognise CpG dinucleotide sequences in DNA is linked to TLR 21.[28, 32] Other PRRs and related genes, such as C-type lectin receptor (CLR), nucleotide-binding oligomerization domain (NOD)-like receptors (NLR) Family Member X1 (NLRX1), and NLR Family CARD Domain Containing 3 and 5 (NLRC3, NLRC5), are also present in these cells. The identification of these substances on thrombocytes linked to pathogen detection supports the claim that, like other leukocytes, these cells may be directly involved in defending the host against infection. In fish and birds, the thrombopoietin receptor (c-Mpl) has been found to be a distinct indicator of thrombocytes connected to the growth of immature cell stages. Additionally, CD62 (P-selectin), a crucial cell adhesion protein for platelet and leukocyte rolling on activated endothelium cells, is expressed by thrombocytes.[33,34] These relationships highlight the potential function of thrombocytes in mediating the gap between innate and adaptive immunity.

3. Immuno-Regulatory Molecules

It has been demonstrated that thrombocytes express, generate, or release a range of inflammatory mediators, antimicrobial agents, and other immune-modulating substances. Thrombocyte PRRs are crucial in the inflammation that follows microbial infections.

In a transcriptome investigation, our lab found several transcripts linked to signaling downstream of TLRs in chicken thrombocytes. Transcripts related to apoptosis, the generation of inflammatory cytokines and chemokines, the activation of T and B lymphocytes, MAPK activation, IFN activation, and JAK/STAT signaling have all been demonstrated to be upregulated by LPS-stimulated chicken thrombocytes.[35] By employing inhibitors for kinases such as extracellular signal-regulated kinase (ERK), p38, mitogen-activated protein kinase (MEK)1/2, and inhibitor of nuclear factor kappa-B kinase (IKK), Winkle et al.[20] were able to map pathways linked with the response of chicken thrombocytes to LPS stimulation. Transcripts for platelet-derived growth factors have also been found in chicken thrombocytes, and these transcripts may play significant roles in the vascular system and in the healing of damaged tissue.[36] Leukocytes release pro-inflammatory cytokines at the outset of injury and tissue damage, which encourage the production of acute-phase proteins by the liver, such as C-reactive protein (CRP), serum amyloid A (SAA), metal-binding protein, lysozyme, lectin, etc.[37] These proteases are in charge of a number of defense-related functions, including the inhibition of proteolytic enzymes, stopping the spread of infectious agents (i.e., either by eliminating microorganisms or enabling microbial cells to respond appropriately by altering surface targets), and restoring damaged tissue to a state of health. In a study that He et al[22] conducted, showed that when grass carp thrombocytes were exposed to bacteria (Aeromonas hydrophila) and reovirus (grass carp reovirus), the RNA expressions of several innate immunity genes were significantly elevated. Furthermore, they discovered that following viral and bacterial stimulation, the number of thrombocytes in peripheral blood increased, suggesting that this rise in thrombocyte counts may be related to immune modulation during pathogen invasion.

4. Response to Pathogens

It has been demonstrated that thrombocytes can become infected or interact with a variety of diseases that affect the poultry and aquaculture industries. Highly pathogenic

(HP) H5N1 avian influenza viruses (AIVs) can infect chicken thrombocytes, which is important in the development of this disease, according to a study done by Schat et al.[38] The ability of the AIV strain A (fowl plague virus) to multiply in chicken thrombocytes has been shown in a different investigation.[39] It has also been demonstrated that the Newcastle Disease Virus, a different virus of significant economic impact, can infect chicken thrombocytes and hinder their capacity for phagocytosis and migration.[40] Mammalian platelets have been demonstrated to engage in diverse viral interactions via their distinct surface receptors for integrins, surface lectins, and TLRs.[41] Numerous investigations have demonstrated that the human immunodeficiency virus (HIV) directly interacts with megakaryocytes and platelets during infection.[42] Viral infections may cause increased platelet breakdown or decreased platelet synthesis, which can result in thrombocytopenia.[43] In addition, platelets can provide pathophysiologic and protective responses during specific viral infections by the production of mediators from these cells and their interactions with other immune and vascular cells.[44] It has been demonstrated that parasites and viruses can interact with thrombocytes. Chicken thrombocytes are infected and undergo development by Gametocytes of leucocytozoon parasites.[45] Trypanoplasma Borreli infections in common carp cause severe thrombocytopenia as a result of nitric oxide-mediated apoptosis.[23] In chickens infected with Plasmodium Gallinaceum, thrombocytopenia may be caused by nitric-oxide-mediated apoptosis.[46] Thrombocytopenia is also reported with infection with most Plasmodium species in humans. Nevertheless, little is known about the mechanisms underlying thrombocytopenia during malaria.[47] Infected erythrocytes and circulating plasmodium parasites can be directly interacted with by platelets, which can then eliminate the infection. In a study where trout were infected with Candida albicans, thrombocytes were seen to interact with erythrocytes, macrophages, other polymorphonuclear cells, and lymphocytes.[48] When interacting with erythrocytes and macrophages, thrombocytes appear to form cellular aggregates in the shape of rosettes.[49] When platelets interact with erythrocytes, neutrophils, or other cells, this behaviour can also be seen. According to Kho et al.[50], platelets are capable of eliminating the main parasites linked to human malaria.

5. Phagocytosis

The immune system's phagocytic cells are vital components. These cells are in charge of consuming pathogens, cellular waste, and other foreign substances and eliminating them. TLRs are among the PRRs that are crucial for pathogen recognition. They cause the release of bioactive, cytotoxic contents from big granules, which degrades pathogens, as well as the following presentation of pathogen-derived peptide antigens. Mammalian platelets can present circulating bacteria and microbial products to neutrophils and other phagocytic cells by binding to them.[51] Contact with some bacteria not only causes germs to bind and internalise, but it also causes platelets to aggregate and degranulate. Platelet granules are known to contain and produce reactive oxygen species[52] and cationic antibacterial/microbicidal proteins known as thrombocidins.[53] First demonstrated by Glick et al.[54], circulating thrombocytes in chickens have the capacity to phagocyte. Dye particles and a variety of bacterial species, such as strains of Salmonella, Escherichia coli, Pseudomonas aeruginosa, and Burkholderia cepaciao, can be phagocytosed by avian thrombocytes.[24, 55] It has been demonstrated that chicken thrombocytes phagocytise around three times faster than heterophils and monocytes combined, and that circulating thrombocytes absorbed almost twice as many bacteria.[4] In avian thrombocytes, the acid-phosphatase-positive granules are thought to be lysosomal structures connected to phagocytic activity.

6. CONCLUSION

Further study by numerous other immunologists is required to completely comprehend the function of thrombocytes in antigen presentation and interaction with other lymphocytes and APCs. Determining how these cells function in immune responses can help with the development of prophylactics and vaccinations for commercially significant agricultural animals like fish and poultry. With the advent of mRNA vaccines and our expanding understanding of the thrombocyte's biological function, developing effective vaccinations may now be done more effectively. We are learning more about the processes that thrombocytes use to function as essential players in both innate and adaptive immunity. We now have proof that thrombocytes are involved in the activation of maintained immunity for long-term protection, in addition to their significance in blood coagulation.

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