Parasite Immunology

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Learning Objectives

1. To understand the immune response of the host against parasites and host immunity.
2. To make the reader aware of the importance of immune evasion by parasites and establishment of chronic infection.
3. To know about the immunoregulation in helminth infections.

Introduction

In 1879, Heinrich Anton de Bary, the German doctor turned botanist and mycologist, stated that "Any two organisms living in close association, commonly one living in or on the body of the other, are symbiotic, as contrasted with free living." The nature of interaction between the symbionts varies considerably, and one such interaction leads to parasitism, i.e., one species, the parasite, lives at the expense of the other, the host, and frequently causes some degree of injury or harm to the host. The parasite, after coming in contact with the host and being a foreign invader, encounters the host's defense system. Whether the host is susceptible or resistant to the infection depends on a complex interplay between the host's immune system and the parasite's ability to combat or evade it. The innate immune response and the adaptive mechanism are equally important in determining the outcome, but one type of adaptive response (humoral or cell mediated) may be predominant over the other. In general, protozoan parasites are frequently intracellular and hence the cell-mediated response plays a prominent role, while for the larval or adult forms of the helminth parasites which are large enough to be extracellular, the antibody response predominates. In spite of these responses, many parasites tend to establish a chronic infection for long-term transmission. This strategy may be facilitated by various mechanisms like immune evasion, immunoregulation, or immunomodulation, which in turn also suppresses or minimizes the immunopathological damage to the host.

Innate Immune Responses

Pathogenic organisms have molecular structures which are shared among similar organisms and are needed for infecting the host. These structures, which are absent in mammalian cells, are termed pathogen-associated molecular patterns (PAMPs). These patterns are recognized

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S. C. Parija, A. Chaudhury (eds.), *Textbook of Parasitic Zoonoses*, Microbial Zoonoses,
https://doi.org/10.1007/978-981-16-7204-0_3

by pattern recognition receptors (PRRs) present in host cells at all levels (cell membrane, cytoplasm, and endosomes). A number of PAMPs have been described in parasites as well as corresponding PRRs in the host. The best studied PRR is the Toll-like receptors (TLRs), a total of 10 of which have been identified in mammalian cells. A number of PAMPs have been found in protozoan parasites, which include glycophosphatidylinositol and phosphoglycans present in trypanosomes, *Leishmania*, *Toxoplasma*, and *Plasmodium falciparum*. These molecules stimulate TLR2 and also TLR4 to upregulate nitrogen oxide synthase production and synthesis of pro-inflammatory cytokines. In addition, parasite nucleic acids also function as ligands for recognition of TLRs. Thus, TLR9 recognizes unmethylated CpG motifs present in protozoan DNA. The profilin proteins of *Toxoplasma* and *Cryptosporidium* trigger IL12 production in murine dendritic cells due to stimulation of TLR11, although this TLR is absent in mammalian cells. In addition to TLRs, other PRRs have been identified which are classical human receptors. These include mannose-binding lectins which bind to lipophosphoglycan of *Leishmania*, *P. falciparum*, and *Trypanosoma cruzi* and pentraxin which binds to sporozoites of malaria parasites. A few other PRRs like cytosolic DNA sensors, NOD-like receptors, and RIG-1-like receptors have been identified, but studies on these receptors are still rare and controversial.

Helminth parasites also express ligands for TLRs, but their role is not clearly elucidated. Certain PAMPs like ES-62, a glycoprotein of filarial worms and lipophosphatidylserine moieties of *Schistosoma* membrane, have been described which can trigger TLR4 or TLR2. Eggs of *Schistosoma* can also trigger TLR3 in dendritic cells.

Cellular Effectors of Innate Immune Response: A number of cell types take an active part in the innate response and form the backbone of this type of immunity:

1. **Macrophages and Granulocytes:** Phagocytosis by macrophages and granulocytes like neutrophils, eosinophils, and basophils plays an important role in innate immune response for protozoan parasites. Activation of the oxidative metabolism and generation of reactive oxygen species for NADPH sets the stage for intracellular killing of phagocytosed parasites. On the other hand, parasites have evolved a number of strategies to avoid or withstand these assaults which increase their chance of survival within these cells. These include, among others, inhibition of respiratory burst by certain parasite molecules, opsonic entry through receptors which do not activate NADPH oxidase, and ability to withstand or escape from the acidified, hydrolytic environment of phagolysosomes. In contrast, helminths, which are too large to be phagocytosed, can be killed by macrophages after activation of adaptive response. Only the eosinophils play some limited role in innate response to helminthic larva by releasing granules containing membrane-damaging enzymes and other proteins.
   Normally, following an antigenic stimulus, the monocytes differentiate into mature macrophages and dendritic cells. Two types of macrophages have been described. The M1 or classically activated macrophages are induced by IFN-γ and microbial products and can kill intracellular pathogens by endocytosis, production of nitric oxide, and synthesis of reactive oxygen intermediates. The second type or M2 (alternatively activated macrophages, AAMs) cells get differentiated in response to IL4, IL13, and some other cytokines and are typically associated with TH2 adaptive immune response and tissue repair seen in helminthic infections. Dendritic cells, which are specialized macrophages, have a dual role to play: as classical macrophages in innate response and also priming of the immune system for the ensuing adaptive response.
2. **Innate Lymphoid Cells (ILCs):** This is a growing family of immune cells that mirror the phenotypes and functions of T-cells of adaptive response. But in contrast to these T-cells, the ILCs do not express antigen receptors or clonal selection when stimulated. Instead, they react to the antigens to produce

various cytokines which direct the immune response needed for the parasite challenge. The natural killer (NK) cells can be considered the innate counterparts of cytotoxic CD8+ T-cells, whereas the ILC1, ILC2, and ILC3 may represent the innate components of TH1, TH2, and TH17 cells, respectively. Tissue signals in the form of IL12, IL15, or IL18 stimulate ILC1 which in turn produce effector cytokines like IFN-γ and TNF-α and help in macrophage activation with generation of reactive oxygen intermediates. Type 2 ILCs are stimulated by IL25, IL33, and TSLP in response to helminthic infections and in turn produce various effector molecules like IL4, IL5, and IL13 which take part in M2 activation and mucus production, along with tissue repair. Survival of ILC2 in the intestine and the lungs is controlled by IL9, a cytokine which also enhances TH2 response. Lastly, the ILC3 plays an important role in bacterial infections and helps in the phagocytic process.

3. **Natural Killer (NK) Cells:** These cells are particularly important for the innate defense against intracellular protozoan parasites. They become activated in response to infections by *Leishmania*, *Toxoplasma*, and *P. falciparum* and also by the excretory-secretory proteins of hookworm. Activation of NK cells occurs as a consequence of PRR-mediated activation of DCs and is both contact dependent and cytokine driven (IL12, IL18). Both mechanisms induce the production of IFN-γ. This cytokine serves as multiple effector for both innate and adaptive responses. Thus it activates macrophages and neutrophils and also helps in transformation of TH1 cells, thereby playing an important role in protozoan infections. The inhibitory action of IL4, IL10, and TGF-β on NK cell activation corresponds to the relatively unimportant role of these cells in helminthic infections where TH2 response predominates. However, the increase in NK cell population in some helminthic infections suggests a role since a few helminths are capable of producing both TH1 and Th2 responses due to the presence of different developmental stages during infection in the host.
   Regulation of NK cell activity is carried out by IL10 and other cytokines which have a downregulatory effect on IFN-γ production or by direct suppression of NK cell activity. This is useful in protecting the host from excessive tissue damage by IFN-γ or TNF-α.
4. **Natural Killer T (NKT)-Cells:** These cells help in rapid cytokine response. They recognize glycolipids in association with CD1d molecules, and these cells have been proposed to be the early sources of TH1 and Th2 cytokines. They express restricted T-cell receptors of limited diversity, and their role in innate response remains controversial. However, they may initiate the adaptive immune response.
5. **γ-δ T-Cells:** These T-cells have T-cell receptors (TCR) made up of γ- and δ-chains in contrast to the more common α- and β-chains. They are found predominantly in gut mucosa and have fewer antigen receptors. These cells are part of innate response since they release cytokines like IFN-γ and TNF-α which can damage infected cells. They also form a bridge between innate and adaptive response by acting as antigen-presenting cells, and they also have regulatory functions. They may contribute to tissue damage by heightened immune response due to the release of IL17. For helminthic infections, various attributes of these cells have been mentioned for different parasites, but the definitive role played by these cells remains unclear.

Apart from the various types of cells mentioned above, for intestinal helminths the first barrier which they encounter is the secreted mucus. There is marked goblet cell hyperplasia noted in such infections, and the secreted mucus gel consists of high molecular weight glycosylated glycoproteins, and Muc2 is the predominant molecule. This mucus production is under the control of both innate and adaptive host response. Type 2 cytokines, particularly IL4, IL13, and IL22 secreted by ILC2 as well as

CD4+ T-cells, are potent inducers of mucin production and resultant goblet cell hyperplasia. This mucin accelerates the expulsion of the helminths from the intestine.

Adaptive Immune Response

Adaptive immune response is primarily mediated by T- and B-lymphocytes with initial priming by various cells of innate immune response. The T-cells are mainly of four types: T-helper cells (CD4+ T-cells), cytotoxic T-cells (CD8+ T-cells, T_c), T17 cells, and T-regulatory cells (T_{REG}). Presentation of the antigen by antigen-presenting cells results in the differentiation of TH1 and Th2 subsets. It is now well established that TH1 response is elicited in infections caused by intracellular protozoan parasites, while the extracellular helminthic infections result in the differentiation of the TH2 subset. However, TH response may vary with the particular type of parasite and its developmental stage.

Adaptive Response to Protozoan Parasites

1. **TH1 Response:** This is mediated by a set of cytokines, chief among which is IFN-γ. The protective role of this cytokine and of TH1 has been conclusively shown in mouse models of *Leishmania* infection. The C57BL/6 mice strains which produce IFN-γ are resistant to *Leishmania* infections, while those which cannot produce it are susceptible to infection. The IFN-γ produced by CD4+ TH1 cells binds to specific receptors on macrophages and causes their activation with the production of antiparasitic molecules. In addition, IFN-γ increases MHC-I expression to help in the recognition and killing by CTLs, together with MHC-II expression to promote antigen presentation to CD4+ T-cells. The TH1 response is important in protection against pre-erythrocytic stage of *Plasmodium* apart from protection against *Leishmania* and *Toxoplasma* infections.
2. **Cytotoxic T-Cells (CTLs, CD8+ T-cells):** These cells function both in the recognition and killing of target cells. As part of adaptive response, they display the necessary specificity, and following antigen stimulus, they start producing cytotoxic granules. The killing mechanism is somewhat nonspecific and involves three types of cytotoxic molecules:
   (a) **Perforins:** It is a 66 KDal molecule which can produce pores or holes in the target cell membrane.
   (b) **Granzymes:** They exist as pro-enzymes and are cleaved by cathepsin. Their entry into cells is facilitated by the pores induced by perforins. Once inside the cells, they can induce apoptosis.
   (c) **Granulysin:** It helps the granzyme to kill the parasite inside the cells by a process similar to apoptosis.

   Whatever may be the mechanism, even if the intracellular parasites are not killed by the above processes, their release from the destroyed cells can lead to killing by activated macrophages. The CTL plays a pivotal protective role by destroying hepatocytes infected with the sporozoites of malaria parasites. It is also important in protection against *Leishmania*, *Toxoplasma*, and *T. cruzi* infections. In *Leishmania* infections, these cells have a dual role to play. On the one hand, they have a protective role in *Leishmania donovani*, *Leishmania major*, and *Leishmania infantum* infections. On the other hand, overproduction of IL10-producing CTLs has been observed in disseminated cutaneous leishmaniasis as well as in post-kala-azar dermal leishmaniasis, pointing to its involvement in disease dissemination. CTLs have also been implicated in tissue destruction and disease progression in mucocutaneous leishmaniasis.
3. **TH2 Response and Role of Antibodies:** All protozoan infection elicits an antibody response, but the role of humoral immunity in protection has not been demonstrated, except for a few selected instances. Thus, for

Trypanosoma brucei, which is an extracellular protozoan parasite, IgG plays an important role in control of infection. The antibodies have also been described to play a role in direct lysis of *T. cruzi* or complement-mediated destruction of plasmodial gametocytes. Antibodies can also facilitate macrophage function by binding with F_c receptors and effective phagocytosis of *Toxoplasma gondii* or RBCs infected with malaria parasites. These antibodies can also prevent the entry of the parasites into target cells by neutralizing certain antigens of the parasite necessary for penetration. This has been demonstrated in *T. gondii* and *P. falciparum.* Thus, it appears that humoral immunity does play a part in containment of protozoan parasites, but by itself it may be less efficient in clearing the infections.

Adaptive Response to Helminth Parasites

The helminths are larger in size compared to protozoan parasites and are extracellular in nature, and hence in such infections, TH2 response predominates over TH1 response. A number of hypotheses have been advanced to explain this phenomenon. It has been shown that helminths exhibit a relatively low number of TLR ligands, leading to a poor production of IL12 by dendritic cells, an interleukin essential for TH1 differentiation. Additionally, the excretory-secretory antigens of helminths may suppress IL12 production and in turn may upregulate cytokines like IL25 and IL33, which enhances TH2 differentiation. Whatever may be the mechanism, the TH2 cells start producing various cytokines like IL3, 4, 5, 9, 10, and 13 which also activate other cells like eosinophils, mast cells, and basophils, along with IgE production by B-cells. Thus a concerted mechanism comes into play to eliminate the helminthic parasite from the body.

Dendritic cells act as classical antigen-presenting cells (APCs) in the body. Apart from this, it has been found that ILCs and basophils can also act as APCs. In the intestine, mucin containing the parasite antigens is taken up by dendritic cells. The induction of highly polarized CD4+ TH2 cell response with the release of a plethora of cytokines promotes immunity through multiple mechanisms and effector cells:

1. **Mast Cells**: IL3 and IL9 produced by TH2 cells act synergistically and cause accumulation of mast cells in the mucosa of the small intestine. The mast cells prevent the adhesion and penetration of parasite into the mucous membrane by releasing chondroitin sulfate. These mast cells also express high-affinity IgE receptors.
2. **Eosinophils**: Elevated eosinophil levels are common in helminthic infections, but their exact role is somewhat controversial. Circulating eosinophils are attracted to the site of helminthic infection by IL4 and IL13 as well as by chemokines. Degranulation or activation of eosinophils occurs under the influence of various cytokines as well as immunoglobulins. In vitro studies have shown parasite destruction by molecules of eosinophilic granules. This has been demonstrated for *Schistosoma mansoni*, *Strongyloides stercoralis*, and *Trichuris muris*, but no such effect could be demonstrated in vivo in animal models. In *Trichinella spiralis*, eosinophils may actually promote infection.
3. **Antibody Response**: IL4 released by TH2 cells is a promoter for immunoglobulin class switching to IgE, which is the prototype immunoglobulin seen in helminthic infections. However, its role in host protection remains unclear, and it is surmised that most of the IgE may not be parasite specific and it may also be a part of parasite evasion strategy. In some cases, IgE contributes to intestinal anaphylaxis due to mast cell degranulation. This can lead to a rapid elimination of the larval stage of the parasite due to intestinal physiology and chemistry of the gut epithelium. In some cases, IgA may neutralize the secreted

metabolic enzymes of the parasite and thus interfere with the feeding of the worm.

In experimental animals and also in natural host animals, the following immune mechanisms have been observed which can restrict helminthic, particularly nematodal infections:

1. **Breed resistance:** It has been seen that individual Merino lambs may be classified as responders and nonresponders on the basis of their immunological response to infection with *Trichostrongylus colubriformis* and these differences are genetically transferable.
2. **Age Resistance:** In older age, the nematodes either fail to develop or get arrested in larval stages in the tissues. *Strongyloides* infections of ruminants and horses are most commonly seen in very young animals and conversely in some parasites such as *Anaplasma*; young cattle are more resistant to infection than older cattle. The reason for this age resistance is unknown. Unlike sheep and cattle, goats do not develop age-related immunity. *Trichostrongylus* spp. stimulate a slower immune response and are therefore sometimes seen in older livestock.
3. As exemplified in infections of the rat with the trichostrongyloid nematode *Nippostrongylus brasiliensis*, the adults may be stunted in size, and in some cases these adult worms are killed and expelled automatically from the animal.
4. Sometimes immunological unresponsiveness is seen in ruminants with gastrointestinal infections. The mechanism is not fully understood. It has been agreed upon that in these animals luminal immunity is due to TH2 type of response. There are increased gut mast cells and gut receptors for worm-specific IgE antibodies. These sensitized mast cells produce vasoactive amines that lead to increased mucus production and capillary leakage. These changes can lead to decreased oxygen tension in the gut, thus leading to detachment and expulsion of the worms. This local gut response by immune cells varies greatly with parasites. For example, mast cell response is required to expel *T. spiralis*, but it is not required in the case of *Nippostrongylus brasiliensis* infection.

Role of T17 Cells in Helminth Infections

The naive T-cells can differentiate into another subset known as TH17 as a result of antigen recognition in the presence of TGF-β and IL16. These TH17 cells produce IL17, which is a pro-inflammatory cytokine. It helps in recruitment of granulocytes and release of other pro-inflammatory cytokines. IL17 may also be produced by cells primarily involved in innate response like NK cells and γδ-T-cells. By promoting inflammation, the TH17 cells contribute to various pathologies associated with helminthic infections, including tissue damage. They may also promote intestinal hypermotility.

T-Regulatory Cells and Immunoregulation

A noteworthy feature of most helminthic infections is their long life span (sometimes many years) and persistence, but causing minimal harm or any life-threatening pathological consequence. This feature is due to a complex interplay of immune evasion and regulation of host immunity. The chronicity of infection causing persistent dominant TH2 response induces the expansion of natural as well as parasite-induced regulatory T-cells (T_{REG}). T_{REG} cells are a distinct population of T-lymphocytes which has the ability to suppress the function of other lymphocytes. Thus they can exert this effect on CD4+ CD25- T-cells, CD8+ T-cells, as well as B-cells. This subset can be identified by the expression of CD4, CD25-, and FOXP3. By its suppression effect, these cells can exert a profound state of immune tolerance in the host. The same response causes an immunoglobulin class switching in B-cells to IgG_4. In effect, the helminth enters into a niche with low parasite

antigen-specific lymphocyte proliferation, higher antigen-specific IgG_4/IgE ratio, and increased levels of regulatory cytokines IL10 and TGF-β. These are the characteristics of an asymptomatic chronic helminthic infection. The complex interplay and the roles played by different cells are depicted in Fig. 1.

In summary, helminths are very complex organisms phenotypically as well as genetically. Due to their physical size, they cannot be ingested by phagocytic cells or destroyed by classic cytotoxic T-cells. The immune cells usually deploy type 2 immune responses or the allergy-type immune responses against the helminths. These responses are characterized by increase in the concentrations of interleukin (IL)4 and other Th2-type cytokines, such as IL5, IL9, IL13, and IL21. There is an increased recruitment and activation of effector cells, such as eosinophils, basophils, and mast cells which can produce various cytokines. In these parasitic infections, innate and acquired components of an active immune system constantly communicate with each other. T-cell signals increase and modify the function of effector B-cell, which in turn induces antibody response.

Immune Evasion by Parasites

Immune evasion is a strategy adopted by various microorganisms including protozoans and helminths to survive in a host in spite of effective immune response. The mechanisms involve one or more of the following strategies:

1. **Antigenic Variation:** Strains of parasite can be distinguished by the presence of immunodominant antigens, and strain-specific immune response defines the parasite population. A loss or gain or alteration in a particular immunodominant antigen group due to the corresponding loss/gain/change of one of the polypeptides or polysaccharide antigen is defined as antigenic variation. Hence, although the adaptive immune response may be effective against the original infective serotype, it becomes ineffective against the same strain displaying the new antigenic variant. Many parasites including malaria parasites, giardia, and agent of African trypanosomiasis undergo antigenic variation by changing the expression of their variant antigen molecules, collectively known as variant specific surface groups (VSG). A parasite may contain a large number of VSG genes but only one will be expressed at a time. Electron microscopy has shown that the VSG form a dense layer on the parasite surface and contain the immunodominant antigen. With the increase in the level of antibody in the host, a small fraction of the antigen population switches to produce a new coat of VSG with a new antigenic character no longer recognized by the circulating antibodies.
2. **Immunosuppression:** The phenomenon of parasite-induced immunosuppression was first described almost 60 years ago when high prevalence of malaria was co-related with low incidence of autoimmune diseases, which led to the foundation of the hygiene hypothesis. In helminthic infections, there is an inability of effector T-cells to proliferate and to secrete pro-inflammatory cytokines, an effect called immunological tolerance. These infections are also characterized by elevated IgG_4 levels and corresponding IL10 production, which is a down-modulatory cytokine. Helminth parasite can induce TGF-β receptor production, which results in generation of T_{REG} cells and suppression of dendritic cells and macrophages and T-cell activation, all of which have an overall immunosuppressive effect. In addition, parasite molecules can also modulate CD4+ T-cell differentiation, B-cell isotype switching, and B-regulatory cell induction and thus can produce a milieu for survival of the immune-shy parasite.
3. **Molecular Mimicry:** Many parasites display some antigens which resemble a host molecule which confers a survival benefit for the parasite. The antigenic resemblance helps in non-recognition of parasite antigen by the host, confusing it as a self-antigen. Sometimes some of these antigens may mimic host hormone receptors or the hormone itself, resulting

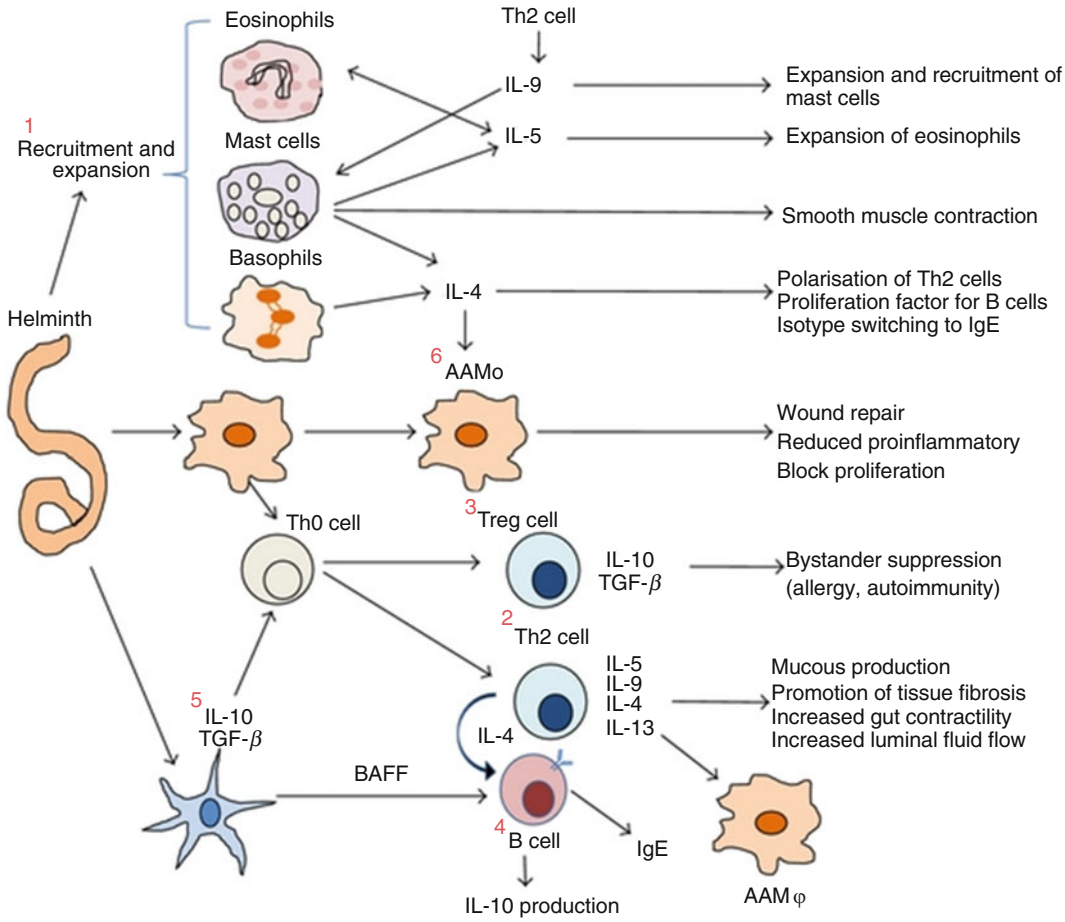

Fig. 1 Helminth infections are strong inducers of a Th2-type immune response. These infections are characterized by the expansion and activation of eosinophils, basophils, and mast cells (1). Their upregulation due to high levels of immunoglobulin E (IgE) and the proliferation of T-cells that secrete IL4, IL5, IL9, and IL13 is part of the host immune response against the parasite (2). However, helminth infections tend to be long-lived and largely asymptomatic because they are sustained through a parasite-induced immunomodulatory network, in particular through activation of regulatory T-cells (3) and systemically elevated levels of IL10 produced by B-regulatory cells (4). They are additionally affected by the expression of the regulatory cytokines IL10 and TGF-β, produced by regulatory dendritic cells (5) and alternatively activated M (AAM) (6). (From: Salazar-Castañon VH, Legorreta-Herrera M, Rodriguez-Sosa M. Helminth parasites alter protection against *Plasmodium* infection. *Biomed Res Int*. 2014;2014: 913696. doi: https://doi.org/10.1155/2014/913696)

in either a response to hormonal signals or sending the signals. This ability of the parasite to mimic host molecules can be the outcome of either transfer (acquisition of host molecule by the parasite) or convergence (evolution of the mimic molecule). The genomic era has opened up a vista where direct comparison of host and parasite proteins and their sequences can be studied and the molecular mimicry candidate proteins or macromolecules can be directly predicted.

Table 1 shows the various immune evasion strategies employed by parasites.

Table 1 Different mechanisms of immune evasion by parasites

SN	Mechanism	Specific mechanism	Parasite
1.	Anatomical seclusion	Intracellular location of parasite	Malaria parasite (RBC) *Leishmania* (macrophages) *Trichinella* (muscle cells)
2.	Antigenic variation	Different antigens in various life stages, variable surface glycoproteins	Malaria parasite, *Trypanosoma*
3.	Size	Large size of parasites	All helminths
4.	Coating with host protein	Blood group antigens and MHC class I and II molecules on the parasite tegument	*Schistosoma*
5.	Molecular mimicry	Fibronectin cell receptors	*Trypanosoma cruzi*
6.	Immunosuppression	Binding of β-integrin CR3 by parasite protein causing neutrophil dysfunction	Hookworm
7.	Parasite enzymes	Glutathione peroxidase and superoxide dismutase cause resistance to antibody-dependent cellular cytotoxicity	Filarial worms

Conclusion

The host-parasite interaction is a highly complex phenomenon and becomes more complicated in helminthic parasites because of the size and myriad of constituent macromolecules. The immune response to parasites is an intricate and interrelated process where there is a large overlap of natural and adaptive immune responses. In addition, parasites have evolved numerous strategies to evade the host's immune onslaught, which has a direct bearing on immunity to parasites and its long-term survival. The present age of genomics, proteomics, and other *-omics* has opened up a floodgate of information concerning various parasites which is expected to elucidate this complex interplay and address many unanswered questions.

Case Study

Lipophosphoglycan (LPG) is an important component of *Leishmania* envelope and has a significant effect on impairment of macrophage function by various mechanisms like cytokine cleavage, prevention of phagolysosome maturation, and activation of negative regulatory factors. Thus it plays an important role in survival of the parasite inside the macrophages. In an experimental mouse model, LPG induced an increased production of IFN-γ and TNF-α by producing reactive nitrogen intermediates and a killing effect on *L. major*. LPG along with BCG has been shown to raise TH1 immune response in mice as well as hamster models. Thus LPG is an important target for the future vaccine development for visceral leishmaniasis.

1. What are the various candidate *Leishmania* vaccines which have entered Phase 1 or 2 of vaccine trials?
2. What is a therapeutic vaccine?
3. Name the parasite vaccine which has shown the most promise to date. What is its composition?

Research Questions

1. What are the PAMPs which are important in different helminth parasites?
2. What is the exact role, if any, of eosinophils in parasitic infections?
3. What is the efficacy of therapeutic worm infection in the treatment of autoimmune diseases and metabolic disorders?

Further Readings

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