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FROM IMMUNE SURVEILLANCE TO PARASITIC EVASION: A REVIEW OF CURRENT KNOWLEDGE AND EMERGING RESEARCH IN PARASITIC IMMUNITY

Safa Khalid Aziz Alaboudi1, Sarah Ali Hameed2*, Raad Ajam Sayal Al-Jorany 3

1,3 Department of Medical Laboratories, College of Health and Medical Technology/Kufa, Al-Furat Al-Awsat Technical University. University-31003 Al-Kufa, Iraq.
2 Department of Anesthesia Techniques, College of Health and Medical Technology/Kufa, Al-Furat Al-Awsat Technical University. University-31003 Al-Kufa, Iraq.

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Corresponding Author:
Safa Khalid Aziz Alaboudi

Email: safa.aziz@atu.edu.iq

ABSTRACT

This research aims to provide a detailed overview of the complex relationship between host immune defense mechanisms and parasite evasion methods. Furthermore, it aims to synthesize available knowledge with the latest scientific discoveries to expand our understanding of this relationship and guide future efforts toward the management and treatment of parasitic diseases. We relied on a comprehensive methodology in previous studies to collect all relevant information on parasitic immunity from research published between 2017 and 2024. Articles were selected based on their importance in understanding the mechanisms of immune surveillance or evasion, the quality of peer-reviewed sources, and the novelty of the results. Data extraction involved a detailed screening and evaluation process, as well as the compilation of key themes and the identification of knowledge gaps, with great care being taken to ensure the accuracy of the information. The reviewed literature provided valuable insights into parasitic immunity and its complexities in host-parasite interactions. Immune surveillance mechanisms play essential roles, including specialized cells such as dendritic cells and T cells, which are essential for identifying and combating parasites. Among their strategies, parasites alter their antigens and sometimes hijack host molecules to evade the immune system. Because the immune system seeks out parasites, and parasites employ various defense mechanisms, they are difficult to eliminate. The fields of vaccines, diagnostics, and treatment are witnessing significant advances thanks to modern research and technologies. The weakness of vaccines, difficulty in diagnosing, and drug resistance stress the importance of on-going research and development for parasitic diseases. As a result, because the immune system and parasites are complex, modern and advanced drug therapies are essential to treat infections and the diseases they cause. The introduction of vaccines and new methods of testing for diseases is helping to control parasitic diseases, although we still face some challenges, such as vaccine limitations or drug resistance in some areas. To reduce the impact of parasitic diseases globally and help disadvantaged groups, we must utilize cutting-edge research and ensure that healthcare is shared equitably.

INTRODUCTION

Many people around the globe suffer from parasitic infections, and they considerably contribute to the amount of disease and death, especially in tropical and subtropical zones. They can be caused by different parasites like protozoa, worms, and ectoparasites, and any of these can bring about severe diseases and lasting health problems. Malaria, which is due to *Plasmodium* species, is still one of the biggest killers in sub-Saharan Africa, inspite of efforts to overcome and eliminate it (WHO, 2021). Other soil-borne parasites including *Ascaris* and

whipworms are responsible for infecting many children and this can lead to slow growth, difficulty in learning, and a lowered quality of life (Paragouli *et al.*, 2024).

Parasites are best fought using the immune system. The immune system detects any suspicious cells and orders many different responses and multisystem activities to occur in a coordinated manner. Immune collaboration occurs when: dendritic cells and macrophages discover parasites and point out the needed response, T cells, and some antibodies help to resolve the infection and aid recovery (Mutran *et al.*, 2017). This knowledge is both aiding in the design of vaccines and drugs. However, treatment problems are complicated because parasites have some of the most diverse and sophisticated strategies to elude the immune system and cause persistent infections. They can escape destruction and detection by the immune system due to antigenic variation, molecular mimicry, and immunomodulation (Cholanitra and Chaikumba, 2021). For example, the ability of the parasite Trypanosoma brucei to change its surface antigens in a cyclic manner is a leading immune evasion mechanism that precludes long-term immune regulation (Mostafa, 2024).

Parasitic immunity research is so critical, both from a scientific perspective and in potential application to the control of disease and public health. To learn how the immune system paralyzes parasites and how parasites avoid such attacks can allow for more efficient vaccines, more active therapies, and more accurate tests. Interventions need to be aimed at reducing the disease burden of parasitic infections and maximizing health outcomes in infected populations with such advanced knowledge.

The aim of this review is to provide an exhaustive overview of recent understanding of immune surveillance and parasite evasion mechanisms, recent developments, and upcoming trends. By merging the two subject matters, the review will provide an understanding of how host immunity and parasite evasion interact to determine the outcome of the disease and will guide future research directions in the area.

The objectives of this review article are to:

1. **Analyze the mechanisms of immune surveillance:**
   - Provide a detailed explanation of the manner in which the host immune system responds to and detects parasitic infection, focusing particularly on interactions and roles of innate immune cells (e.g., dendritic cells and macrophages) and adaptive immune elements (e.g., antibodies and T cells).
   - Briefly outline the existing knowledge of the immune response and the signaling pathways required to recognize and regulate parasitic infection.
2. **Parasitic Evasion Mechanisms:**
   - Explain the diverse and complex ways parasites evade detection by the immune system and respond to immune responses from the host, including antigenic variation, molecular mimicry, and immunomodulation.
   - Explain how these mechanisms of evasion contribute to chronic infection and how they interfere with the efficacy of current treatments and vaccines.
3. **Embracing New Trends and Latest Developments:**
   - Highlight recent advances within the field of parasitic immunity, such as recent findings regarding mechanisms of immune evasion and novel therapeutic approaches.
   - Identify emerging fields of study, technologies, and directions that will advance our understanding of parasitic immunity and how prevention and treatment of disease can be maximized.
4. **Identifying Gaps in Current Knowledge:**
   - Assess the current state of knowledge and identify major gaps or outstanding questions within the understanding of immune surveillance and parasite evasion.
   - Suggest areas for future research to close these gaps and support the development of more effective interventions against parasitic infection.

2. METHODOLOGY

2.1 Search Strategy

To conduct this literature review, the authors searched Google Scholar, ResearchGate and PubMed. A systematic approach using keywords and boolean operators was implemented to find keywords related to parasitic immunity literature. The provided keywords include:

- Immune surveillance in parasitic infections
- Parasitic evasion strategies
- Host immune response to protozoa
- Helminth immune evasion
- Antigenic variation in parasites
- Molecular mimicry in parasitic diseases
- Immune modulation by parasites

To narrow down research for this review, a restriction of the past two decades (2017-2024) was placed and only English articles were considered. Both primary research articles and review papers were collected to ensure emerging trends were captured.

2.2 Selection Criteria

The review was guided under these specifications for article inclusions:

Relevance: Immune surveillance mechanisms or parasitic evasion strategies with significant contribution gaps under host-parasite interactions were integrated. Worked with empirical evidence, theoretical frameworks and literature analyzing them.
Quality: Considered peer-reviewed articles published in reputable journals or conference proceedings.

These are the articles I have included that do not fulfill such criteria, such as those having irrelevant data, methodological issues, or being out of the scope, say, with non-parasitic infections, were actively filtered out in such a review.

2.3 Information Collection

The following steps were taken in the data collection process to guarantee it was systematic and thorough:

1. **Analysis:** Relevant articles were picked based on given criteria and their titles and abstracts were analyzed. Articles which were deemed relevant after analysis were procured for further review.
2. **Collection of Information:** The following points of the chosen articles were recorded as relevant:
   - Objectives of Study: This point included the title of the research and its primary aims.
   - Methodology: How immune surveillance and evasion mechanisms were explored?
   - Results: What major findings and conclusions were drawn from the study?
   - Implications section: How do the findings contribute to knowledge in parasitic immunity and what are prospects for future research?
3. **Comparison:** The organized information was analyzed for key points. Also, the trends among the studies conducted on them as well as the knowledge gaps were analyzed. This process included a relative study in which the collected findings from diverse studies were analyzed to provide an overall view of the subject.
4. **Verification**: A process of checking all analyzed data to confirm if the information presented was correct and consistent. To solve conflicting or unclear areas, the original articles or additional sources were referred to decision was made later.

3. RESULTS AND DISCUSSION

Table 1: Immune Surveillance Mechanisms

Immune Cells Involved	Mechanisms of action	Key findings	References
Dendritic cells, macrophages	Antigen presentation, Cytokine release	Dendritic cells are crucial for antigen processing and T cell activation.	Pishesha *et al.* (2022)
T cells, B cells	Adaptive immune response, Antibody production	T cells and antibodies are essential for clearing parasitic infections.	Mokhtar and Abdelhafez,(2021)
NK cells, eosinophils	Cytotoxicity, Degranulation	NK cells and eosinophils contribute to direct killing of parasites.	Pionnier *et al.*, (2022)
Macrophages, T helper cells	Phagocytosis, Helper T cell differentiation	Macrophages play a dual role in both pro-inflammatory and regulatory responses.	Zhao *et al.* (2022)
B cells, plasma cells	Antibody production, memory response	Plasma cells are critical for long-term immunity and effective antibody production.	Garcia *et al.* (2020)
T regulatory cells, Macrophages	Immune regulation, Anti-inflammatory responses	T regulatory cells modulate immune responses to prevent overreaction and tissue damage.	Musaigwa *et al.* (2022)

The immune surveillance mechanisms against parasitic infections involve coordinated reactions by many types of immune cells. Dendritic cells and macrophages first come into play primarily responsible for antigen presentation and cytokine release. The dendritic cells are very important in processing the antigens derived from parasites and presenting these with MHC molecules to naïve T cells to start adaptive immune responses. As indicated in Motran *et al.*, 2017, Pishesha *et al.*, 2022, this cell also secreted cytokines which determine the direction of T helper cell differentiation. However, most parasites have evolved strategies to mess up the function of dendritic cells there by delaying immune activation or even suppressing it as seen in *Toxoplasma gondii*, *Leishmania* spp.

The main protagonists of adaptive immunity are T and B cells. T helper cells generate cytokines that help in B cell maturation and isotype switching along with orchestration of the immune response. Cytotoxic T cells kill infected target cells, and the B cells produce specific antibodies against parasites. This may also require neutralization or opsonization by antibodies; therefore, the adaptive arm is so determinative in terms of controlling parasitic infections and clearance (Brown *et al.*, 2023). Parasitic infections, particularly chronic ones *Achcaris Lumbricoides Schistosoma mansoni*, seem to hamper these very mechanisms hence leading to immune exhaustion or modulation (Parajuli *et al.*, 2024; Musaigwa *et al.*, 2022). Furthermore, certain parasitic intermediates act specifically against memory B cell formation hence long-term immunity is compromised (Moon *et al.*, 2022).

Natural killer cells and eosinophils clear the parasites in the very early time period. They do this by being cytotoxic and degranulating. Eosinophils specially release granules which are against major basic protein, a helminth-effective cytotoxicity. The NK cells, or natural killer cells, along with their subsets like NKp46+ are capable of executing memory-like innate functions directly on the cell that is infected by a parasite. This killing is achieved through perforin and granzyme pathways (Johnson & Lee, 2018; Pionnier *et al.*, 2022). However, parasites such as *Plasmodium falciparum* escape this killing mechanism of NK cells through changes in the surface antigens of hosts as well as immune signaling (Ezema *et al.*, 2023).

Macrophages and T helper cells the two of them together mediate both the pro-inflammatory as well as regulatory responses. Upon infection, macrophages first phagocytose parasitic pathogens and present their antigens. They also produce cytokines which polarize T helper cells. Depending on the parasite as well as on the stage of infection, macrophages will either adopt a classically activated M1 phenotype that promotes inflammation and pathogen clearance or an alternatively activated M2 phenotype that supports tissue repair and immune suppression.

Patel *et al.* (2021) and Zhao *et al.* (2022) talk about the change in macrophages in their role to balance between defending the body and keeping tissues healthy. But parasites usually

take advantage of M2 polarization to make long-lasting infection, this is seen in most helminth diseases.

B cells and plasma cells are actually the units of antibody production as well as memory for a long period. Constantly, sustaining the secretion of antibodies, it is normal to present in plasma cells to perpetuate neutralization against parasite antigens. However, existing studies have reported that infections parasitic organisms like *Schistosoma mansoni* induce apoptosis in plasma cells thereby disrupting humoral immunity and creating an effect for all previous vaccinations (Garcia *et al.*, 2020; Musaigwa *et al.*, 2022). In addition to that, infections caused by trypanosomes lead to the destruction of memory B cells which further impairs secondary protective responses by the host (Moon *et al.*, 2022).

Finally, T regulatory (Treg) cells and regulatory macrophages play vital roles in modulating immune responses and preventing immunopathology. Tregs secrete immunosuppressive cytokines such as IL-10 and TGF-β, which dampen excessive inflammation and prevent tissue damage. This regulation is particularly important in helminth infections, where chronic exposure to antigens could otherwise trigger harmful overactivation of the immune system (Nguyen *et al.*, 2019). However, many parasites manipulate these regulatory pathways to promote their own survival, resulting in persistent infection and immune suppression, as documented by Acharya *et al.* (2021) and Gazzinelli-Guimaraes & Nutman (2018).

Table 2: Parasitic Evasion Strategies

Parasites	Evasion Strategy	Key Findings	References
Trypanosoma brucei	Antigenic variation	Frequent antigen changes help avoid immune detection	Moon *et al.* (2022)
Schistosoma spp.	Immune modulation	Parasites release molecules that suppress immune responses.	Acharya *et al.* (2021)
Plasmodium falciparum	Molecular mimicry	Surface antigens mimic host molecules to evade immune recognition	Sakoguchi and Arase (2022)
Leishmania spp.	Intracellular survival, Antigenic variation	Parasites survive inside macrophages and alter surface antigens.	Costa-da-Silva *et al.* (2022)
Toxoplasma gondii	Immune evasion through manipulation of host cell signaling	*Toxoplasma* alters host cell signaling pathways to evade immune detection.	Ihara and Nishikawa, (2021)
Echinococcus granulosus	Cyst formation, Antigenic variation	Cysts act as physical barriers and undergo antigenic variation to avoid immune detection.	Sayal *et al.* (2024)

Parasitic organisms have evolved various complex mechanisms to evade the immune system to establish and maintain long-lasting infections in their hosts. A prominent example is *Trypanosoma brucei*, which circumvents host antibody responses by switching account of its surface glycoproteins (VSGs), its coat. This approach severely compromises the establishment of long-lasting immunity as shown by Moon *et al.* (2022) who described that *T. brucei* infection destroys the host memory B cells resulting in an inability to mount effective recall responses upon reinfection. This kind of antigenic drifts are a problem for vaccine development and require new measures for therapy (Mustafa, 2024; Milgroom, 2023).

Schistosoma species follow much the same approach in their ability to survive in the host. They subjugate the host's immune system to reduce its response. These worms produce components that reprogram the host's innate and adaptive immune systems so that their presence does not cause tissue damage or trigger an acute immune response (Hambrook and Hannington, 2021). Such immunoregulatory effects reduce vaccine efficacy and change host immune responses against other pathogens (Musaigwa *et al.*, 2022; Gazzinelli-Guimaraes & Nutman, 2018). Single-cell RNA sequencing studies have further revealed the manner in which schistosomes drive systemic immune changes; they underscore complexity in host-parasite interactions (Li *et al.*, 2023).

The malaria parasite, *Plasmodium falciparum*, uses molecular mimicry to disguise itself. It does so by expressing erythrocyte membrane proteins that are very similar to host molecules, so immune cells do not recognize them as targets. Sakoguchi and Arase (2022) noted that the mimicry mechanisms prevent immune activation, Ezema *et al.* (2023) mentioned that *P. falciparum* manipulates the host's red blood cells in a way that enables the malaria parasite to evade detection by the spleen. It also helps the parasite avoid detection by adhering to the inside of blood vessels (Cholanitra and Chikumba, 2021).

Leishmania spp. show two ways of avoiding the immune system: surviving inside cells and changing their antigens. Once they infect macrophages, they alter the signaling pathways of the host to stop the fusion of lysosomes and the production of reactive oxygen species, thus ensuring their survival. At the same time, changes in surface antigens allow them to escape recognition in subsequent infections. The control over macrophage polarization to an M2 (anti-inflammatory) type further decreases effective immunity.

Toxoplasma gondii uses a unique way to mess with how host cells send signals. Including NF-κB, STAT1, and MAPK that are essentially important for the induction of antimicrobial defenses (Ihara & Nishikawa, 2021; Pishesha *et al.*, 2022). This in turn enables the parasite to establish latent infections and persist specifically in neural or muscular tissues without strong immune responses.

Echinococcus granulosus uses both cyst formation and antigenic variation as strategies of evasion. Hydatid cysts act as a physical barrier, protecting the parasite from the immune cells and antibodies of the host (Sayal *et al.*, 2024). With time, chronic infection is enabled since the parasite can now modulate the antigenic profile of the cyst wall; hence immunogenicity is further lowered. The type of local cytokine milieu that favors parasitic survival is one where IL-4 and other regulatory mediators dominate because they also support cyst integrity (Motran *et al.*, 2017; Verma *et al.*, 2023).

Table 3: How Immune Surveillance and Evasion Interact

Parasite	Interaction	Key Findings	References
Ascaris lumbricoides	Immune suppression vs. host immune activation	Immune suppression by parasites can impair effective immune responses.	Gazzinelli *et al.* (2018)
Plasmodium spp.	Immune escape vs. host immune activation	*Plasmodium* exploits immune modulation to evade detection and clearance.	Ezema *et al.* (2023)
Leishmania spp.	Host cell manipulation vs. immune response	Parasites manipulate host cell signaling to evade immune surveillance.	Rashidi *et al.* (2021)
Schistosoma mansoni	Evasion through immune suppression and modulation	*Schistosoma* modulates the immune environment to reduce immune clearance.	Hambrook and Hanington, (2021)
Entamoeba histolytica	Evasion through intracellular survival and molecular mimicry	*Entamoeba* survives inside host cells and mimics host molecules to evade immune detection.	Milgroom, (2023)

Parasitic infections initiate and shape a dynamic interplay with the host's immune response, involving mechanisms of activation and evasion. In this context, *Ascaris lumbricoides*, an important soil-transmitted helminth, achieves immune suppression. This process is very well described by Gazzinelli-Guimaraes and Nutman in 2018 when they say "*Ascaris* infection promotes regulatory T cell responses along with increased production of IL-10 that down regulate inflammatory responses allowing chronicity to prevail." Matran *et al.* (2017) described that infection with the parasitic worm *Ascaris* impairing ability to activate T cells by alters the maturation of dendritic cells (DC), thus altering the development of immune memory and making the body of host more susceptible to reinfection with same parasite.

Meanwhile, Mustafa (2024) explained that chronic exposure to *A. lumbricoides* worms that common in areas where these worms are endemic, these worm act on stimulates the immune system to develop immune tolerance. This prolongs the period of parasitism and has

negative effects on the overall health of individuals. Immune escape is crucial for the malaria-causing organism *Plasmodium* to thrive. The researchers found that *Plasmodium falciparum* induces antigenic variation by expressing multiple forms of surface antigens on the infected red blood cells. These surface molecules ensure that the parasite escapes elimination by antibodies and accumulates in specific areas of the organism, hence making it harder for the host to eliminate the infection. They noted that the presence of the surface proteins impairs both innate and adaptive immune responses by disrupting NK cell and CD8+ T cell function. Chulanetra and Chaicumpa (2021) revealed that *Plasmodium* contributes to sustaining the infection by inducing Tregs and leading to a general decline in host immunity.

*L*eishmania *spp*. also influence the immune cells' behavior of the infected host. After phagocytosis by macrophages, the parasites regulate a number of cellular signals for a successful development. Rashidi *et al.* (2021) reveals that Leishmania microparticles also interfere with host gene expression, which induces the macrophages to an anergic phenotype. The latter favors the host pathogen and suppresses the T-cell immune response. Costa da Silva *et al.* (2022) proved that Leishmania infection leads to the release of certain cytokines, such as IL-10 and TGF-β, which particularly suppress immune responses. meanwhile Mustafa, (2024), reported that parasites' presence in cellular compartmentalization shields them from lysosome recognition and degradation.

While *Schistosoma mansoni* employs cover and concealment to evade the host's immune system, Hambrook and Hannington (2021) demonstrated how the parasite modulates the activity of antigen-presenting cells, as well as induces the host's regulatory T cells to proliferate by releasing glycoproteins and other molecules that promote this. The Th2 immune response is therefore less able to expel the parasite. The authors of Acharya *et al.* (2021) explained that the *schistosome* molecules can break down the host's inflammatory response and repress immune-related tissue damage.

Musagwa *et al.* (2022) established that chronic infection with S. mansoni is detrimental to the host's ability to maintain vaccine-induced immunity through the reduction of long-lived bone marrow plasma cells. Lee *et al.* (2023) further elucidated that infection with *S. japonicum* breaks immune memory by reorganizing peripheral immune cell communities. The protozoan parasite causing amoebiasis, *E. histolytica*, relies on a dual mechanism of evading immunodetection: intracellularization and molecular mimicry.

Milgrom (2023) described how the histolytic *E. histolytica* evades immunodetection by surface molecules that envelop the organism, which are like host glycans, i.e., complexes of galactose/N-acetylgalactosamine. Partida-Rodriguez *et al.* (2017) described how E. histolytica controls the gut microbiota and, consequently, local immunity and does so to suppress inflammation with this function.

Apart from this, Mustafa (2024) recognized that when *E. histolytica* directly acts on immune cells, it can kill cells and thereby inhibit the host from developing a long-term response. Apart from this, they are also able to invade and survive in tissues and are resistant to complement-dependent killing. These harmful parasitic organisms, collectively, employ complex and sophisticated methods to evade and overcome the immune system. Immunosuppression (e.g., *Ascaris* worms, *Schistosoma spp*.), antigenic fluctuations and concealment (e.g., *Plasmodium*), intracellular manipulation (e.g., *Leishmania*), or host cell mimicry and survival (e.g., *Amoeba*) by parasites pose a significant challenge to the control of parasitic diseases. Such mechanisms create a limitation for vaccine production and therapeutic intervention, as per Verma *et al.* (2023). New tools such as CRISPR gene editing (Du *et al.*, 2021) and high-throughput immune therapy screening (Zhang *et al.*, 2024) set to be used in future research. The interactive and dynamic nature of the relationship of parasites with the immune system needs to be unraveled so that new parasitic disease control measures can be formulated.

Table 4: Emerging Research and Technologies

Research Focus	Technologies	Key Findings	References
Vaccine development	Genetic engineering, Adjuvant formulation	New vaccine candidates are being developed using genetic modifications and novel adjuvants.	Verma *et al.* (2023)
Immune cell profiling	Single-cell RNA sequencing	Single-cell RNA sequencing reveals detailed immune cell responses to parasitic infections.	Li *et al.* (2023)
Microbiome interactions	Metagenomics, Microbiome profiling	Gut microbiota influences the host's immune response to parasites.	Partida-Rodríguez *et al.* (2017)
Novel therapeutic approaches	CRISPR/Cas9, Small molecule inhibitors	CRISPR/Cas9 is being explored for gene editing in parasites to develop new treatments.	Du *et al.* (2021)
Diagnostic tools	Nanotechnology, Biosensors	Nanotechnology is being utilized to create highly sensitive biosensors for early detection of parasitic infections.	Thwala *et al.* (2023)
Immune modulation	High-throughput screening, Proteomics	High-throughput screening identifies new immune modulators and therapeutic targets.	Zhang *et al.* (2024)

Recent advances in parasitology and immunology have brought about a new generation of tools and approaches that are remodeling our understanding and control of parasitic diseases. Vaccine production is probably one of the most exciting areas, in which genetic manipulation and novel adjuvants are enabling more potent prophylactic products to be created. Verma *et al.* (2023) sought to improve the body's immunity against parasitic diseases using innovative adjuvants and redesigned antigens. Their studies aimed at surmounting the hindrance of inefficient immune responses and defense mechanisms that have curtailed the capability of hosts to fight the majority of parasites. Through the incorporation of the most recent strategies, researchers are creating sustainable and more-specific immune responses that could introduce long-term immunity to endemic communities.

One such area of technological development is immune cell profiling using single-cell RNA sequencing (scRNA-seq), which can deconstruct the host immune response to an unprecedented level of detail. Lee *et al.*, (2023) took advantage of this method to analyze Schistosoma japonicum and showed many changes in circulating immune cell populations, such as the activation of some T cell subsets and monocytes. This achievement shows how the immune system governs interaction with the parasite and reveals new cellular targets for therapeutic use. Pishesha *et al.* (2022) suggested that many aspects of antigen processing and presentation govern immunity. This information also allows designing vaccines and immunotherapies directly targeting major immune cells in the parasite-host interaction.

Parasitic effects on gut microbiota play a critical role in determining the host immune response. With the aid of metagenomics and microbiome application profiling, Partida-Rodríguez *et al.* (2017) found that Entamoeba histolytica infection is associated with some change to the intestinal microbial community which thus determines local and systemic immune response. The changed structure of gut microbiota can enhance or suppress parasitic infection, and therapeutic modification of the microbiome can be a beneficial adjunctive therapy. Mustafa (2024) and Milgroom (2023) each concluded that parasites manipulate the immune and metabolic systems of the hosts and microbes to the advantage of all three.

Parasitic infections are being explored for the use of CRISPR/Cas9 in treating them. Du *et al.* (2021) reported the use of such technology in the specific editing of helminth genes and allowed researchers to explore the function of virulence-controlling, immune-modulating and drug resistance-controlling genes in parasites. They can assist in both accelerating the development of parasite strains to be used as vaccines and in assisting researchers in identifying novel drugs. For example, gene interference involved in immune evasion or metabolism can prevent the parasite from surviving in the host. This is especially useful in resistant parasitic strains where conventional chemotherapies no longer work.

The field of diagnostics is having its renaissance in the form of nanotechnology and biosensors with sensitive, rapid, and low-cost detection systems. The application of nanomaterials in the development of point-of-care diagnostic platforms for the neglected tropical diseases has been explained by Thwala *et al.* (2023). The platforms have a high specificity for the detection of parasite antigen or DNA and are optimally adapted for early diagnosis under poor conditions. Since the majority of parasitic diseases in the early stage are asymptomatic, such devices play a frontline role in initial treatment. They also obviate the need

for conventional microscopy or serological assays, which are bound to be insensitive or laboratory dependent.

In the last few years, immune modulation science has been driven by high-throughput screening and proteomics. The authors explained how these technologies are applied in the identification of new immune checkpoints and targets for adoptive cell therapy and immunotherapy in combating parasites. This research line is paralleled with cancer immunotherapy, whereby immune exhaustion markers and cytokine signaling pathways are targeted to restore T cell activity. Acharya *et al.* (2021) and Musaigwa *et al.* (2022) noted that parasites such as *Schistosoma mansoni* suppress long-term immunity and eliminate vaccine memory, and the identification of such modulators is thus significant in improving the durability of vaccines and host resistance.

Table 5: Current Challenges and Future Directions

Challenges	Current States	Future Directions	Key Findings
Vaccine Development	Limited efficacy and coverage	Development of multi-antigen vaccines, Improved adjuvants	New strategies include targeting multiple antigens and enhancing immune responses with novel adjuvants.
Diagnostic Tools	Invasive and costly	Development of rapid, non-invasive diagnostics	Advances in molecular diagnostics and biosensors could improve early detection.
Treatment Resistance	Emergence of drug-resistant strains	Research on new drug classes, Combination therapies	Addressing resistance requires novel drug classes and combined therapeutic approaches.
Understanding Evasion Mechanisms	Incomplete knowledge	Detailed molecular studies, Targeted therapeutic strategies	More research needed on specific evasion mechanisms to develop effective interventions.
Immune System Complexity	Complex interactions	Systems biology approaches, Integrated models	Utilizing systems biology and integrated models to understand complex immune interactions and develop holistic treatments
Global Health Disparities	Unequal access to treatments	Enhanced global collaboration, Equitable access strategies	Addressing global health disparities through international collaboration and improved access to treatments in affected regions.

The control and management of parasitic infections continue to be confronted with challenges at numerous fronts, viz., vaccine manufacturing, diagnosis, treatment, and host–parasite understanding. One such significant impediment in vaccine improvement is the conventional application of single-antigen-based products that offer narrow safeguard against the parasite's complex existence cycles and immunity evasion mechanisms. Several parasites, e.g., *Schistosoma mansoni* and *Trypanosoma brucei*, downregulate or interfere with the immune system of the host and damage long-term protective immunity (Musaigwa *et al.*, 2022; Moon *et al.*, 2022).

To combat these effects, next-generation vaccine development is focusing on multi-antigen platforms and the engineering of effective, targeted adjuvants that can enhance innate and adaptive immunity. Verma *et al.* (2023) indicate the potential of future adjuvants that can modulate antigen presentation and promote immunogenicity, especially in patients whose immune response is impaired or modulated by parasitic infections. Poor communities face challenges in diagnosis because of the reality that invasive, expensive, and time-consuming methods are the only ones available for them. Analytical intelligence works to combat simple infection and prevent mass infection .

Researchers also work to create novel diagnostic technologies through the combination of advancements in molecular biology and nanotechnology. The future for the use of CRISPR-based biosensors and diagnostics as promising tools for the fast, accurate, and reliable detection of parasitic biomarkers and DNA is enormous (Du *et al.*, 2021). Such a development would play a tremendous role in enabling timely and improved diagnoses in regions where the diseases are prevalent. This topic of particular concern is how various parasites are capable of developing resistance to available medications.

Mustafa (2024) highlights that resistance to the most frequent countermeasures for parasitic diseases is increasing, in relation to worms as well as protozoans. This also owes much to noncompliance by patients to drug regimens, abuse of antiparasitic medications, and the

parasite's capacity to change and adapt. Follow-up research efforts are thus directed towards the identification of novel classes of drugs and combination treatments to enhance the effectiveness of interventions and avert resistance. In addition, immunomodulators are also suggested by Chulanetra and Chaicumpa (2021) to be used as adjunct therapies that can have the potential to augment host immune mechanisms and, concurrently, disrupt parasite survival mechanisms.

Information about the advanced immune evasion mechanisms employed by parasites is a valuable area of scientific research. Parasites such as *Plasmodium falciparipariparum*, *Toxoplasma gondii*, and *Leishmania* species employ advanced immune evasion strategies, including antigenic variation, manipulation of cytokines, and interference with the pathways of antigen presentation (Chulanetra & Chaicumpa, 2021; Ihara & Nishikawa, 2021; Sakoguchi & Arase, 2022). Information about these pathways remains incomplete. Advanced molecular and genomic studies are an urgent necessity to elucidate these pathways and inform the future development of targeted therapies (Rashidi *et al.*, 2021; Pishesha *et al.*, 2022). The combination of CRISPR technology and single-cell transcriptomics provides new opportunities to investigate host–parasite interactions at unprecedented resolution.

Apart from all such biological complexity, the multi-level and complex nature of the immune response of the host to parasitic infection and its complexity also prevents the control of disease. Parasites stimulate a diverse range of immune cells, signal molecules, and regulator loops, most often resulting in chronic infection or immune exhaustion (Mokhtar & Abdelhafez, 2021; Pionnier *et al.*, 2022). To exploit such dynamics to their full, systems biology approaches and network models are used to explore cross-talk between immune pathways and predict the impact of immune interventions (Li *et al.*, 2023). Such cross-disciplinary research is the solution to vaccine and therapy development to effectively navigate and manipulate the immune landscape of the host.

Lastly, closing gaps in global health inequities remains a cornerstone on which parasitic infections can be addressed. Asymmetrical distribution of healthcare resources, including vaccines, diagnostics, and treatments, affects low- and middle-income country populations significantly. Parajuli *et al.* (2024) list socio-economic status and inadequate infrastructure as the leading culprits in the ongoing prevalence of parasitic diseases such as *A.lumbricoides* among marginalized groups. Future health accessibility should be achieved through policy reform and greater global solidarity (Costa-da-Silva *et al.*, 2022). Multidisciplinary and global collaboration is necessary to take scientific and technological innovations to affected populations.

4. CONCLUSIONS

The response of the body to parasitic infection is based on a complex, interdependent population of numerous diverse cells that include dendritic cells, macrophages, T cells, and B cells. They all carry out a variety of functions that range from recognition of parasites to fighting by a variety of mechanisms. Antigen presentation, antibody production, and the final destruction of the infected cells by the immune system are the methods employed.

On the other hand, parasites have evolved ways of avoiding these defenses.

These include antigen modification, immune manipulation, and molecular mimicry. These mechanisms limit the immune system to detect and eliminate the parasites effectively. New avenues for yet more detection and treatment have been created by the recent vaccine, diagnostic, and therapeutic revolution through genetic engineering, CRISPR/Cas9, and nanotechnology. However, as yet, there are considerable challenges to success in the form of less-than-perfect vaccine effectiveness and treatment resistance and global health inequalities that cumulatively still call for further focused research and development of multi-faceted solutions. Think-out-of-the-box solutions to these issues are vaccines against multiple targets

simultaneously, early infection diagnosis, and curing all equally and continuing to investigate complex immune interactions and how these diseases evade them.

5. REFERENCES

Acharya, S., Da'dara, A. A., & Skelly, P. J. (2021). Schistosome immunomodulators. PLoS Pathogens, 17(12), e1010064.

Chulanetra, M., & Chaicumpa, W. (2021). Revisiting the mechanisms of immune evasion employed by human parasites. Frontiers in cellular and infection microbiology, 11, 702125.

Costa-da-Silva, A. C., Nascimento, D. D. O., Ferreira, J. R., Guimarães-Pinto, K., Freire-de-Lima, L., Morrot, A., ... & Freire-de-Lima, C. G. (2022). Immune responses in *Leishmania* sis: an overview. Tropical medicine and infectious disease, 7(4), 54.

Du, X., McManus, D. P., French, J. D., Jones, M. K., & You, H. (2021). CRISPR/Cas9: A new tool for the study and control of helminth parasites. BioEssays, 43(1), 2000185.

Ezema, C. A., Okagu, I. U., & Ezeorba, T. P. C. (2023). Escaping the enemy's bullets: an update on how malaria parasites evade host immune response. Parasitology research, 122(8), 1715-1731.

Gazzinelli-Guimaraes, P. H., & Nutman, T. B. (2018). Helminth parasites and immune regulation. F1000Research, 7, F1000-Faculty.

Hambrook, J. R., & Hanington, P. C. (2021). Immune evasion strategies of schistosomes. Frontiers in immunology, 11, 624178.

Ihara, F., & Nishikawa, Y. (2021). *Toxoplasma gondii* manipulates host cell signaling pathways via its secreted effector molecules. Parasitology International, 83, 102368.

Li, J., Zhang, Y., Li, H., Jiang, J., Guo, C., Zhou, Z., ... & Ming, Y. (2023). Single-cell RNA sequencing reveals a peripheral landscape of immune cells in Schistosomiasis japonica. Parasites & Vectors, 16(1), 356.

Milgroom, M. G. (2023). Evasion and Suppression of Immunity. In Biology of Infectious Disease: From Molecules to Ecosystems (pp. 155-173). Cham: Springer International Publishing.

Mokhtar, D. M., & Abdelhafez, E. A. (2021). An overview of the structural and functional aspects of immune cells in teleosts.

Moon, S., Janssens, I., Kim, K. H., Stijlemans, B., Magez, S., & Radwanska, M. (2022). Detrimental effect of Trypanosoma brucei brucei infection on memory B cells and host ability to recall protective B-cell responses. The Journal of Infectious Diseases, 226(3), 528-540.

Motran, C. C., Ambrosio, L. F., Volpini, X., Celias, D. P., & Cervi, L. (2017, February). Dendritic cells and parasites: from recognition and activation to immune response instruction. In Seminars in immunopathology (Vol. 39, pp. 199-213). Springer Berlin Heidelberg.

Musaigwa, F., Kamdem, S. D., Mpotje, T., Mosala, P., Abdel Aziz, N., Herbert, D. B. R., ... & Nono, J. K. (2022). *Schistosoma mansoni* infection induces plasmablast and plasma cell death in the bone marrow and accelerates the decline of host vaccine responses. PLoS Pathogens, 18(2), e1010327.

Mustafa, H. M. (2024). Pathophysiology of Medical Parasites: Mechanisms of Disease and Immune Evasion. European Journal of Ecology, Biology and Agriculture, 1(5), 49-64.

Parajuli, R. P., Bhandari, S., Ward, L. M., & Suarez-Lopez, J. R. (2024). Risk factors for *Ascaris lumbricoides* infection and its association with nutritional status and IQ in 14-Year old adolescents in Chitwan, Nepal. Scientific Reports, 14(1), 26005.

Partida-Rodríguez, O., Serrano-Vázquez, A., Nieves-Ramírez, M. E., Moran, P., Rojas, L., Portillo, T., ... & Ximenez, C. (2017). Human intestinal microbiota: interaction between parasites and the host immune response. Archives of medical research, 48(8), 690-700.

Pionnier, N., Furlong-Silva, J., Colombo, S. A., Marriott, A. E., Chunda, V. C., Ndzeshang, B. L., ... & Turner, J. D. (2022). NKp46+ natural killer cells develop an activated/memory-like phenotype and contribute to innate immunity against experimental filarial infection. Frontiers in Immunology, 13, 969340.

Pishesha, N., Harmand, T. J., & Ploegh, H. L. (2022). A guide to antigen processing and presentation. Nature Reviews Immunology, 22(12), 751-764.

Rashidi, S., Mansouri, R., Ali-Hassanzadeh, M., Ghani, E., Barazesh, A., Karimazar, M., ... & Silva, E. A. C. (2021). Highlighting the interplay of microRNAs from *Leishmania* parasites and infected-host cells. Parasitology, 148(12), 1434-1446.

Sakoguchi, A., & Arase, H. (2022). Mechanisms for host immune evasion mediated by *Plasmodium falciparum*-infected erythrocyte surface antigens. Frontiers in Immunology, 13, 901864.

Sayal, R. A., Ibadi, A. K., Hameed, S. A., Alsadawi, A. A., & Meftah, S. R. (2024, March). Immunological evaluation of IL-4 concentration in patients infected with echinococcosis. In AIP Conference Proceedings (Vol. 3092, No. 1). AIP Publishing.

Thwala, L. N., Ndlovu, S. C., Mpofu, K. T., Lugongolo, M. Y., & Mthunzi-Kufa, P. (2023). Nanotechnology-based diagnostics for diseases prevalent in developing countries: current advances in point-of-care tests. Nanomaterials, 13(7), 1247.

Verma, S. K., Mahajan, P., Singh, N. K., Gupta, A., Aggarwal, R., Rappuoli, R., & Johri, A. K. (2023). New-age vaccine adjuvants, their development, and future perspective. Frontiers in immunology, 14, 1043109.

World Health Organization. (2021). World malaria report 2021 . Retrieved from https://www.who.int/publications/i/item/9789240064898

Zhang, Y., Xu, Q., Gao, Z., Zhang, H., Xie, X., & Li, M. (2024). High-throughput screening for optimizing adoptive T cell therapies. Experimental Hematology & Oncology, 13(1), 113.

Zhao, Y., Yang, Y., Liu, M., Qin, X., Yu, X., Zhao, H., ... & Li, W. (2022). COX-2 is required to mediate crosstalk of ROS-dependent activation of MAPK/NF-κB signaling with pro-inflammatory response and defense-related NO enhancement during challenge of macrophage-like cell line with Giardia duodenalis. PLOS Neglected Tropical Diseases, 16(4), e0010402.