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Advances in Tropical Medicine

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Editorial

An Issue Particular To Biomedicines: Parasitic Infection And Immunity.

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INTRODUCTION

Animal and human infectious parasite illnesses continue to be a major global health concern. Protozoan-caused parasitic diseases are linked to significant health expenditures for both humans and animals as well as direct and indirect financial loss. The main human protozoan parasite illnesses, which result in 82.4 million Disability Adjusted Life Years and 810,000 fatal cases annually, are predicted to have a prevalence of about 790 million individual cases, according to [1].

The majority of protozoan parasitic diseases are linked to economically disadvantaged populations [1], unsanitary water supplies and conditions [2], and host immunodeficiency [3]. These diseases are frequently spread by vectors (vector-borne diseases), contaminated food (food-borne diseases), or water (water-borne diseases). An integrative and multidisciplinary strategy is necessary for the control and prevention of these protozoan parasites because many of them are zoonotic [4].

Leishmania spp., Trypanosoma brucei, Toxoplasma gondii, Plasmodium falciparum, Giardia duodenalis, Cryptosporidium parvum protozoan parasites, and Rhipicephalus bursa, a multi-host hard tick that spreads several economically significant pathogens in ruminants, such as Babesia, Anaplasma, Theileria, Rickettsia, and Coxiella, as well as several zoonotic pathogens, are all covered in the nine research papers in this Special Issue of Biomedicines (MDPI), "Parasitic Infection and Immunity" [5]. These studies fall into three major categories: vaccine and therapeutic development, protozoan parasitic immunology, and novel biological characteristics of protozoan parasites.

NOVEL BIOLOGICAL FEATURES OF PROTOZOAN INSECTS

Basic biology discoveries could aid in the creation of novel therapeutic medications by illuminating the molecular strategies used by protozoan parasites to endure in their hosts. Marucci and colleagues [7] sequenced four Giardia lamblia viruses and examined their biological characteristics, whereas Karamysheva and associates [6] disclosed novel biological features of Leishmania spp. in this Special Issue.

Leishmania species are dimorphic protozoan parasites that are spread by sand fly vector bites. They alternate between non-flagellated amastigotes that live in the phagolysosomal compartment of mammalian macrophages and flagellated, extracellular promastigotes that reside in the vector's midgut. Prophylactic tools are scarce, and available treatment medications are linked to hazardous side effects and the quick evolution of drug-resistant strains. Karamysheva and colleagues [6] investigated the C14-demethylase (CD14DM) enzyme, which catalyzes the formation of ergostane-based sterols, to uncover the function of lipids in regulating gene expression.Since Leishmania produces ergostane-based sterols rather of cholesterol like mammals do, CD14DM is a promising therapeutic target. According to in vitro research, L.major CD14DM inactivation results in lower virulence, hypersensitivity to stress, increased plasma membrane fluidity, and mitochondrial dysfunction. The researchers discovered that CD14DM Leishmania deletion mutants showed signs of gene dysregulation, which resulted in decreased translation, increased DNA degradation, and a compromised heat shock response. It was also mentioned that the identification of the process causing RNA instability brought on by sterol deficiencies would open up new therapeutic targets for the creation of anti-Leishmania medications.

High-throughput sequencing of four Giardia lamblia viruses (GLVs) from human and animal isolates was described in the study created by Marucci and associates [7]. The flagellated protozoa parasite G. duodenalis colonizes the small intestine and causes diarrhea in both people and animals, including cattle and pets. Children and young animals are more vulnerable to this infection, which is mostly linked to

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Received: 07-Jan-2025, **; Editor Assigned:** 08-Jan-2025 **; Reviewed:** 20-Jan-2025, **; Published:** 28-Jan-2025,
Citation: Marie Peraira. An Issue Particular to Biomedicines: Parasitic Infection and Immunity. Advances in Tropical Medicine. 2025 January; 1(1).

immunosuppression and inadequate cleanliness. Acute and chronic symptomatic infections can happen, even though it is usually asymptomatic in humans and animals. Moreover, Giardia may result in long-term extra-intestinal and gastrointestinal problems after infection [8]. New tactics to combat G. duodenalis have been accelerated by the rise of resistance and the high toxicity of traditional medications [9]. Research on protozoan parasite endosymbiont viruses is still in its infancy but is rapidly growing. These viruses have been linked to the severity of the illness, and treating giardiasis with them has been contemplated. However, before their use in the treatment of parasitic illnesses can be considered, basic and applied research is required [1].The study's sequencing and integrated mass spectrometry-based proteomic analysis yielded fresh insights into the biology and organization of the GLV genome, underscoring the significance of these novel "omic" approaches in exposing the possible diversity of GLV and advancing our knowledge of protozoan endosymbionts.

IMMUNOLOGY OF PROTOZOAN PARASITIC

A constant adaptation between the parasite and its host may be the cause of the chronic course of many protozoan parasitic illnesses. Through intricate host-parasite molecular interactions, parasites and hosts have put pressure on one another throughout millions of years of co-evolution. The host initiates a number of immunological processes to eradicate the parasites as soon as they enter the body. Parasites use a variety of tactics to avoid or undermine the host's innate and adaptive immune responses in order to survive in this harsh environment. These tactics include diversifying their genome, altering the expression of the host immune system's targets, and obstructing or suppressing the host immune response [10–12].Therefore, finding a host immune response that is successful in controlling parasitic infections and minimizing the chronicity or recurrence of disease is a key area of research in parasitic immunology. This Special Issue contains two papers that address the immunological aspects of illnesses caused by protozoa.

In order to assess the immunological response of canine hepatocytes exposed to L. infantum and the effect of inflammation on the metabolic activity of these cells in a milieu that mimics in vivo tissues, Rodrigues and colleagues [13] established a novel three-dimensional (3D) hepatic spheroid. The scientists came to the conclusion that 3D hepatic spheroids detect and respond to L. infantum parasites, resulting in an innate immune response at the price of a reduction in the liver's ability to metabolize xenobiotics.

Vacas and associates investigated the possible immunomodulatory impact of L. major's phosphotransferase serine/threonine protein kinase (LmjF.22.0810) both in vitro and in vivo [14]. According to the in vitro investigations, promastigote parasites showed reduced expression levels of virulence factors in comparison to control parasites, while transgenic parasites overexpressing LmjF.22.0810 shown decreased infectivity in vitro. Furthermore, transgenic parasite-infected BALB/c mice had noticeably less footpad edema, most likely as a result of a Th2 immune response deficiency that favors Th1 cytokines. LmjF.22.0810 is a good target for researching the immune response brought on by Leishmania parasites, the investigators stated.T. brucei, the causative agent of African trypanosomiasis, which was regarded as a neglected tropical disease until recently, was the subject of research by Dias-Guerreiro and associates [15]. This parasite, which causes nagana in cattle and sleeping sickness in humans, is spread by the hematophagous dipteran Glossina spp. (tsetse fly) while the bug is feeding on blood. The extracellular vesicles (EVs) released by T. b. brucei were described by the scientists, who also looked at the immunological response that the EVs produced in a mouse macrophage cell line and lymphocytes. It was discovered that EVs promoted the development of regulatory CD4+ and CD8+ T cells while inducing the differentiation of both M1- and M2-macrophages and eliciting the increase of MHCI+, MHCII+, and MHCI+MHCII+ macrophage populations.

It's interesting to note that it was confirmed that EVs and T. b. brucei parasites appear to have complementary but opposing impacts on the host immune response, most likely creating a balance between parasite proliferation and immune response regulation.

Vaccine and Drug Development

The majority of protozoan parasite infections are underdiagnosed, especially those that impact tropical nations and are linked to poverty. Concerns about their control and eradication are growing as a result of the lack of anti-protozoan immunizations and the shortage of therapeutic medications linked to rising drug resistance. As a result, a significant amount of biomedical research has been devoted to finding novel compounds and targets for parasite management. The selection of antigenic peptide candidates for use in the creation of anti-tick vaccines based on sialotranscriptome data and in silico analysis is described in one paper in this Special Issue. Three other research papers also feature new compounds that were tested against protozoan parasites, such as C. parvum, T. gondii, and P. falciparum.

The creation of antitick vaccines, especially transmission-blocking vaccines, is an alternate method of preventing tick-borne illnesses. These vaccines alter the biology and behavior of the vector, preventing it from spreading disease. In order to find antigenic sites that might be utilized in the creation of anti-tick vaccines, Couto and colleagues [16] investigated the R. bursa sialosecretome using a reverse vaccinology

technique. Potential candidates for upcoming vaccination trials include two secreted (EVASIN and RICIN) and one membrane-related (MARVEL) proteins that are specific to R. bursa and absent from the mammalian host. These antigens were shown to be able to elicit a long-lasting and protective immune response against this tick.

Human non-bloody diarrhea is caused by C. parvum, especially in immunocompromised people and children living in environments with little resources. As a water-borne zoonosis, cryptosporidiosis is primarily contracted by ingestion through the fecal–oral route. The parasite cannot be completely eradicated from the host by any successful chemotherapy. S-Methylcysteine (SMC), one of the primary organosulfur components of garlic, was evaluated for its impact on C. parvum in vivo by Elmahallawy and colleagues [17].In comparison to infected, non-treated mice, Swiss Albino mice showed significantly lower oocyst counts, fewer enteritis, hepatitis, and splenic lesions, lower serum hepatic transaminases and cytokine levels, and significantly higher levels of antioxidant enzymes, glutathione and superoxide dismutase, in the intestines two weeks after receiving SMC treatment. The authors came to the conclusion that SMC might be a promising and useful substance for treating infestations of C. parvum.

The obligatory intracellular apicomplexan parasite T. gondii is found throughout the world and infects almost all homoeothermic animals, including humans as intermediate hosts and cats as definitive hosts. Pregnant women's placentas can vertically transfer Toxoplasma gondii to the fetus; in immunocompromised people, Toxoplasma infections can result in stillbirth and spontaneous abortion. High toxicity, adverse effects, and drug resistance are some of the issues linked to traditional pharmacological therapy. Therefore, there is an urgent need to find novel alternative therapeutic choices.In this regard, the novel spider peptide XYP1, which was discovered from the cDNA library of the spider Lycosa coelestis' venom gland, was examined by Liu and associates [18]. According to the authors, XYP1 exhibits strong anti-Toxoplasma properties both in vivo and in vitro. In particular, the spider peptide improved the survival of mice with acute T. gondii infection and markedly reduced the viability, invasion, and multiplication of tachyzoites in vitro. XYP1 may be a viable novel medication candidate for the treatment of toxoplasmosis because of its mechanism of action, which is linked to membrane perforation, swelling, and tachyzoite disintegration.

Plasmodium protozoan parasites are the cause of malaria, an infectious disease spread by mosquitoes. Humans and Anopheles mosquito females are the two hosts in the life cycle of P. falciparum. The clinical manifestation of the disease is caused by the sexual blood stage of Plasmodium parasites. The sexual stages of the parasite that mosquitoes can contract are called mature gametocytes. The majority of anti-malarial medications only work against the blood stage of asexual parasites. Furthermore, controlling malaria is extremely challenging due to the development of parasite drug resistance to the existing medications, which can also raise the rates of morbidity and fatality. The design and in vitro effects of eleven organoarsenic compounds on P. falciparum's asexual blood stage and sexual transmission stage were reported by Basova and colleagues [19]. In addition to inhibiting gametocyte growth and exflagellation, the authors discovered that the As-8 molecule demonstrated strong efficacy against P. falciparum strains that were both CQ-sensitive and CQ-resistant, with acceptable IC50 values. Additionally, there was no cytotoxic or hemolytic impact, suggesting that the As-8 molecule is harmless and primarily targets the parasite. The authors came to the conclusion that As-8 is a promising starting point for the development of new organoarsenic medications with multi-stage anti-P. falciparum efficacy.

CONCLUSION

In order to promote the flow of new discoveries and the high caliber of published studies, this Special Issue covers the key areas of research in protozoan parasitic diseases, including the study of parasitic immunology, basic research into the biology of protozoan parasites, and research applied to the development of new prophylactic and therapeutic tools.Innovative 3D cultures that more closely resemble tissue architecture, new research tools like genomics and proteomics, and in silico research offer the answers needed to control these diseases, many of which have been neglected for many years.

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