DEVELOPMENT OF THERAPEUTIC AGENTS: METHODS AND APPROACHES IN THE DEVELOPMENT OF VACCINES AGAINST PROTOZOAN PARASITES

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1 INTRODUCTION

Parasitic infections make up a large percent of diseases in tropical countries and pose a significant threat to human health worldwide. Parasites are complex pathogens associated with chronic disease, high reinfection rates, and host immune depression. Furthermore, parasitic infections, unlike most viral and bacterial infections, are more complex and chronic, requiring special consideration when developing therapeutic agents. Designing strategies against parasitic infections demands that scientists address the multifactorial aspects of special pathogens. The challenge in developing therapeutic agents against parasites lies in the nature of the parasites and their close relationship with both human immunity and anthropogenic activities.

2 PARASITE LIFE CYCLES AND VECTORS

The leading cause of death from parasitic disease, malaria, presents unique obstacles for scientists trying to develop effective therapies [1]. *Plasmodium falciparum,* the etiological agent of malaria, is transmitted to humans via the *Anopheles gambiae* mosquito. Sporozoites are introduced into the human host and enter a hepatic cycle before being released into the blood for the erythrocytic cycle (Fig. 1). After a blood meal, the mosquito vector will ingest parasite gametocytes, which undergo a sporogonic cycle (sexual cycle) giving rise to infective sporozoites that perpetuate the life cycle. Looking at the malaria life cycle, one can identify two main obstacles: (1) the parasite develops within two different hosts and different cells, and (2) there are multiple immunologically distinct parasite stages. For this reason, scientists have concentrated their efforts on formulating a vaccine targeted at multiple stages and multiple antigens to mimic the array of immunological responses activated during a natural infection [2]. The strategy here is to find optimal antigens from different parasite stages that could mount proper immune responses at various stages in parasite development. Another problem with malarial disease is that different stages require different immunological responses to effectively eradicate the infective parasite [3]. Strong antibody responses are required to fight blood stage sporozoites as well as gametocyte transmission to the mosquito. In the liver stage, however, a strong cytotoxic T-cell-mediated response has been associated with clearance of infected host cells. Combining the need for a multiantigen approach with the need to stimulate both humoral and cell-mediated

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