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Vaccine against Protozoan Parasites: A Failure

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ABSTRACT

Protozoan parasites are unicellular, eukaryotic and heterotrophic organisms which get entry in the appropriate host after responding to the cues that indicate the presence of host. These cues can be generated by the host itself, any byproduct of the host or the plants consumed by the host. The host range of protozoan parasites i.e., *Plasmodium, Trypanosoma, Leishmania, Babesia, Theileria, Giardia* etc. ranges from companion animals to bovines and humans posing a serious threat to these species. Among these, *Plasmodium* causes a life-threatening disease in human and is transmitted by the bite of Anopheles mosquito. *Trypanosoma* and *Leishmania* are responsible for causing African sleeping sickness, Chagas disease and tropical and visceral Leishmaniasis. Similarly in bovines, *Babesia* causes hemoglobinuria which may lead to death of animal. It is the need of hour to control these deadly protozoan parasites through effective control strategies i.e., vaccination. The development of DNA vaccines is considered as a dynamic field of research and have been used in the last 15 years offering a new alternative for the control of protozoal infections. Vaccination against these deadly pathogens have not been proved effective yet because of multiple reasons including immunological non-responsiveness to individual vaccine antigens, antigenic variation and polymorphism, immune deviation because of maternal immunity, parasite-induced apoptosis of immune effector and memory cells and alterations of dendritic cell function.

Introduction

The word protozoa is derived from Greek words **protos** meaning first and **zoan** meaning animals. Protozoa are eukaryotic, unicellular, heterotrophic organisms that come under the Kingdom Protista. They feed on organic matter such as other microorganisms or organic tissues and debris. They comprise of four organization types i.e., ciliates, amebae, flagellates and parasitic sporozoans. There are more than 6500 species of protozoan parasites [1].

Protozoa may be free-living or parasitic. This statement is elaborated in the sense that;

i) The body of protozoa is covered by a pellicle or cuticle.
ii) For locomotion, they have flagella.
iii) Freshwater forms of protozoa have a contractile vacuole (Figure 1).
iv) Reproduction is done by Binary fission that is called as longitudinal division.

Examples of protozoan parasites are *Plasmodium, Trypanosoma, Leishmania, Babesia, Theleria, Giardia*, etc [1].

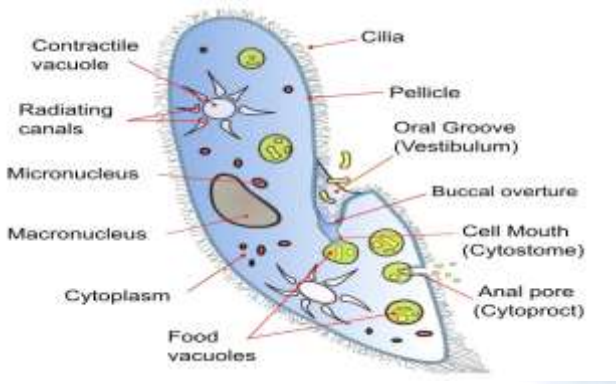

Figure 1: Structure of a protozoan parasite

Habitat:

Protozoa are found in most of the habitats worldwide. Almost all protozoa require moist habitat while some may survive in dry environment for longer duration by developing resting cysts. The cyst makes them enable to remain dormant until the availability of favorable conditions [2].

Characteristics:

Most of its species are free-living and are abundantly found in salt, fresh and brackish water, and other moist environments such as soils and mosses. Examples include *Amoeba, Paramecium* etc. Some species of protozoa require extreme environment like hot springs and hypersaline lakes and lagoons. They may be parasitic and symbiotic means that they live on or within other organisms. The organisms may include vertebrates, invertebrates, plants or other unicellular organisms. Parasitic protozoa include *Trypanosoma, plasmodium, Entamoeba* spp., *Toxoplasma gondii* etc. Symbiotic protozoa include fleas, mosquitos etc. Some protozoa are entomopathogens. These are those pathogens that may be viral, bacterial, or fungal that kill or disable insects. They play vital role in natural vegetation of insect pests. They are commonly called as microsporidians. Examples include fall webworm, cabbage looper, borer etc.

Some protozoa are harmless to their host organisms. The examples include:

- Flagellates such as *Trichomonas* and ciliated protozoa such as *Isotricha* and *Entodinium* that live commensally in the rumen of ruminant animals such as cattle and sheep.
- GIT protozoa i.e., *Pyrsonympha* and *Trichonympha* that lives in the termite's gut and enables them to digest the wood by breaking the complex sugar in to easily digested molecules.

Some may cause or may be the source of significant diseases like malaria (causative agent: *Plasmodium*), toxoplasmosis (causative agent: *Toxoplasma gondii*), leishmaniasis (causative agent: *Leishmania tropica*) etc [3].

Haemoprotozoan diseases such as Babesiosis, Anaplasmosis, Theileriosis and Trypanosomiasis are taken into special consideration as impediments in the health, productive performance of cattle, and increased cost for control measures along with the loss to livestock industry.

Ticks are mostly related to initiation of many diseases. Ticks are considered as natural vectors for Anaplasmosis, Babesiosis and Theileriosis.

Bovine Theileriosis is caused by *Theileria annulata* and *Theileria parva*. Anaplasmosis is a disease of adult cattle caused by *Anaplasma Marginale* and *Anaplasma centrale*.

- Babesiosis is a tick-borne disease affecting wide range of animals causing bovine babesiosis.
- Anaplasmosis is a disease that affects red blood cells caused by *Anaplasma marginale*.
- Diarrheal illness in animals is caused by *Cryptosporidium* and *Giardia* which are intestinal parasites.
- *Trypanosoma Brucei* transmitted by tsetse fly, affecting livestock and human and cause Trypanosomiasis and African sleeping sickness.
- *Trypanosoma Cruzi* transmitted by triatomine bug causing American Trypanosomiasis [4]

Vaccine Development:

Vaccine is the suspension of weakened or killed pathogen, their toxins or other biological fluid containing antibodies, messenger RNA (mRNA) or lymphocytes administered to the host to prevent them from disease. Effective vaccines are available for many protozoal diseases of animals,

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including vaccines for zoonotic pathogens and for several species of vector-transmitted haemoparasites.

The development of DNA vaccines is considered as a dynamic field of research and have been used in the last 15 years offering a new alternative for the control of protozoal infections. Instead of success of vaccines in public health, there are still various protozoal pathogens such as *Plasmodium falciparum*, *Trypanosoma* sp., or *Leishmania* sp. against which no effective vaccine is developed. But discovery of direct injection of plasmid DNA encoding foreign proteins could lead to synthesis of endogenous protein and a specific immune response generated against it leading to new perspectives in vaccine development [5]

Vaccine Failure:

The major reasons for failure of protozoal vaccine are immunological non-responsiveness to individual vaccine antigens, antigenic variation and polymorphism, immune deviation because of maternal immunity, parasite-induced apoptosis of immune effector and memory cells and alterations of dendritic cell function. The vaccines in case of viruses are effective as they are unicellular in nature but in case of multicellular organisms there are multiple factors involved that may lead to create hindrance in development of antibodies.

In case of trypanosomes the vaccine failure is due antigenic variation by the involvement of glycoproteins i.e., there are more than 500 glycoproteins in trypanosomes. In case of leishmania the major cause of vaccine failure is its complex life cycle and the involvement of various polyproteins [6, 7].

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