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Journal of Cell Signaling

Short Communication

# The cAMP-Regulated Pathways Seen in Apicomplexan Parasites for Drug Development

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## DESCRIPTION

One of the most significant tropical diseases affecting humans is malaria, which is brought on by several *Plasmodium* species, which are protozoan parasites from the apicomplexa. The *Plasmodium*, *Toxoplasma*, and *Cryptosporidium* genera of apicomplexan parasites, which can cause malaria, toxoplasmosis, and cryptosporidiosis, have a plastid-like structure called the "apicoplast" [1]. Despite of enormous efforts and advancements in drug development, there are still few medications available for the treatment of these neglected diseases, largely because of developing drug resistance to commercially available medications. It's essential to have a productive centre focused on finding new routes that contain new therapeutic targets. The distinct cAMP-regulated pathways seen in apicomplexan parasites are unique makes them an attractive resource for the development of new drugs. Here, with a particular emphasis on *Plasmodium*, the most significant distinctions from the human host are outlined.

### *Plasmodium* lacks G-proteins and GPCRs in its non-canonical cAMP-regulated pathway

*Plasmodium*, the deadly parasite that causes malaria, is the most significant member of the apicomplexa. The malaria parasite must grow in two distinct settings after infecting the human host, namely the preerythrocytic stage in the liver and the erythrocytic blood stages. After that, the mosquito enters a sexual stage, which causes the growth of ookinetes in its midgut to create an oocyst that produces sporozoites in the salivary glands [2]. Only signalling processes can enable the parasite to quickly respond to these developmental changes. The dearth of available genome data has prevented research on apicomplexan parasites from progressing as quickly as that on cyclic nucleotide controlled pathways in humans. However, new genome sequencing discoveries have shown that the components of their cyclic nucleotide pathways differ.

### *Toxoplasma gondii* is dependent on GPCR-mediated signalling from the infected human host cell

The common protozoan parasite *Toxoplasma gondii* is the cause of toxoplasmosis [3]. 30% of people are affected by it. The oocyste, tachyzoite, and bradyzoite are the three developmental forms that it takes on throughout its life cycle. Feces from cats, where the oocysts are found, are the means of transmission. Congenital toxoplasmosis, caused by the rapidly replicating tachyzoite form of the parasite, causes tissue damage and foetal infection in pregnant women. Tachyzoites can transform into bradyzoites in particular in muscles and the Central Nervous System (CNS) depending on the immunological response of the human host. Some tachyzoites, however, have the ability to evade the host's immunological reaction and transform back into bradyzoites. Bradyzoites can be consumed in meat and transform into tachyzoites when they are swallowed by a human host.

### *Cryptosporidium,* a non-intracellular parasite, reproducing without canonical G-proteins and GPCRs

Both *Cryptosporidium* hominis and *Cryptosporidium* parvum, which can infect both humans and animals, produce human cryptosporidiosis, a self-limiting diarrhoea in healthy individuals. The condition can progress into severe diarrhoea with effects on the biliary tree and the respiratory organs in immunocompromised individuals, such as HIV-1 infected individuals or young children [4]. The life cycle begins with the expulsion of sporulated oocysts through the respiratory system or in the faeces. Sporozoites are secreted after intake or inhalation and parasitize epithelial cells. After then, asexual reproduction (schizogeny or merogony) begins before the sexually mature micro- and macrogamonts form the oocyste.

## CONCLUSIONS

The discovery of pathways with novel targets is crucial for the control and eradication of major worldwide parasite diseases at a

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**Received:** 21-Jul-2022, Manuscript No. JCS-22-19304; **Editor assigned:** 26-Jul-2022, PreQC No. JCS-22-19304 (PQ); **Reviewed:** 09-Aug-2022, QC No. JCS-22-19304; **Revised:** 16-Aug-2022, Manuscript No. JCS-22-19304 (R); **Published:** 23-Aug-2022, DOI: 10.35248/2576-1471.22.07.300

**Citation:** Salmona A (2022) The cAMP-Regulated Pathways Seen in Apicomplexan Parasites for Drug Development. J Cell Signal. 7:300

time when traditional treatment is becoming less effective. The non-canonical cAMP-regulated pathways of apicomplexan parasites that cause toxoplasmosis, cryptosporidiosis, and malaria offer a useful tool in this situation. This discussion demonstrates various approaches to solving the issue.

- Inhibition of the host proteins may lessen parasite load because canonical G-proteins and GPCRs are missing in these parasites but present in the mammalian host. The canonical, cAMP-regulated pathways of the human host are very important for the survival of all three genera of apicomplexan parasites.
- An appealing strategy to stop the parasite's invasion and egress is to inhibit the Rap1 protein in the guanine nucleotide exchange pathway.
- Kinase G is the most promising target in *Plasmodium* out of the secondary effector proteins, or the family of ACG kinases, because it performs crucial regulatory roles throughout the whole parasite life cycle. The WHO's criteria that a single treatment eliminates the parasite in each embryonic stage is already met by an inhibitor with an imidazopyridine lead structure.
- Small Ras GTPases in all three genera, which interact with certain host enzymes to speed up parasite invasion and proliferation, have not yet been fully utilized in drug discovery.

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