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Ubidercarenone Decelerates the Manifestation of Experimental Cerebral Malaria in C57BL/6J Mice by ameliorating the Host Inflammatory Response

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Abstract

Cerebral Malaria (CM), a highly lethal form of severe malaria is known to cause inflammation that exacerbates pathology in the brain predominantly due to inflammatory immune response as a result of *Plasmodium falciparum* infection. There is limited progress in the development of new approaches for the treatment of CM. Therefore, in this study we investigated whether oral Ubidercarenone (Ubn) can regulate the induction of inflammatory immune response in experimental cerebral malaria (ECM). Three groups of mice were utilized for this study, one group of C57BL/6J mice was used as control; group two was only infected with *Plasmodium berghei ANKA* (PbA) and group three orally supplemented with 200mg/kg ubn followed by infection with PbA. Here we show that Ubn was able to protected majority of mice against ECM. Importantly, Ubn supplementation significantly hampered infiltration of inflammatory monocytes, T cells and cytotoxic granzyme B into the brain. Serum analysis showed a reduction in the levels of TNF-α in Ubn administered mice. Furthermore, Ubn administration resulted in decreased expression of chemokine CCR2 in the brain, leading to reduced levels of activated pathogenic T cells. Notably, anti-inflammatory cytokines IL-10 and IL-22 together with T-regulatory cells, which are associated with protection during ECM, were up-regulated in Ubn treated mice. These results demonstrates that Ubn can assuage PbA-mediated inflammatory responses usually witnesses during ECM.

Keywords: Ubidercarenone; Experimental Cerebral Malaria; Inflammatory Response

1.0 INTRODUCTION

Cerebral malaria (CM), is considered to be a highly fatal neurological syndrome caused by *Plasmodium falciparum* and is characterized by delirium, body ache, fever, coma and ultimately impaired consciousness [1]. Additionally, the pathology that is usually witnessed during CM is mediated by inflammatory processes following *Plasmodium falciparum* infection [2]. Animal models of CM show sequestration of the parasite in microvasculature and the adherence of parasitized erythrocytes in the endothelial lining of the brain [3]. Furthermore, pro-inflammatory mediators which include; infiltrated leukocytes, pro-inflammatory cytokines and chemokines play a major role in the pathogenesis of CM.

Moreover, considerable evidence suggests that overwhelming induction of inflammatory processes is an important trigger mechanism that aids in malaria parasite clearance, but can also play a key role in the development of ECM [4]. Additionally, the situation is further worsened when the generation of pro-inflammatory cytokines overwhelms anti-inflammatory processes during plasmodium infection. Also the indispensable role of infiltrated inflammatory monocytes in the development of immunopathology in ECM has been described [5]. Both innate and adaptive immune systems play an important role during malaria

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