First steps towards the identification of a new hybrid antimalarial therapeutic agent targeting PfAQP

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Malaria became a public global health priority and matter of discourse during the transition between millennia. Although most malaria variants are currently successfully treated with the existing antimalarial drugs, in 2019, this disease was still responsible for approximately 409 000 deaths globally [1]. Severe malaria in humans is mostly caused by infection with *Plasmodium falciparum* whose complications include severe anemia and end-organ damage, pulmonary complications, and hypoglycemia or acute kidney injury [2].

The development of hybrid antimalarial agents has been actively pursued as a promising strategy to overcome the problem of resistant parasite strains since it provides treatment for all *P. falciparum* that infects human red blood cells and at the same time eliminates the replicative and dormant liver forms of the parasite [3]. In this communication, we will present the first steps towards the development of a multi-target strategy based on the use of keystone antimalarial drugs coupled to inhibitors of the *P. falciparum* aquaporin (PfAQP). This protein acts as a constitutive water and glycerol channel [4], with a key function in the reproduction of the Plasmodium, making it a promising target for the development of antimalarial therapeutics [5]. An initial structural characterization of PfAQP along with a qualitative assessment on the dynamics and function of the protein will be presented, together with an evaluation of the effect different membrane sizes on simulation times and quality of the model. These results are of utmost importance for the next steps of the project, where the inhibitory efficiency of different glycerol derivatives will be evaluated.

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