HYPOTHESIS AND OBJECTIVES

The parasite encoded *clag3* genes, which are regulated at the epigenetic level and present clonally variant expression, determine the formation of the main channel for the transport of solutes at the membrane of the infected RBC (PSAC). Hence, we hypothesize that *P. falciparum* parasites can modify the permeability of the membrane to specific solutes by epigenetic regulation of *clag3* genes expression. This phenomenon may be of relevance for parasite adaptation to fluctuating conditions in the environment, such as presence of toxic compounds; this way, parasites could develop resistance to antimalarial drugs by altering the erythrocyte membrane permeability.

To explore this hypothesis, we aimed to further characterize *clag3* genes, with particular interest in their epigenetic regulation and its effect on the infected RBC permeability, and to study the significance of this potential drug resistance mechanism.

The detailed objectives of this PhD thesis are the following:

Objective 1. To explore the role of switches in *clag3* expression in the acquisition of resistance to the antibiotic BS.

Objective 2. To characterize *clag3* genes expression dynamics in *P. falciparum* human infections, with a special interest in the mutually exclusive expression property and the epigenetic memory of *clag3* genes after going through transmission stages.

Objective 3. To identify the specific polymorphic regions of *clag3* genes that determine transport properties.

Objective 4. To identify drugs susceptible to failure by parasite resistance through epigenetic switches in *clag3* genes.