Federico Valerio

Synthesis of novel PfDHODH inhibitors based on 4-amino-5-hydroxy/5-methoxy-coumarin structures

Malaria is an infectious disease caused by five species of the genus *Plasmodium* (*P. falciparum, P. vivax, P. ovale, P. malariae* and *P. knowlesi*) that is transmitted by infected female Anopheles mosquito. The mosquito bite introduces the parasite into a host's blood and those parasites travel to the liver where they multiply before infecting and destroying red blood cells causing anaemia. *Plasmodium falciparum* is the deadliest parasite and is responsible for majority of all Malaria cases that occurs mainly in Sub-Saharan Africa. A vaccine is still not available and malaria treatment depends on chemotherapeutics. It is important to find new targets and new antimalarial drugs versus *Plasmodium* parasite because it develops resistance against all classes of antimalarial medicines.

Dihydroorotate dehydrogenase (DHODH) is the enzyme that catalyzes the fourth step of *de novo* pyrimidine biosynthesis. It is an interesting target because unlike the humane, the parasite has not pyrimidine salvage pathway and if *Pf*DHODH is inhibited, it will not be able to synthesize DNA so it is growth will be stopped.

In this project we synthetized new 4-amino-5-hydroxy-coumarin and 4-amino-5-methoxy-coumarin derivatives in search for new *Plasmodium falciparum* dihydroorotate dehydrogenase inhibitors.

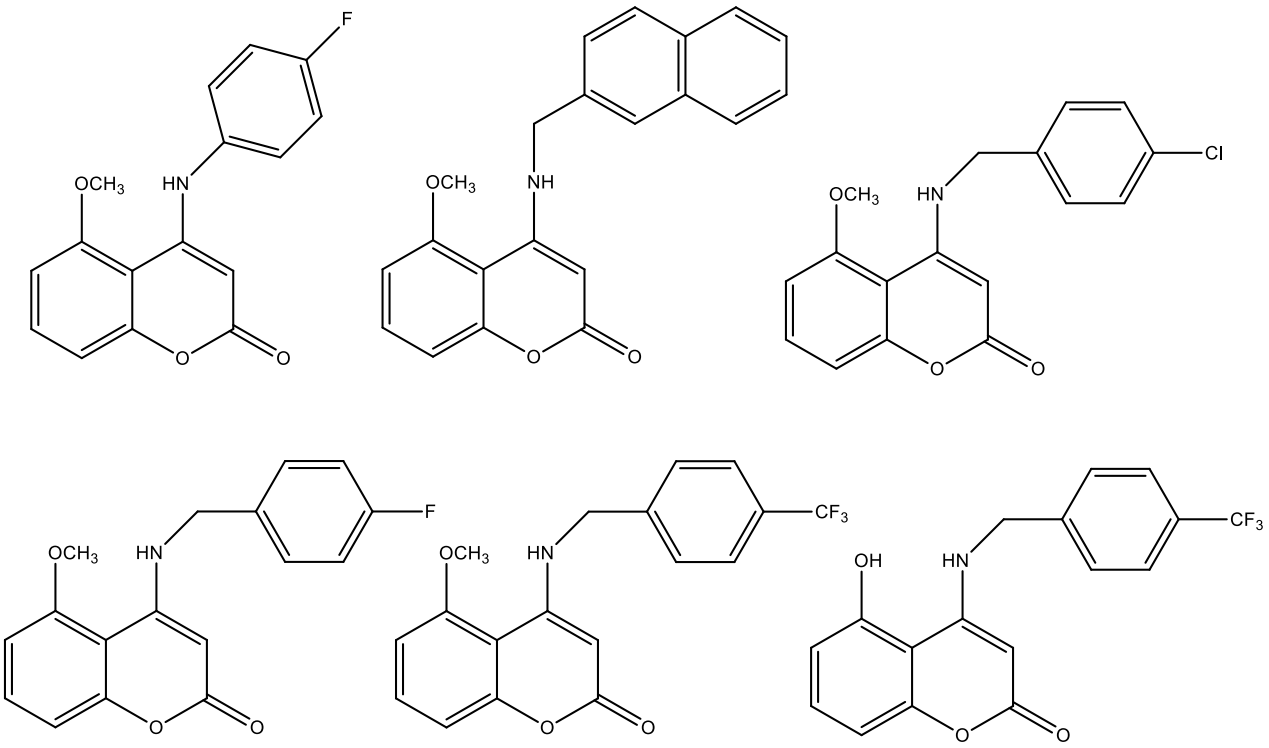

Figure 1. 4-Amino-5-hydroxy-coumarin and 4-amino-5-methoxy-coumarin structures synthesized.

In conclusion we synthetized six compounds which will be tested on the *Pf*DHODH.

Supervisor: Prof. **Ulf J. Nilsson** and PhD student **Maria Luisa Verteramo**
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CAS - Centre for Analysis and Synthesis, Lund University