Project FI-2

Complement escape by malaria parasites

(Supervisors: **Prof. Seppo Meri, Prof. Veronique Fremeaux-Bacchi**)

The fact that various stages of the malaria parasites can survive in human blood suggest that they are capable of escaping destruction by the host complement system. Moreover, mosquito's midgut is also exposed to human blood during and after blood meal. We have hypothesized that the Plasmodium parasite and the Anopheles mosquito's midgut express surface proteins that interfere with complement activation and complement-mediated cell damage. In our preliminary studies, we have identified two immune evasion mechanisms that allows the invasive sporozoite stage of the P. falciparum parasite to escape complement-mediated killing. The parasite evasion molecule has been identified and will be further characterized. In the second mechanism, another parasite protein was found to hijack the central complement component C3 and its activation product, the opsonin C3b from host blood. Here, we will study how the hijacked C3 and C3b molecules exert their inhibitory activity on complement.

Under the same topic, we have also discovered that mosquito's midgut cells utilize an evasion mechanism to escape destruction by complement activity. It targets the alternative pathway of complement activation. Specifically, we found that the mosquito midgut epithelial cells captured factor H, a natural complement regulator, from the ingested blood. Consequently, the deposition of C3b, a key complement component, on the surface was impaired and cell death was avoided. In this project, we will analyze the mosquito's factor H receptor and its interaction with factor H. The sporozoite and midgut proteins that mediate human complement evasion are vaccine candiodates. As vaccines they would lead to an immune response that could interfere with the interaction between the immune evasion molecules and complement. This could eventually lead to enhanced parasite killing in the case of parasite-based vaccine or to mosquito killing (when fed on the blood of the vaccinated individuals) in the case of a mosquito-based vaccine.

General description of your individual PhD-schedule:

- Your main university will be University of Helsinki (Finland) with Prof. Meri as supervisor.
- You will have a 12-months research secondment at Sorbonne University (France) with Prof. Fremeaux-Bacchi as supervisor, where you continue to scientifically work on your thesis project.
- You will have a 1-month clinical training at Tirol Kliniken Innsbruck (Austria).
- You will have a 1-month entrepreneur training at RCB (Borstel, Germany).
- You will finally receive a PhD issued by Sorbonne University and University of Helsinki if you fulfil the respective requirements.

Application

The position is advertised from 10.03.2020 – 10.05.2020 on **www.corvos.eu**. Please apply via this homepage during that time.