Project NO-2

Single and double inhibition of complement and CD14 in opportunistic conditions

(Supervisors: **Prof. Tom Eirik Mollnes, Prof. Reinhard Würzner, Prof. Garred**)

The group of professor Mollnes has worked with a combined inhibition of complement (at the level of C3 and C5), and the Toll like receptors (TLRs) targeting CD14, a key co-receptor for TLR4, TLR2 and others, based on an hypothesis to attenuating the upstream innate immune activation when it is over- or dys-activated. This occurs in conditions like sepsis, trauma and ischemia reperfusion injury. The effect of this combined inhibition has been shown both in vitro (human whole blood model) and in vivo (mice and pigs) with impressive effect on the detrimental inflammatory reaction, including activation of complement, cytokines, hemostasis and leukocytes induced by bacteria. Gram-negative *E. coli* and *N. meningitides*, as well as several Gram-positive *Staphylococci species* have been investigated with principally the same beneficial effects have been investigated. In this program we will investigate this therapeutic approach on opportunistic species including the fungi *Candida* and *Aspergillus*, which never has been studied in these models before. It will be a major scientific step forward to show whether fungi behave similar or different with respect to bacteria. Furthermore, inhibitors of the terminal pathway (C7) will be added in the program (produced by prof Würzner, Innsbruck).

The second part of this project will be to develop a commercial assay for detection of C3 activation. We have, for many years used an in-house assay based on the antibody bH6, characterized by professor Garred (Copenhagen). This antibody is unique in the sense that it detects a neoepitope which is exposed on the C3 molecule immediately after activation, but not on native C3. The epitope is exposed on C3b, iC3b and C3c, thus detection of the total amount of these fragments present in a sample. In collaboration with the company SVAR life science (Malmö, Sweden), this assay will be developed.

General description of your individual PhD-schedule:

- Your main university will be University of Oslo (Norway) with Prof. Mollnes as supervisor.
- You will have a 6-months research secondment at Medical University of Innsbruck (Austria) with Prof. Würzner as supervisor, where you continue to scientifically work on your thesis project.
- You will have a further 6-months research secondment at SVAR LifeSciences (Malmö, Sweden) where you will develop a new complement activation assay, based on the mab bH6, detecting a neoepitope exposed on C3 fragments.
- You will have a 1-month clinical training at Research Center Borstel Hospital (Borstel, Germany).
- You will have a 1-month entrepreneur training at SVAR LifeSciences.
- You will finally receive a PhD issued by University of Oslo and Medical University of Innsbruck if you fulfil the respective requirements.

Application

The position is advertised from 10.09.2019 – 10.11.2019 on **www.corvos.eu**. Please apply via this homepage during that time.