Project HU-1

Development of immunoassays for specific classical and lectin pathway activation markers

(Supervisors: Prof. Zoltan Prohaszka, Prof. Reinhard Würzner)

Infections and various immune-inflammation mediated conditions are characterized by the activation of the complement system. Antibodies (immune complexes) activate the classical pathway whereas repetitive carbohydrate structures give rise to the initiation of the lectin pathway. The activation state of the various complement pathways can individually and specifically be measured by levels of the generated specific split products or protein-protein complexes. There are several well known and widely used complement activation biomarkers currently in the market (for example sC5b-9 for the terminal pathway), but specific markers for the early classical- and early lectin pathways are still missing. C1 inhibitor, forming covalent linkage with active proteases of the classical and lectin pathway, is promising target for the development of such novel immunoassays. We already generated monoclonal antibodies against human C1 inhibitor, C1s and MASP-1, and started the selection of appropriate clones to set up sandwich immunoassays to measure C1 inhibitor-C1s, and C1 inhibitor-MASP-1 covalent complexes. The aim is to develop sensitive and specific assays appropriate for the quantitative measurement of the above complexes in human plasma and serum samples. Clinical studies will be organized by enrollment of patients with iatrogenic- (in-hospital acquired pneumonia and sepsis) and opportunistic (pulmonary tuberculosis) infections. As additional patient control group several conditions with classical and/or lectin pathway activation (immune-complex diseases, fungal infections) will also be included. If the newly developed assays turn out to be specific, and generate clinically meaningful results, commercialization (assay development at Hycult Biotech) will be done. External validation of the new Kits will be done in Medical University of Innsbruck using patient's samples with opportunistic infections.

General description of your individual PhD-schedule:

- Your main university will be Semmelweis University (Budapest, Hungary) with Prof. Prohaszka 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 Hycult Biotech (Uden, Netherlands) where you will develop commercial assays using generated mAbs.
- You will have a 1-month clinical training at Research Center Borstel Hospital (Borstel, Germany).
- You will have a 1-month entrepreneur training at Hycult Biotech.
- You will finally receive a PhD issued by Semmelweis University 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.