Project AT-1

Generation, characterisation and commercialisation of native-restricted and neoepitope-specific monoclonal antibodies directed against the terminal complement protein C7

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

Complement is one of the most important players in innate immune defense. Three activation pathways are triggered by multiple interactions and are amplified in cascades, leading to the activation of the terminal complement (TC) pathway. This pathway is especially important in Neisserial infections, and thus subjects deficient in these TC components are particularly affected by these gram-negative bacteria. Furthermore, insufficiently protected human cells (for various reasons) are also attacked. Of the several TC proteins C7 plays a particular role, as it is the only component predominantly synthesized extrahepatically. Thus, locally produced C7 will enhance complement attack at the site of inflammation.

Monoclonal antibodies (mabs) against C7 are already available, but those which are clearly native-restricted or neoepitope-specific are lacking. The former will detect only native C7 and may even block TC complex assembly, whereas the latter may be useful for the quantitation of this complex. The aim of this PhD thesis project is the generation and commercial production of anti-C7 mabs.

To achieve the goals, first, short amino acid regions of C7 will have to be identified, especially those which are likely accessible in either the native or the incorporated C7 protein, of which the former may be likely involved in TC pathway interactions. Peptides, representing these sequences will be used for immunization of mice to generate specific mabs, very likely with a partner in Copenhagen (DK). The first intensive tests, however, will be performed in Innsbruck. A thorough control evaluation using an array of different kits will follow at the Semmelweis University in Budapest (HU) for 6 months, where the inhibitory and potentially connected therapeutic functions of these mabs will be assessed. During another 6-months stay at the biochemical company Hycult (NL), all suitable mabs will be conditioned for good manufacturing practice and mass production to coin commercial products, when all IPR issues have been accomplished.

General description of your individual PhD-schedule:

- Your main university will be Medical University of Innsbruck (Austria) with Prof. Würzner as supervisor.
- You will have a 6-months research secondment at Semmelweis University (Budapest, Hungary) with Prof. Prohaszka 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 use your mAbs for development of commercial assays.
- You will have a 1-month clinical training at University Hospital Helsinki (Finland).
- You will have a 1-month entrepreneur training at Hycult Biotech.
- You will finally receive a PhD issued by Medical University of Innsbruck and Semmelweis University 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.