**2018 Helmholtz – OCPC – Program**

**for the involvement of postdocs in bilateral collaboration projects**

**PART A**

**Title of the project: “Immune control of hepatitis B virus”**

**Helmholtz Centre and institute: Helmholtz Zentrum München, Institute of Virology**

**Project leader: Prof. Ulrike Protzer, MD**

**Web-address:** www.helmholtz-muenchen.de/viro

**Description of the project** (max. 1 page)**:**

Chronic hepatitis B affects 255 million humans worldwide and puts them at high risk to develop liver cirrhosis or hepatocellular carcinoma (HCC). 880.000 humans die every year due to the consequences of a hepatitis B virus (HBV) infection (WHO 2017). For HCC, HBV infection is the leading cause. Antiviral therapies mainly build on nucleos(t)ide analogues that are safe and well tolerated and suppress HBV replication, but seroconversion from HBsAg to anti-HBs, which is regarded as a “cure”, remains very rare committing most patients to long term therapy. In addition, HCC rates remain unexpectedly high. Entry inhibitors, capsid assembly modulators and siRNAs are newer antivirals under development. However, none of them directly targets HBV persistence form, the episomal HBV cccDNA. So far, the only potentially curative approach remains interferon which is already available for more than 20 years but this treatment has high side effects and is only effective in 5-20% of patients.

We hypothesize that triggering immune control of HBV will be needed to achieve HBV cure and allow to terminate antiviral therapy. A cure will require (i) the elimination of infected hepatocytes, (ii) non-cytolytic purging of the HBV persistence form by cell-intrinsic defense mechanisms, or alternatively (ii) its loss by cell division if new infection is blocked. T cell responses seem to be essential to achieve at least a functional cure of hepatitis B. While HBV-specific CD4 and CD8 T-cell responses are readily detectable in patients resolving HBV infection, HBV-specific T cells are scarce and partially impaired in chronic hepatitis B most likely due to high amount of circulating viral antigens.

Novel therapeutic approaches have been stimulated by the availability of cell lines and mouse models as well as therapeutic candidates and tools that have been established in cancer research. Immune therapeutic approaches activating T cells have been developed or co-developed for antiviral therapy by Ulrike Protzer’s group in Munich. A particular interest is on activating antiviral T cells using a therapeutic vaccine or on the redirection of T cells to HBV-infected hepatocytes. This is achieved either by grafting T cells with a recombinant T cell receptor (TCR) or a chimeric antigen receptor (CAR) or by using bi-specific antibodies as T cell engangers. As in therapy of solid cancers, however, antiviral immunity seems to be skewed by the high antigen load. The aim of the project will thus be to determine why HBV-specific T cell-responses are skewed in HBV infection and how immune tolerance to viral antigens can be overcome.

**Description of existing or sought Chinese collaboration partner institute** (max. half page)**:**

Fudan University, Shanghai, School of Basic Medical Sciences, Department of Medical Microbiology & Parasitology: Professor Zhenhong YUAN, MD, PhD (Director Key Laboratory of Molecular Medical Virology). Collaboration on the regulation of HBV replication

Wuhan University, School of Basic Medical Sciences, Institute of Medical Virology: Professor Yuchen XIA, PhD. Collaboration on the control of hepatitis B virus by cytokines

**Required qualification of the post-doc:**

* PhD in Biochemistry / Molecular Biology / Virology
  + Experience with research in liver physiology / diseases; mouse experiments; primary liver cells
* Additional skills in Immunology or in Bioinfomatics

**PART B**

**Documents to be provided by the post-doc, necessary for an application to OCPC via a postdoc-station:**

* + Detailed description of the interest in joining the project (motivation letter)
  + Curriculum vitae, copies of degrees
  + List of publications
  + 2 letters of recommendation
  + Proof of command of English language

**PART C**

**Additional requirements to be fulfilled by the post-doc:**

* Max. age of 35 years
* PhD degree not older than 5 years
* Very good command of the English language
* Strong ability to work independently and in a team