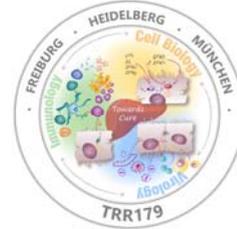




HEIDELBERG
FACULTY OF
MEDICINE



MOLECULAR VIROLOGY
HEIDELBERG



OPEN POSITION for a PhD student

Project: Dynamics of hepatitis B virus morphogenesis and its alterations during persistent infection

Research area: Virology, biochemistry, structural biology

Infections with the human hepatitis B virus (HBV) are a health burden of global importance with at least 257 million people being chronic virus carriers. About 890,000 individuals die each year due to HBV-driven liver disease, including liver cirrhosis and hepatocellular carcinoma. HBV belongs to the large and ancient family *Hepadnaviridae*, members of which are found in all bony vertebrate classes (1). These viruses coevolved in intimate association with their hosts over several hundred million years, which explains their successfulness in establishing persistent infections.

The HB virion, termed Dane particle, appears as double-shelled spherical particle. Its central structure is an icosahedral capsid that is built from core protein and harbors a reverse transcribed DNA genome together with the viral polymerase P. This nucleocapsid is surrounded by a lipid envelope into which the surface glycoproteins are embedded.

We regard the HBV Dane particle as an effective nanomachine in which several concentric shells are highly interconnected, and changes in any zone might trigger secondary changes in the neighboring zone (2). Based on our previous work, we propose that HBV particles are subject to defined ultrastructural dynamics with a series of thermodynamically driven, temporally and spatially regulated events during particle morphogenesis (3,4). In this project, we aim at a detailed characterization of nucleocapsids containing the authentic replication complex by biochemical and structural biology methods. Nucleocapsids will be arrested in different maturation states and subjected to structure determination by cryo-electron microscopy. Moreover, we will perform thorough biochemical interaction studies to quantitatively describe the binding kinetics of nucleocapsids to the HBV surface glycoproteins. Nuclear magnetic resonance techniques will be applied to resolve the structure of surface protein segments bound to nucleocapsids. The insight gained into the structural details and biochemical parameters of the interactions determining nucleocapsid envelopment will allow us the quantitative modelling of the morphogenetic pathways with respect to their variability during chronic infection.

The candidate holds an MSc (or equivalent degree) preferentially in biotechnology or biology with a focus on biochemistry, cell biology or molecular biology. Profound knowledge in cell biology and practical experience with biochemical methods are prerequisite. Experience in working with viruses and cell culture is highly desired. Practice in electron microscopy and liquid chromatography on an ÄKTA system is a plus, but not essential. Strong motivation and enthusiasm for research as well as high accuracy and reliability are required. Excellent communication and team skills are mandatory.

References:

1. Lauber C, Seitz S, et al. 2017. Deciphering the origin and evolution of hepatitis B viruses by means of a family of non-enveloped fish viruses. *Cell Host Microbe* 22(3):387–99
2. Seitz S, et al. 2020. The hepatitis B virus envelope proteins: Molecular gymnastics throughout the viral life cycle. *Annu Rev Virol*. Online ahead of print.
3. Seitz S, et al. 2007. Cryo-electron microscopy of hepatitis B virions reveals variability in envelope capsid interactions. *EMBO J*. 26(18):4160–67
4. Seitz S, et al. 2016. A slow maturation process renders hepatitis B virus infectious. *Cell Host Microbe* 20(1):25–35

The position is open immediately and secured for three years; an extension is possible.

Applications must comprise:

- 1) a detailed CV, including an abstract of the master's thesis and copies of the graded certificates
- 2) a description of research experiences including applied methodologies
- 3) a list of three references with complete contact details
- 4) a short (~one page) letter focusing on the candidate's scientific interests and motivation

Applications should be sent by email no later than September 15, 2020 to **Stefan Seitz:**
stefan.seitz@med.uni-heidelberg.de

Further information about our research can be found at:

<https://www.klinikum.uni-heidelberg.de/zentrum-fuer-infektiologie/molecular-virology>

This project is funded by the German Research Foundation (DFG) in the frame of TRR179 (www.trr179.de). The TRR179 is an interdisciplinary research consortium and has a highly active Graduate School offering multiple training possibilities. Payment and social benefits are in accordance with regulations of the German TV-L (E13, 65%).

Heidelberg is a very active and lively centre for research in the field of life sciences and medical research (http://www.uni-heidelberg.de/index_e.html). It is one of the leading centres in virus research, cancer research, systems biology and imaging techniques in Europe. The campus provides unique opportunities for basic research in life sciences and is well connected to several institutions such as the German Cancer Research Centre (DKFZ), the European Molecular Biology Laboratory (EMBL) and the Max-Planck Institute for Medical Research.