Open PhD student / postdoc positions

Call: January 22nd, 2024

The Department of Infectious Diseases, Virology at Heidelberg University offers positions for **PhD students** and **postdocs at all career levels** to investigate **assembly, maturation** and **post-entry events in retrovirus replication.** Research will be conducted in the groups of **Hans-Georg Kräusslich** and **Barbara Müller** within the DFG funded collaborative research center 1129 (https://www.sfb1129.de/).

Our groups study multiple aspects of HIV-1 assembly and maturation as well as the fascinating events occurring after virus entry in the early phase of the retroviral replication cycle. Virus assembly occurs at the producer cell plasma membrane in specialized membrane microdomains and the inner virion organization is dramatically altered by proteolytic maturation concomitant with and after particle release. We are studying structural aspects of particle formation with a particular focus on protease activation and subsequent changes (Schimer et al., 2015; Hanne et al., 2016; Qu et al. 2021). After the mature viral capsid has entered the cytosol of a newly infected cell, retroviruses convert their RNA genome into dsDNA, transport it into the nucleus and integrate it into host chromatin after release from the viral capsid (uncoating). The role of the capsid in these steps recently underwent a major paradigm shift: capsid is no longer seen as a passive delivery container. Instead, it is now recognized as a key organizer of post-entry events that is instrumental for escape of HIV-1 from recognition by the innate immune system and serves as an attractive target for antiviral therapy. Recent data from us and other groups revealed that - contrary to text book knowledge - the cone-shaped capsid of HIV-1 can enter intact nuclei through nuclear pores, and indicate involvement of the capsid in nuclear events resulting in either productive or latent infection.

The complex assembly, maturation and post-entry events escape analysis by traditional bulk approaches. We therefore use advanced microscopy to visualize events at the single particle level with high temporal or spatial resolution. We will further develop our established systems to visualize HIV-1 DNA (Müller *et al.*, eLife 2021) and capsid (Schifferdecker *et al.,* MBio 2022), and apply them to investigate host interactions and structural changes using live imaging, STED and MINFLUX nanoscopy as well as correlative light and electron microscopy and cryo electron microscopy (Zila *et al.*, Cell 2021). These studies will be complemented with cell biological approaches to discover and characterize relevant host dependency and restriction factors, and will involve application of chemical biology tools (Schimer et al., 2015) and capsid-targeted pharmacological interventions.

We offer several exciting and highly interdisciplinary research topics with biomedical relevance in an interactive and international scientific environment, including collaborations with national and international partners, at an internationally competitive level. The projects are part of SFB1129 and involve close interactions with groups from different disciplines within the research center. The lab is located in the Center for Integrative Infectious Disease Research (www.ciid-heidelberg.de) which also houses the unique state-of-the-art IDIP imaging platform (www.idip-heidelberg.org). Successful PhD student candidates will be enrolled in the HBIGS International Graduate School (http://www.hbigs.uni-heidelberg.de/) to benefit from the excellent scientific training of this program. Postdocs will be eligible for structured career support

by the HeiTracks program of Heidelberg University (https://www.uni-heidelberg.de/en/research/support-for-early-career-researchers/career-support).

Applicants should have a master's or doctoral degree in a relevant discipline (molecular and cell biology, biochemistry, biophysics or molecular medicine). They should be interested in addressing basic virological questions using a variety of methods, with a strong focus on imaging techniques and image analysis. A good background in standard molecular biological methods is expected. Ideally, candidates have already experience in fluorescence microscopy and image analysis, together with a background in cell biology, biochemistry or biophysics.

We are looking forward to meet curious and motivated applicants who are really excited about science. You should like to work independently, but also enjoy to interact, discuss and collaborate with researchers from different disciplines and nations.

The positions are open immediately. Please send your application (CV, academic transcript, motivation letter and reference letters or contact details of two referees) until **February 22nd, 2024** as a **single** pdf file to **Propaedeutik.Lehre@med.uni-heidelberg.de**

PhD student candidates can also apply directly through the HBIGS platform **http://www.hbigs.uni-heidelberg.de/**

Relevant publications:

Hanne et al. (2016). Stimulated Emission Depletion Nanoscopy Reveals Time-Course of Human Immunodeficiency Virus Proteolytic Maturation. ACS nano 10, 8215-8222.

Müller *et al.* (2021) HIV-1 uncoating by release of viral cDNA from capsid-like structures in the nucleus of infected cells. *eLife* 10, e64776 doi: 10.7554/eLife.64776

Qu et al. (2021) Maturation of the matrix and viral membrane of HIV-1. Science, Vol. 373, Issue 6555, pp. 700-704. DOI: 10.1126/science.abe6821

Schifferdecker *et al.* (2022) Direct capsid labeling of infectious HIV-1 by genetic code expansion allows detection of largely complete nuclear capsids and suggests nuclear entry of HIV-1 complexes via common routes. mBio. 2022 Oct 26;13(5):e0195922. doi: 10.1128/mbio.01959-22

Schimer et al. (2015). Triggering HIV polyprotein processing by light using rapid photodegradation of a tight-binding protease inhibitor. Nature communications 6, 6461. doi: 10.1038/ncomms7461.

Zila *et al.* (2021) Cone-shaped HIV-1 capsids are transported through intact nuclear pores. *Cell* 184, 1032-1046.e18 doi: 10.1016/j.cell.2021.01.025

Bejarano *et al.* (2019) HIV-1 nuclear import in macrophages is regulated by CPSF6-capsid interactions at the Nuclear Pore Complex. *Elife* 8, e41800 doi: 10.7554/eLife.41800

Reviews:

Müller TG, Zila V, Müller B, Kräusslich HG (2022) Nuclear Capsid Uncoating and Reverse Transcription of HIV-1. Annu Rev Virol. 2022 Sep 29;9(1):261-284. doi: 10.1146/annurev-virology-020922-110929.

Müller *et al.* (2019) A Spotlight on Viruses - Application of Click Chemistry to Visualize Virus-Cell Interactions. *Molecules*; 24(3), E481. doi: 10.3390/molecules24030481