Open PhD student / postdoc positions

The Department of Infectious Diseases, Virology at the University Hospital Heidelberg offers positions for **PhD students** and **postdocs** to investigate **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 the fascinating events occurring in the early phase of the retroviral replication cycle. After entering the cytosol of the host 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. Our ongoing research aims at defining the mechanistic details of these processes that will be further translated into pre-clinical models.

Our recent data 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 (Zila *et al.*, Cell 2021 and PLoS Pathogens 2021). In contrast, murine leukemia virus requires breakdown of the nuclear envelope for its genome to integrate into host chromatin. Since this requires a balance between shielding the viral genome from innate immune sensing and exposing the dsDNA at the right time and place for integration, MLV needs to tightly coordinate viral uncoating with cell division. By characterizing post entry processes of HIV-1 and MLV in different cell types we want to define crucial common pathways as well as key differences.

The complex 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., BioRxiv), 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, immunological and proteomics approaches to discover and characterize relevant host dependency and restriction factors, and will include capsid-targeted pharmacological interventions affecting intracellular trafficking, host factor interactions and capsid integrity.

We offer an exciting and highly interdisciplinary research topic 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 students who are truly excited about science. You should enjoy working independently, but also love 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) as a **single** pdf file to **martina.nierle@med.uni-heidelberg.de.**

Relevant recent publications:

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

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

Schifferdecker *et al.* 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. BioRxiv.
https://www.biorxiv.org/content/10.1101/2021.09.14.460218v2

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:

Zila V, Müller TG, Müller B, Kräusslich HG (2021) HIV-1 capsid is the key orchestrator of early viral replication. PLoS Pathog 17(12):e1010109. doi: 10.1371/journal.ppat.1010109.

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