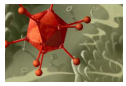
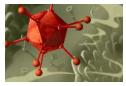


## Fraefel / Eichwald

| New antivirals targeting elephant endotheliotropic herpes viruses | |
|---|---|
| **Short description** | Elephant endotheliotropic herpes viruses (EEHVs) cause highly acute and often lethal elephant hemorrhagic disease (EHD) in young animals that die within hours after the onset of clinical illness due to organ failure and extensive hemorrhages. Unfortunately, antivirals such as ganciclovir, famciclovir, and aciclovir resulted ineffective for EHD treatment. This research project aims to evaluate new antiviral compounds to treat EHD. For this, a library of 990 nucleoside analogs will be tested in cell culture using a recombinant herpes simplex virus-1 (HSV-1) system encoding for EEHV thymidine kinase (TK) and herpesvirus-conserved protein kinase (CPK). |
| **Keywords** | elephant endotheliotropic herpes virus, antivirals, protein kinase, thymidine kinase |
| **Supervisor** | Prof. Dr. Cornel Fraefel/Dr. Catherine Eichwald |
| **Institute / Department** | Institute of Virology, University of Zurich |
| **E-mail** | cornel.fraefel@uzh.ch/ceichwald@vetvir.uzh.ch |
| **Phone** | +41 44 635 87 11 |
| **Requirements** | A highly motivated student with an interest in virology and molecular biology. |
| **Web links** | https://www.vetvir.uzh.ch/en.html |

## Metzner

| **Short description** (100 words) | **As part of its life cycle, HIV-1 integrates its genome into the host genome. This is an error-prone process that results in many replication incompetent proviruses harboring large deletions. It is unknown which cellular factors are involved in this process. We aim to identify these host restriction factors using our HIV-1 model system (PMID: 33282555) and human genome-scale CRISPR/Cas9 screenings.**<br><br>**Techniques: CRISPR-Cas9 screenings, FACS, NGS, cell culture, molecular biology** |
|---|---|
| **Keywords** | virology |
| **Supervisor** | Prof. Karin Metzner |
| **Institute / Department** | Department of Infectious Diseases and Hospital Epidemiology |
| **E-mail** | Karin.Metzner@usz.ch |
| **Phone** | +41 44 255 30 29 |
| **Requirements** | Commitment, motivation and interest in virology / molecular biology |
| **Web links** | https://www.usz.ch/en/clinic/infectiology/research/research-group-karin-metzner/ |

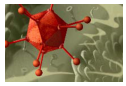


## Münz

| Epstein Barr virus (EBV) transcription and protein expression in autophagy-knockout lymphoblastoid cell lines (LCLs) | |
|---|---|
| **Short description** | The Epstein Barr Virus (EBV) is the underlying cause of several malignancies in humans and persists primarily in B cells, using several different latency programs as well as lytic reactivation. In B cells, EBV protein expression and the intracellular degradation pathway macroautophagy are closely connected and can regulate each other (De Leo, A., *et al., Cell Death Dis.* (2015)).<br>In order to further investigate the connection between different AuTophaGy (ATG)-related proteins and viral protein expression in EBV-transformed B cells (lymphoblastoid cell lines = LCLs), several knockout LCLs have been established in out lab.<br><br>The aim of the proposed masters project will be to characterize latent and lytic viral replication in these cell lines, using a combination of cell culture techniques, RT-qPCR, Western Blot, Fluorescent Microscopy and Flow Cytometry. |
| **Keywords** | Epstein Barr virus, Autophagy-related proteins, lymphoblastoid cell lines |
| **Supervisor** | Prof. Dr. Christian Münz |
| **Institute / Department** | Viral Immunobiology, Institute of Experimental Immunology |
| **E-mail** | christian.muenz@uzh.ch |
| **Phone** | +41 44 635 37 16 |
| **Requirements** | High motivation and solid understanding in virology and immunology. Prior experience in molecular biology techniques (qPCR, Western Blot, Immunofluorescence) is an advantage. Good communication skills and fluency in English. |
| **Web links** | https://www.immunology.uzh.ch/en/researchunit/immunobiology/research.html |

| Characterization of EBV specific T cell clones | |
|---|---|
| **Short description** | The global seroprevalence of the Epstein-Barr virus (EBV) is over90%. It is the causative agent of infectious mononucleosis, and it is estimated that 1.8% of cancer deaths are due to EBV-induced malignancies such as Burkitt's lymphoma or nasopharyngeal carcinoma. Although EBV was discovered in 1964, little is known about the cells that initiate the immune response, which is crucial for developing an effective vaccine.<br>Additionally, methods to detect EBV-infected cells are primarily indirect; for instance, epitope-specific T cell clones and direct methods using immunoglobulins, such as T cell receptor (TCR) -like antibodies, are currently under investigation; however, sufficient target specificity has never been achieved.<br>This project will aim to characterize the specificity and sensitivity of EBV-specific T cell clones(TCC) and compare these cells with EBV epitope-specific chimeric antigen receptor (CAR) T cells. EBV-specific T cells have already been sorted and tested for their reactivity. To characterize these TCCs, a combination of cell culture techniques, peptide titration, and alanine scanning will be performed. To compare TCC with virally transduced T cells, co-culture ELISAs, and cytotoxicity assays are used. |
| **Keywords** | Cell culture, flow cytometry, ELISA, ELIspot,lentiviral transduction, virus production |
| **Supervisor** | Prof. Christian Münz |
| **Institute / Department** | Institute of Experimental Immunology |
| **E-mail** | muenzc@immunology.uzh.ch and schmid@immunology.uzh.ch |
| **Phone** | |
| **Requirements** | |
| **Web links** | https://www.immunology.uzh.ch/en/researchunit/immunobiology.html |

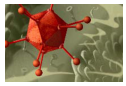
## Stertz



| Title of the project | |
|---|---|
| **Short description** | Influenza viruses are of high medical concern in humans and can cause devastating economic problems for the poultry and pig livestock industries. Currently, we have vaccines and antiviral drugs available, but both come with severe limitations. Vaccines cannot protect against novel strains of influenza virus and must be continually updated. In particular, novel influenza viruses of zoonotic origin would not be covered by currently available vaccine formulations. Furthermore, we experience increasing problems with drug-resistance of influenza viruses, and new antivirals with lower chances of resistance developing are urgently sought.<br>In our research, we study entry of influenza viruses into their host cells, and the virus-host interactions required during this process. This is the first key stage of infection that all influenza viruses must accomplish, and is therefore an excellent target for antiviral drugs. Moreover, differential host cell requirements for influenza viruses of different host origin can impact the zoonotic potential of viruses and are thus important to understand.<br>Methodologies employed in our lab to study influenza virus entry include RNAi screening, proteomic approaches, transcriptomics and state-of-the-art microscopy. |
| **Keywords** | Influenza virus, virus entry, virus-host interactions |
| **Supervisor** | Prof. Dr. Silke Stertz |
| **Institute / Department** | Institute of Medical Virology |
| **E-mail** | Stertz.silke@virology.uzh.ch |
| **Phone** | +41 44 634 2899 |
| **Requirements** | Solid background in virology (BIO615, Blockkurse) |
| **Web links** | https://www.virology.uzh.ch/en/research/Group-Stertz.html |

## Greber

| Title of the project | |
|---|---|
| **Short description** | **Co-infection of human airway cells with rhinovirus and coronavirus**<br><br>**Context**<br>Viruses are abundant and infect all organisms. Frequently, they are transmitted between individuals through aerosols, droplets or smear contact. Yet, not all individuals exposed to virus are infected equally. To address infection variability, we explore if viral infection protects cells against infection by unrelated viruses. The project examines how two of the most abundant human respiratory pathogens, rhinovirus (RV) and coronavirus (CoV) co-infect human airway explant cell cultures. These cultures harbor primary epithelial cells, basal cells, mucus secretion cells and immune cells, and represent an intermediate model system between cell cultures and whole organisms.<br><br>**Procedures**<br>Upon RV and CoV co-inoculation, virus released to the apical medium of the polarized cell cultures is assessed by quantitative assays in virus-specific indicator cell lines. Viral replication is determined by multiplexed quantitative reverse transcription PCR in the extracellular medium. Single cell resolved viral replication assays with image-based RNA-fluorescence in situ hybridization assess the impact of interferon on CoV infection as triggered by co-infecting RV, as well as inhibitors to suppress IFN signaling, such as Ruxolitin blocking the JAK/STAT pathway [1]. It employs chemical inhibitors specific for RV and CoV to assess the nature of viral interference in the coinfection settings. Inhibitors include agents blocking RV, such as the PI-4-kinase 3-beta inhibitor PIK93 [2], or Remdesivir, Methylene blue, Mycophenolic acid and Nirmatrelvir (Paxlovid) blocking CoV replication [3, 4].<br><br>**Importance** |



| | |
|---|---|
| | A better understanding of the interplay between different viral agents is crucial because viruses co-circulate and co-infect individuals. This can exacerbate disease or attenuate infection, but underlying mechanisms have been largely unknown. A scalable coinfection system with rhinoviruses and coronaviruses might facilitate prediction of coinfection outcome and contribute to unravel infection variability.<br><br>**Literature**<br>(1) Hu, X.; Li, J.; Fu, M.; Zhao, X.; Wang, W. The JAK/STAT signaling pathway: from bench to clinic. *Signal Transduct Target Ther* **2021**, *6* (1), 402. DOI: 10.1038/s41392-021-00791-1<br>(2) Roulin, P. S.; Murer, L.; Greber, U. F. A single point mutation in the rhinovirus 2B protein reduces the requirement for phosphatidylinositol 4-kinase class 3beta in viral replication. *J Virol* **2018**. DOI: 10.1128/JVI.01462-18.<br>(3) Murer, L.; Volle, R.; Andriasyan, V.; Petkidis, A.; Gomez-Gonzalez, A.; Yang, L.; Meili, N.; Suomalainen, M.; Bauer, M.; Policarpo Sequeira, D.; et al. Identification of broad anti-coronavirus chemical agents for repurposing against SARS-CoV-2 and variants of concern. *Curr Res Virol Sci* **2022**, *3*, 100019. DOI: 10.1016/j.crviro.2022.100019.<br>(4) Liu, J.; Pan, X.; Zhang, S.; Li, M.; Ma, K.; Fan, C.; Lv, Y.; Guan, X.; Yang, Y.; Ye, X.; et al. Efficacy and safety of Paxlovid in severe adult patients with SARS-Cov-2 infection: a multicenter randomized controlled study. *Lancet Reg Health West Pac* **2023**, 100694. DOI: 10.1016/j.lanwpc.2023.100694 |
| **Keywords** | Human airway epithelial explants, rhinovirus, coronavirus, co-infection, innate immunity |
| **Supervisor** | Dr. Romain Volle (Greber lab, UZH) |
| **Institute / Department** | Department of Molecular Life Sciences |
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| **Requirements** | Bsc degree in Life Sciences from UZH (or equivalent) |
| **Web links** | https://www.mls.uzh.ch/en/research/greber |