

## Meeting report of the 22nd workshop "Cell Biology of Viral Infections" of the German Society for Virology (GfV) in Schöntal

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The „Cell Biology of Viral Infections“ Workshop of the German Society of Virology (GfV) was held from November 4–6<sup>th</sup> for its 22<sup>nd</sup> edition. It is already 10 years ago that the meeting moved to the scenic Schöntal and its monastery, in Baden-Württemberg. This year's meeting attracted 36 participants, including 21 undergraduate or PhD students, 6 postdocs or senior scientists and 9 PIs. For the second time, the meeting was organized by Gabrielle Vieyres (University of Lübeck) and Christian Sieben (Helmholtz-Centre for Infection Research).

The spotlight of this year's meeting was set on "membranes" with four invited keynote speakers from Germany, Switzerland, Sweden and the Netherlands and a full session devoted to this topic. The program included 3 additional sessions, following viral infections through entry, viral replication and morphogenesis as well as host-virus interactions.

Prof. Montserrat Bárcena opened the workshop with the first keynote lecture on "Intracellular makeover: viral replication organelles". Dr. Bárcena is an assistant professor at the Leiden University Medical Center where she uses classic and novel electron microscopy approaches to study the replication of positive-strand RNA viruses. She gave an overview of the intracellular membrane reshuffling occurring during viral infections, presenting similarities and differences between her main working horses, including poliovirus and coronaviruses. She also guided us through a deep dive into the structure of SARS-CoV-2 replication organelles, with the structural elucidation and molecular identification of the crown-shaped pores connecting the virus-induced double-membrane vesicles to the cytosol. The following session of the meeting was then devoted to early events in virus infection and included presentations on virus receptor interactions and their inhibition, on the routes of virus internalization and the barrier function of mucus in influenza A virus (IAV) infection.

Prof. Francesca Bottanelli from the Free University of Berlin kicked off the second day of the meeting with a lecture on "Unravelling the inner secrets of cells with gene editing and live-cell super-resolution microscopy". Prof. Bottanelli illuminated the intracellular vesicular trafficking along the endocytic and secretory pathways using live cell microscopy and a collection of CRISPR-Cas9-based fluorescent knock-in cell lines. Her presentation underscored the organization of cellular membranes

in microdomains and shook up textbook knowledge of vesicular transport by presenting clathrin vesicles carried on larger tubular structures. Finally, Prof. Bottanelli shared her newest findings on the membrane organization of the immunological synapse during T-cell activation.

The following session on virus-host Interactions gave the stage for talks assessing the coinfection between emerging flaviviruses, the antiviral activity of cyclosporin A against Nipah virus, or the relevance of the phosphorylation of the arenavirus matrix protein. A presentation on a host-virus binding screening platform set the stage for the use of reductionist synthetic membrane models in studying infection. Another contribution highlighted the potential of confocal interferometric scattering microscopy (C-iSCAT) to track viral infections in label-free conditions.

The third keynote lecture was given by Dr. Markku Hakala, from the University of Geneva. His presentation tackled "the interplay between protein scaffolds and membrane domains at the plasma membrane and endosomes". Dr. Hakala presented his recent work on the ESCRT protein HRS during the formation of intraluminal vesicles in multivesicular bodies. By presenting intriguing biophysical in vitro and cell culture data, Dr. Hakala showed that HRS can form dense multilayer condensates, which supported by clathrin can cluster cargo molecules and aid vesicle formation. Dr. Hakala furthermore highlighted his role in a recently published study showing the organization of membrane domains retained in isolated yeast eisosome filaments.

The following session focused on membranes and further brought them into the context of viral infection with new insights on the role of ceramides in the formation of the coronaviral replication organelle or of lipid mediators in flavivirus replication. Strikingly, the IAV hemagglutinin was shown in cryo-electron microscopy to remodel and zipper intracellular membranes into a so far unrecognized compartment that likely participates in the bundling of the viral ribonucleoproteins for accurate genome packaging.

To round off this exciting day, Prof. Erdinc Sezgin, from the SciLifeLab / Karolinska Institute in Sweden, reported on "Synthetic biology tools to study host-pathogen interactions".

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Prof Sezgin's lab engineers biomimetic systems with reduced complexity such as giant unilamellar vesicles or functionalized bead-supported membrane bilayers. He presented the usefulness of these models to unravel membrane properties but also to study virus-host interactions, for instance by incorporating the SARS-CoV-2 receptor ACE2 in the system and screening for inhibitors of virus binding. The final session was devoted to virus replication and morphogenesis. Unbiased proteomic approaches showed promise in giving new insights into the replication machinery of pestiviruses or in preventing the formation of ebolavirus replication organelle. A presented cryo-electron tomography study also shed light onto the peculiar poxvirus envelopment process.

As usual, the workshop featured several hot topics and cutting-edge techniques in the field of cell biology that currently drive forward our understanding of host-virus interactions. This included the fields of synthetic membrane models, the topic of membrane microdomains and membrane remodeling but also of molecular condensates. The latter was underscored by several speakers including Yannick Jensen, PhD student from the Leibniz Institute of Virology in Hamburg, who revealed how the phosphoprotein pp150 drives liquid-liquid phase separation and tegument formation during human cytomegalovirus assembly. In recognition of this insightful talk, the attendees awarded Yannick Jensen the prize for the best oral presentation (see photo). In terms of methods, the meeting highlighted the usefulness of proximity labeling to unravel the protein machinery involved in viral replication and morphogenesis, with examples on ebolavirus, bovine viral diarrhea virus and Lassa virus. It stressed the potential of gene editing to fluorescent-



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ly tag endogenous proteins with simplified protocols. It also featured striking examples of cryo-electron microscopy studies and their impact on our understanding of multiple aspects of the viral replication cycles, from the entry and morphogenesis of influenza A virus to the replication organelles of plus-strand RNA viruses or the assembly of the large poxviruses. Finally, the iSCAT technology opened new perspectives to investigate virus infections with minimal perturbations.

We are grateful to all participants of this 22<sup>nd</sup> edition for sharing their exciting research, participating in the lively discussions and contributing to the friendly atmosphere of the meeting. Our gratitude also goes to our four guest speakers and to our faithful sponsors, the German Society for Virology (GfV), the German Society for Cell Biology (DGZ), and the company ReBlikon GmbH, whose continued financial and administrative support over the years make this meeting durable. The 22<sup>nd</sup> workshop "Cell Biology of Viral Infection" of the German Society of Virology (GfV) will take place from October 8<sup>th</sup> to 10<sup>th</sup> 2025, again at Schöntal Monastery. For updates, please visit our website at <https://cellviro.g-f-v.org/>.

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