

Virus Species Determinants and Transmission

Meeting report of the 1st GfV Workshop on 'One Health and Zoonotic Viruses' in Goslar, Germany, 27-29 July 2022

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Group photo with 2022 workshop participants at the Hessenkopf Convention Center, Goslar, Germany

Aiming to unite young scientists and experts working on *One Health and Zoonotic Viruses*, as well as to foster interdisciplinary interactions and cross-career collaborations, the newly established working group on *One Health and Zoonotic Viruses* within the German Society for Virology (GfV), organized the 1st workshop on the central theme '*Virus Species Determinants and Transmission*' from 27-29 July 2022 at Hessenkopf Convention Center, Goslar. The workshop attracted 34 participants from several fields, including virologists, infectiologists, immunologists,

clinicians and veterinarians, to exchange their latest findings on viral zoonoses. The workshop commenced with a welcome note by the workshop chairs, Gisa Gerold (University of Veterinary Medicine Hanover Foundation) and Yvonne Börgeling (University of Münster), directly followed by the first keynote lecture by Ana Fernandez-Sesma from Icahn School of Medicine at Mount Sinai, USA, on the modulation of innate immunity by RNA viruses in primary human systems. In her presentation, she discussed the mechanisms by which arboviruses like Dengue

virus and Chikungunya virus counteract the innate immune response, emphasizing the various ways these viruses interfere with the cGAS - STING pathway. In addition, she introduced dendritic cells and human tonsil explants as models to overcome the problem of immune deficiency of commonly used cell lines. During a later career development session involving all keynote speakers and participants, she answered many questions from the younger participants, highlighting particularly the boost in professional development when working in another country or when switching research focus after the PhD.



Anja vom Hemdt (Center) - the student winner of the Best Oral Presentation Prize, along with the Workshop Chairs Yvonne Börgeling (Left) and Gisa Gerold (Right)

The first session of the workshop on *Host Restriction and Dependency Factors* included talks on viral factors facilitating entry into host cells, discussing cases of bat coronaviruses with spike proteins bearing specific single amino acid exchanges that enhance entry through human ACE2, and GlcCer glycolipids incorporated into the phenuivirus envelope favoring binding to host cells. The session also included talks on host factors promoting intracellular virus replication, quoting cases of endoplasmic reticulum import proteins favoring Zika virus replication, and the proviral roles of fatty acid elongases and desaturases in Dengue virus infection. Further talks highlighted host factors restricting infection or intracellular replication, like the RNAi response against insect-specific alphaviruses and USP10 inhibiting stress granule formation upon Chikungunya virus Infection. Emphasis was also

laid on highlighting molecular probes, quoting examples of hepatitis C virus NS3/4A protease to identify key host factors, and proximity labeling mass spectrometry to map early Chikungunya virus - host cell interactions. The session concluded with a discussion on designing therapeutic interventions that target potential proviral factors or exploit promising antiviral factors to counteract virus infection.

The last session of the first day ended with a special Q&A session on *Science Communication through New Media* hosted by Björn Meyer from Otto-von-Guericke-University Magdeburg, Germany. Björn shared his experience on communicating science via twitter and encouraged the workshop participants to take on the challenge of communicating latest research in a concise and understandable way. This induced a lively debate about the pros and cons of exposing oneself as a scientist on social media. The concerns of many participants were weighted against the career possibilities that can come with being visible as a professional online as well as the social responsibility to act against misinformation.

The second day commenced with the keynote lecture on *Hantavirus Entry into Host Cells and Molecular Features of the Gn/Gc Spikes* by Nicole Tischler, Fundación Ciencia and Vida, Santiago, Chile, highlighting the structural features of the hantavirus entry machinery and its high degree of flexibility and resistance to high temperatures. The second session of the workshop on *Species Tropism: Reservoirs and Adaptation* focused on the molecular determinants of adaptation and pathogenicity, discussing examples of NS1 mutations facilitating adaptation of seal influenza viruses to mammalian and avian cells, polymerase proteins as pathogenicity determinants of avian influenza viruses in infected poultry, and polymerase compatibility as a molecular determinant of reassortment between human and Eurasian avian-like swine influenza viruses. The session also had talks on zoonotic hantaviruses and human noroviruses with similar context, as well on the multimammate rat *Mastomys natalensis* with respect to Arenavirus persistence

and host species barriers restricting Lassa viruses, ending with talks on zoonotic spillovers of coronaviruses and replication-mediated spread of delta-like agents. Overall, the session appreciated the broad, multifactorial determinants of adaptation, evolution, persistence and host tropism of diverse viruses with high zoonotic potential.

The second session was followed by a guided tour of the beautiful UNESCO World Heritage city of Goslar, where the workshop participants got to know the medieval architecture and the rich history of the area. The third session of the workshop on *Species Tropism: Vectored and Insect-Specific Viruses* highlighted key interplay between virus pathogenesis and host processes, like the Toscana virus NS-controlled activation of an extrinsic apoptotic pathway in human cells, and the comparative characterization of Bourbon viruses from ticks and humans, in terms of their replication capacity and interferon sensitivity. The session was quickly oriented to discuss mosquito-borne viruses: Of special mention, student talks on the molecular roles of T-cell immunoglobulin and mucin domain 1 in cross-species transmission of alphaviruses, and on the recognition of Cap 1 and Cap 0 flaviviruses in mosquito cells, provided both immunology and cell-biology perspectives to the session theme. The day ended with the third keynote lecture by Björn Meyer on the *Adaptation Potential of SARS-CoV-2 Spike*, stitching important literature and recent interesting results from his own research group, on the mutational hotspots and structural flexibility of SARS-CoV-2 spike, mediating faster evolution of new variants, and its overall implications over immune-escape, rapid transmission, Ab-neutralizing activity, and vaccine efficacy.

The last day of the workshop commenced with the final keynote lecture by Stefan Pöhlmann from the German Primate Center, Germany, on *SARS-CoV-2 Entry into Cells and its Inhibition*, highlighting the key scientific discoveries of his research group since 2020, including the identification of human ACE2 as an entry receptor for SARS-COV-2, and the serine protease TMPRSS2 for spike priming. A

major focus of this keynote lecture was on evaluating diverse entry inhibitors, including TMPRSS2 inhibitor Camostat and convalescent sera from infected patients as potential therapeutics for SARS-CoV-2, extending to present-day omicron subvariants. The last session of the workshop on *Detection, Prevention and Treatment* included talks on interesting modern platforms favoring detection and safety-evaluation, for instance the serological assays for detection of orthonairovirus infections in ruminants, and a Measles vaccine platform as a safety standard for vaccine development against highly pathogenic *Francisella tularensis*. Presentations on advanced therapeutics, exploiting the CRISPR Cas13 system and IFN α subtype diversity for treating respiratory zoonotic viruses, promising antiviral approaches were discussed. With viruses escaping selection pressure imposed by therapeutics, the workshop rightly included discussions on spike variants escaping the selection pressure imposed by single and combined SARS-CoV-2 neutralizing monoclonal antibodies. The session concluded with a unanimous acknowledgement of the diverse molecular-biology based modern approaches that enable effective management of zoonotic infection outbreaks.

Anja vom Hemdt, a PhD student at the University of Bonn Medical Center, bagged the *Best Oral Presentation Prize* with a cash award of €100 from the GfV and a participation voucher for the 2023 One Health workshop, having received the maximum votes from student participants. The workshop concluded with formal closing remarks by Gisa Gerold and Yvonne Börgeling, thanking all the participants for their active interaction, and the keynote speakers for their constructive comments, across all sessions of the workshop. The workshop chairs also acknowledge the sponsors German Society for Virology and Joachim Herz Foundation for their financial support. The participants look forward to the 2nd workshop on *One Health and Zoonotic Viruses* planned to be organized in fall 2023, focused on yet-another interesting theme.