Third
N-RENNT Symposium
on Neuroinfectiology

February 15th and 16th, 2016
University of Veterinary Medicine
Hannover | Germany
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N-RENNT is a new research network that started in October 2013 and is funded by the Ministry of Science and Culture of Lower Saxony with 5.4 million €. N-RENNT brings together a unique consortium of leading experts and institutions, to join forces with an unparalleled expertise and knowledge in the integrated fields of neuroscience and infection medicine. Medical and veterinary research institutions of Lower Saxony are linked together in a network for an ‘One Health – One Medicine’ approach. This will establish a highly skilled, globally unique and versatile expertise center that will address challenges posed by present and emerging infectious agents that target the central nervous system and cause largely unresolved neurological disorders.

N-RENNT comprises 17 principal investigators from universities and other academic institutions of the three cities Hannover, Göttingen and Braunschweig. At the heart of N-RENNT will be the new Research Center for Emerging Infections and Zoonoses (RIZ) at the University of Veterinary Medicine in Hannover, which was opened in 2014. Prof. Albert Osterhaus, an internationally renowned virologist, became the Founding Director of the RIZ. The main mission of N-RENNT is to establish a neuroinfectiology-network in Lower Saxony as an internationally renowned center of excellence in this rapidly emerging interdisciplinary field. Besides creating a highly active network, scientific training of graduate students is a major task of N-RENNT.

Wolfgang Baumgartner (speaker) & Wolfgang Löscher (co-speaker)
University of Veterinary Medicine Hannover, Foundation
Conference & contact

Conference venue

Department of Pathology
Lecture hall
The University of Veterinary Medicine Hannover, Foundation (TiHo)
Bünteweg 17
30559 Hannover (Germany)

Date
February 15th - February 16th, 2016

Registration
Please register for this event
www.tiho-hannover.de/nrennt
E-Mail: tina.basler@tiho-hannover.de
No participation fee.

Conference language
The official language of the meeting is English.

Meals
Lunches will be provided.

Wifi
You’ll find your personal access key on your name badge
General informations

Accommodation

**Hotel Bischofshol**
Bemeroder Straße 2
30559 Hannover
+49 511/953900
bischofshol@t-online.de
www.hotel-bischofshol.de
Room rate (single): 75 € including breakfast

Social program

The dinner for speakers and registered participants will take place on Monday 15th, 2016 at the restaurant „Gasthaus Meyer“. The restaurant ist located at the Zoo Hannover. We will meet at 18:00h!

Find the way:

Adenauerallee 3
30175 Hannover
+49 511/856266200
The University of Veterinary Medicine Hannover, Foundation (TiHo) stands for long-standing competence in the field of veterinary medicine. It is an eminent scientific institution connecting modern science with university tradition. Since its founding in 1778 as the Roß-Arzney-Schule it has kept its independent status up until today thereby assuming an exceptional position in Germany. At the beginning of 2003 the TiHo was transformed to a university foundation – the State of Lower Saxony granting the university a greater personal responsibility and thereby more flexibility for legal arrangements. The TiHo has built up six specialist centers and integrates six clinics, 19 institutes, three special units, and an affiliated independent organisation located at two sites in Hannover. Additionally, in Ruthe, south of Hannover, in Bakum near Vechta and in Büsum at the North Sea the TiHo runs two field stations training students, and conducting research projects.

Research at the TiHo stands for research on and for animals – and in a translational manner for human research. Main research interests of the TiHo are:

- Infection medicine
- Systems neuroscience
- Animal health and food quality
- Clinical research

There is a great demand for the course of studies at the TiHo. In April 2003 a Graduate School was founded for the scientific postgraduate training of veterinarians and natural scientists. Under its umbrella are three PhD courses of study. The PhD program Veterinary Research and Animal Biology was set up in 1998 – the first PhD course of studies nation-wide.

Besides research and teaching, services are one of the core tasks of the TiHo. Patient care in the six clinics of the TiHo are of signifificant importance. Clinical work is well-known far beyond the borders of Hannover and the clinics are frequented by patient owners from abroad.
Dear Participants of the “3rd N-RENNT Symposium on Neuroinfectiology”!

In 2012, the Volkswagen Foundation jointly with the Ministry of Science and Culture of Lower Saxony launched a call for proposals which was addressed to research institutions in Lower Saxony with the aim to foster the development of their disciplinary and interdisciplinary profile, and to strengthen their national and international competitiveness and visibility. The “Niedersachsen-Research Network on Neuroinfectiology (N-RENNT)” was one of four successful concepts and has been funded with 5.4 million euros from October 1st, 2013 onwards. This remarkable neuroinfectiology-network comprises three important research locations in Lower Saxony: Hannover, Göttingen, and Brunswick. Here in Hannover two universities, the University of Veterinary Medicine and the Hannover Medical School, both having strong profiles in infection medicine and the neurosciences, closely collaborate within the N-RENNT framework. This integration of these two institutions greatly exemplifies the network’s “One Health – One Medicine” approach which aims at learning more about infectious diseases which affect both, humans and animals.

N-RENNT is a strong research cluster with unique perspectives for both medicine and veterinary medicine, not only for Lower Saxony but also on an international level. The high number of distinguished experts from abroad participating in this third N-RENNT symposium is, I think, a good proof for this. I wish you the best of success for your conference!

Dr. Franz Dettenwanger
Volkswagen Foundation
Program Director „Niedersächsisches Vorab“
Program February 15th

09:00 Opening words: Wolfgang Baumgärtner, Hannover
Speaker of N-RENNT

09:10 Opening address: Gerhard Greif, Hannover
President of the TiHo

09:20 Welcome address: Franz Dettenwanger, Hannover
Volkswagen Foundation

Chair: Albert Osterhaus

09:30 – 10:30 Adriano Aguzzi, Zurich
Understanding prions: how far have we gotten?

10:30 – 11:30 Trevor Owens, Odense
CNS-resident microglia regulate neuroinflammation

11:30 – 11:45 Coffee break
Chair: Wolfgang Baumgärtner

11:45 – 12:45 Martin Beer, Isle of Riems
Virus discovery using metagenomics: The bornavirus example

12:45 - 13:15 Albert Osterhaus, Hannover
MERS: history and options for intervention

13:15 – 13:45 Lunch
Chair: Beate Sodeik

13:45 - 14:30 Poster flash: presentation of selected abstracts (3 slides / 3 min)
Program February 15th

14:30 - 15:00  Thomas Schulz, Hannover
Location, location, location:
an estate agent’s view of latent viral persistence

15:00 - 16:00  Oral presentations of selected abstracts

15:00  Hannelore Ehrenreich et al., Göttingen
Autoantibodies against the NMDR receptor subunit NR1:
Comparable functionality and epitopes across health and disease

15:15  Lydia Stork et al., Göttingen
High CCR5 expression in natalizumab-associated PML IRIS
supports anti CCR5 therapy with maraviroc

15:30  Klaus Jung et al., Hannover
A bioinformatic approach for linking multiple omics data from
infection research by meta analysis and global testing

15:45  Victor González-Motos et al., Hannover
Discovery of a novel chemokine binding activity in
varicella zoster virus

16:00 – 16:30  Coffee break

Chair: Alexander Flügel

16:30 - 17:00  Klaus-Armin Nave, Göttingen
Myelin assembly and models of myelin diseases

17:00 - 17:30  Wolfgang Baumgärtner, Hannover
Schwann cell remyelination in demyelinating diseases

18:00  Dinner at Gasthaus Meyer, Zoo Hannover
Program February 16th

Chair: Peter Valentin-Weigand

09:00 - 10:00 Kelly Doran, San Diego
Group B streptococcal meningitis: mechanisms of blood-brain-barrier penetration

10:00 - 10:45 Alexandra Schubert-Unkmeir, Würzburg
Differential activation of acid sphingomyelinase and ceramide release determines invasiveness of Neisseria meningitidis into brain endothelial cells

10:45 - 11:15 Coffee break

Chair: Peter Claus

11:15 - 11:45 Bernd Lepenies, Hannover
The role of C-type lectin receptors in the pathogenesis of cerebral malaria

11:45 - 12:45 Oral presentations of selected abstracts

11:45 Chintan Chhatbar et al., Hannover
Viral encephalitis is controlled by IFNAR triggering of astrocytes and neurons via rectuiment of microglia and monocytes

12:00 Patrick Waindok et al., Hannover
Neurobehavioral alterations in mice during Toxocara canis- and Toxocara cati-brain infection

12:15 Alexandra Jablonka et al., Hannover
Satisfactory Measles, Mumps, Rubella and Varicella sero-prevalence in adult refugees in Western Europe - but don´t forget the kids
Program February 16th

12:30  Svenja Drave et al., Hannover
Extra-hepatic replication and infection of hepatitis E virus in neuronal-derived cells

12:45 - 13:15  Lunch

13:15 - 13:45  Poster viewing, entrance foyer

Chair:  Ulrich Kalinke

13:45 - 14:45  Branka Horvat, Lyon
Emerging contagion: immunopathogenesis of neurotropic Nipah virus infection

14:45 - 15:15  Reinhold Förster, Hannover
In vivo cytotoxic T cell-mediated killing of virus-infected cells

15:15  Closing remarks: Wolfgang Baumgärtner, Hannover

15:30  Information session on PhD programs at the TiHo
Beatrice Grummer, HGNI
Transmissible spongiform encephalopathies (TSEs) are neurodegenerative diseases of humans and many animal species caused by prions. The main constituent of prions is PrPSc, an aggregated moiety of the host-derived membrane glycolipoprotein PrPC. Prions were found to encipher many phenotypic, genetically stable TSE variants. The latter is very surprising, since PrPC is encoded by the host genome and all prion strains share the same amino acid sequence. Here I will review what is known about the infectivity, the neurotoxicity, and the neuroinvasiveness of prions. Also, I will explain why I regard the prion strain question as a fascinating challenge – with implications that go well beyond prion science. Finally, I will report some recent results obtained in my laboratory, which is attempting to address the strain question and some other basic issues of prion biology with a “systems” approach that utilizes organic chemistry, photophysics, proteomics, and mouse transgenesis.
Following injury, the peripheral nervous system (PNS) possesses a pronounced regenerative capacity, while regeneration is insufficient in central nervous system (CNS) diseases in most cases. Regeneration of the PNS is in part attributed to the plasticity of Schwann cells, the major class of PNS glia. Schwann cells undergo a remarkable transformation in response to injury, characterized by a transient period of proliferation and changes in gene expression. Although Schwann cells are not a physiological component of the CNS, recent evidence indicates that they contribute to the cellular response following CNS injury. Schwann cell-mediated remyelination is a well-known phenomenon in patients with spinal cord injury and multiple sclerosis. Although data upon the exact role of these cells in terms of functional effects are lacking so far, it is suggested that Schwann cells might contribute to CNS regeneration.

The origin of Schwann cells within the CNS is controversially discussed. On the one hand, experimental and naturally occurring spinal cord injury studies demonstrated that immature/dedifferentiated Schwann cells expressing the prototype marker p75 neurotrophin receptor (p75N-TR) migrate into the lesioned site from PNS sources such as spinal nerve roots. On the other hand, lineage-tracing studies have clearly shown that CNS-resident precursors are the major source of Schwann cell-mediated remyelination within toxic CNS demyelinating lesions of mice, while only very few remyelinating Schwann cells invade the CNS from PNS sources in this model. Additionally, in vitro studies suggest that canine p75NTR expressing Schwann cells derived from the CNS share properties with oligodendrocyte precursor cells, including similar voltage-gated potassium channel (Kv) activation and antigenic expression. Irrespective of their exact origin, it remains to be resolved, which mechanisms function as triggering factors for the occurrence of Schwann cells in the CNS. To address these various questions concerning the role Schwann cells in CNS lesions naturally occurring infectious and degenerative diseases such as canine distemper virus encephalitis and spinal cord injury as well as experimentally induced toxic and virus-associated myelopathies in mice were comparatively investigated.
The first metagenomic analyses focussed on the detection of microbes found in diverse habitats, and were based on sequencing the microbial diversity independent of the isolation of individual strains. With the now available various next-generation sequencing (NGS) platforms, metagenomics can be broadly used to identify pathogens in different sample materials, and the power of NGS-driven metagenomic approaches to identify infectious agents is defined by the extreme amount of sequencing information that can now be obtained in a single sequencing run. However, these extreme number of sequence fragments resulting from NGS-analyses requires novel diagnostic pipelines including powerful software tools to identify relevant pathogen information within the background sequences including host sequences as well as genome information of non-pathogenic microbes. Moreover, the sequence information gained can be useful for downstream analyses like PCR-screening of additional samples for instance for confirmation, quantification, and epidemiological purposes.

The presentation will focus on the available possibilities of metagenomics for virus discovery in general, and a workflow example from sample handling to sequencing and bioinformatics will be presented. Furthermore, the detection of a novel zoonotic bornavirus in Germany by metagenomics will be presented, and both the power and the current limitations of the new diagnostic possibilities will be discussed.
Bacterial meningitis is a serious infection of the central nervous system and occurs when blood-borne bacteria cross the blood-brain barrier (BBB). Group B Streptococcus (GBS) is the leading cause of neonatal meningitis, however the molecular mechanism regulating bacterial BBB disruption and penetration is not well understood.

We found that infection of human brain microvascular endothelial cells (hBMEC) with GBS and other meningeal pathogens resulted in the induction of Snail1, a host transcriptional repressor of tight junction genes. These results were substantiated in vivo in murine and zebrafish models of GBS infection. Transcript and protein levels of tight junction components ZO-1, Claudin-5 and Occludin were decreased in hBMEC following GBS infection, which was dependent on Snail1 induction. We further demonstrate that Snail1 is sufficient to facilitate tight junction disruption, promoting bacterial passage and permeability of the BBB. GBS induction of Snail1 expression was dependent on the Erk1/2 MAPK signaling cascade and bacterial cell wall components. Finally, overexpression of a dominant negative Snail1 homolog in zebrafish was sufficient to increase transcript levels of tight junction proteins and increase zebrafish survival in response to GBS challenge.

Taken together our data suggests a novel mechanism of BBB disruption and penetration by meningeal pathogens.
CD8+ cytotoxic T lymphocytes (CTLs) detect viral peptides and subsequently kill infected cells by targeted secretion of death-inducing effector proteins. Novel vaccines inducing CTL responses, adoptive transfer of pathogen-specific CTLs, and drugs counteracting immune-suppressive signals in CTLs have shown to provide immunity against virus infections or malignant diseases. However, the efficacy and dynamics of CTL killing in vivo remain unclear and even basic parameters such as how efficiently individual CTLs kill virus-infected cell in vivo are unknown.

Applying 2-photon microscopy and different virus infection models in mice, we show that the antiviral killing efficiency of single effector CD8 T cells is unexpectedly low. Disruption of herpesvirus- or poxvirus-infected cells requires collaborating effector CD8 T cells. Even then, effector CD8 T cells destroy on average only 2-12 virus-infected cells per day.

Furthermore, we reveal that viral immune evasion by MHC class I down-modulation completely prevents contact-dependent killing of virus-infected cells, but has no effect on T cell priming since that is mediated by cross-presentation.

Thus, this study establishes per capita T cell killing efficiency, viral MHC class I immune evasion, and formation of swarms of cooperating effector T cells as major determinants of protective antiviral CD8 T cell immunity in vivo.
Nipah virus (NiV) is a highly pathogenic neurotropic zoonotic paramyxovirus of Henipavirus genus that causes human outbreaks annually in South-East Asia. Although Henipavirus outbreaks remain sporadic until now and seem to affect only small areas, NiV may have a global pandemic potential and is an agent of particular concern in the field of human and agricultural biodefense. Immuno-neuropathogenesis of this recently emerged virus is still poorly understood. Although lymphocytes are not susceptible to Henipavirus infection, they bind efficiently the virus via heparan-sulfate and transinfect susceptible cells. We have analyzed different type of mice, bearing defects in either innate or adaptive immune system, for the susceptibility to NiV infection and development of fatal encephalitis. In contrast to wild-type, mice deficient for type-I interferon (IFN-I) receptor were highly susceptible to NiV. Although viral sensing through either TLR or RLR alone was not critical in anti-viral defense, mice devoid in both TLR and RLR signaling succumbed to the infection, with similar survival rate as IFN-I deficient mice. Utilization of mice with tissue-specific deletion of IFN-I receptors suggested that IFN-I signaling in any of single cell population, including macrophages, dendritic cells (DC), natural killer cells and neurons, neither in plasmacytoid DC, is not crucial for the protection from lethal NiV infection. Interestingly, presence of T-cell but not B-cell compartment was critical in allowing resistance to the infection, and this effect was independent from perforin production. Finally, depletion of macrophages allowed rapid systemic propagation of NiV infection and high lethality in mice, suggesting their important role at the crossroads between innate and adaptive immunity. Altogether, these results revealed important novel aspects of immuno-regulation of NiV infection, which could help in development of new strategies to control this highly lethal infectious disease.
Malaria is one of the main global causes of death from infectious diseases. One of the most severe complications is cerebral malaria (CM). Besides the high mortality rate, persistent neurocognitive deficits after recovery have become an increasing concern. To date, little is known about how pattern recognition receptors in innate immunity impact the pathogenesis of CM. Myeloid C-type lectin receptors (CLRs) are mainly expressed by antigen-presenting cells such as macrophages and dendritic cells and recognize pathogen-derived ligands or self-antigens. Previously, we have generated a comprehensive library of CLR-Fc fusion proteins to screen for yet unknown CLR ligands on pathogens (Maglinao et al., 2014).

To investigate the role of CLRs in CM pathogenesis, we employed the murine Plasmodium berghei ANKA (PbA) infection model. PbA infection is a generally accepted CM model since it shares some characteristics with the human disease. In a recent study, we have shown a crucial role for the CLR Dendritic cell immunoreceptor (DCIR) in CM development (Maglinao et al., 2013). While wild-type control mice developed neurological symptoms, DCIR-deficient mice were highly protected from CM. Protection from CM was accompanied by a markedly reduced brain sequestration of CD8+ T cells, ameliorated brain inflammation, and decreased TNF-alpha levels in sera of PbA-infected DCIR-/- mice. In addition, DCIR deficiency impacted CD4+ and CD8+ T cell activation in the spleen. Recent results of our lab indicate that other CLRs such as SIGNR3 and CLEC-12a also contribute to Plasmodium recognition by antigen-presenting cells and thus impact the initiated immune response during PbA infection.

In conclusion, we demonstrate a critical role for CLRs in the pathogenesis of CM. Our results suggest that interfering with CLR signaling might be a strategy to dampen immune-mediated neuropathology during malaria.

*Co-Authors: T Johannssen¹, M Maglinao¹, PH Seeberger¹, R Klopfeisch²: ¹Max Planck Institute of Colloids and Interfaces, Potsdam, and Institute of Chemistry and Biochemistry, Freie Universität Berlin; ²Veterinary Pathology, Freie Universität Berlin
Myelin speeds up axonal impulse propagation and is a prerequisite for fast motor-sensory and higher cognitive functions. Myelination is the result of a complex interaction between axons and their ensheathing glial cells that have only recently been understood at the molecular and subcellular level. Loss of myelin in hereditary diseases of the central and peripheral nervous system, or in inflammatory autoimmune disorders, including multiple sclerosis, are of major clinical relevance. Infectious diseases with secondary CNS demyelination, such as progressive multifocal leukoencephalopathy (PML) in man or Theiler’s virus encephalomyelitis in mice, are caused by gliotropic viruses, but loss of oligodendrocytes, the myelinating cells of the CNS, leads invariably also to axonal degeneration.

We recently identified a novel aspect of neuron-glia interactions, the oligodendroglial support of axonal energy metabolism, which provides glucose-derived lactate as a fuel for axonal mitochondria. This supportive function of glycolytic oligodendrocytes is even more important for myelinated tracts because the insulating myelin sheath physically shields the axonal compartment from metabolites of the extracellular milieu. Loss of metabolic support by injured oligodendrocytes is likely a contributing factor for axonal degeneration in various demyelinating diseases.
In 2012 we identified a previously unknown human coronavirus, Middle East respiratory syndrome corona virus (MERS-CoV), from a patient in Saudi Arabia presenting with fatal acute pneumonia\textsuperscript{1}. To date, several clusters and more than 1000 confirmed cases have been reported with around 40\% of the reported human cases being fatal. Although clusters of nosocomial spread of MERS have been identified, dromedary camels were shown to be the reservoir of this virus\textsuperscript{2} and recent studies have indicated that persons working with dromedary camels are at increased risk of becoming infected with MERS-CoV. Given that zoonotic transmission from the reservoir is expected to continue and that outbreaks of human-to-human transmission such as recently experienced in South Korea have a huge impact on society, intervention strategies are urgently needed. Control of MERS will have to rely on the combination of several intervention strategies, from adequate syndrome surveillance and diagnostic services, to advanced patient isolation, treatment and vaccination options. The primary goal of vaccination may be aimed to reduce the risk of transmission of MERS-CoV from dromedary camels to humans. In addition vaccines may be used to vaccinate certain groups of individuals at increased risk of infection, like healthcare workers. Progress towards the development of MERS-CoV vaccines however has been hampered by problems in developing animal models. We have put considerable effort in the development of MERS animal models and novel vaccine candidates that may be applied both in dromedary camels and in humans. Currently we further evaluate the efficacy of candidate vaccines like a MVA vaccine that encodes the MERS-CoV spike gene, in rabbits and dromedary camels as model and target species respectively\textsuperscript{2}. We recently showed that this vaccine confers mucosal immunity and significantly reduces MERS-CoV excretion in dromedary camels. MVA-specific antibodies would also provide protection against camelpox, endemic in dromedary camels in the region\textsuperscript{3}.

Introducing Microglia: Microglia are the tissue macrophages of the central nervous system (CNS). Their primary functions are as part of innate CNS immunity, to clear debris and damaged cells, and to signal for lymphocyte response in adaptive immunity. Microglia can function as antigen presenting cells (APC) for T cell proliferative response. The CD11c+ microglial subset are very effective APC for proliferative response although ineffective at inducing effector T cells. Microglia play a major role in homeostatic regulation in the CNS, including by production of Type I interferons (IFN), as well as other cytokines and chemokines. Cytokine secretion profiles and microglial phenotypes are themselves influenced by developmental and degenerative cues, including bidirectional interaction with astrocytes, and their recent phagocytic experience. They therefore interpret local needs and conditions for appropriate immune response.

Aim: To understand how these regulatory profiles are triggered and how they control neuroinflammation.

Methods: Experimental ligands that drive regulatory cytokine production are applied in mouse models for multiple sclerosis and neuromyelitis optica and outcomes measured using transgenic reporter and gene-deficient mice to establish mechanism. Gene expression profiles of microglia from neonatal and adult mice are compared.

Results: Results show induction of Type I IFN in the CNS, and the effect of this on neuroinflammatory disease, as well as a role in neuronal development for microglia that produce the cytokine insulin-like growth factor-1 and other factors implicated in neuronal guidance and survival.

Conclusions: Microglia play an important role in neuronal development in the neonatal CNS. Microglia play a regulatory role in the adult CNS and this can be exploited for therapeutic benefit.
Differential activation of acid sphingomyelinase and ceramide release determines invasiveness of *Neisseria meningitidis* into brain endothelial cells

The interaction with brain endothelial cells is central to the pathogenicity of *Neisseria meningitidis* infections. Recent studies demonstrated that distinct membrane microdomains, named lipid rafts, and ceramide play an important role in infectious biology. Ceramide forms larger ceramide-enriched membrane platforms that are required for segregation of receptors and diverse signal transduction.

In this study, we show that *N. meningitidis* causes transient activation of acid sphingomyelinase (ASM) followed by ceramide release in brain endothelial cells. In response to *N. meningitidis* infection, ASM and ceramide are displayed at the outer leaflet of the cell membrane and condense into large membrane platforms wherein ErbB2, an important receptor involved in bacterial uptake, clusters. Mechanistically, *N. meningitidis*-mediated ASM activation relied on binding of the outer membrane protein Opc to heparan sulfate proteoglycans followed by activation of phosphatidylinositol-specific phospholipase C. Pharmacologic or genetic ablation of ASM abrogated meningococcal internalization without affecting bacterial adherence. In accordance, the restricted invasiveness of a defined set of pathogenic isolates of the ST-11/ST-8 clonal complex into brain endothelial cells directly correlated with their restricted ability to induce ASM and ceramide release. In conclusion, ASM activation and ceramide release are essential for internalization of Opc-expressing meningococci into brain endothelial cells, and this segregates with invasiveness of *N. meningitidis* strains.
Location, location, location: An estate agent’s view of latent viral persistence

A characteristic feature of several virus families is their ability to persist long term in infected individuals. This property is characteristic for all herpesviruses, including the neurotropic alphaherpesviruses, retroviruses, hepadnaviruses, papillomaviruses, polyomaviruses and some adenovirus species. In addition to these DNA viruses, a few RNA virus families can persist long-term, most famously among them hepac- and pestiviruses. Recent observation also point to the possibility that, on occasion, acutely infecting RNA viruses such Ebola virus, may on occasion persist in individuals who have apparently recovered from an acute Ebola infection.

Longterm viral persistence may involve the replication of an episomal viral genome during the S phase of the latently infected cell and its partitioning to daughter cells, the survival of latent viral genomes in terminally differentiated resting cells, integration of a viral genome into cellular DNA and its subsequent silencing, vegetative DNA replication or the low level production of new viral progeny and reinfection of new cells. Epigenetic mechanisms play an important role in the transcriptional silencing of episomal or integrated viral genomes. Recently accumulating evidence suggests that the location of an integrated or episomal viral genome in particular chromatin regions may be an important factor in determining latent persistence. In addition, long-lived cell types enable the persistence of viral genomes. Location, either in particular chromatin regions or in a suitable cell type, therefore determine latent viral persistence.
Short oral presentations

Castillo-Gomez E¹, Oliveira B¹, Tapken D², Bertrand S³, Trippe R², Zafeiriou P⁴, Pan H¹, Steiner J⁵, Jurek B⁶, Klein-Schmidt C², Prüss H⁶, Zimmermann WH⁴, Bertrand D³, Hollmann M², Nave KA¹,⁷, Ehrenreich H¹,⁷

Autoantibodies against the NMDA receptor subunit NR1: Comparable functionality and epitopes across health and disease

¹ Max Planck Institute of Experimental Medicine, Göttingen
² Department of Biochemistry I – Receptor Biochemistry, University of Bochum
³ HiQscreen, 1222 Vesenaz, Geneva, Switzerland
⁴ Institute of Pharmacology, University Medical Center, Göttingen
⁵ Department of Psychiatry, University of Magdeburg
⁶ Department of Neurology, Charité, University Medicine, and DZNE, Berlin
⁷ DFG Research Center for Nanoscale Microscopy and Molecular Physiology of the Brain (CNMPB), Göttingen

Chhatbar C¹, Detje CN¹, Grabski E¹, Spanier J¹, Ghita L¹, Borst K¹, Döring M¹, Gudi V², Chittappen KP², Stangel M²,³, Kalinke U¹

Viral encephalitis is controlled by IFNAR triggering of astrocytes and neurons via recruitment of microglia and monocytes

¹ Institute for Experimental Infection Research, TWINCORE, Center for Experimental and Clinical Infection Research GmbH, Hannover
² Clinical Neuroimmunology and Neurochemistry, Department of Neurology, Hannover Medical School, Hannover
³ Center of Systems Neuroscience, Hannover

Drave SA¹, Debing Y², Walter S¹, Todt C¹, Engelmann M¹, Friesland M¹, Wedemeyer H³, Neyts J², Behrendt P¹,³, Steinmann E¹

Extra-hepatic replication and infection of hepatitis E virus in neuronal-derived cells

¹ Institute for Experimental Virology, TWINCORE, Centre for Experimental and Clinical Infection Research; a joint venture between the Medical School Hannover (MHH) and the Helmholtz Centre for Infection Research (HZI), Hannover
² Rega Institute for Medical Research, Department of Microbiology and Immunology, KU Leuven, Leuven, Belgium
³ Hannover Medical School, Department of Gastroenterology, Hepatology and Endocrinology, Hannover
Short oral presentations

González-Motos V¹, Ritter B¹, Lenac T², Jonjic S², Arenzana-Seisedos F³, Kalinke U⁴, Viejo–Borbolla A¹

**Discovery of a novel chemokine binding activity in varicella zoster virus**

1 Institute of Virology, Hannover Medical School, Hannover
2 Center for Proteomics and Department of Histology and Embryology, Faculty of Medicine, University of Rijeka, Rijeka, Croatia
3 Viral Pathogenesis Unit, Institut Pasteur, Paris, France
4 Institute for Experimental Infection Research, TWINCORE, Centre for Experimental and Clinical Infection Research, Hannover

Jablonska A¹,², Happle C³, Grote U⁴, Schleenvoigt B⁵, Hampel A⁶, Schmidt RE¹,², Behrens GMN¹,²

**Satisfactory Measles, Mumps, Rubella and Varicella seroprevalence in adult refugees in Western Europe – but don´t forget the kids**

1 Hannover Medical School, Department of Clinical Immunology and Rheumatology, Hannover
2 German Center for Infection Research
3 Hannover Medical School, Department of Pediatrics, Neonatology and Allergology, Hannover
4 Hannover Medical School, Department of Hematology and Oncology, Hannover
5 Jena University Hospital, Center for Infectious Diseases and Infection Control, Jena
6 Hospital Wolfsburg, Department for Surgical Intensive Care Medicine, Wolfsburg

Jung K

**A bioinformatics approach for linking multiple omics data from infection research by meta analysis and global testing**

University of Veterinary Medicine Hannover, Institute for Animal Breeding and Genetics, Hannover
Short oral presentations

Stork L¹, Brück W¹, Bar-Or A², Metz I¹

High CCR5 expression in natalizumab-associated PML IRIS supports anti CCR5 therapy with maraviroc

1 Department of Neuropathology, University Medical Center, Georg August University, Göttingen
2 Department of Neurology and Neurosurgery and Neuroimmunology Unit, Montreal Neurological Institute, McGill University, Montreal, Canada

Waindok P¹, Janecek E¹, Bankstahl M², Löscher W², Strube C¹

Neurobehavioral alterations in mice during Toxocara canis- and Toxocara cati-brain infection

1 Institute for Parasitology, University of Veterinary Medicine Hannover, Hanover
2 Department of Pharmacology, Toxicology, and Pharmacy, University of Veterinary Medicine Hannover, Hannover
3 Center for Systems Neuroscience
1. **Anjum M\(^1,2\), Bröer S\(^1,2\), Kaeufer C\(^1,2\), Löscher W\(^1,2\)**

*Inter-ictal spikes and seizures in EEG recordings: Possible read-outs of epileptogenesis in animal models of epilepsy*

1. Department of Pharmacology, Toxicology, and Pharmacy, University of Veterinary Medicine Hannover, Hannover
2. Center for Systems Neuroscience, Hannover

2. **Beyer M\(^1,2\), Heneka MT\(^3\), Korte M\(^1,2\)**

**Enduring changes in neuronal structure and function upon acute and systemic administration of LPS**

1. Division of Cellular Neurobiology, Zoological Institute, TU Braunschweig
2. Helmholtz Centre for Infection Research, AG NIND, Braunschweig
3. Clinical Neuroscience, University Bonn, German Center for Neurodegenerative Diseases

3. **Bröer S\(^1\), Hage E\(^2\), Kaeufer C\(^1\), Gerhauser I\(^3\), Anjum M\(^1\), Lin L\(^3\), Schulz TF\(^2\), Löscher W\(^1\)**

**Functional and genomic differences in the neurovirulence of two substrains of Theiler’s murine encephalomyelitis virus**

1. Department of Pharmacology, Toxicology, and Pharmacy, University of Veterinary Medicine Hannover & Center for Systems Neuroscience, Hannover
2. Institute of Virology, Hannover Medical School, Hannover
3. Dept. of Pathology, University of Veterinary Medicine Hannover, Germany & Center for Systems Neuroscience, Hannover

4. **Budida R\(^1\), Stankov MV\(^1\), Döhner K\(^2\), Tappe KA\(^2\), Buch A\(^2\), Panayotova-Dimitrova D\(^3\), Sodeik B\(^2\), Behrens GMN\(^1\)**

*Herpes Simplex Virus 1 interference with dendritic cell autophagy impairs CD8+ T lymphocyte immunity*

1. Hannover Medical School, Department of Clinical Immunology and Rheumatology, Hannover
2. Hannover Medical School, Institute for Virology, Hannover
3. Mannheim Clinic of University of Heidelberg, Department of Dermatology, Venerology and Allergology, Mannheim
Reduced antiviral immunity following regulatory T cell expansion is dependent on cytotoxic T cells

1 University of Veterinary Medicine Hannover, Department of Pathology, Hannover
2 Center for Systems Neuroscience, Hannover
3 Helmholtz Centre for Infection Research, Department of Experimental Immunology, Braunschweig

Neutrophil extracellular trap (NET) formation in the S. suis-infected cerebrospinal fluid compartment

1 University of Veterinary Medicine Hannover, Institute for Microbiology, Dept. of Infectious Diseases, Hannover
2 University of Veterinary Medicine Hannover, Research Center for Emerging Infections and Zoonoses (RIZ), Hannover
3 University of Veterinary Medicine Hannover, Department of Physiological Chemistry, Hannover
4 Heidelberg University, Department of Pediatrics, Pediatric Infectious Diseases, Medical Faculty Mannheim, Mannheim
5 The Nippon Dental University, School of Life Dentistry at Tokyo, Department of NDU Life Sciences, Chiyoda-ku, Tokyo, Japan
6 University Leipzig, College of Veterinary Medicine, Institute for Bacteriology and Mycology, Centre for Infectious Diseases, Leipzig

Influence of innate pattern recognition receptors and host type-1 interferon response on murine herpes simplex encephalitis

1 Institute for Experimental Infection Research, TWINCORE, Centre for Experimental and Clinical Infection Research, Hannover, Germany
2 Institute of Virology, Hannover Medical School, Hannover, Germany
3 Institute for Laboratory Animal Science, Hannover Medical School, Hannover, Germany
4 Department of Neuroanatomy, Hannover Medical School, Hannover, Germany
Döhner K\textsuperscript{1}, Bialy D\textsuperscript{1}, Anderson F\textsuperscript{1}, Buch A\textsuperscript{1}, Koithan T\textsuperscript{1}, Hinz A\textsuperscript{1}, Binz A\textsuperscript{1}, Rudolph K\textsuperscript{1}, Hügel S\textsuperscript{2}, Rother F\textsuperscript{3}, Hartmann E\textsuperscript{2}, Bauerfeind R\textsuperscript{4}, Bader M\textsuperscript{3}, Sodeik B\textsuperscript{1}

**The importins of nuclear targeting of herpes simplex virus in fibroblasts and neurons**

1 Institute of Virology, Hannover Medical Center, Hannover  
2 Department of Biology, University of Lübeck, Hannover  
3 Max-Delbrück Centre for Molecular Medicine, Berlin  
4 Institute of Cell Biology, Hannover Medical School, Hannover

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Halle S, Liu X, Förster R

**Killer immune cell infiltration during CNS infection**

Hannover Medical School, Institute of Immunology, Hannover

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Hansmann F\textsuperscript{1,3}, Jungwirth N\textsuperscript{1,3}, Zhang N\textsuperscript{1,3}, Salinas Tejedor L\textsuperscript{2,3}, Skripuletz T\textsuperscript{2}, Stangel M\textsuperscript{2,3}, Baumgärtner W\textsuperscript{1,3}

**Opposing effects of canine adipose tissue-derived mesenchymal stem cells in a viral model of multiple sclerosis**

1 Department of Pathology, University of Veterinary Medicine Hannover, Hannover  
2 Department of Neurology, Hannover Medical School, Hannover  
3 Center of Systems Neuroscience, Hannover

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Hinz A\textsuperscript{1}, Koithan T\textsuperscript{1}, Döhner K\textsuperscript{1}, Urbé S\textsuperscript{2}, Sodeik B\textsuperscript{1}

**Cytosolic restriction factors for incoming HSV1 particles**

1 Institute of Virology, Hannover Medical Center, Hannover  
2 Institute of Translational Medicine, University of Liverpool, UK
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Jo W¹, Baumgärtner W², Osterhaus A¹, van der Vries E¹

**Implementation of a NGS platform for novel pathogen discovery: Evaluation of viral enrichment techniques**

1 Research Center for Emerging Infections and Zoonoses, University of Veterinary Medicine Hannover, Hannover
2 Department of Pathology, University of Veterinary Medicine Hannover, Hannover

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Käufer C¹, Bröer S¹, Anjum M¹, Gerhauser I², Li L², Bankstahl M¹, Baumgärtner W², Löscher W¹

**Encephalitis–induced epilepsies: Studies with the murine Theiler encephalomyelitis virus (TMEV)**

1 Department of Pharmacology, Toxicology, and Pharmacy, University of Veterinary Medicine Hannover, Hannover
2 Department of Pathology, University of Veterinary Medicine Hannover, Hannover
3 Center for Systems Neuroscience, Hannover

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Koczula A¹, Willenborg J¹, Jarek M², Goethe R¹, Valentin-Weigand P¹

**Transcriptome profiling of Streptococcus suis during growth in porcine blood and cerebrospinal fluid**

1 Institute for Microbiology, University of Veterinary Medicine, Hannover
2 Genome Analytics, Helmholtz Centre for Infection Research, Braunschweig

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Li L¹, Gerhauser I¹, Klein S¹, Elmobaret SA¹, Deschl U³, Kalkuhl A³, Baumgärtner W¹, Ulrich R², Beineke A¹

**Dynamic changes of cell-specific apoptosis in a murine model for multiple sclerosis**

1 Department of Pathology, University of Veterinary Medicine Hannover, Hannover
2 Center for Systems Neuroscience Hannover, Hannover
3 Department of Non–Clinical Drug Safety, Boehringer Ingelheim Pharma GmbH & Co. KG, Biberach (Riss)
4 Department of Experimental Animal Facilities and Biorisk Management, Friedrich-Loeffler-Institut, Greifswald – Insel Riems
Brain transcriptional changes over the course of neurotoxocarosis

1 University of Veterinary Medicine Hannover, Institute for Parasitology, Hannover
2 Helmholtz Center for Infection Research, Department Infection Genetics, Braunschweig
3 University of Veterinary Medicine Hannover, Hannover
4 University of Tennessee Health Science Center, Memphis, USA
5 Helmholtz Center for Infection Research, Research Group Genome Analysis, Braunschweig

Visualization of immune response to viral infection in the central and peripheral nervous system

1 Institute of Immunology, Hannover Medical School, Hannover
2 Institute of Virology, Hannover Medical School, Hannover

Neurotrophic Fibroblast Growth Factors are up-regulated in brain cells in response to herpes simplex virus infection

1 Institute of Neuroanatomy, Hannover Medical School
2 Institute of Virology, Hannover Medical School, Germany
3 Institute for Pathology, University of Veterinary Medicine
4 N-RENNT (Niedersachsen-Research Network on Neuroinfectiology), Hannover
5 Center for Systems Neuroscience, Hannover

Autoimmune CNS disease is triggered by myelin-reactive autoantibodies

Institute for Multiple Sclerosis Research, Department of Neuroimmunology, Gemeinnützige Hertie-Stiftung and University Medical Centre Göttingen
Mitterreiter JG\textsuperscript{1}, Ouwendijk WJD\textsuperscript{2}, Osterhaus ADME\textsuperscript{1}, Verjans GMGM\textsuperscript{1,2}

**Comparative analysis of Toll-like receptor expression by glial cells of the human central and peripheral nervous system**

1 Research Center for Emerging Infections and Zoonoses, University of Veterinary Medicine Hannover
2 Department of Viroscience, Erasmus MC Rotterdam, The Netherlands

Pägelow D\textsuperscript{1}, Beineke A\textsuperscript{2}, Hornef MW\textsuperscript{3}, Fulde M\textsuperscript{1,4}

**A neonatal CNS infection model following mucosal challenge with *Listeria monocytogenes***

1 Institute of Microbiology, University of Veterinary Medicine Hannover, Hannover
2 Institute for Pathology, University of Veterinary Medicine Hannover
3 Institute for Medical Microbiology, University Hospital RWTH Aachen, Aachen
4 Freie Universität Berlin, Institute of Microbiology and Epizootics, Berlin

Prajeeth CK\textsuperscript{1}, Gudi V\textsuperscript{1}, Floess S\textsuperscript{2}, Huehn J\textsuperscript{2}, Stangel M\textsuperscript{1*}

**Epigenetic regulation of adult glial response following neonatal LPS challenge**

1 Clinical Neuroimmunology and Neurochemistry, Department of Neurology, Hannover Medical School, Hannover
2 Experimental Immunology, Helmholtz Centre for Infection Research, Braunschweig
* Center of Systems Neuroscience, Hannover

Seitz M\textsuperscript{1}, Seele J\textsuperscript{1}, Nau R\textsuperscript{2}, Stangel M\textsuperscript{3}, Valentin-Weigand P\textsuperscript{1}

**Establishment and characterization of a primary astrocyte-microglia co-culture system for *Streptococcus suis* infection**

1 Institute of Microbiology, University of Veterinary Medicine Hannover, Hannover
2 Institute of Neuropathology, University Medical Center Göttingen, Göttingen
3 Institute for Clinical Neuroimmunology and Neurochemistry, Department of Neurology, Hannover Medical School, Center for Systems Neuroscience, Hannover
Uhde A-K1, Herder V1,2, Teich R3, Flöß S3, Baumgärtner W1,2, Huehn J3, Beineke A1,2

Disturbed interleukin-10 signaling enhances virus-induced brain damage in a mouse model for multiple sclerosis

1 Department of Pathology, University of Veterinary Medicine Hannover, Hannover
2 Center for Systems Neuroscience, Hannover
3 Department of Experimental Immunology, Helmholtz Centre for Infection Research, Braunschweig

Wilk E1, Hosseini S4, Michaelsen-Preusse K4, Korte M4, Schughart K1,2,3

Impact of influenza A infections on the CNS

1 Department of Infection Genetics, Helmholtz Centre for Infection Research, Braunschweig
2 TU-Braunschweig, Zoological Institute, Cellular Neurobiology Div., Braunschweig
3 Neuroinflammation and Neurodegeneration Group – AG NIND, Helmholtz Center for Infection Research, Braunschweig
4 University of Veterinary Medicine Hannover, Hannover
5 University of Tennessee Health Science Center, USA

Zhu S1, Stanslowsky N2, Ritter B1, Kaufer BB3, Verjans GM4,5, Wegner F2, Viejo-Borbolla A1

Generation of human peripheral neurons to study varicella zoster virus

1 Institute of Virology, Hannover Medical School, Hannover
2 Department of Neurology, Hannover Medical School, Hannover
3 Institute of Virology, Freie Universität Berlin, Berlin, Germany
4 Department of Viroscience, Erasmus Medical Centre, Rotterdam, The Netherlands
5 Research Center for Emerging Infections and Zoonoses, University of Veterinary Medicine Hannover, Foundation, Hannover
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Chair: Beate Sodeik, MHH

13:45 Implementation of a NGS platform for novel pathogen discovery: Evaluation of viral enrichment techniques
Jo W, Baumgärtner W, Osterhaus A, van der Vries E

13:50 Inter-ictal spikes and seizures in EEG recordings: Possible read-outs of epileptogenesis in animal models of epilepsy
Anjum M, Bröer S, Käufer C, and Löscher W

13:55 Enduring changes in neuronal structure and function upon acute and systemic administration of LPS
Beyer M, Honeka MT, Korte M

14:00 Neutrophil extracellular trap (NET) formation in the S. suis-infected cerebrospinal fluid compartment

14:05 Killer immune cell infiltration during CNS infection
Halle S, Liu X, Förster R

14:10 Functional and genomic differences in the neurovirulence of two substrains of Theiler’s murine encephalomyelitis virus

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Budida R, Stankov MV, Döhner K, Tappe KA, Buch A, Panayotova-Dimitrova D, Sodeik B, Behrens GMN