

UNIVERSITÄT ZU LÜBECK **STUDENTS' SYMPOSIUM**

PROGRAM GUIDE

8th Biomedical Students' Symposium FROMINFEC TO THERAP Trends in Virology



www.lifescience-symposium.de 31.10. - 03.11.2013 University of Lübeck



IM FOCUS DAS LEBEN.



Welcome to Lübeck

Foto: Ann-Kristin Gebhardt



Dear fellow colleagues, scientists and friends, and, last but not least: Dear students!

Thomas Peters

It is my pleasure to welcome you to the 8th Biomedical Students' Symposium "From Infection to Therapy - Trends in Virology". Virus epidemics are a long-standing and ever increasing challenge to men. Yet, antiviral therapies are sparse as this is highlighted by an almost complete lack of potent antiviral drugs against any viral infection. There is a need to improve this situation, and this year's students' symposium aims at bringing some of the key issues to your attention. I am grateful to our - sic! - Molecular Life Science students for their enthusiasm, their motivation, and their efforts to compile a stimulating scientific agenda. I am looking forward to enjoyable two and a half days of science, fruitful discussions and new ideas!

Have Science - Have Fun! Thomas Peters

Thanas Id

Professor of Chemistry and Chairman of the *Life Science Association Lübeck e.V.*

Welcome

Venue

Universität zu Lübeck Ratzeburger Allee 160 23562 Lübeck (DE)

Homepage

www.lifescience-symposium.de

Patronage

Gesellschaft für Biochemie und Molekularbiologie e.V. (GBM) (Prof. Dr. Carmen Villmann) Life Science Lübeck e.V. (Prof. Dr. Thomas Peters, Dr. Rosa Pulz, PD Dr. Thomas Weimar)

Organizer

We are students of the bachelor's and master's degree program Molecular Life Science:

Anika Alberts · Hannes Baukmann · Kevin Becker Robert Creutznacher · Johannes Dittmer · Alexander Domnick Jasmin Dülfer · Ann-Kristin Gebhardt · Yasmin Gül Christin Krause · Antje Lindae · Anna Oberle Nikolai Schieweck · Felicia Schlotthauer Tobias Schöne · Philipp Seidel · Till Zickmantel



Dear students,

We are proud to be able to host the 8th Biomedical Students' Symposium in Lübeck. For this occasion we have chosen a topic that is particular for Lübeck: From Infection to Therapy – Trends in Virology.

This year's participation of more than 200 students from all over Germany, and also neigbouring countries, exceeds previous expectations and promises an enjoyable weekend and the possibility to meet other involved students of bioscience, biomedicine, biotechnology or related subjects.

You have the chance to listen to different talks about viral infection and latest trends in therapy of and also with the use of viruses. Of course you won't lose sight of some practical experiences in topic related workshops which will also show the advantages of virology research in Lübeck.

In this brochure you will find an overview of general information about arrival, accommodation, catering and evening program, furthermore abstracts of the talks and workshops during this symposium.

We wish you an enjoyable stay in Lübeck!



Table of Contents

General Information	7
Campus Plan	9
Schedule	10
Introduction to Virology	11
Talks	12
Talks on Friday	12
Talks on Saturday	26
Special Talk on Sunday	
Workshops	
Social Program	46
Exhibition	46
Evening Program	47
Where to go in Lübeck	48
Acknowledgements	49
Sponsors	50
Contact and Imprint	

Check-In

Please be sure to Check-In between 15:00 and 19:00. There we will pay the deposit back to you (minus possible costs for accommodation and city tour). You can buy some coupons for canteen, therefore please bring some loose cash.

Accommodation

Halle der Paul-Klee-Schule Alexander-Fleming-Straße 6 – 12 23562 Lübeck St. Jürgen Halle Kalkbrennerstraße 5 23562 Lübeck

Bus information

To university Bus lines 1 and 9 – stop 'Fachhochschule' (Direction 'Hochschulstadtteil'/ 'Grillenweg') Bus line 6 – stop 'Universität' (Direction 'Blankensee')

Parking information

Parking on campus is possible at parking areas of 'Zentralklinikum'. Due to limited space it will cost 1 EUR per started hour. There are some free parking areas in Anschützstraße, which is about 5 minutes by foot to AM1.

Wardrobe

The wardrobe is in the basement floor of AM1 and free of charge. Please note that we can take no liability for lost or stolen items.

Certificate of attendance

Certificates of attendance are available at the Check-In.

Access to the Internet

During the Symposium you can get free access to WLAN. You will get the accession code at the Check-In.

General Information

Catering

Breakfast including drinks will be provided on Friday, Saturday and Sunday in the Foyer of AM1 from 8:00.

We will have a welcome barbecue on Thursday evening.

For Friday noon you can buy coupons for canteen at the Check-In or you can go to various snack bars or restaurants near the University. On Friday evening we go for dinner provided by Euroimmun. Again you can also go to various snack bars or restaurants on your own.

For Saturday noon we provide lunch in the Foyer of AM1. On Saturday evening you can go to various restaurants in the city centre.

For the members of BuFaTa we will order some pizza on Sunday noon.

Evaluation

Please turn in your completed and legible evaluation form to the Check-In on the last day. Thank you for your active participation and constructive criticism.

Explanation of acronyms

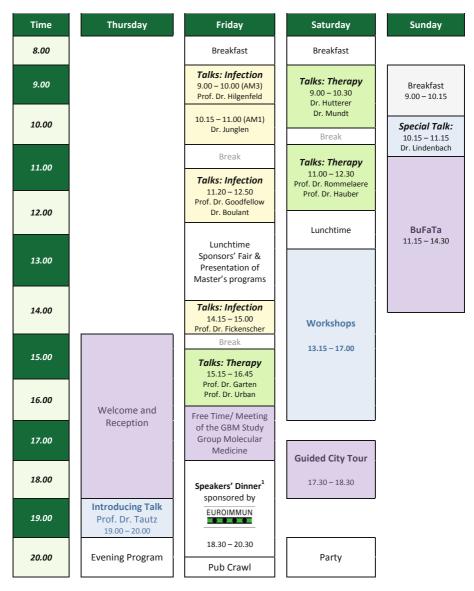
- WS# Number of your chosen workshop
 - D If you have chosen to participate at the EUROIMMUN dinner
 - C If you have chosen to participate at the guided city tour
- G1/2 Gym: Paul-Klee-Schule or St. Jürgen Halle

Campus Plan



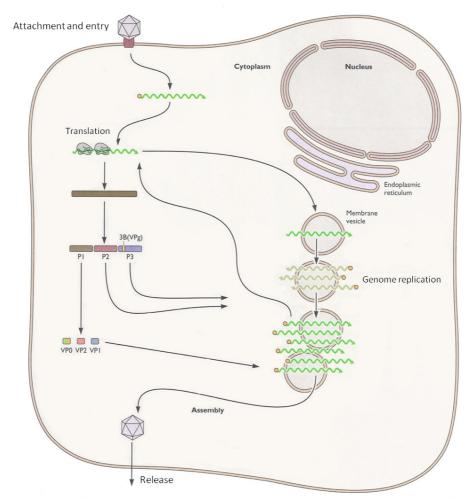
B1: Bus stop 'Fachhochschule' B2: Bus stop 'Universität' G1: Paul-Klee-Schule G2: St. Jürgen Halle

Schedule



¹All participants are invited including students and non-speakers.

The viral infectious cycle



(from Principles of Virology, Vol I, S.J. Flint)

Talks on Friday - Infection

We are glad to welcome excellent speakers in Lübeck. We highly encourage you to ask questions after the lectures. Moreover, you should seize the chance to meet one or more speakers to arrange an internship or Master's thesis.

Prof. Rolf Hilgenfeld (Lübeck) – Epidemiology and Zoonosis 09.00 – 10.00 / AM3

	since 2003	Full professor (C4) of Biochemistry,
1		University of Lübeck
1 and 1	1998 - 2000	Director, Institute of Molecular Biotechnology e.V., Jena
	1995 - 2002	Head of Department,
		Institute of Molecular Biotechnolog e.V., Jena
	1995 - 2002	Full professor (C4) of Structural Biochemistry,
		University of Jena
	1987 - 1988	Postdoc, Biocenter, University of Basel, Switzerland

FROM BAT CORONAVIRUSES TO SARS AND MERS

In recent years, it has been shown that bats constitute a rich reservoir of RNA viruses. Occasionally, these viruses are transmitted into the human population by zoonosis, often via an intermediate species. Thus, the outbreak of Severe Acute Respiratory Syndrome (SARS) in 2002/2003 was caused by a coronavirus (SARS-CoV) that probably crossed species barriers from bats to the civet cat and other animals treated at markets in Southern China, and from there to humans. A very recent event is the emergence of a new human coronavirus in countries on and surrounding the Arab peninsula. Designated Middle-East Respiratory Syndrome coronavirus (MERS-CoV), this virus appears to have a high case-fatality ratio (57 documented cases, 27 deaths at the time of writing this abstract), although at the moment, we probably only see the "tip of the iceberg". Similar to SARS, MERS is characterized by severe atypical pneumonia, but in addition, renal failure is observed in most cases. Through functional and structural characterization of components of the huge replicase/transcriptase complex of the coronaviruses, we try to under-



stand the evolution of these viruses. How do they adapt to the new host after entering the human population? We also examine interactions between viral proteins and host proteins, with a focus on viral components that seem to influence protein synthesis in the host cell. The structural findings are also used to design antiviral compounds. In preparation against future zoonotic transmissions, we develop and synthesize antivirals on the basis of our structures of bat-CoV proteins; these compounds can immediately enter preclinical development should another epidemic caused by a novel human coronavirus strike. Using this approach, we already had an antiviral in our hands when MERS-CoV was first described in September, 2012.

Talks on Friday - Infection

Dr. Sandra Junglen (Bonn) – Epidemiology and Zoonosis



GENETIC DIVERSITY AND DILUTION EFFECTS DURING VIRUS EMER-GENCE FROM PRISTINE TO MODIFIED LANDSCAPES

Tropical rainforests show the highest level of terrestrial biodiversity and may be an important contributor to microbial diversity. Exploitation of these ecosystems may foster the emergence of novel pathogens. At present, however, we lack both an understanding of pathogen prevalence in remote rainforest areas and reliable detection systems for novel pathogens. Monitoring of pathogen prevalence and circulation at the interface of pristine rainforests and disturbed landscapes is crucial for emerging disease surveillance and forecasting.

We investigated the variation in mosquito distribution and mosquito-associated viruses along anthropogenic disturbance gradients in Africa and the Neotropics. Mosquito species composition and diversity greatly differed between natural and modified habitat types. Investigating concomitant viral infections revealed an extremely high diversity of numerous previously unknown RNA viruses belonging to the families Bunyaviridae, Flaviviridae, Reoviridae, and Rhabdoviridae, as well as to the discovery of the first insectassociated nidovirus (Cavally virus, CAVV) that is likely to represent a novel family within the order Nidovirales.



General virus abundance and diversity was examined along the gradient, yielding a decrease in diversity and an increase in prevalence, from natural to modified habitat types. Phylogenetic analyses indicated

ancestral relationships of the newly discovered viruses to established virus groups suggesting that tropical ecosystems may contain a larger spectrum of viruses than currently known from epidemic isolates. Knowledge on the biological mechanisms behind ecosystem modification and arbovirus emergence could provide innovative approaches for epidemic risk assessment and intervention strategies.

Talks on Friday - Infection

Prof. Ian Goodfellow (Cambridge) – Viral Replication

11.20 - 12.05 / AM1



After an undergraduate degree at the University of Warwick where Ian Goodfellow studied microbiology and virology, he then spent three years undertaking a PhD in the Iab of Liz Sockett at the University of Nottingham studying bacterial flagellar motility. After a PhD, Ian Goodfellow returned to virology working at the University of Reading with Jeff Almond and David Evans on picornavirus host cell interactions. After a few years he moved to the University of Glasgow with David Evans to continue as a post doc studying picornavirus receptors and RNA structures.In 2003

lan Goodfellow was awarded a Wellcome Trust Career Development Fellowship and moved to the University of Reading to establish his own research group. His research now focuses on the biology of family of small RNA viruses within the Caliciviridae family. He relocated to the Section of Virology, Imperial College London in January 2006 where his group has grown in size to typically 10 people. He was awarded a Wellcome Senior Fellowship in 2007, recently renewed in 2012, to continue his studies, focusing primarily on the noroviruses.

Prof. Ian Goodfellow will provide you with up-to-date information about the work of his Calicivirus Research Group.



Talks on Friday - Infection

Dr. Steeve Boulant (Heidelberg) – Viral Replication

12.05 - 12.50 / AM1

2008-2012 Post doctoral associate, Harvard Medical School Boston MA, USA	
Harvard Medical School Boston MA LISA	
Harvard Medical School Boston MA, OSA	
2006-2008 Marie curie Post doctoral fellow,	
MRC Virology Unit Glasgow, UK	
2005-2006 Post doctoral associate, MRC Virology Unit Glasgow, UK	
2004-2005 Bridging grant fellow, IBCP-CNRS Lyon, France	
2001-2004 PhD in Molecular Biology and Biochemistry,	
IBCP-CNRS, France	

FROM VIRUS ENTRY TO REPLICATION: A HITCHHIKER GUIDE TO THE CELL

Viruses are intracellular parasites. They must enter the cells to deliver their genetic information to replication-competent compartments within the host cell. The first barrier that a virus must face to establish an infection in the host is breaching the cellular membrane. Viruses have developed efficient ways to hijack existing cellular processes to breach this barrier. They either directly penetrate the plasma membrane or hijack endocytic pathways to gain access to the host cells. For viruses that enter cells by endocytosis, after uptake, they traffic to the endosomal pathway. In the endosomal compartments, viruses will encounter acidic environments and proteases that are often required for the viruses to undergo fusion or membrane penetration, which will allow either the release of the viral particles or of the viral genome into the cytoplasm so that infection/replication can occur.

In this lecture, the students will have an overview of the various strategies used by viruses to enter and to replicate in the host. By using examples from non-enveloped and enveloped viruses, the participants will have an introduction to the methodologies used in laboratories to study virus entry and replication.



This seminar will mainly focus on imaging methods (live-cell confocal microscopy and super-resolution microscopy) that allow researchers to visualize and track individual virus particles as they infect the host. Finally, we will examine the advantages and disadvantages of these methods and discuss how molecular mechanisms could be concluded from these microscopy approaches.

Talks on Friday - Infection

Prof. Helmut Fickenscher (Kiel) – Tumor Viruses

14.15 - 15.00 / AM1

	since 2005	Chair of Virology, Director of the Institute for Infection
		Medicine and Head of the Central Unit
a and		for Environmental and Hospital Hygiene, Kiel
	2002-2005	University Professor of Clinical Virology of the
		Ruprecht-Karl University of Heidelberg
	1991 - 2001	Principal investigator at the Institute for Clinical and
		Molecular Virology, Erlangen
	1989 - 1991	DFG fellowship at the Max-Planck Institute for
		Biophysical Chemistry in Göttingen with Prof. Dr. Peter
		Gruss (Developmental Biology)
	1988 - 1989	Postdoctoral fellow in Virology with Prof. Dr. Bernhard
		Fleckenstein, Erlangen
	1989	Promotion to Dr. med. on gene regulation in human
		cytomegalovirus

RHADINOVIRAL T-CELL VECTORS

(by Linda Bremer and Helmut Fickenscher)

The adoptive immunotherapy of malignant tumors represents an additional option to established tumor therapies. However, its applicability is limited by the availability of large numbers of MHC-restricted tumor-antigen specific T cells. We improved a rhadinoviral vector system based on herpesvirus saimiri in order to provide a stable long-term transgene expression in transduced primary T cells which are easy to amplify to large cell numbers. A chimeric recombinant MHC-independent T-cell receptor against ErbB2 was stably expressed by a rhadinoviral expression vector from a tricistronic transcript which also encodes the viral functions for T-cell amplification. The stable cytotoxic activity of vector-transduced T cells was shown against ErbB2-positive cell lines and primary tumor cultures in contrast to ErbB2-negative cells. This proof of concept allows further applications for basic research as well potentially in the development of novel therapeutic options against malignant tumors.



Talks on Friday - Therapy

Prof. Wolfgang Garten (Marburg) – Drug Design

15.15 - 16.00 / AM1

since 1992 1988 1987 1976-1986 1972-1974	Full Professor for Molecular Virology, Philipps-University of Marburg Professor, Philipps-University of Marburg, Medical School, Institute of Virology, Director: Prof. Dr. HD. Klenk Habilitation in Molecular Virology, Justus-Liebig-University of Giessen, Medical School Research Assistant, Institute of Virology, Liebig-University of Giessen, Medical School, DFG-Habilitation Scholarship Scholarship of the Max-Planck Society, PhD at the Max Planck-Institute, Biology, Tübingen (Prof. Dr. U. Henning)
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A NEW CONCEPT OF INFLUENZA TREATMENT BY A COMBINATION OF ANTIVIRAL DRUGS AND INHIBITORS TARGETING HEMAGGLUTININ AC-TIVATING HOST PROTEASES

Human and animal influenza virus infections are caused by numerous genetically variable influenza virus strains with an outcome of severe illnesses, high burden on the healthcare system, and serious economic losses. A development of a more efficacious anti-influenza therapy on the basis of existed drugs and newly created agents is considered to be needed, since the limitations and usefulness of vaccination against influenza and the emergence of drug-resistant influenza viruses. Host proteases activating viral hemagglutinin spikes were discovered in recent years. Moreover, highly efficient protease inhibitors were designed and chemically synthesized by my colleague Prof. Dr. Torsten Steinmetzer, Pharmaceutical Chemistry, University of Marburg. Now we examined influenza virus propagation in presence of these inhibitors, alone in double-combination with neuraminidase inhibitors or in triple-combination with virus replication inhibitors. Combinatorial treatment of virus infected cells showed a more significant inhibitory effect compared



with that treated with a single drug. Such a combination therapy may reduce the emergence of resistant influenza viruses. Our data of combined therapies will be presented, proposing a viable strategy for treatment of humans afflicted with seasonal influenza or with a highly pathogenic avian influenza virus infection.

Talks on Friday - Therapy

Prof. Stephan Urban (Heidelberg) – Drug Design

16.00 - 16.45 / AM1

	since 2008	Professorship (apl.) at the faculty for Biowissenschaften at the University of Heidelberg
	since 2001	Independent group leader at the Department of molecular virology of the University Hospital Heidelberg
	2000-2001	Stipendium at the ZMBH, University of Heidelberg
	2000	Habilitation at the faculty for biosciences, venia legendi
		molecular biology at the Ruprecht-Karls Universität
and the second se		Heidelberg
	1995-2000	Postdoc Center for Molecular Biology (ZMBH),
		Heidelberg University (Prof. Dr. H. Schaller)
	1991-95	PhD, Dept. Of Virology (Prof. Dr. mult. P. H.
		Hofschneider), Max-Planck-Institut für Biochemie,
		Martinsried

Prof. Stephan Urban will provide you with up-to-date information about the work of his HBV Research Group

Areas of Interest

Molecular mechanisms of Hepatitis B- and Hepatitis D Virus/host interactions with a focus on the early and late events of viral infection. Structural analyses of hepadnaviral particles and virus receptor interactions. Clinical development of entry inhibitors for HBV and HDV infection. Development of hepatotropic drugs for the therapy of liver diseases.



Talks on Saturday - Therapy

Dr. Corina Hutterer (Erlangen-Nürnberg) – Drug Design

09.00 - 09.45 / AM1

since 2010	Post-doctoral Fellow, Institute for Clinical and Molecular Virology (Chair Prof. Dr. B. Fleckenstein), University of Erlangen-Nuremberg, GE
2005-2010	PhD thesis, "Functional characterization of the small terminase subunit of Human Cytomegalovirus" (supervisor Prof. Dr. E. Bogner):
2004	Diploma thesis, Institute for Microbiology, Erlangen, Germany, "Analyses of RNA regulator elements"
2003	Diploma examinations in microbiology (major), forensic medicine, organic chemistry and plant physiology, Friedrich-Alexander-University of
	Erlangen-Nuremberg, GE
1999-2004	Studies in Biology, Friedrich-Alexander-University of Erlangen-Nuremberg, GE

DESIGN OF NOVEL ANTIVIRAL DRUGS ON THE BASIS OF CELLULAR TARGETS

Infections with human cytomegalovirus (HCMV) represent a serious, sometimes life-threatening danger for immunosuppressed individuals, including transplant recipients and patients under antitumoral chemotherapy. Currently approved antiviral drugs have the disadvantage of inducing side effects and drug-resistant virus mutants. These limitations create an increasing need for new antiviral drugs, particularly for drugs that exhibit low levels of toxicity and activity against HCMV variants that are resistant to conventional drugs. Viral replication is a complex process regulated on a network of interacting viral and cellular proteins that are expressed during infection. Here, we describe innovative anticytomegaloviral approaches based on novel, potent and selective small-molecule inhibitors targeting cellular host factors crucial for the efficiency of virus replication. These antiviral principles are based on the targets dihydroorotate dehydrogenase (DHODH, an enzyme that medi-



ates de novo biosynthesis of pyrimidine ribonucleotides) or cyclin-dependent kinase 7 (CDK7, a CDK-activating kinase and a co-activator of RNA polymerase II). Our findings demonstrate that both targets play important roles during viral gene expression and replication and may be efficiently exploited for novel antiviral strategies. Thus, we conclude that DHODH- and CDK7-inhibitors represent highly interesting candidates for the development of novel antiviral drugs.

Talks on Saturday - Therapy

Dr. Egbert Mundt (Böhringer-Ingelheim, Hannover) - Vaccines 09.45 – 10.30 / AM1

10-	Since 2012	Boehringer-Ingelheim Veterinary Research Center, Global Head R&D Poultry Vaccines, Business unit: Animal Health
	2011-2012	IDT Biologika GmbH, Head Viral Vaccines, Business unit: Animal Health
	2006 - 2011	PDRC, University of Georgia as Associate Professor, Caswell Eidson Chair in Poultry Medicine,
		Georgia Alliance Eminent Scholar
	1994-2006	Biosafety officier at the Federal Research Institute for
		Animal Health, Insel Riems, Germany
	1992-2006	Employed as scientist and group leader at Federal
		Research Institute for Animal Health,
		Insel Riems, Germany

MODERN TECHNOLOGY HELPS TO DISCOVER NEW VIRUSES FOR VACCINE DEVELOPMENT

The development of vaccines relays on the knowledge of the pathogen which caused the disease. Most known viral pathogens are able to replicate in either cell culture or embryonated hen eggs. But 99% of all pathogens are not able to replicate in such systems. Thus the identification of such pathogens is restricted. With the availability of new technologies to determine nucleotide sequences the identification of potential viral pathogens which are not able to replicate in vitro became possible. This approach was used to identify a pathogen which caused an enteric disease in chickens. The use of gut content for comparative viral metagenomics between affected and non-affected chickens allowed the identification of a group of possible candidates which might cause the enteric disease. Based on the obtained data appropriate tools were generated which supported the isolation of a new chicken astrovirus. In subsequent experiments it was shown that the virus isolate was able to cause the enteric disease and can now be used for the



development of a vaccine. This example demonstrates that combination of classical virological techniques with latest molecular technologies allows the identification of viral pathogens which might become candidates for vaccine development.

Talks on Saturday - Therapy

Prof. Jean Rommelaere (Heidelberg) – Gene Therapy

11.00 - 11.45 / AM1

	1993-2011	Director of two INSERM research Units at the DKFZ
	1992-present	Professor at Heidelberg Univ; Director of the Division of
19 61		Tumor Virology at the DKFZ
1-1	1984-1992	Research Director (French Natl Inst of Health & Med Res,
1		INSERM) at Pasteur Inst, Lille, France
	1984-1992	Lecturer & Lab Director (ULB)
011	1976-1979	Postdoctoral training
		(Mass Inst Technol & Yale Univ, USA)
	1974-1984	Qualified Researcher (Belgian Natl Fund for Sci Res)
	1974	PhD in Mol Biol (Brussels Free Univ, ULB)

PARVOVIRUS INFECTIONS: PROSPECTS FOR CANCER TREATMENT

Rodent parvoviruses (PV) are recognized for their intrinsic oncotropism and oncolytic activity. These features contribute to the natural capacity of PV for tumor suppression, for which human cancer cells can be targets in animal models. Although PV uptake occurs in most host cells, some of the subsequent steps leading to expression and amplification of the viral genome and production of progeny particles are upregulated in malignantly transformed cells. By usurping cellular processes such as DNA replication, DNA damage response, and gene expression, and/or by interfering with cellular signaling cascades involved in cytoskeleton dynamics and cell integrity, PVs can induce cytostasis and cytotoxicity. Furthermore, there is growing evidence that parvoviral oncosuppression involves an immune component. Besides exerting direct oncolytic effects, PV can indeed serve as adjuvants to hand further tumor destruction to the immune system in animal models. Current and planned parvovirotherapy clinical trials should indicate whether PV oncolysis can be translated into long-term protection by the immune system with improved tumor destruction and patient survival.



Talks on Saturday - Therapy

Prof. Joachim Hauber (Hamburg) – Gene Therapy

11.45 - 12.30 / AM1

	since 2002	Full Professor (C4), Heinrich Pette Institute – Leibniz Institute for Experimental Virology, Hamburg
1000	1996-2002	Associate Professor (Extraordinarius, C3), Institute for
		Clinical and Molecular Virology, Friedrich Alexander University Erlangen-Nürnberg
	1988-1996	Head of Molecular Biology, Sandoz/Novartis Research
		Institute, Department of Antiretroviral Therapy, Vienna,
		Austria
	1987-1988	Postdoctoral Fellow, Howard Hughes Medical Institute,
		Duke University Medical Center, Durham NC, U.S.A.
	1986-1987	Postdoctoral Fellow, Hoffmann-La Roche Inc.,
		Department of Molecular Genetics, Nutley NJ, U.S.A.
	1983-1986	Ph.D., Institute for Physiological Chemistry, Physical
		Biochemistry and Cell Biology, Ludwig Maximilians
		University München

TOWARDS AN HIV CURE BY PROVIRUS EXCISION

HIV-1 integrates into the host chromosome and persists as a provirus flanked by long terminal repeats (LTR). To date, treatment regimens primarily target the virus enzymes or virus entry, but not the integrated provirus. Therefore, current antiviral therapy (HAART) requires lifelong treatment which, unfortunately, may be accompanied by the occurrence of substantial drug-related toxicities and/or the development of drug-resistant viruses. Moreover, HAART cannot cure HIV infection.

Previously, we engineered a LTR-specific recombinase (Tre-recombinase) that effectively excises integrated HIV-1 proviral DNA from infected human cell cultures, suggesting that customized enzymes might someday help to eradicate HIV-1 from the body. Here we analyzed potential cytopathic effects in Tre-expressing cells and demonstrate pronounced antiviral Tre-activity in HIV-1 infected Rag2-/-yc-/- mice, which were either engrafted with Tre-trans-



duced human CD4+ T cells or with Tretransduced human CD34+ hematopoietic stem cells (HSC). The presented data suggest that Tre-recombinase may be a valuable component of future antiretroviral therapies of the post HAART era that aim at virus eradication.

Special Talk on Sunday

Ph.D. Brett Lindenbach (Yale, USA)

10.15 - 11.15 / AM1

	since 2012	Associate Professor, Department of Microbial Pathogenesis, Yale University School of Medicine, New Haven, CT
	2006–2012	Assistant Professor, Section of Microbial Pathogenesis, Yale University School of Medicine, New Haven, CT
	2005–2006	Research Associate, Center for the Study of Hepatiti C, Laboratory of Virology and Infectious Disease,
		The Rockefeller University, New York, NY
	2002–2005	Postdoctoral Research Associate, Center for the Study of
		Hepatitis C, Laboratory of Virology and Infectious
		Disease, The Rockefeller University, New York, NY
	1999–2002	Postdoctoral Research Associate, Howard Hughes
		Medical Institute, University of Wisconsin, Madison, WI
	1999	Postdoctoral Research Associate, Department of
		Molecular Microbiology, Washington University,
		St. Louis, MO

VIRAL NONSTRUCTURAL PROTEINS IN RNA REPLICATION

RNA viruses generate diverse mutant populations, which provide the genetic foundation for the emergence of drug resistance. Because viral diversity arises within infected cells, trans-complementation is an important type of genetic interaction for RNA viruses. For hepatitis C virus (HCV), defects in only two of the five nonstructural (NS) genes required for RNA replication have been shown to be trans-complemented, leading to suggestions that other viral NS genes only work in cis. Here we describe a quantitative system to measure the cis- and trans-requirements for HCV NS gene function in RNA replication. In contrast to previous results, we found that NS3, NS4A, NS4B, NS5A, and NS5B can all be supplied in trans, either individually or in combination. Interestingly, the NS5B polymerase displays an unusual cis-preference: when expressed by a functional replicon, NS5B is unavailable for complementation;



however, when expressed outside the context of a functional HCV replicon, NS5B is capable of trans-complementation.

Further analysis indicated that NS5B function co-segregates with NS5A function; i.e., the functional form of NS5B comes from the same polyprotein as the functional NS5A. These findings reveal new insights on the organization and interaction of viral proteins within replication complexes and provide a facile genetic system to dissect the cis- and trans- functions of viral NS proteins.

Workshops

All participants will be guided to the workshops by members of the organization team.

1 Cellular and viral determinants of the life cycle of positive strand RNA viruses of the family Flaviviridae & Cellular and viral determinants for Norovirus Entry

Prof. Dr. Taube & Dr. Isken, Institute of Virology and Cellbiology

Part I: Cellular and viral determinants of the life cycle of positive strand RNA viruses of the family Flaviviridae (Dr. Isken)

The focus of this workshop will be an introduction of our work with positive strand RNA viruses of the family Flaviviridae. The main focus of research is the elucidation of determinants of viral RNA replication, virion morphogenesis and virus-host interactions. This workshop will consist of a seminar that outlines current research on Hepatitis C Virus (HCV) and related viruses such as bovine viral diarrhea virus (BVDV). The second part will focus on the practical techniques used in our group. Here, we will demonstrate the different applications of reverse genetic approaches to dissect determinants important for different aspect of the viral life cycle. Demonstrations will include methods such as cell culture techniques to determine viral biotypes and virus titers of BVDV or Vaccinia Virus, immunofluorescence assays to control for viral protein expression during replication (HCV and BVDV) and luciferase reporter assays for the quantitative measurements of viral RNA replication.

Part II: Cellular and viral determinants for Norovirus Entry (Prof. Dr. Taube)

The focus of this workshop will be an introduction of our work with positive strand RNA viruses of the family Caliciviridae. The main focus of research is the elucidation of determinants for virus attachment and entry. This workshop will consist of a seminar that outlines current research on Human Norovirus (HuNoV), Murine Norovirus (MNV) and related Caliciviruses, receptor specificity and host restriction factors. The second part will focus on the practical techniques used in our group. Here, we will demonstrate the diffe-



rent applications of protein expression and purification of virus like particles (VLPc). Reverse genetic approaches will be used to dissect determinants important for different aspect of the viral life cycle. Demonstrations will include methods such as cell culture techniques to determine amplify Murine and Human Norovirus in tissue culture, generation of complete and subviral particles using the baculovirus expression system.

2 Looking for the needle in a haystack - how to develop novel drugs using NMR experiments

Prof. Dr. Peters, Institute of Chemistry

NMR spectroscopy provides powerful tools at different stages in the process of drug design. In particular, so called fragment based approaches benefit significantly from NMR techniques that have been developed over the past fifteen years. The workshop will give an introduction into the basic experiments used in NMR based drug design. In general, ligand based and proteinbased approaches can be applied. The pros and cons of either approach will be illustrated using case studies ranging from enzymes as drug targets to membrane proteins to native viruses to whole cells. The emphasis of this workshop is on practical aspects of this novel methodology and no prior knowledge in the theory of NMR spectroscopy is expected.

3 Structure-based design of an antiviral compound

Prof. Dr. Hilgenfeld, Institute of Biochemistry

This workshop will consist of an introduction to structure-based drug design (SBDD) and a tour of the Institute of Biochemistry where various techniques required for SBDD (recombinant target protein production, crystallization, and diffraction data collection) will be briefly explained. This will be followed by hands-on inhibitor docking experiments in the computer pool.

4 Kristallographie und Röntgenbeugung

Dr. Mester, Institut für Biochemie

Kurz nach der Entdeckung des Röntgenlichts durch Wilhelm Röntgen in 1895 (Nobelpreis 1901) zeigte Max von Laue in 1912 (Nobelpreis 1914) die Beugung von Röntgenlicht an Kristallen. Dies ebnete letztendlich den Weg für die Bestimmung der ersten Proteinstruktur, Myoglobin, durch John Kendrew in 1958 (Nobelpreis 1962). Die PDB umfasst gegenwärtig mehr als 90.000 Strukturen wie zum Beispiel die Struktur des Ribosoms oder die der GPCRs. Den Großteil dieser Strukturen (±90%) verdanken wir der Kristallographie und Röntgenbeugung. Kenntnis der dreidimensionalen Struktur ist zwingend erforderlich für die Aufklärung der Beziehungen zwischen Struktur und Funktion. Außerdem sind die Strukturen für die gezielte Optimierung wichtiger Enzyme und erfolgversprechender Leitverbindungen in der Forschung unerlässlich. Im Workshop wird nebst einer kurzen Einführung in die Kristallographie und Röntgenbeugung ein kleines Protein kristallisiert. Wie damals Max von Laue, wird im Labor die Beugung von Röntgenlicht an diese Proteinkristalle gezeigt und besprochen. Ziel des Workshops ist es u.a. Barrieren abzubauen und die Methodik zugänglicher für junge Forscher(innen) zu machen.

5 Quantitative analysis of protein nucleic acid interactions using the example of HIV-1 reverse transcriptase

Prof. Dr. Restle, Institute of Molecular Medicine

Decoding the role of protein nucleic acid interactions in the regulation of transcription, translation, DNA replication, repair and recombination as well as RNA processing, translocation and RNAi has revolutionized our understanding of many cell biological processes and mechanisms in pathogenesis. This workshop gives an insight to some key technologies for quantitative and structural analysis of protein nucleic acid interactions using the example of retroviral replication. Practical examples of techniques based on fluorescence (e.g. equilibrium and pre-equilibrium measurement) and single-molecule



FRET will be elucidated. Depending on the number of participants working out a concrete experiment is possible.

6 Gezielte Modifikation der Blut-Hirn-Schranke mittels rekombinanter Adeno-assoziierter Viren

Dr. Helge Müller-Fielitz, Institut für experimentelle und klinische Pharmakologie und Toxikologie

Die Erforschung von neurodegenerativen Erkrankungen (z. B. Alzheimer und Multipler Sklerose) ist ein wichtiger Teil der aktuellen Neurowissenschaften. Allerdings ist die Untersuchung und Entwicklung möglicher Therapieansätze schwierig, da das Gehirn ein immunprivilegiertes Organ und im Vergleich zu anderen Organen nur schwer zugänglich ist. Ein Hauptfaktor dafür ist die Blut-Hirn-Schranke. Sie stellt eine Barriere dar, über die die Migration von Zellen (z. B. Immunzellen) und Pathogenen sowie der Stofftransport von Metaboliten und Signalmolekülen reguliert werden. Durch ihre Funktionen bildet die Blut-Hirn-Schranke ein attraktives Ziel für Grundlagen- aber auch Therapie-orientierte Forschung. Aufgrund des komplexen Aufbaus und der Interaktion von mehreren Zelltypen sind in vitro Experimente nur bedingt möglich. Das Seminar soll die Möglichkeiten der gezielten Modifikation der Blut-Hirn-Schranke und insbesondere des Gehirnendothels in vivo behandeln. Dabei liegt der Fokus auf der Verwendung rekombinanter Adeno-assozijerter Viren, die mittels Cre-loxP Systems oder Kapsid-spezifischem Targeting für Knockout/in-Studien verwendet werden können.

7 Magnetic Particle Imaging

Prof. Dr. Buzug, Institute of Medical Engineering

MPI is a new tomographic imaging modality capable of imaging the distribution of superparamagnetic nanoparticles (SPIOs) and was recently invented at Philips research, Hamburg (2005). The institute of medical engineering started to investigate in MPI in 2007 and was the first to demonstrate

the feasibility of the new single-sided MPI scanner geometry. Our further research activities are magnetic particle spectroscopy (MPS), efficient reconstruction, simulation studies and design of optimal nanoparticles for MPI. The principle of MPI is based on the nonlinearity of the particles' magnetization curve. When exposed to an oscillating magnetic field (drive field), the spectrum of the responding magnetization contains not only the base frequency f but also higher harmonics that are exploited for imaging. Spatial encoding is achieved by superposition of a static non-uniform selection field providing a single field-free point (FFP) and high field strength in its vicinity. The FFP is steered through the object of interest by means of the aforementioned drive field. In this way, data for reconstructing the particle distribution can be acquired with a recording coil. Here, it is exploited that only particles in the direct neighborhood of the FFP contribute to the signal, whereas afar particles stay in saturation.

8 The molecular ruler poly proline with single molecule FRET

Prof. Dr. Hübner, Institute of Physics

In the workshop, the students will get a brief introduction into fluorescence resonance transfer with single molecules. There will be a hands-on in the lab were the students make smFRET experiment where the energy transfer in the classical molecular ruler poly proline will be measured. In the Institute of Physics smFRET is applied to study viral or bacterial proteins. The main focus lies on the investigation of protein folding and the formation of a protein-protein-complexes, for example the RNA-polymerase, assembled from non-structural protein 7 (nsp7) and non-structural protein 8 (nsp8), from the Feline Coronavirus or the complex formation of ESAT-6/CFP-10 complex from Mycobacterium tuberculosis. With the advent of single-molecule methods the process of complex formation is becoming accessible to direct observation.



9 Current therapy strategies in HIV infections

Prof. Dr. Rupp, Institute of Medical Microbiology and Hygiene

The incidence of newly detected HIV- patients in Germany did not change in the last decade. Almost 3000 people get diagnosed with acute or chronic HIV- infection per year, sometimes already progressed to AIDS. However, the perspective for those patients increased tremendously in

recent years, due to the availability of highly active antiretroviral therapy. In this seminar we will discuss current treatment options in patients with HIV infection. Patient cases will be presented to make the attendants familiar with daily routine in HIV clinics. A special focus will be given the different molecular ways to attack HIV in a human cell. Additional targets in the HIV-host interaction will be highlighted to reconsider current treatments and speculate about novel drugs that might improve treatment efficacy. Drug-drug interactions and side-effects of the most common substances in treating HIV will be addressed in the context of the life-long necessity to treat the infection. Students with interest in virology, antiviral treatments and infectious diseases are highly welcome to join the seminar.

10 Key position of stem-like cells in malignant human glioma

PD Dr. Zechel, Clinic for Neurology

Malignant glioma, such as glioblastoma multiforme (GBM) and gliosarcoma (GSarc), harbor a subpopulation of cells, referred to as BTSC (brain tumor stem cells). BTSCs exhibit similarities to neural stem cells (NSC) and neural progenitors (NPC), self- renew and produce orthotopic tumors in mouse models. Recent data proposed that BTSCs constitute a lineage of self- renewing cell types expressing a range of markers of forebrain lineages. Moreover, experimental data provided evidence that BTSCs survive standard radio- and chemotherapy and become responsible for tumor regrowth. In 2012, a genetically engineered mouse model proved this and showed that a restricted

cell population of slowly dividing GBM cells propagated tumor growth after standard chemotherapy. Notably, BTSCs also contribute to the rich network of vessels and capillaries developing during gliomagenesis by secretion of growth factors, vascular mimicry and transdifferentiation. Together these findings suggest that elimination of BTSCs by specific targeting or differentiation will be the crucial step on the way to improved glioma therapy.

11 Heart and Heredity - Functional Genomics of Atherosclerosis and Myocardial Infarction

M.Sc. Jaafar Al-Hasani, Institute of Integrative und Experimental Genomic

Myocardial infarction (MI), commonly known as a heart attack, is a major cause of morbidity and mortality worldwide, thus also called killer number one. MI is not only influenced by many environmental factors or physical conditions, such as smoking, alcohol, stress, diabetes or high blood pressure, but the risk can also be inherited. The aim of our group, led by Prof. Erdmann, is to identify and to understand the genetic basis of cardiovascular diseases (CVD), such as Atherosclerosis, a major predisposition for MI, and MI. Very recently, and together with Prof. Schunkert, Prof. Erdmann contributed successfully in identifying risk genes for MI using genome wide association studies (GWAS). Until now, 46 risk genes have been identified. In the coming years, we aim to go beyond GWAS and elucidate the functional role of each of the already identified risk genes using in vitro and in vivo models. Especially, we combine different approaches, integrating systems biological aspects with genomic, transcriptomic and metabolomic data, to understand the underlying pathomechanism of each risk gene. The workshop will include two parts: a theoretical and a practical part. The theoretical part will include an overview about Heart and Heredity as well as a short introduction into GWAS. The second, practical part will take the participants to learn about several methods of molecular and cell biology which are used in our lab, like cell culture techniques for differentiation of murine Embryonic Stem Cells (mESC) to cardiomyocytes or calcifying cells, and the transfection of mammalian cells using plasmids with reporter genes, to name a few. Also, the participants will



learn about histological analysis of mouse heart sections and go throughout the different anatomical structures of the heart under microscopy.

12 Viruses - blessing or a curse

Dr. Dominik Mahr, Institute for History of Medicine and Science Research

In this workshop you will get the possibility to discuss a ethical topic from the area of conflict of virology and gene technology. The introduction may be a provoking question or a short text to make sure everybody is arguing on the same basis.

13 Immunologic Research at the Institute for Systemic Inflammation Research

Prof. Dr. Manz, Institut für Systemische Entzündungsforschung

The ISEF conducts leading basic and translational immunological research focusing on the crosstalk between the innate and the adaptive immune system (www.isef.uni-luebeck.de). ISEF researchers contribute to multiple research and teaching consortia at the University of Lübeck (UzL), such as the Excellence Cluster "Inflammation at Interfaces", the SFB/TR 22 "Allergic Immune Responses of the Lung", the SFB 654 "Plasticity and Sleep" and the Research Training Group (GRK) 1727 "Modulation of Autoimmunity". Further, the ISEF initiated and organizes the recently funded International Research Training Group (IRTG) 1911 "Immunoregulation of Inflammation in Allergy and Infection" in close collaboration with the University of Cincinnati and Cincinnati Children's Hospital, a leading research organization in the US. This seminar will provide an overview of the ISEF activities, with a particular focus on research and training opportunities in the context of the IRTG1911 (www. irtq1911.uni-luebeck.de). In this consortium, state of the art immunological methods based on genetically modified mouse models, multicolor flow cytometry, cell sorting and confocal microscopy are applied to study the immune mechanisms controlling the development of allergic asthma and food allergy

and diseases triggered by infection with intracellular pathogens including Toxoplasma gondii, Leishmania major, Mycobacterium tuberculosis and Lymphocytic choriomeningitis virus. The main goal of the IRTG projects is to broaden our understanding of pathogen sensing, activation and modulation of innate immune cells, their crosstalk with pathogen-specific adaptive immunity and the resolution of such immune response. The students working within the IRTG1911 projects closely collaborate with other ISEF students and UzL scientists involved in studies on autoimmune diseases and are integrated in local research and training networks.

14 From Bench to Bedside – Ein Überblick über die translationale chirurgische Forschung in Lübeck

Prof. Dr. Dr. Habermann, Sektion für Translationale Chirurgische Onkologie & Biomaterialbanken

Die Sektion für Translationale Chirurgische Onkologie & Biomaterialbanken der Universität zu Lübeck unter der Leitung von Prof. Dr. Dr. Habermann führt schwerpunktmäßig Untersuchungen auf dem Gebiet der kliniknahen onkologischen Forschung durch. Hierbei werden alle üblichen Labortechniken sowie die meisten molekularbiologischen Untersuchungsmethoden in fünf spezialisierten Laboreinheiten angewandt: Klinische Probenaufbereitung, Histologie, Zellkultur, Biomics (Genome-, Transkriptom- und Proteinanalysen), Mikroskopie mit DNS-Cytometrie. Auf dem Gebiet der Tumorforschung gilt das besondere Interesse dem kolorektalen Karzinom, dem häufigsten Tumor des Verdauungstraktes. Untersuchungen zu Veränderungen auf DNA-, RNA- und Protein-Ebene sollen dabei helfen, grundlegende Mechanismen der Karzinomentstehung zu entschlüsseln und hierbei innovative Biomarker zu identifizieren, die für eine verbesserte Früherkennung, Individualdiagnostik, Therapie, Prognose und Nachsorge eingesetzt werden können. Die grundlegenden Untersuchungen hierfür werden insbesondere mittels Chip- bzw. Array-Technologien (arrayCGH, microarrays, protein-chips, SELDI, tissue-arrays) als auch mit Hilfe der 2-DE Technik durchgeführt. Identifizierte Biomarker insbesondere des Zellzyklus, der Tumorzellproliferation, der Meta-



stasierung und der Apoptoseregulierung stehen im Vordergrund weiterführender Analysen, mittels derer die Wertigkeit einzelner Marker für innovative Therapien getestet wird.

Ein weiterer Schwerpunkt der Tumorforschung gilt dem Aufbau der überregionalen Tumorbank "Kolorektales Karzinom", der dazu führen soll, eine qualitativ hochwertige Gewebe-, Blut- und klinische Datensammlung aufzubauen. Für die Betreibung der überregionalen Tumorbank wurden gemeinsame Standard Operation Procedures (SOP's) entworfen, die sich an den aktuellen datenschutzrechtlichen und ethischen Vorgaben ausrichten. In der Kryobank werden sowohl Gewebe als auch Blutproben mit ihren klinischen Parametern gemäß der jeweiligen SOP's erfasst. Das Seminar wird einen Überblick über den aktuellen Alltag in der Sektion Translationale Chirurgische Onkologie & Biomaterialbanken bieten. Es wird exemplarisch ein kompletter Workflow in der klinischen Forschung von der Probensammlung im Operationssaal, über die molekulare Untersuchung bis hin zum klinischen Test dargestellt. Neben illustrativen Vorträgen wird eine Laborführung den Ablauf in der chirurgischen Forschung untermalen.

15 Human neurons derived from induced pluripotent stem cells

Dr. Capetian and Dr. Seibler, Institute of Neurogenetics

A new type of pluripotent cells known as induced pluripotent stem (iPS) cells has recently gained increasing importance to study disease mechanisms in a biologically relevant cell system. These cells share the pluripotent characteristics of embryonic stem cells but are instead generated via direct reprogramming of the patients' own somatic cells. The workshop will give an introduction to the generation of iPS cells and their subsequent differentiation into disease-relevant neuronal subtypes. Further, participants will get the opportunity to have a look on cells in the differentiation process and to perform a short live-cell imaging experiment in our lab.

Exhibition stalls

A few sponsors and collegiate groups will introduce oneself.

Presentation of Master's Programs

The reason for the Biomedical Students' Symposium is not only expanding your knowledge in a specific subject but it also provides a good opportunity to learn from each other in order to maintain or even increase the scientific standard. Moreover, it is useful to receive first hand information about your favored universities before you start your master's degree. Therefore, every university may display its master's program

For further information visit:

molmednet.de or gbm-online.de



Thursday

We will welcome you in the foyer of the Audimax. During the **introducing talk** Prof. Dr. Tautz will provide you with basic knowledge about virology. Moreover, we want to present the short, but exciting story about our university.

Afterwards, we will get together in the foyer in order to get to know each other. Our 'Fachschaft MINT' will provide a **barbecue** where you can buy sausages and some veggie-food for low budget. Accordingly to the cold weather we serve hot wine punch.

Friday

In the evening we will have **dinner** in the company Euroimmun. It will be possible to go by bus. It is definitely worth it (It's for free!!). Prof. Dr. med. Winfried Stöcker (director of Euroimmun) will introduce his company to you and you will have the perfect opportunity to talk to some of the speakers. Subsequently we will go to the city to explore the **pub culture** of Lübeck.

Saturday

Visiting the city of Lübeck, the queen of the Hanseatic League, one should not miss a **guided tour** through the **historic city centre**. Let the guides in their historical suits take you to the different epochs of Lübeck's town history, from the middle age until the modern age. This journey will go from the impressing brink-lined town hall to the small and cosy alleys and backyard and is definitely going to bring you close the inimitable charm of our home town, which so many of us learned to greatly appreciate. (It will be charged with 5EUR at the Check-In.)

P++ Party: P++ is a group of students who have already organized a lot of parties at our university. We are sure that we will have a good time with you.

The medieval city centre of Lübeck is part of the UNESCO-world heritage and favored by all students. To get a first overview of the city, we advise to visit the **Tower of Sankt Petri**, Petrikirchhof 1. For only a few Euros a modern lift will take you to the viewing platform in a height of 50m.

Only a far meters down the road you can see the beautiful **Holstentor**, landmark of Lübeck. You should have a look from both sides! Another typical hallmark of Lübeck is our **marzipan**. Near the Holstentor (An der Untertrave 98) you can see an exhibition about the history of marzipan in Lübeck. Of course you can also buy some marzipan there. The popular Niederegger Marzipansalon, another marzipan, factory', can be found in Breite Straße 89.

Across the road you find yourself at the market place facing the **town hall** of Lübeck. Directly aside there is the imposing church of **Sankt Marien**. If you are interested in history and literature, you may want to visit the **Budden-brookhaus** (Mengstraße 4) where the family of the famous author Thomas Mann lived in. Today it harbours two exhibitions: ,Die Buddenbrooks - Ein Jahrhundertroman' and,Die Manns - eine Schriftstellerfamilie'. The **Günther-Grass-Haus**, in Glockengießer-Straße 21, offers alterning exhibitions.

You also should not miss to see the famous **7 towers of Lübeck:** Marienkirche, St. Jakobikirche, Petrikirche, Aegidienkirche and the Dom of Lübeck.

If you want to learn more about our beautiful **,Queen of the Hanseatic League**, you are welcome to participate in the guided city tour on Saturday evening or visit www.luebeck.de. This symposium could not have been organized without help and contributions from many individuals. We are more than grateful to the Life Science Verein Lübeck, in person Dr. Rosa Pulz, PD Dr. Thomas Weimar and Prof. Dr. Thomas Peters. Moreover, we want to thank the speakers and the organizer of the workshops for their intrinsic motivation to inspire students and young scientists and for uncovering many secrets of virology and science in general. We also are grateful to those who supported us during the event, especially the 'Fachschaft MINT', Medisert (Frau Kanina Botterweck, Herr Thomas Zeidler and Saskia Koch) and P++ (Kevin Becker, Nikolai Schieweck and Matthias Hardtmann). Thanks to the sponsors and the GBM (Prof. Dr. Carmen Villmann) for the financial support. And finally, we would also like to thank you for coming to Lübeck.

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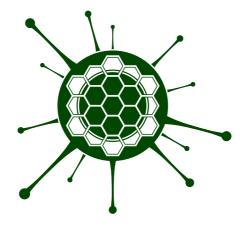


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Content and Layout Christin Krause · Antje Lindae · Tobias Schöne

Graphics and Design Till Zickmantel

Print www.flyeralarm.de

Moderation Anna Oberle · Philipp Seidel · Felicia Schlotthauer

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March/April 2014:

Spring Students' Symposium in Furtwangen/Villingen Schwenningen

30.10. - 02.11.2014:

Students' Symposium in Erlangen

