03
Winter
2020

NEWS
RESIST – Resolving Infection Susceptibility

RESIST

Looking back and forward

GREETINGS FROM PROFESSOR SCHULZ AT THE TURN OF THE YEAR

I imagine that most people will look back on 2020 with rather mixed feelings – the SARS-CoV-2 pandemic has complicated life for everybody, and for some among us it has even had life-changing or existence-threatening consequences. Against this background it is therefore with immense gratitude that I look back on what 2020 has brought for RESIST. In this year we have completed the recruitments of our 7 new assistant and associate professors and this newsletter will introduce them to all of you. Not only do they substantially strengthen the research portfolio and the academic community in the MHH research priority area of 'Infection & Immunity', many of them also bring new skills and expertise to our campus and some will enhance the links with partnering institutions such as Center for Structural and Systems Biology in Hamburg, of which MHH is a partner, or the Center for Chronic Immunodeficiencies in Freiburg. Their presence will help us mount new initiatives for cooperative funding networks. It is also with gratitude that we in RESIST acknowledge the additional substantial support to be provided by our Ministry for Science and Culture of Lower Saxony (MWK) for the four RESIST associate professors in order to help them 'come up to speed' as quickly as possible.

The RESIST speaker team: Professor Dr. Thomas Schulz (in the middle) and the two co-speakers Professor Dr. Gesine Hansen (left) and Professor Dr. Reinhold Förster (right).

A second important achievement is our new Master of Science program in 'Biomedical Data Analysis'. This is a joint effort of RESIST and the Peter L. Reichertz Institute of Medical Informatics, directed by Prof. Michael Marschollek, and could not have been set up as efficiently without the substantial help of the office of the MHH Dean of Studies, in particular Drs. Volke and Celik. They organized the challenging accreditation process and guided us through the required myriad formal steps. With their help, this new degree course has now been officially accredited by the accreditation agency, approved by our Ministry (MWK) as well as the MHH Senate, and we now look forward to the first student intake in the autumn of next year. Having this MSc course in place will be one important step in positioning MHH for the 'information age'.

This year has also seen important research achievements and some are illustrated in this newsletter. They show that all research areas in RESIST generate cutting-edge research and that many MHH clinicians and scientists, as well as scientists at our partner institutions, contribute substantially. This year, of course, everybody's attention has been on SARS-CoV-2 and its disease, COVID-19, and RESIST has also taken up this challenge. With additional substantial financial support from our Ministry (MWK), RESIST investigators have initiated two discovery programs to identify new small molecule inhibitors as well as recombinant neutralizing antibodies with broad activity not only against SARS-CoV-2 but also against related coronaviruses that could represent potential starting points for future epidemics: after all, our current problem, the SARS-CoV-2 pandemic, stems from the fact that, for the third time in less than 20 years, a highly pathogenic coronavirus has 'jumped' from bats to humans to cause an epidemic outbreak of a new disease. Since we know that many more closely related coronaviruses exist in several bat species, it is therefore a reasonable assumption that such a zoonotic outbreak may happen again. The current pandemic has made it abundantly clear that we need to be better prepared next time. RESIST scientists are therefore working to make a contribution to this challenge. Others in RESIST are laying the scientific basis for alternative and improved ways to apply SARS-CoV-2 vaccines and produce an improved immune response.

I therefore believe that in RESIST we can look back on a successful year 2020. On behalf of the RESIST-speaker team I therefore wish everybody in RESIST and all the readers of this newsletter a Merry Christmas and equally successful, but hopefully less strenuous and more 'normal' year 2021.

NOW THE TIME HAS COME: THE SEVEN PROFESSORSHIPS FINANCED FROM RESIST FUNDS ARE ON BOARD

All RESIST professorships awarded

„We are very pleased that we were able to appoint seven professorships financed by RESIST with outstanding young scientists as planned this year. They enrich and support our already existing RESIST research areas with their expertise and complement them, for example in the field of biomedical data analysis. Moreover, our new RESIST professorships are intensifying the connection to the RESIST partners TWINCORE, CSSB and CCI," says RESIST speaker Professor Dr. Thomas Schulz.

Sarina Ravens is W2 Professor for "Systemic Human Immunology" since May 2020. She was already involved in development and leading of two existing RESIST research projects. Together with Professor Dr. Dorothee Viemann she is working on project B3 on influence of the microbiome on the development of the immune system. And within the project B5 Professor Ravens analyses in cooperation with Professor Dr. Thomas Werfel, Professor Dr. Immo Prinz and Professor Dr. Reinhold Förster the susceptibility of elderly people to herpes. Within the framework of her professorship, she works together with her research group at the MHH-Institute of Immunology on B and T cells of the immune system and investigates how these white blood cells functionally adapt depending on environmental factors and age.

The 34-year-old received her master's degree in Biomedicine at the MHH and graduated at the Université de Strasbourg in 2014. Since 2015 she is working at the Institute of Immunology at MHH. "Together with my team and in close cooperation with other RESIST working groups, I am analysing the diversity of antigen receptors and gene expression patterns of B and T cells in relevant patient cohorts, such as the cohort with premature infants recruited by the MHH Clinic of Paediatric Pneumology, Allergology and Neonatology," says Professor Ravens. She uses special high-throughput sequencing technologies and bioinformatical methods. For example, she tries to find out, how intestinal bacteria and infections affect the fitness of immune cells in early childhood and whether this influence might be associated with susceptibility to infections over the course of a lifetime. Her long-term goal is to gain a better understanding of the susceptibility of patients with weakened immune systems to infections so that improved therapeutic approaches can be developed in future.
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Chris Lauber received a junior professorship financed by RESIST in June 2020. "I am very pleased that I can support RESIST now to achieve its goals", says the MHH Professor of "Computational Virology". He works at the Institute for Experimental Virology at TWINCORE.

Professor Lauber and his team are bioinfomatically analysing the complex interaction of genetic variations in the human genome. He aims to identify changes in the genome that are related to disease susceptibility or to the course of disease. The 39-year-old is particularly interested in infections by the respiratory syncytial virus (RSV), which can be severe or even life-threatening in small children. He is working closely with Professor Dr. Gesine Hansen and Professor Dr. Thomas Pietschmann in order to uncover genetic determinants of severe RSV disease progression.

Moreover, Professor Lauber investigates a possible connection of an individual susceptibility by a person's virom, which is the totality of viruses associated with a human being. In order to link already known and newly discovered viruses with diseases of unknown cause, he, his team and cooperation partners in Heidelberg have recently developed a workflow for high-throughput calculations. "The huge amount of bioinformatical data that we analyse in our research requires application of efficient computer-based methods. That is why we use high-performance computers that can run up to 50,000 analyses simultaneously," explains the researcher.

Chris Lauber studied bioinformatics in Jena, received his PhD in 2012 in Leiden, Netherlands. He continued his research at the Technical University of Dresden. Since 2017, he also worked for the German Cancer Research Centre in Heidelberg.
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Jens Bosse is junior professor for "Quantitative and Molecular Virology" since May 2020. His team is the first MHH group located at the Center for Structural Systems Biology (CSSB) in Hamburg, a joint venture of nine scientific partners from Northern Germany. Professor Bosse's group is associated with the MHH Institutes of Virology and Biophysical Chemistry and, in addition, supported by the Heinrich-Pette-Institute, Leibniz Institute for Experimental Virology (HPI).

The 38-year-old analyses how the assembly of individual viral particles in infected cells is coordinated in time and space and which viral and cellular factors play a role during this process. He is particularly interested in herpes viruses. Methodologically Professor Bosse uses and develop highly sensitive live cell microscopy systems. He has been cooperating with RESIST scientists for years.

Jens Bosse studied molecular and applied biotechnology in Aachen and received his PhD at the Max von Pettenkofer-Institute for Hygiene and Medical Microbiology at the Ludwig-Maximilians University Munich in 2011. He subsequently did his research at Princeton University, New Jersey, USA. Since 2016 he heads the group "Quantitative Virology", which moved from the HPI to the CSSB in October 2020. "At CSSB, my team and I are able to combine particularly well the latest structural biology results with data on the dynamics of virus replication in living cells, and thus identifying weak points in the viral life cycle as basis for new antiviral agents," he says.

This professorship will strengthen the relationship between RESIST and the MHH and the CSSB. „The motivation for founding the CSSB arose from the desire to create an internationally visible centre for equipment-intensive biomedical research in the region," explains RESIST researcher Professor Manstein. The director of the MHH Institute of Biophysical Chemistry has been a member of the CSSB's steering committee since 2013 and was its deputy director from 2018 to 2020. „Since the completion of the CSSB research building, considerable third-party funding has been raised for excellent equipment of five instrumental centres focusing on protein production, protein characterisation, light and fluorescence microscopy, electron cryomicroscopy and high-throughput crystallisation. The international leadership of the institution is further strengthened by its close proximity to large-scale research facilities such as eXFEL and Petra III on the DESY campus in Hamburg-Bahrenfeld," adds Professor Manstein.
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Michele Proietti is junior professor for "Genetics of Immundysregulation" since July 2020 and works in the MHH Clinic for Rheumatology and Immunology. "I am very pleased to join this community of excellent scientists and physicians and support RESIST now", he says.

Professor Proietti analyses, in close collaboration with RESIST-scientists Professor Dr. Reinhold E. Schmidt and Professor Dr. Torsten Witte at MHH, and Professor Dr. Bodo Grimbacher and Dr. Andrés Caballero at Center of Chronic Immunodeficiency (CCI) Freiburg, the genetic landscape of individuals with immunodeficiency and defective regulation of the immune response. Their goal is to identify genetic changes that predispose individuals to infections and to immune-mediated pathology. To efficiently analyse the large amount of genetic data efficiently, Professor Proietti and his cooperation partners in Freiburg are currently developing an immunogenetic bioinformatic platform, containing genetic andfunctional data as well as according literature.

The 44-years-old is a physician and scientist with a background on clinical medicine, experimental immunology and bioinformatics. He obtained a degree in medicine and his residency in internal medicine in Rome (University "La Sapienza"), subsequently he received his PhD in clinical and experimental Immunology in 2010 at the University of Genova, Italy. Afterwards, he moved to the Institute of Research in Biomedicine to focus on experimental immunology, before joining the CCI at the Uniklinikum Freiburg in 2015. During that time he developed a particular interest and expertise in data analysis and bioinformatics with focus on genetic data. These skills supported him in his position as Head of the genetic and genomic Unit of the CCI from 2017
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„The RESIST professorship of Michele Proietti represents a bridge professorship between the MHH and the CCI. It also links the MHH Clinic for Rheumatology and Immunology with the internationally leading German centre for this topic, thus significantly strengthening future cooperations," says RESIST researcher Professor Dr. Reinhold E. Schmidt.

Nico Lachmann is W2 professor for "Control of Respiratory Infections" financed by RESIST since September 2020. He works in the MHH Clinic for Paediatric Pneumology, Allergology and Neonatology. "The development of new therapeutic approaches to treat lower respiratory tract infections is urgently needed," he says.

The 38-years-old investigates the role of macrophages in the development and control of infections. For example, his team is conducting detailed research into how these scavenger cells of the immune system are formed in the lungs and what function they have in bacterial lung infections. Different types of stem cells are used therefore.

In order to gain new insights into the development of lung diseases and derive new therapies, Professor Lachmann's team is also establishing different disease models in the laboratory. His work is supported by close cooperations with other RESIST-scientists at MHH, such as Professor Dr. Burkhard Tümmler, Professor Dr. Dorothee Viemann and Professor Dr. Ulrich Kalinke from TWINCORE, but also with international partners such as Professor Dr. Jean-Laurent Casanova from Paris.

The scavenger cells in the lungs can be attenuated – for example due to a genetic defect, a misdirected pulmonary immunity or an infection that has already occurred. „One of our latest approaches is to replace the weakened macrophages with healthy macrophages from the laboratory, which then provide protection against bacteria, such as mycobacteria, and viruses," describes Professor Lachmann.

Nico Lachmann studied biomedicine at MHH and Yale University (School of Medicine) and received his doctorate from the MHH in 2012. Subsequently he did research at MHH, at the Max Planck Institute for Biomedicine in Münster and the Cincinnati Childrens Hospital Medical Center in Cincinnati.
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Marco Galardini is RESIST funded W2 Professor for „Systems Biology of Microbial Communities" at MHH since October 2020. He heads the research group with the same name at the Institute for Molecular Bacteriology at TWINCORE.

"Just as every human being is different from the others, although we are all humans, bacterial strains inside one species can differ. If the species exist in different surroundings, mutations create genetic variations that can affect more than half of their genetic content", says Marco Galardini.

The 36-year-old focuses on the question how this genetic differences influence the variable bacterial characteristics. This question is particularly important with regard to the pathogenicity of the bacteria and their resistance to antibiotics.

„I am interested in how these differences between the strains can affect the development of antimicrobial resistance, in particular its speed and predictability," explains Marco Galardini. Using bioinformatic tools and molecular biology, he is trying to predict how the differences in the pathogens' genomes will evolve.

Marco Galardini studied biotechnology and bioinformatics and holds a PhD in microbial genetics. After working as a postdoctoral researcher in Cambridge and Boston, he now arrived in Hanover. His expertise complements the specialised portfolio of Professor Dr. Susanne Häußler's Institute for Molecular Bacteriology, where multi-resistant pathogens and biofilm-forming bacteria are analysed.
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Sabrina Schreiner is W2 RESIST professor for "Virus Replication in Cellular Chromatin" at the MHH Institute of Virology since October 2020. She focuses her research on human adenoviruses, which cause conjunctivitis, gastrointestinal disorders or pneumonia, among other things.

In most cases, such a disease proceeds in healthy adults either without any clear or with very mild symptoms. „It can be assumed that everyone has already had several adenovirus infections," explains Professor Schreiner. The human adenovirus, of which there are currently more than 85 different types known, were previously not considered particularly dangerous. However in immunocompromised people such an infection can become severe and even fatal. The disease is particularly dangerous for children after stem cell transplantation.

"Since 2006, it has also been known that infections with adenoviruses can cause severe pneumonia in healthy people as well, which can have fatal consequences. We do not yet understand the molecular background in detail," says Professor Schreiner. So far, there is no drug that is specifically effective against adenoviruses. There are also no vaccinations for the healthy population available.

Professor Schreiner investigates together with her team how the virus multiplies in the cell. „We have observed that an adenoviral infection causes a significant change of so-called PML core bodies in the cell, a complex of several proteins," she says. The name PML body is derived from the acute promyelocytic leukaemia, as they are destroyed in this disease, but also in various viral infections. The otherwise round structures dissolve and elongated fibrils are formed. „It is suspected that the PML core bodies have an antiviral function – not only in human adenoviruses," explains the 38-year-old Sabrina Schreiner.

„Adenoviruses destroy the round structures of the protein complexes and then use this manipulation of the cell for their own reproduction," describes Professor Schreiner. Her team is therefore working on an antiviral agent that acts against these cell structures and not directly against the virus. This is important, because viruses often develop resistance to drugs that target them directly. For example, they can mutate so that they are no longer recognisable by the drug.
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New in the RESIST team: Dr. Atschekzei

SHE IS DEDICATED TO PRIMARY IMMUNE DEFICIENCIES IN ORDER TO HELP AFFECTED PEOPLE WITH INDIVIDUAL THERAPIES

Since November 2020 Dr. Faranaz Atschekzei is now associated with RESIST. She has been successfully researching in the field of immunogenetics at the MHH Clinic for Rheumatology and Immunology for eight years and has been involved in the RESIST subproject A2 since 2019. Her research group focuses on the molecular genetics of primary immunodeficiencies and how epigenetic factors influence immunodeficiency diseases. Primary immunodeficiencies are congenital and often genetically determined defects of the immune system that manifest themselves in childhood or even in adolescence or adulthood.

There are very heterogeneous disease patterns among the approximately 400 known primary immunodeficiencies, but a high and usually severe susceptibility to infection unites most of them. In addition to the increased susceptibility to infection, some patients also develop immune dysregulations including autoimmunity, lymphoid hyperplasia and tumours. Dr. Atschekzei's research group is investigating the molecular basis of the disease in order to enable patients with these heterogeneous diseases to receive a very individual and targeted therapy in the near future.

Dr. Atschekzei is pleased to be associated with RESIST now: „Being part of the RESIST team opens up new opportunities for cooperation and exchange with experienced scientists and experts in various research areas," she says.

More information (in german) about Dr. Atschekzei's work can be found on the Internet at: https://www.mhh.de/kliniken-und-spezialzentren/kir/forschung/ag-atschekzei

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NEW: Biomedical Data Science

MASTER'S PROGRAMME AT THE INTERFACE BETWEEN LIFE SCIENCES, MEDICINE AND COMPUTER SCIENCE

Dr. Melina Celik

Digitalisation is increasing. Hence, it is becoming more and more important in research, diagnostics and therapy to be able to handle large amounts of data – for example, for planning and evaluating clinical studies or complex experiments. But there are still too few experts in this field.

The new four-semester Master's programme Biomedical Data Science, accredited in September 2020 and financed by RESIST, will help to remedy this situation. „We are very pleased that the Master's programme can start in the winter semester 2021/2022 with a total of 24 students. The analysis of large amounts of data is indispensable for individualised medicine and thus, for example, for people with a weak immune system," says RESIST speaker Professor Dr. Thomas Schulz, head of the MHH Institute of Virology. Together with Professor Dr. Michael Marschollek, Director of the Peter L. Reichertz Institute for Medical Informatics at MHH, he is responsible for the schedule of the study programme. „The focus of this interdisciplinary and multiprofessional study programme is on the collection, maintenance, processing, analysis and communication of data in the field of infection biology. The students learn to generate and handle large, heterogeneous and complex data sets and to develop and apply IT solutions," explains Professor Marschollek. They can work as scientists in research institutions or in (research) companies, biotechnological / clinical laboratories and government agencies – at the interface of life sciences, medicine and computer science.

The study programme can also form the basis for a doctorate.

Applications are open to graduates of a bachelor's programme in biology or medicine from 30 April to 15 July 2021. The main language of instruction is German with some elements in English. Most of the study programme takes place online, although there will be periods of attendance at MHH lasting several days.

More information is available on the programme's homepage:
www.mhh.de/master-biomeddat

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Become a data professional: In autumn begins the new program for 24 students.

CONGRATULATIONS!

Professor Dr. Charles M. Rice awarded the 2020 **Nobel Prize**

Professor Dr. Charles M. Rice, member of the Scientific Advisory Board of the Cluster of Excellence RESIST, received the 2020 Nobel Prize in Physiology or Medicine – together with Professor Dr. Harvey J. Alter and Professor Dr. Michael Houghton. This was announced by the Nobel Prize Committee on 5th of October 2020 at the Karolinska Institutet in Stockholm.

The three scientits are being honoured for their discovery of the hepatitis C virus. They have found the cause of chronic hepatitis cases and made blood tests and new drugs available, that have saved millions of lives.

Professor Rice of the US Center for the Study of Hepatitis C, the Rockefeller University, New York, is one of the leading experts in the fields of infection and immunity of the RESIST Scientific Advisory Board. This board supports the Research Management Board of RESIST in questions of research strategy. RESIST researcher Professor Dr. Thomas Pietschmann, head of the TWINCORE Institute for Experimental Virology, also working on the hepatitis C virus, has been cooperating with Professor Rice for many years. „His work has laid an important foundation stone in hepatitis C research. Personally, I am especially pleased for Charlie about this great honor for him and our field of research." RESIST researcher Professor Dr. Gisa Gerold from TiHo jointed the group of Professor Rice as a postdoc and is very happy for him. „His basic research has paved the way for the development of hepatitis C cures. Basic research is the key. If we understand the molecular details of an infection, we can develop strategies to prevent or treat infections," she explains.

The hepatitis C virus is transmitted via blood, can cause chronic liver inflammation (hepatitis) and liver cancer, and is a common cause of liver transplants. Around 71 million people worldwide have chronic hepatitis infections. Antiviral drugs can cure most people, but the expensive drugs are not available across the globe, and successful treatment does not protect against re-infection, which can occur often in populations with frequent exposure to the virus.

Studies suggest that global control of this disease is only possible by a combination of antiviral treatment and prophylactic vaccination. This is why the team of the RESIST project B10 is focusing on vaccination as a protection against Hepatitis C. The aim of this team is to identify particularly efficient immune responses and contribute to the development of a new vaccine.

School competition:

Infektions-forschung @ home

It starts with the question, what bacteria, viruses and fungi are, followed by the cultivation of bacteria and, last but not least, even epidemiological observations using the example of SARS-CoV-2 are considered: A RESIST team involving Dr. Henrike Ahsendorf, PD Dr. Jens Bohne, Carla Seegers and Dr. Annett Ziegler has come up with tasks for schoolchildren for the „B!G B4NG Challenge" online competition in cooperation with the University Hannover (LUH). The challenge around infection biology will be presented at the beginning of January 2021 outside the series as a single task. The tasks are addressed to students from the 9th to the 13th grade, which they can work on alone or in teams using all available. The best teams can look forward to monetary and material awards to promote their studies. Further information and the opportunity to register are available at https://www.lehrerbildung.uni-hannover.de/en/school-projects/offers-grade-10-13/bg-b4ng-challenge/

Impressum

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Design and printing
Digital media of the Hannover Medical School (MHH)

Online edition
The RESIST newsletter is also available on the Internet at www.RESIST-cluster.de.

Photos (Edition 3_2020)
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Nico Herzog / Fokuspokus (1)
Rockefeller University (7)
TWINCORE / Carpentier (10 below)
private: (5 below)
Bettina Bandel (11, 12 below)
Isabel Winarsch for VolkswagenStiftung (12 middle)

Dr. Bosnjak (right) and Professor Förster (left) in the Institute of Immunology.

Recovered but not protected

SARS-COV-2: SIMPLE TEST DEVELOPED FOR DETECTION OF PROTECTIVE NEUTRALISING ANTIBODIES

Infections with the coronavirus SARS-CoV-2 can take very different courses: While some people have no symptoms, others get seriously ill. An important question that often arises after surviving an infection is whether neutralising antibodies against the virus have been generated. These particulary important antibodies dock to the virus and prevent the virus from entering and multiplying in human cells. In this manner these antibodies protect the body from re-infection. For detection of neutralising antibodies there are usually complex requirements as infectious viruses, living cells and laboratories with a high safety standard required. That's why only a very limited amount of blood samples from convalescent patients can be tested for the presence of neutralising antibodies. „To change this, we have developed a very simple and rapid procedure that requires only two proteins that are important for the infection process: The spike protein of the virus and the protein ACE2 of the cell. If the binding of the spike protein to ACE2 is suppressed by serum antibodies, these antibodies are also able to prevent the infection of cells with the virus," says Dr. Berislav Bosnjak from the Institute of Immunology at MHH. He is the first author of the study now published in the journal Cellular and Molecular Immunology.

The corresponding research project was funded by RESIST and the Corona Research Funding Programme of the State of Lower Saxony.

„Our developed test provides the possibility now to analyse a large number of patients over a long period of time in clinical trials and to determine how long these important antibodies are present in the blood," says Professor Dr. Reinhold Förster. The RESIST co-speaker leads the MHH Institute of Immunology and is the senior author of the study. At the moment, the new method is only available for research purposes. However, it could potentially be adapted for routine diagnostics in the future.

Using already available techniques and comparing them with the new method, the team was able to show that about ten percent of people infected with SARS-CoV-2 had no protective antibodies in their blood. Those were mostly people who showed few symptoms ill only for a short time. On the contrary, patients with severe symptoms and longer disease courses produced much more antibodies. „It is still unclear which amount of neutralising antibodies is required to protect convalescents from re-infection. But with the test now available, it will be possible to answer this important question more quickly," says Professor Förster.

There were other members of his Institute also involved in the study – as well as the MHH Institute of Virology, led by RESIST speaker Professor Dr. Thomas Schulz, the Institute of Transfusion Medicine and Transplant Engineering, teams from the MHH Clinic for Rheumatology and Immunology, the MHH Clinic for Pneumology and the German Primate Centre in Göttingen.

netzwerk universitäts medizin

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Together against the **Corona pandemic**

RESIST RESEARCHERS ARE PART OF THE NETWORK OF UNIVERSITY MEDICINE

To better tackle the corona pandemic the German university hospitals have joined forces by establishing the „Network of University Medicine". The Federal Ministry of Education and Research (BMBF) is supporting 13 projects of this network with a total of 150 million euros. One of these projects, NAPKON, is co-coordinated by RESIST researcher Professor Dr. Thomas Illig and RESIST researchers are cooperation partners in other projects.

„The aim of the NAPKON project ‚National Pandemic Cohort Network' is to create a basis for a better understanding of the course of COVID-19 and to research possible therapies. We bring together clinical data, biosamples and imaging data in scientific studies," says Professor Illig. NAPKON is closely linked to another project of the network called CODEX, which aims to create a nationwide uniform infrastructure for the storage of COVID-19 research data sets. NAPKON is also cooperating with the project „Determination and use of SARS-CoV-2 Immunity" (COVIM).

Central COVIM issues are: Who is immunologically protected from a SARS-CoV-2 infection? When does the protection start and how long does it last? And how can the immunity be transferred to other people and be used for new therapeutic approaches? In order to find answers, immunological data from population studies and the investigation of COVID-19 genesis will be combined and concepts for the immunotherapy of this disease will be developed. COVIM cooperation partners include RESIST speaker Professor Dr. Thomas Schulz and RESIST researcher Professor Dr. Gérard Krause.

COVIM works together with the B-FAST project, the „Nationwide Research Network Applied Surveillance and Testing", among others. Within B-FAST a platform is being developed in which test and surveillance strategies can be tested. They are intended to serve the observation, analysis, interpretation and reporting of health data. RESIST-scientists Professor Dr. Reinhold Förster and Professor Dr. Dirk Schlüter are involved in B-FAST.

More information about the „National Network of University Medicine on COVID-19" can be found on the Internet (in german): https://www.netzwerk-universitaetsmedizin.de/.

Farewell **and loyalty**

RESIST researcher Professor Dr. Immo Prinz has accepted the appointment to the professorship Systems Immunology at the Medical Center Hamburg Eppendorf (UKE) as of January 2021. „I am leaving the MHH, but will continue to work on three RESIST projects. The projects include the reactivation of varicella zoster viruses and hepatitis B therapy and vaccination," he says. The new professorship is located at the „Hamburg Center for Translational Immunology" (HCTI), whose aim is to close the „translation gap" between basic immunological research and the clinical application of innovative therapeutic approaches. Professor Prinz will head the Institute for Systems Immunology.

Stable – and therefore attackable

RESEARCH TEAM COMES A STEP CLOSER TO PROTECTION AGAINST HERPES VIRUSES

Professor Grünewald

When herpes viruses enter the human host cell, the viral membrane fuses with the cellular membrane. Specific viral proteins are required for this process: As these proteins fold in a defined way, they manage to fuse the two membranes. The shape of the proteins before the fusion is the one, which is found on the viral surface. It is an attractive target for the development of drugs and vaccines. But this form is highly unstable.

A team led by RESIST researcher Professor Kay Grünewald has now succeeded in structural and functional stabilisation of this unstable form of the membrane fusion protein B of herpes simplex virus 1. This was done by directed mutations and served structural determination of the protein. The results were published in the journal „Science Advances". First author is Dr. Benjamin Vollmer.

It is a study of the Heinrich-Pette-Institute, Leibniz Institute for Experimental Virology (HPI), the Centre for Structural Systems Biology (CSSB), Oxford University, Birkbeck University of London, Friedrich-Loeffler-Institute and the Pasteur-Institute. It was financed by RESIST, among others.

Professor Grünewald's team was able to identify the major structural changes required for the membrane fusion reaction. Moreover, it was found that the conformational changes are similar to those of the so-called vesicular stomatitis virus glycoprotein G. „Antibodies or antiviral drugs affecting this conformational change could provide clinically relevant protection. Our results thus represent a first step towards the development of new drugs against human-pathogenic herpes viruses," summarises first author Dr. Vollmer his results.

What protects against **hepatitis C**

VACCINE RESEARCH: BASIS FOR THE DEVELOPMENT OF A MOUSE MODEL FOUND

Humans are the only natural host of the hepatitis C virus. Mice, in contrast, are not susceptible. "The reasons for this were not exactly known", says Professor Dr. Thomas Pietschmann, Director of the Institute for Experimental Virology at TWINCORE. Now, with the support from national and international colleagues, his team has succeeded in identifying two factors that protect mice liver cells from infection with the hepatitis C virus (HCV): These are Cd302, a lectin, and Cr1l, a complement receptor-like protein. These results, published in the journal Science Advances, lay the foundation for the future development of a mouse model for HCV vaccine research. First author is Dr. Richard Brown, one of the other authors is RESIST-scientist Professor Dr. Thomas Krey.

In the mouse, the two factors are constantly expressed in the liver and can function independently from the interferon system. Together these two mouse proteins are sufficient to dramatically reduce the proliferation of HCV in human liver cell cultures when they are artificially introduced. To further characterise the identified restriction factors, the TWINCORE scientists sought support from several colleagues at the TWINCORE, at MHH and HZI, but also from England, Belgium and the USA. Over 40 authors from more than 20 research institutions contributed to the publication, including this year's Nobel Prize winner Professor Charles M. Rice.

In TWINCORE: Dr. Brown (right), Professor Pietschmann (in the middle) and co-author Birthe Tegtmeyer.

Annual Meeting of the Society of Virology

The 30th annual meeting of the Society of Virology (GfV) will take place from March 24 to 26, 2021. The entire scientific programme will be presented online. In addition, it should be possible for a limited number of colleagues to attend the meeting in person, if the restrictions at the scheduled time due to the SARS-CoV-2 pandemic will allow it. The meeting will also be able to give enough time to SARS-CoV-2 as a topic to allow everyone to catch up with the latest developments and to discuss hot issues with experts in this field. Further information can be found on the homepage . www.virology-meeting.de.

RESIST seminar series 2021

Every Thursday (except during school holidays) two RESIST scientists or top-class researchers from external institutions present their work at the RESIST seminar series. The seminars are taking place from 5 to 6 pm and the titles of the presentations are published on the homepage www.RESIST-cluster.de as soon as they are known.

Due to coronavirus pandemic, the event will only take place virtually. If you are interested in participating via video (online) and not receiving the seminar announcements, please contact RESIST@mh-hannover.de.

14. January	Professor Dr. Sarina Schreiner und Professor Dr. Chris Lauber
21. January	Professor Dr. Michele Proietti und Professor Dr. Nico Lachmann
28. January	Professor Dr. Mala Maini (Guest lecture)
11. February	Professor Dr. Rolf Müller und Professor Dr. Marco Galardini
18. February	Professor Dr. Dirk Schlüter und Professor Dr. Kay Grünewald
25. February	Professor Dr. Luka Čičin-Šain und Professor Dr. Thomas Schulz
11. March	Professor Dr. Andre Franke (Guest lecture)
18. March	PD Dr. Susanne Eschenburg
22. April	Professor Dr. Ulrich Kalinke und Professor Dr. Torsten Witte

Move to a **new office**

Working in the new office (from left): Olga Klimenkova, PhD, Dr. Maike Hinrichs, Dr. Eugenia Faber and Dr. Eugenia Gripp.

From the RESIST sign in front of the MHH building J6 it is only a few steps to the recently newly occupied office, where Dr. Eugenia Gripp and Dr. Eugenia Faber from the RESIST management work – together with Dr. Maike Hinrichs, coordinator of the Collaborative Research Centre (SFB 900), and Olga Klimenkova, PhD, project manager of the research area „Infections in immunocompromised hosts" at the German Centre for Infection Research (DZIF). She is currently also a parental leave substitute for Dr. Faber.

You can get to the new office by walking through the main entrance of the building and then turning left immediately. Walk past the lift to the second door on the left (room number 3030).

Contact:
RESIST: RESIST@mh-hannover.de
phone: 0511 532-4107

SFB 900:
SFB900.Sekretariat@mh-hannover.de
phone: 0511 532-19822

Project Manager Infections of the immunocompromised Host/DZIF:
Klimenkova.Olga@mh-hannover.de
phone: 0511 532-83160

Science **in motion**

In a new video clip, Professor Dr. Torsten Witte reports on the research of the RESIST project B2, which focuses on rheumatological diseases. He explains the disease and its treatment with the help of a patient. This video in German language can be viewed on the RESIST homepage at: https://www.resist-cluster.de/news-events/nachrichten-uebersicht/

Drinks, drugs **and the liver**

ON THE INTERNET: RESIST RESEARCHERS PROVIDE INFORMATION ABOUT THE CENTRAL METABOLIC ORGAN

Are red wine, fruit, coffee and sweets good or bad for the liver? On 16 November, RESIST researcher Professor Dr. Markus Cornberg (to see on the photo on the left) and his colleague Dr. Benjamin Maasoumy presented exciting facts about the metabolic organ responsible for detoxifying the body live on the MHH Facebook channel. The MHH scientists and physicians illustrated the current RESIST research on diseases of the liver and of course also described how to keep this 1.5 kilogram organ healthy. Missed the programme? No problem: A recording from the event can be seen on the RESIST homepage at www.RESIST-cluster.de. This much in advance: Too much fructose can cause fatty liver and consequently liver cirrhosis, for example, while drinking coffee is good for the liver. In order to be able to detect diseases early on, it is worthwhile having your liver values checked regularly by your family doctor. The transmission of this exciting and relaxed lecture met with great interest: It reached around 4,600 people, many of whom had questions answered during and after the transmission.

SAVE THE DATES:

RESIST RETREAT AND SYMPOSIUM

On 4 and 5 February 2021, the RESIST Retreat will take place as an online event. RESIST researchers and members of their working groups will have the opportunity to present the current results and next steps of their RESIST projects. As soon as the programme is available, you will find it together with further information on the homepage www.RESIST-cluster.de.

The RESIST Symposium together with CRC 900 Symposium is scheduled to take place on 28 and 29 June 2021. Further information on this will also be published on the RESIST homepage as soon as it is available. The photo was taken at the RESIST symposium 2019 on the stairs of the castle in Herrenhausen.

RESIST – About us

Funded by DFG Deutsche Forschungsgemeinschaft German Research Foundation

The clinicians and scientists working in the Cluster of Excellence RESIST (Resolving Infection Susceptibility) aim to offer scientific excellence for the people most vulnerable to infections. RESIST researchers work at **Hannover Medical School** (MHH), **TWINCORE** Centre for Experimental and Clinical Infection Research, **Helmholtz Centre for Infection Research** (HZI) in Braunschweig, **Center for Structural Systems Biology** (CSSB) in Hamburg, **Centre for Chronic Immunodeficiency** in Freiburg (CCI) and the **University of Veterinary Medicine Hannover, Foundation**. The work of the Cluster of Excellence RESIST is funded by the **German Research Foundation** (DFG).