01
Spring
2022

NEWS

RESIST – Resolving Infection Susceptibility

Mid-term review

PRAISE FOR RESIST: MOST PROJECTS ARE OF VERY HIGH QUALITY AND UNIQUE WORLDWIDE

It's half-time at RESIST – half of the first funding period is already over – and so it's time for an interim review in the form of an internal evaluation of the ongoing RESIST research projects. This serves to sharpen the strategic orientation of RESIST and to prepare for the external evaluation by the DFG in 2025.

For this evaluation, the RESIST researchers first wrote reports on their respective projects, which they made available to the international review panel in a report volume together with a general presentation of the Cluster of Excellence. During the subsequent online meeting on 31 January and 1 February 2022, the researchers then presented their work again in individual talks before the panel of around 20 people – members of the scientific advisory board, the research management board, representatives of research units A to D and the RESIST spokesperson. During the meeting, the seven RESIST professors also presented their research activities.

After detailed analysis and discussion, the reviewers identified the strengths and weaknesses of the individual projects and also documented them in written form. The members of the scientific advisory board praised RESIST as a whole as well as most of the RESIST projects, they described as being very high quality and unique worldwide. Based on this evaluation, and taking strategic aspects into account, the research management board approves the continued funding of most of the projects until the end of the first funding period, which runs until the end of 2025, as well as the inclusion of a new project centering on hepatitis D virus infections.

We

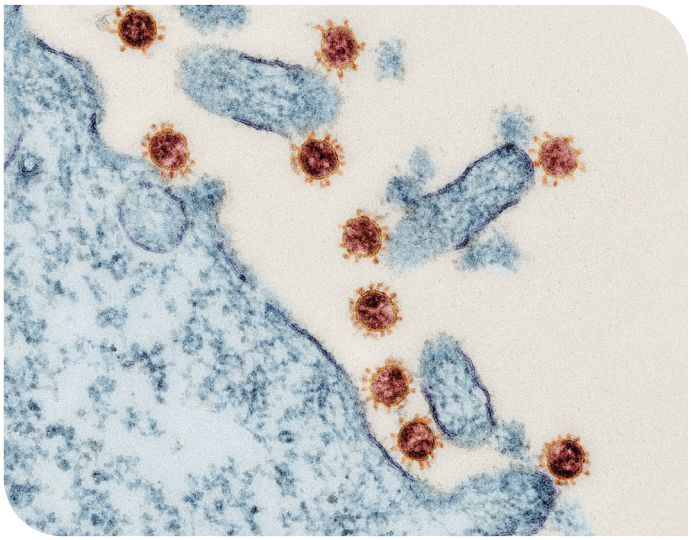
are very pleased to present you the new RESIST newsletter. Right on this page you can read more about the praise RESIST has received at the halftime of the first funding period.
The articles on pages 6 to 8 focus on research: for example, the results of work on hepatitis and cytomegaloviruses, but also on *E. coli* bacteria and the "cultivation" of healthy phagocytes. The topic of SARS-CoV-2 also continues to keep many RESIST researchers very busy, and they are partly funded in this context within the framework of COFONI. You can read more about this on page 2.
The first semester of the Master's programme in Biomedical Data Science has been a success (page 9). And for the first time, there is now an exchange within the framework of HAGIS as well as a symposium in Glasgow (page 10).
Sadly, we had to bid farewell to Prof. Schmidt, as he passed away in January. You can read an obituary on page 4.
RESIST is becoming more and more visible to the outside world – among other things through the participation of RESIST researchers in the Patient University of the MHH (page 11). But RESIST is also involved, for example, in a DFG app and in an speed dating event – take a look at page 12. We hope you enjoy reading,

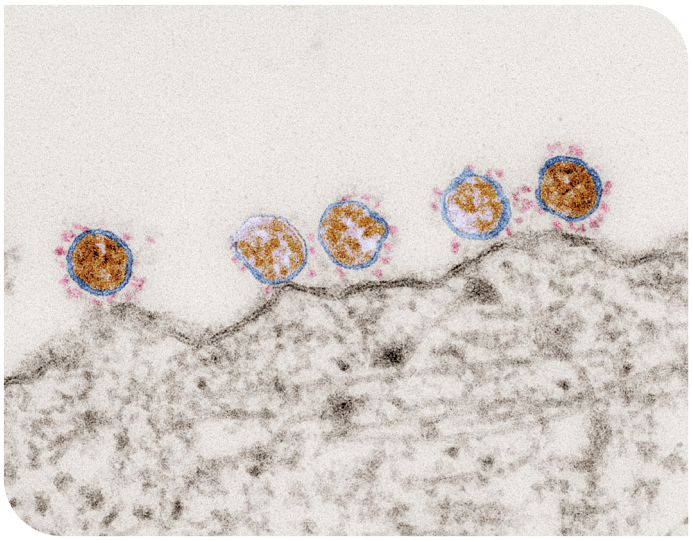
Your RESIST speaker team

The RESIST speaker team: Prof. Schulz (in the middle) and the two co-speakers Prof. Förster (left) and Prof. Hansen (right).

Research on COVID-19

THE COFONI NETWORK BRINGS TOGETHER CORE SCIENTIFIC COMPETENCIES





SARS coronavirus 2 particles on the surface of a cell (electron micrograph, ultra-thin section)

What works against SARS-CoV-2? Who falls ill despite vaccination? What role do genes play in the immune response? Numerous questions continue to revolve around the topic of corona. In order to be able to answer them, the "COVID-19 Research Network Lower Saxony" (COFONI) is funding 13 projects with a total of about six million euros. Six of these projects are led by scientists who also conduct research in RESIST or are associated with RESIST. The projects are each supported with up to 500,000 euros and could start between February and April 2022:

The best test

To be able to inhibit SARS-CoV-2 infections with antibodies – this is the goal of the project "Activity of human broadly neutralizing antibodies in a SARS-CoV-2 primate model", which is headed by Prof. Schulz and whose co-applicant is also RESIST researcher Prof. Krey.

The researchers' aim is to ensure that the antibodies can neutralize as many SARS-CoV-2 variants as possible – and if possible also closely related animal coronaviruses that infect human cells and could therefore possibly be transmitted to humans in the future and cause further outbreaks. The researchers have already succeeded in developing so-called broadly neutralizing antibodies. These can specifically inhibit the original SARS-CoV-2 virus, all variants that have appeared so far and even related beta-corona viruses – for example, viruses from pangolins and bats that are related to SARS-CoV-2. The team has also already demonstrated that several of these broadly neutralizing antibodies can protect hamsters from infection with both the original and Omicron variants of SARS-CoV-2. "Now we want to test the best of these antibodies in a non-human primate model and develop new antibodies with an even broader neutralizing potential," says Prof. Schulz. Prof. Schulz and Prof. Krey are conducting the project together with Prof. Pöhlmann (German Primate Center, DPZ).

Preventing escape

The project "Preclinical development of a neutralizing monoclonal antibody against SARS-CoV-2 (PREHUMAB)", coordinated by Prof. Kalinke, also revolves around highly potent SARS-CoV-2 neutralizing monoclonal antibodies.

His team has already succeeded in developing highly potent SARS-CoV-2 neutralizing monoclonal antibodies from memory B cells of recovered COVID-19 patients. "We will now further develop these as so-called multivalent bispecific reagents. The aim is to use these reagents to prevent the emergence of variants of the virus that can escape the immune defenses," says Prof. Kalinke. In addition, the team will test different ways to express such reagents in the lung epithelium. In addition to experiments in mice and hamsters, preclinical investigations in non-human primates are also planned. Thus, the prerequisites for a clinical phase I investigation of the most promising antibodies will be fulfilled. Prof. Kalinke is conducting the project together with Prof. Schambach (MHH) and Prof. Pöhlmann (DPZ).

New binding sites sought
Evasive variants of the virus are also the topic of the project "Prediction of Escape Mutants (PREMUS)" coordinated by Prof. Čičin-Šain.

The SARS-CoV-2 coronavirus needs the spike proteins on its surface to bind to specific receptors on the surface of human cells and thus be able to invade the cells. The corresponding binding site of the spike protein is called the receptor binding domain (RBD). Antibodies of the human immune system can bind to the RBD and thus ensure that the viruses cannot penetrate the cells.

"PREMUS aims to identify mutations in this binding site of the spike protein that can prevent currently available monoclonal antibodies from being effective against the viruses," says Prof. Čičin-Šain. The research team plans to create a library of mutations of these RBDs.

The long-term goal is to identify antibody binding sites on the virus that are not able to mutate. This should prevent the viruses from using mutations to prevent the antibodies from binding and thus escaping the immune system. The project's applicants are Prof. Čičin-Šain, Prof. Dübel and Prof. Hust (TU Braunschweig) and Prof. Pöhlmann (DPZ).

The response of the ageing immune system
The project "LISE – Long-term Immune Response of senior Individuals to SARS-CoV-2", coordinated by Prof. Hühn, focuses on the long-term consequences of a SARS-CoV-2 infection in older people. The team is looking at how strong the cellular and humoral immune response is in older people after SARS-CoV-2 vaccination, how long it lasts and how it declines over time. The applicants also include Prof. Förster, Prof. Li, Prof. Illig, Prof. Pöhlmann (DPZ), Dr. Rösner and Prof. Werfel.

The researchers are also investigating whether there are different patterns of immune responses and which molecular mechanisms underlie them. "In addition, we are addressing the extent to which vaccination has induced antibodies that are able to neutralize current and future variants," says Prof. Hühn. Further questions are: Does the cellular composition of the immune system correlate with the ability to mount a protective immune response after vaccination? Which fully vaccinated individuals are at high risk of infection with current and also future virus variants?

The Lower Saxony Ministry of Science and Culture provides special funding for LISE, as it is a project to research the long-term effects of COVID-19. Prof. Hühn's team is applying multi-omics analyses, integrating the SARS-CoV-2 specific data with existing multi-omics data and also considering personal risk factors. Multi-omics is an analysis approach in which the data sets are multiple "omes". For example, the genome, all material carriers of a cell's heritable information; the transcriptome, all gene transcripts present in a cell; or the epigenome, all chemical modifications of DNA and histone proteins that temporarily determine the activity of genes and thus the functional properties of the cell.

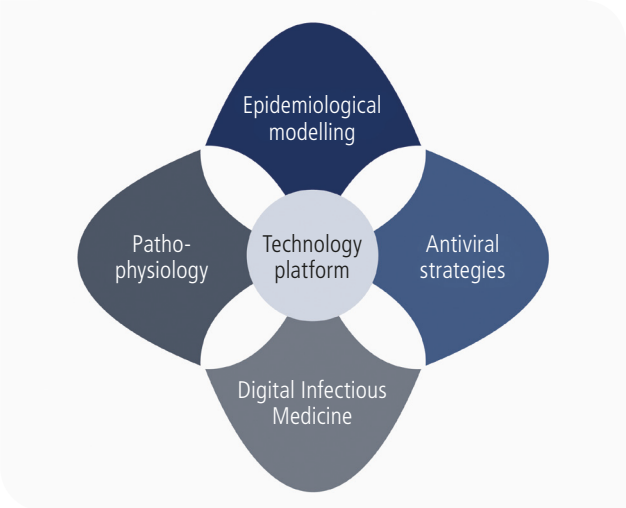
Prediction through multi-omics data
The project coordinated by Prof. Yang Li, "Revealing genetic regulation of immune response to SARS-CoV2 infection using single-cell omics approaches", also uses multi-omics analysis. Since the extent of disease varies widely among individuals, she addresses the question of what role genetic regulation plays in the immune system's response to SARS-CoV-2 infection. Prof. Cornberg is also the project's co-applicant.

The team is studying mechanisms of immune response and disease progression at the single-cell level, including using the genome, transcriptome and epigenome of patients. "We have already been able to show in previous studies that the human immune response to infections is determined by genetic factors, among others, and can be predicted by integrating multi-omics data," says Prof. Li. "Therefore, we expect that we can also use 'omics data' to identify the molecular changes in COVID-19 patients and those that form immune system responses to SARS-CoV-2 infections."

The results should help make predictions about disease progression and develop effective therapies.

The target: proteases
Prof. Čičin-Šain wants to find out what role a very specific protein plays in SARS-CoV-2 infection in the PROTECT project he is coordinating: "The role of TMPRSS2 proteolysis in the spread of SARS-CoV-2 in cells of the respiratory tract and in vivo". In addition to himself, the applicants are Prof. Pöhlmann (DPZ), Prof. Ulrich (MHH) and Prof. Braun (Fraunhofer ITEM).

Together with his team, he is concentrating on the transmembrane serine protease 2 (TMPRSS2). This is a cell surface protein that occurs in the respiratory tract and is involved in the cleavage of peptide bonds of certain proteins. The central question here is: What role does this protein play in the entry of the SARS-CoV-2 virus into the cell and in the infection? The team assumes that this cellular protease could be a molecular target for therapeutic strategies against COVID-19 disease. "This is particularly interesting since the emergence of the Omicron variant, for which it has been shown in vitro that the TMPRSS2 protease is less clearly required," says Prof. Čičin-Šain. The laboratory teams involved in this project will study SARS-CoV-2 infection in human tissue cultures as well as in lung sections and in rodent and primate models.



COFONI: The four key areas around the central technology platform.

RESIST mourns the loss of **Prof. Schmidt**

PROF. DR. REINHOLD E. SCHMIDT DIED ON 23 JANUARY 2022 AT THE AGE OF 70

Prof. Dr. Reinhold E. Schmidt

After his training as an internist and rheumatologist in Bonn and in London (Royal Hammersmith) and his post-doctoral period at the Dana-Farber Cancer Institute at Harvard University in Boston, Reinhold Schmidt became a senior physician in the Department of Clinical Immunology at the MHH in 1986. At that time he researched the role of NK cells and Fc receptors in immune defense and in the pathophysiology of autoimmune diseases. From 1995 onwards he headed the Department of Clinical Immunology and from 2007 until his retirement in 2020 the Department of Immunology and Rheumatology. With great perseverance, he worked to establish clinical immunology as an independent subject in medicine. With success: in addition to the specialist immunologist qualification, DGfI, the qualification of immunology for specialists has also recently been established.

Reinhold Schmidt was a pioneer and made many of his visions become reality, for example the founding of the Hannover Biomedical Research School (HBRS) as an institution where all graduate courses at MHH are supervised today and where he was the first dean from 2003. The promotion of young researchers was important to him. He supported medical researchers in his own clinic and organized, among many other things, the Translational Immunology School (TIS) to bring medical researchers and basic researchers closer together. In his clinic, he promoted research into primary and secondary immunodeficiencies and intensified research into collagenoses and vasculitides.

He was involved in numerous collaborative projects at the MHH, for example as spokesperson of the KFO 250 "Molecular and cellular mechanisms of autoimmunity" or as a member of the boards of the excellence clusters REBIRTH and RESIST. Reinhold Schmidt was involved in the founding of RESIST and played an important role as a member of the Research Management Board and the Internal Advisory Board. He was also co-project leader of the A2 research project, which investigates the causes of susceptibility to infection – in particular the role of genes as well as the influence of congenital immunodeficiencies.

His work has been honored with numerous prizes and awards. He was chairman of the scientific advisory board of the Paul-Ehrlich-Institut as well as of the research institutes of the Federal Ministry of Health, a member of the German National Academy of Sciences – Leopoldina, chairman of the IUIS Committee for Clinical Immunology (CIC), president of the German Society for Immunology as well as president of the foundation board of the German Rheumatism Research Center Berlin. Reinhold Schmidt was full of irrepressible stamina and joie de vivre, both professionally and in his private life. The meetings and congresses he organized became legendary because they were scientifically outstanding, but human interaction was also never neglected. In addition, he was characterized by an enthusiasm for endurance sports of all kinds. Even after his retirement, he still outran some of the younger staff members.

Reinhold Schmidt will be remembered as an extremely energetic and positive-thinking, multi-faceted and fun-loving personality whose achievements for clinical immunology were outstanding and who left his mark on the MHH.

Prof. Dr. Torsten Witte

RESIST **in the Council**

CORONA PANDEMIC: PROF. FALK AND PROF. MEYER-HERMANN ARE MEMBERS OF THE EXPERT COUNCIL

Advising the German government on Corona:
Prof. Meyer-Hermann and Prof. Falk (from left).

In order to effectively combat the corona pandemic, the German government has set up a council of scientific experts to advise them on the basis of current scientific findings on the COVID-19 pandemic and its consequences. Prof. Falk (MHH) and Prof. Meyer-Hermann (HZI) are members of this committee, which consists of 19 scientists from various disciplines.

RESIST researcher Prof. Dr. Michael Meyer-Hermann is a physicist and heads the HZI "Systems Immunology" department at the Braunschweig Integrated Centre of Systems Biology (BRICS), a joint research facility of the HZI and the Technische Universität Braunschweig. Prof. Dr. Christine Falk, member of the RESIST Internal Advisory Board, is President of the German Society for Immunology. She heads the Institute for Transplantation Immunology at the Hannover Medical School (MHH).

The Council informs the Federal Chancellery on the basis of current scientific findings on developments in infection biology, epidemiology, the health system, psychosocial issues and society. It works on an honorary and independent basis, advises on a regular basis, which is adjusted as needed, and develops recommendations for pandemic management and for the prevention of further pandemics.

New RESIST-members

We are very pleased to welcome Prof. Dr. Anna K. H. Hirsch, Head of the Department of "Drug Design and Optimisation" at the Helmholtz Institute for Pharmaceutical Research Saarland (HIPS) in Saarbrücken, as a new RESIST member. She is now part of the leadership team of RESIST project D1, which aims to find substances that can inhibit the replication and survival of herpes viruses in the body.

Within the framework of RESIST, Prof. Hirsch is concentrating in particular on active substances that can inhibit the so-called accessory DNA polymerase protein. This is involved in the multiplication of the Kaposi's sarcoma-associated herpes virus. "This antiviral target, which has been little researched so far, has the potential to offer new therapeutic options for herpesvirus diseases," she says.

Anna Hirsch studied natural sciences with a focus on chemistry at the University of Cambridge. She received her PhD from ETH Zurich in 2008 and then worked at the Institut de Science et d'Ingénierie Supramoléculaires in Strasbourg before taking up a position at the Stratingh Institute for Chemistry at the University of Groningen in 2010, where she was appointed professor in 2015. In 2017, she moved to the Helmholtz Institute for Pharmaceutical Research Saarland (HIPS).

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We also welcome Dr. Georgios Sogkas as a new member of RESIST. The rheumatologist from the MHH Department of Rheumatology and Immunology is now working in the teams of the RESIST projects A2 and B2. The first project revolves around congenital immunodeficiencies and in particular the question of how diagnosis can be improved to achieve early identification of as many affected individuals as possible. The second project is looking into the extent to which intestinal bacteria can trigger rheumatological diseases.

Within the framework of RESIST, Dr. Sogkas focuses on identifying common disease mechanisms of immunodeficiency and autoimmunity in inborn errors of immunity. "The discovery of monogenic disorders, characterized by both autoimmunity and susceptibility to infections, has provided novel insights into the common pathophysiological origins of immunodeficiency and immune dysregulation," he says. With his work, he wants to contribute to finding new therapeutic starting points to reverse the dysregulation of the immune system. "The goal is that patients with immunodeficiency are not additionally burdened with immunosuppression," he says.

Dr Sogkas studied medicine at the University of Thessaly, Greece, and then completed his Master's degree in "Integrated Immunology" at the University of Oxford, United Kingdom. He received his PhD at the MHH Clinic for Immunology and Rheumatology, where he has worked ever since.

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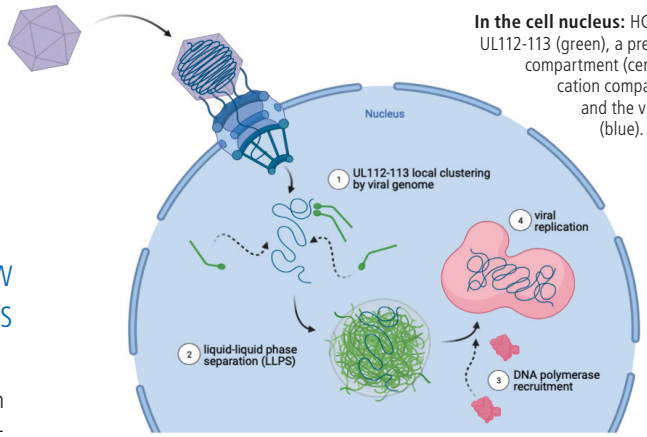
Prof. Dr. Anna K. H. Hirsch

Dr. Georgios Sogkas

Replication **space**

RESEARCH TEAM FURTHER ELUCIDATES HOW CYTOMEGALOVIRUS REPLICATES



In the cell nucleus: HCMV proteins UL112-113 (green), a pre-replication compartment (center), a replication compartment (red) and the viral genome (blue).

Human cytomegalovirus (HCMV) is a major cause of illness and mortality in immunocompromised transplant patients and the most common cause of infection in newborns worldwide.

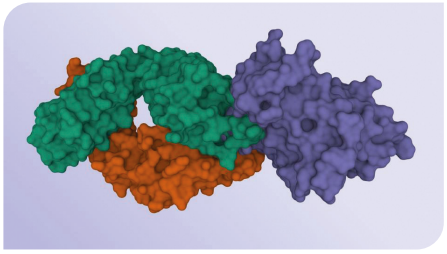
In HCMV infection, the virus replicates its DNA genome in specialized replication compartments in the nucleus of the host cell. These membraneless organelles arise as round structures and increase in size over time. However, the exact mechanism of biogenesis of the replication compartments is still unknown. A team led by Professor Dr. Wolfram Brune (HPI) and RESIST Professor Dr. Jens Bosse (MHH, CSSB, HPI) has now been able to show that the HCMV proteins UL112-113 undergo phase separation, which supports the formation of the replication compartments in the cell nucleus. The phase-separated pre-replication compartments formed in this way are necessary to recruit the viral DNA polymerase for the genome replication of the viruses. The results were published in the journal "Cell Reports". The team of scientists, in which RESIST researcher Prof. Grünewald was also involved, used so-called live-cell imaging and photo-oligomerisation methods for their work.

The elucidation of these replication processes contributes to achieving the long-term goal of being able to better ward off and treat HCMV infections.

The text is based on a press release by Dr. Franziska Ahnert-Michel, Press and Public Relations of the Heinrich Pette Institute - Leibniz Institute for Experimental Virology (HPI).

Antibody characterized

ANOTHER STEP ON THE WAY TO DEVELOPING A HEPATITIS C VACCINE



In the form of a crystal structure: The binding of an antibody (red and green) to the HCV surface protein "E2" (purple).

RESIST researcher Prof. Pietschmann from the Twincore Institute for Experimental Virology developed a test system with his team in 2021 that can be used to precisely measure the immune response against a large spectrum of hepatitis C viruses (HCV). With the help of this test system, it has now been possible within the framework of the study to isolate HCV antibodies that attack an extraordinary number of virus variants simultaneously – so-called broadly neutralizing antibodies. They could be isolated from a group of patients who, as "elite neutralizers", can attack exceptionally many virus variants simultaneously.

This analysis of the antibodies shows where the virus is particularly sensitive, which is another step on the way to developing a hepatitis C vaccine. The study, which also involved RESIST researcher Prof. Krey from the University of Lübeck, was led by the team of Prof. Dr. Florian Klein, University Hospital Cologne and German Centre for Infection Research. The results were published in the highly respected journal Immunity.

The team of scientists examined the data of 435 hepatitis C patients. Up to five percent showed exceptional HCV-neutralizing activity. From the blood of four of these "elite neutralizers", the team isolated more than 300 antibodies, including those that were particularly efficient at rendering various hepatitis C viruses harmless. With the help of structural and mutation analyses, the researchers characterized these special antibodies and were able to identify, for example, which amino acid sequences have an influence on the neutralization ability.

The scientists now plan to test the most potent antibodies in animal models.

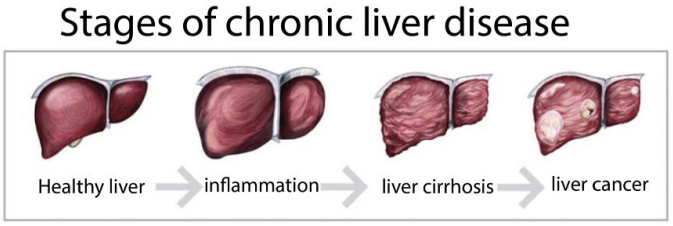
Infection with the hepatitis C virus still leads to about 400,000 deaths per year worldwide, despite treatment methods that have improved in the meantime. The development of a vaccine is urgently needed, but has so far failed due to the genetic diversity and high mutation rate of the virus.

Who benefits from **immunotherapy?**

HEPATITIS B: BIOMARKERS SHOULD ENABLE PROGNOSIS OF THERAPY SUCCESS

Hepatitis B can lead to liver cirrhosis and liver cell cancer. So far, most therapies can suppress this viral infection, but not cure it. There are some novel immunotherapies that can actually cure it, but it is still unclear which patients will benefit most from these new therapies. A research team led by Prof. Cornberg and PD Dr. Anke Kraft, and in which Prof. Li and Prof. Wedemeyer as well as other scientists from the CiiM, the MHH and the DZIF also worked, has now identified a biomarker that should enable predictions about the success of the therapy. The results were published in the scientific journal Gut.

The team found that the T-cell responses of patients with chronic hepatitis B virus infection, which are particularly important for fighting the virus, were not – as previously assumed – associated with the level of hepatitis B surface protein complex (HBsAg) in the blood, but were rather influenced by the age of the patients. "Younger patients, who have presumably not been chronically infected with the virus for so long, show a stronger T-cell response to the virus," says Prof. Cornberg. "Since this is the prerequisite for successful immunotherapy against the virus, new immunotherapies should be studied primarily in these patients."



Hepatitis B can lead to liver cirrhosis and liver cell cancer. © Deutsche Leberstiftung

In addition, the team looked for alternative biomarkers to make therapy predictions. They found that the T-cells of infected patients with a low blood level of another viral marker ("hepatitis B core-related antigen", HBcrAg) had better immune function.

The text is based on an article by Charlotte Wermser / HZI

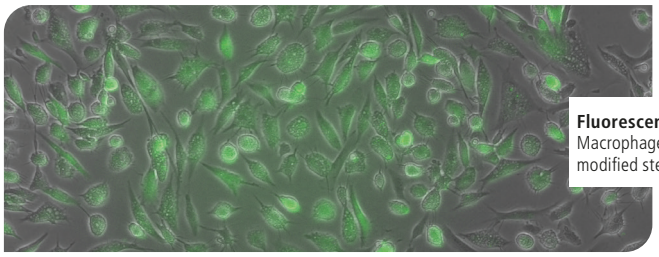
Healing with cells

MACROPHAGES CAN ENABLE THE DEVELOPMENT OF CELL-BASED THERAPIES FOR NUMEROUS DISEASES AND TEST SYSTEMS FOR INFECTIOUS DISEASES

Macrophages are essential for the immune response as well as for tissue repair and the elimination of cancer cells. In addition, these scavenger cells of our immune system fight off bacteria and viruses in the lungs. But they can be weakened, for example due to a genetic defect or an infection that has already passed through. A variety of diseases can also cause the function of these important cells to be impaired. Replacing these diseased cells with healthy ones from the laboratory – this is one of the latest cell therapy approaches that RESIST researcher Professor Dr. Nico Lachmann is currently investigating.

To this end, he and his team have now created detailed instructions for the continuous mass production of macrophages and published them in the journal **Nature Protocols**. The macrophages are derived from human stem cells by the artificial reprogramming of somatic cells. "This strategy is simple and robust, can be performed in suspension culture or stirred tank bioreactors, and 20-50 million functional and highly pure macrophages can be produced continuously per week over several months," says Prof. Lachmann.

The ability to produce fully standardized macrophages, however, allows for even more: innovative test systems can now be developed to improve novel anti-bacterial or anti-viral agents and test them for safety. Potential contaminants of drugs can also be detected with the cells. "The new technique is an important contribution for RESIST to break new ground in tomorrow's infection medicine."


Fluorescence image:
Macrophages from genetically modified stem cells (iPSC).

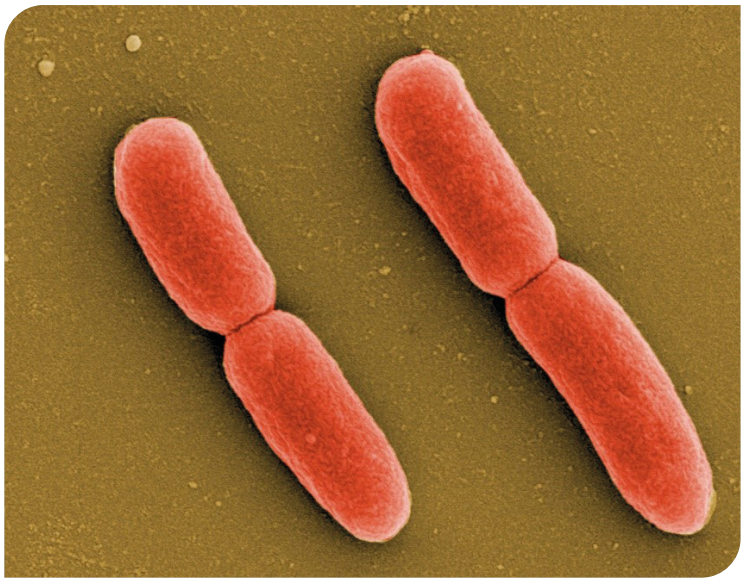
Prof. Grünewald **is CSSB-Director**

Prof. Dr. Kay Grünewald, Leibniz Institute for Experimental Virology (HPI) and Department of Chemistry at the University of Hamburg, is the new scientific director of the Centre for Structural Systems Biology (CSSB) as of the beginning of 2022. At the CSSB, state-of-the-art technologies and methods are used to study how pathogens infect cells. Prof. Grünewald also heads the research group "Structural Cell Biology of Viruses" there.

Prof. Grünewald is co-leader of the RESIST projects D1 and D2, whose goal is to be able to better treat infections with herpes viruses. In addition, he represents project area D on the RESIST board, which revolves around the question of how viruses manage to settle in the body.

Prof. Grünewald

How are bacterial genes and disease severity related?



Escherichia coli: electron micrograph of these bacteria ©HZI/ Rohde.

The bacterium *Escherichia coli* is found in the human intestine, among other places. It is generally harmless there, but under certain circumstances it can also become a pathogen. It can cause bladder infections or even blood poisoning. A team of researchers led by RESIST-Professor Dr Marco Galardini at TWINCORE, together with colleagues from the medical faculty of the University of Paris, have investigated whether certain genes of the bacterium are linked to the severity of the diseases it causes. They have published their results in the journal **PLOS Genetics**.

E. coli is part of the human intestinal flora. As a so-called commensal, it normally causes no harm there. But it can also become a pathogen: In the urogenital tract, for example, it causes bladder infections and in the bloodstream it causes blood poisoning. Until now, it has not been possible to predict the severity of such an infection on the basis of the germ's genetic make-up.

Researchers from TWINCORE have now analyzed whether certain genetic variants of *E. coli* are associated with a severe course. "We sequenced bacterial samples from two large patient studies and correlated them with the course of the infection," says Prof. Galardini, head of the RESIST research group Systems Biology of Microbial Communities. Characteristics such as age, gender or known previous diseases were also included in the analysis.

The team was unable to identify genes that determine the severity of the disease. However, they made another interesting discovery: a certain gene cassette was clearly associated with infections that started in the urinary tract. From this, a strategy for avoiding life-threatening diseases can be derived. "In future, one could sequence the pathogens from a bladder infection and then decide whether the drug treatment should be adjusted as a precaution."

The fact that the researchers could not prove a link between the genome of the bacteria and the course of the disease does not necessarily mean that there is none. "It could just as well be that the number of samples we studied was too small," says Prof. Galardini. "A simulation showed that ten times the number of samples would be needed to detect or exclude the compound with higher certainty." He is therefore preparing a more extensive follow-up study with his French cooperation partners.

Text source: Jan Grabowski / Twincore

Wide spectrum **view**

PASSED THE ACID TEST: ONE SEMESTER OF BIOMEDICAL DATA SCIENCE COMPLETED

Very good. That's how Marie Mikuteit, Adrian Schulz and Julia Winkler described the first semester of the Master's programme in Biomedical Data Science – both the content and style.

Together with their fellow students, they were able to delve into topics such as 'Introduction to Data Science', 'Basics of Informatics' and 'Clinical Studies and Biobanking', for example. "The course is well structured and has many practical examples," reports Julia Winkler. What was new for many was the style of studying. Instead of lessons on site, daily laboratory routine and internships on wards – which was familiar from previous medical or natural science degree programmes – everyone now learns at times of their own choosing, from home and online. "I like that because it allows me to coordinate my studies well with my work at the MHH," says Marie Mikuteit. For others, it's practical because they don't live in Hanover. The small size of the group of 18 people is also new and popular, for example for Adrian Schulz: "I like that everyone knows each other and teamwork is very much encouraged."

Working as equals

The students are particularly enthusiastic about the lecturers and coordinators. They find them just as committed, respectful and cooperative as they are flexible and accommodating. "You can tell that the lecturers are keen to teach us something. They think it's relevant that people study something like this and interact with us as equals," Marie Mikuteit tells us. "You get a quick answer to your questions and it's a real togetherness," agrees Julia Winkler. The fact that the study programme is still in its infancy is noticeable in individual points – for example, there were times when the assignments were too extensive, but they were adjusted after feedback. "They are genuinely interested in our opinion and our feedback. We can help shape this new degree programme – and I want to live up to my responsibility," Adrian Schulz says. The Corona restrictions were hardly noticeable in the study programme, as most of the appointments were planned online from the outset. It was important for everyone to get to know each other during a week of attendance at the beginning of the programme.

The students are looking forward to the next three semesters - as well as to the time afterwards. Adrian Schulz is excited about the topics of artificial intelligence, big data and biostatistics. He can imagine working in the field of data science later on. Marie Mikuteit would like to work at a university as a doctor and researcher later on, but also finds it important to be able to evaluate large data sets when working exclusively clinically. And Julia Winkler had a job in the field of clinical studies in mind when she started her studies. But now she knows: The spectrum of knowledge she is acquiring with this degree is much broader and offers many more possibilities than she thought.

Start of applications for the coming winter semester

From 30 April 2022, interested students can apply for the Master's programme in Biomedical Data Science, which was developed within the RESIST Cluster of Excellence with significant participation from the Peter L. Reichertz Institute for Medical Informatics at MHH and TU Braunschweig. The application deadline is 15 July 2022.

In the MHH building J1:
Julia Winkler, Adrian Schulz and Marie Mikuteit (from left).

More information can be found on the homepage at: www.mhh.de/master-biomeddat. The contact person is Dr. Melina Celik, telephone: (0511) 532-5700, e-mail: www.mhh.de/master-biomeddat.

Publications: **Please specify RESIST**

The German Research Foundation (DFG) funds RESIST with around 32 million euros from 2019 to 2025. Without this support, our scientific work in RESIST would not be possible. RESIST is evaluated by the DFG not least on the basis of its published work. Therefore, the research results that RESIST scientists publish in journals must mention the German Research Foundation as well as the cluster's identification number (ID) in the acknowledgements. The following wording is correct: "Funded by the Deutsche Forschungsgemeinschaft (DFG, German Research Foundation) under Germany's Excellence Strategy – EXC 2155 – project number 390874280."

Publish research results:
Please ensure that you quote the correct project number.

Off to **Glasgow**

At a workbench:
Franziska Hüsers in a laboratory at MHH Virology.

THE FIRST STUDENT IS RESEARCHING WITHIN THE FRAMEWORK OF HAGIS / FIRST HAGIS SYMPOSIUM IN APRIL

Here we go: On 20 April 2022, the first doctoral student will travel to Glasgow for two months as part of the "Hannover-Glasgow Infection Strategy" (HAGIS). Franziska Hüsers from the research group of Prof. Dr Beate Sodeik from the MHH Institute of Virology will learn a method there in the team of Dr Chris Boutell at the "MRC-University of Glasgow Centre for Virus Research" (CVR), which she needs for her doctoral thesis.

So far, Franziska Hüsers only knows Scotland as a holidaymaker, but she has already gained experience abroad during a four-month internship in London. "I like the international atmosphere, which I also know well from our MHH team, and I am looking forward to living for a time where others go on holiday," she says. Her work revolves around the herpes simplex virus and in particular the human cell protein MxB. Her task is to investigate whether this protein can disassemble the protective capsules (capsids) of herpes viruses in cells, and in which cell types this mechanism is active. With the new method she is now learning, the genome of the herpes viruses can be specifically labelled before its incorporation into the capsids and its possible release from the capsids in infected cells can be tracked. This should clarify at which stages in the infection cycle the cell protein MxB attacks the capsids.

Franziska Hüsers will already be on site when several RESIST researchers travel to Glasgow on 29 April to meet with the CVR team for a joint symposium.

HAGIS was launched in August 2021 by RESIST and the CVR. The aim is to conduct research together on a permanent basis, complementing each other and thus advancing the development of new therapies for infectious diseases and enabling doctoral students to benefit from the combined research strengths of the two sites. The Lower Saxony Ministry of Science and Culture is providing financial support for HAGIS. According to current plans, a joint DFG application for an international research training group will be submitted from 2023.

HAGIS
Hannover-Glasgow Infection Strategy

The HAGIS logo:
It shows the bridge over the River Clyde in Glasgow and the Ernst August Monument.

RESIST Seminars

THURSDAY LUNCHTIME IS RESIST SEMINAR TIME

Exciting topics, interestingly presented: Every Thursday (except during school holidays), one or two RESIST scientists or top-class researchers from external institutions present their RESIST projects at the seminar series from 1 to 2 p.m. – for all RESIST and SFB 900 members as well as other colleagues and, of course, interested students. In April, we are looking forward to the presentation for project A4 on the 21st and for project B1 on the 28th. In May, project B2 will be presented on the 12th. On 19 May, Dr Helge Dorfmüller from the University of Dundee, Scotland, will give a talk. On the Thursdays in June (9th, 16th, 23rd and 30th), presentations of projects B3 to B6 are scheduled. The announcements of the seminars with the seminar titles can be found on the homepage **www.RESIST-cluster.de**. We wish everyone interesting Thursday lunchtimes.

Health education **for all**

Patienten UNIVERSITÄT

In this year's spring series, the MHH's Patient University provides new and interesting information on the topic of "Infections" – and the team of the Cluster of Excellence RESIST is actively involved: The RESIST scientists will report, among other things, on the research results they have been able to gain in the context of so-called cohort studies. These are studies in which data, blood samples or tissue donations from patients are collected over a longer period of time. Such studies are indispensable for answering many scientific questions. RESIST researchers use about a dozen different cohorts.

The information is provided in the form of videos. They will be available to anyone interested from the end of April on the Patient University homepage under the link https://www.patienten-universitaet.de.

In addition to the RESIST research results, there will be other lectures on the topic of infections, including a virtual short tour of the special exhibition "Epidemics. Curse of the past - threat of the future" of the Roemer- und Pelizaeus-Museum Hildesheim as well as an interesting explanation by the curator of the museum Oliver Gauert.

Impressum

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Appetizer

Last year, RESIST scientists in Hanover, Braunschweig, Hamburg and Saarbrücken stood in front of the camera to report on the infection research for which they are "on fire"! The resulting 44 videos show what research in RESIST is all about and with what aims and passion it is carried out. All videos can be viewed at the click of a mouse on our homepage (**www.resist-cluster.de**). In addition, we have now created a little appetizer as a surprise: A video teaser that you can find at the top of the page; enjoy.

The start page of our video teaser

Human Microbe

What are microbes? How do epidemics develop? How can infectious diseases be controlled? The DFG's free interactive tablet app "MenschMikrobe" offers a fascinating tour through the world of microorganisms and insights into the interplay between humans and microbes.

In the "Research" section, scientists present projects from DFG-funded research – Including the one from RESIST project D2, which revolves around herpes viruses.

Under the heading "How a human defense protein blocks herpes viruses", app users can learn interesting facts about herpes viruses and our immune system from Prof. Sodeik's team from the MHH Department of Virology - in particular about the protein MxB, which plays an important role in the defense against herpes virus infections because it can destroy the protein packaging of the viral genome (the capsid).

The app MenschMikrobe:
Getting to know the interplay between humans and microbes.

Spring

We wish you all a colourful, light-filled and hopeful spring despite the many problems in the world.

Your Neswletter editorial team

Colourful reception:
At the entrance of building J6.

Speed dating with science

"Book a Scientist" – organised by the Leibniz Association – is similar to speed dating: interested people can talk to an expert for 25 minutes and ask everything they've always wanted to know about their favourite topic. The most recent of these one-on-one meetings took place online on 8 April and Prof. Dr. Kay Grünewald also gave out appointments. Under the heading "Making viruses ice-coldly visible" people could ask him questions about cryo-electron tomography – a technique he uses to analyse the structure and dynamics of cellular infection processes. The next "Book a Scientist" event is on 15 June. That' s when interested people can once again ask experts questions. You can find more information at www.leibniz-gemeinschaft.de/bookascientist.

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, **Centre for Structural Systems Biology** (CSSB) Hamburg, **Centre for Chronic Immunodeficiency** Freiburg (CCI) and the **University of Veterinary Medicine Hannover**, Foundation (TiHo). The work of the Cluster of Excellence RESIST is funded by the **German Research Foundation** (DFG).