

I wish you a successful year 2023

GREETINGS FROM PROF. SCHULZ AT THE TURN OF THE YEAR

In the last RESIST newsletter of 2021, I had wished everyone a "successful and hopefully this time really 'more normal' year 2022" at the turn of the year 2021/22. 2022 has been 'more normal' in the sense that the restrictions on daily life due to the SARS-CoV-2 pandemic are now largely gone, thank goodness. Less stressful? Everyone will have their own opinion on this. In RESIST we certainly had enough to do. The big topic this year was the internal evaluation of our research projects, which we conducted together with our SAB in February 2022. In the course of a two-day event, which unfortunately could only be held 'online', the SAB took an in-depth look at the current RESIST projects and made recommendations on the continuation of those that have been running since 2019, and on the inclusion of some new projects. The commitment of the SAB and the willingness to deal intensively with individual projects was impressive and we as an association benefited greatly from this meeting. We are therefore very grateful to the SAB members for their commitment and hope that we will be able to wel-

come them next year in Hanover to meet and exchange ideas in a relaxed setting. On the basis of this internal evaluation, most of the projects could be continued, if necessary after adaptation, which we took as confirmation that the path we have taken with our projects is the right one.

This year was also the 'half-time' of the first RESIST funding period. In the coming year, our focus will therefore be on writing the continuation application, which we will have to submit in August 2024. To start this process, we are planning a joint RESIST retreat on 20 and 21

April 2023, at which we will discuss the future direction of RESIST and the framework of the continuation application. This will be a very important date and I ask everyone to reserve the date. We will also hold a meeting of the RESIST board with the boards of the other two clusters of excellence in the field of infection, "Balance of the Microverse" in Jena and "CMFI (Controlling Microbes to Fight Infection)" in Tübingen, to coordinate our respective orientations and prepare a joint scientific symposium of all three

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I think it is
extremely important
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regularly again.



The RESIST speaker trio Prof. Schulz, Prof. Hansen and Prof. Förster (from bottom to top) with the new RESIST roll up.

clusters in 2024. This joint first meeting of the boards will take place on 22 and 23 June 2023.

As we are now returning to 'normal' procedures, we have also started to organise the regular "live" RESIST seminars again, with an 'online option'. I think it is extremely important that we all meet regularly again to exchange and develop new ideas, and also to think about things that do not occupy us on a daily basis, inspired by a stimulating seminar. Dr. Eugenia Faber, Dr. Eugenia Gripp and Dr. Maïke Hinrichs, our managers, put a lot of effort into creating the framework conditions for this and

organise cake, canapés and also beer after the regular RESIST seminar at 5 p.m. to spur on the discussions. For Christmas, I would therefore like all members of RESIST working groups to make a 'good resolution' for the new year 2023 to regularly attend the RESIST Seminars. Of course, all other readers of this newsletter are also cordially invited to the seminars.

All in all, I think we can look back on another successful year for RESIST at the end of 2022. I wish all members of RESIST and all other readers of this newsletter a Merry Christmas and an equally successful 2023.

The first RESIST Satellite Symposium

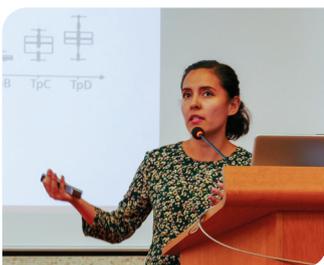


Reunion joy (from left): Greta Ehlers, Maïke Willers, Prof. Viemann and Prof. Grimbacher.

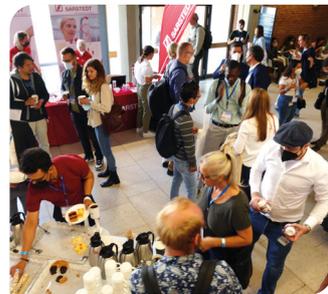
PRESENTATIONS ON SARS-COV-2, THERAPEUTIC MEASURES AND SYSTEMS IMMUNOLOGY

On 7 September, a RESIST satellite symposium was held for the first time – as part of the annual meeting of the German Society for Immunology (DGfI) and the Austrian Society for Allergology and Immunology (ÖGAI). Ten speakers enriched the guests' knowledge of the topics of SARS-CoV-2, therapeutic measures and systems immunology in well-attended talks in the MHH lecture theatre H.

Prof. Pöhlmann from the German Primate Center kicked things off with



Exciting lectures: Ximena Leon Lara explains how certain T cells mature in premature and newborn babies.



Also important: Breaks offer opportunities for exchange and invigoration.

his lecture on SARS-CoV-2 variants. Dr. Bosnjak from the MHH Institute of Immunology then presented his work on the inhalable SARS-CoV-2 vaccine, his colleague Dr. de Barros reported on immune reactions to SARS-CoV-2 vaccination and Prof. Krey from the Institute of Biochemistry at the University of Lübeck explained the activity of broadly neutralising antibodies against SARS-associated coronaviruses.

On the topic of "Therapeutic Measures", Ximena Leon Lara from the MHH Institute of Immunology explained the

maturation of $\gamma\delta$ - and $\alpha\beta$ -T cells in premature and newborn infants. Prof. Viemann from the Translational Paediatrics of the University Hospital Würzburg clarified the perinatal programming of the innate immune system by S100 alarmins and Prof. Lachmann from the MHH Clinic for Paediatrics, Paediatric Pneumology, Allergology and Neonatology spoke on the role of macrophages in modern infection medicine.

Dr. Kefalakes from the MHH Clinic for Gastroenterology, Hepatology and Endocrinology focused on systems immunology. She explained how T cells can be used to control hepatitis D infection. Dr. Rösner from the MHH Clinic for Dermatology, Allergology and Venerology reported on risk factors for severe courses of varicella zoster virus infections and Lennart Riemann rounded off the programme with his talk on mechanisms of immune responses to COVID-19 vaccines.

Prizes for RESIST researchers

RESIST researcher Maïke Willers from Prof. Viemann's Experimental Neonatology group received the "AAI Bright Sparks Award", endowed with 300 euros, from the American Association of Immunologists (AAI) for her lecture at the congress. The topic of her lecture was the age-dependent programming of the innate immune defence against the influenza A virus. "With our studies on this topic, we would like to understand, among other things, which type of immune programming is associated with increased susceptibility and severe courses of influenza diseases," she says.

RESIST Medicine PhD students Greta Ehlers and Annika Tödtmann jointly received a prize of 200 euros for their poster "Ontogenesis of postnatal innate immune metabolism", sponsored by Merck.

Internal advisory board enriched

In addition to Gabriele Gründl, who we introduced in the last RESIST newsletter, Egbert Trowe now also represents patients on the RESIST internal advisory board:

Mr Trowe, you had a liver transplant in 2002 due to viral hepatitis. Since then, organ donation has been your topic and you are very active in numerous committees. In your opinion, what should be researched as a priority in this regard?

Work should be done to avoid reinfection and to make immunosuppressants more tolerable, so that there are fewer side effects. But above all, I would like to see progress in curing the diseases. Then organ transplants would no longer be necessary.

In addition to caring for patients waiting for an organ, you are particularly committed to the issue of organ donation. What is particularly important to you?

By saying "yes" to organ donation, you can help people. But I also understand very well if people are against it. It is important to me that people deal with the issue, decide for or against organ donation and record this in an organ donor card or a living will. In this way, one can avoid the relatives having to determine this if the worst comes to the worst.

In Germany, organs and tissue are only removed if the deceased person consented to organ donation during his or her lifetime. What do you think about this?

I am clearly in favour of the objection solution, whereby – if the deceased person has not expressly objected to organ donation during his or her lifetime – organs can be removed for transplantation. At the same time, it should still be possible for relatives to refuse the removal of organs if they cannot cope with it – this is how it is regulated in Spain, for example.

However, the solution to the objection is only one building block in the whole issue of organ donation. Another more important component is that



Egbert Trowe

there must be more binding procedures for organ removal in the clinics.

What do you think should change in this regard?

The removal of organs always takes place in an intensive care unit, and in the daily clinical routine there is often hardly any time for discussions with the relatives – which is why they often reject the removal of organs. I think that more space needs to be given to the topic there, which also means that both the relatives and the medical and nursing staff need psychological support. There is something wrong there.

How has your work changed as a result of the corona pandemic?

We have no direct contact between us members or with the patients. And the doctor-patient seminars only take place online. This has increased the number of participants, but personal communication has suffered. It is a particular pity that our educational work in schools is dormant. Unfortunately, the topic of organ donation is not yet integrated into the curriculum. Yet this would be so important, because social acceptance for this topic is still largely lacking.

Dear Mr Trowe, thank you very much for the interview.

Egbert Trowe is very active. He is an honorary ...

- Member of the board of the Association of Liver Transplant Patients Germany e.V.
- Member of the Board of Trustees of the German Organ Procurement Organization
- Member of the Board of Trustees and Foundation Council of the German Liver Foundation
- Topic-related patient representative in the Federal Joint Committee
- Member of the patient advisory board of the MHH Transplant Centre
- Member of the Hanover Admissions Committee of the Association of Panel Doctors of Lower Saxony
- Member of the Lower Saxony Organ Donation Network

A worthy conclusion:

The SFB 900-Symposium

THE SFB 900 FORMED THE BASIS FOR RESIST – A REVIEW AND OVERVIEW OF THE DEVELOPMENT OF THE 19 CURRENTLY RUNNING PROJECTS OVER THE LAST DECADE



Participants of the symposium

On 13 and 14 October 2022, the final symposium of the Collaborative Research Centre 900 "Chronic Infections: Microbial Persistence and its Control" took place. The SFB 900 started on 1 July 2010 and will come to an end on 31 December 2022 after 12½ years of funding by the German Research Foundation – it has thus reached the maximum possible funding period after two successful interim evaluations in 2014 and 2018 and a 6-month pandemic-related extension. The SFB 900 is the first Collaborative Research Centre at the MHH to focus entirely on infections: infection topics had previously been dealt with in Collaborative Research Centres at the MHH with other foci. With its focus on chronic infections, the SFB 900 took into account the strengths of infection research at the MHH in the fields of hepatitis and herpes viruses and chronic bacterial pathogens, which had grown in the first decade of the 21st century. Together with the International Research Training Group IRTG 1273 "Strategies of human pathogens to establish acute and chronic infections", the SFB 900 formed the basis for the Cluster of Excellence RESIST, which was launched in 2019.

The SFB 900 Symposium in October 2022 was therefore dedicated to a review and overview of the development of the 19 currently running projects over the last decade. The presentations by the SFB 900 project leaders were accompanied by talks by invited external speakers on the same research topics. On the pathogens *Helicobacter pylori* and

Pseudomonas aeruginosa, which had been focal points of the SFB 900, there were talks by S. Suerbaum, C. Josenhans, S. Bartfeld (Berlin) and B. Tümmler. They shed light on the evolution of bacterial genomes, the molecular mechanisms of the plasticity of bacterial genomes, the role of a lipopolysaccharide metabolite in the inflammatory response triggered by *H. pylori* and new organoid models to study the tropism of *H. pylori* for certain cell types in the gastrointestinal mucosa. These presentations were complemented by an overview by X. Didelot from the University of Warwick, UK on new phylogenetic methods for reconstructing the evolution of bacterial genomes and by a lecture by G. Graßl from the MHH on chronic *Salmonella* infections.

The major topic of "Immune responses in chronic infections" was introduced by an engaging talk by A. Hayday, King's College London; he spoke about immune mechanisms that restore homeostasis after infection and cancer. This was followed by talks by I. Prinz, S. Ravens and B. Eiz-Vesper on $\gamma\delta$ and $\alpha\beta$ T cells in viral infections and by A. M. Leen from Texas on antiviral T cell therapies. H. Wedemeyer and M. Cornberg shed light on the ongoing changes in the immune system after hepatitis C virus infections, and R. Förster, L. Cicin-Sain, U. Kalinke and M. Brinkmann reported on their many years of work on the confrontations between the innate and adaptive immune system and cytomegalovirus. A lecture by S. Urban, Heidelberg, summarised his many years of work, which have led to the development of an inhibitor of the hepatitis B and D viruses that has now been approved for the clinic. A subsequent visit to the Wilhelm Busch Museum to view drawings by Wilhelm Busch and English caricatures from the 18th century exhibited there provided an occasion for interesting discussions – especially for doctoral students from other cultural backgrounds – about the development of freedom of the press and freedom of opinion in the 18th and 19th centuries.

The second day of the symposium was dedicated to chronic viral infections, in particular the three herpes viruses worked on in SFB 900, Herpes simplex virus (HSV; B. Sodeik, A. Viejo-Borbolla, A. Cliffe), human cytomegalovirus (HCMV; M. Messerle, N. Stern-Ginossar), Kaposi's sarcoma-associated herpes virus (KSHV/HHV8; T. Schulz), as well as two hepatitis viruses, hepatitis C virus (HCV; T. Pietschmann, G. Gerold, J. Marcotrigiano) and hepatitis E virus (HEV; T. Krey). C. Goffinet reported on her recent work on SARS-CoV-2. Finally, two invited speakers gave talks on new ways of defending the cell against intracellular pathogens: P. Lehner (University of Cambridge) on his work on the HUSH

complex and epigenetic mechanisms in defence against retroviral genomes, and M. Gack (Lerner Research Institute, Cleveland Clinic, Florida) on the role of cellular non-coding RNAs in stimulating the innate immune response.

All in all, we all felt that this symposium, which reflected a twelve-year research programme and had also offered many new suggestions and insights, had been a worthy scientific conclusion to our SFB 900.

Thomas Schulz

RESIST researchers are highly regarded

Prof. Manns



Prof. McHardy



Prof. Osterhaus



Prof. Werfel



Prof. Manns, Prof. McHardy, Prof. Werfel and Prof. Osterhaus are among the most cited scientists in the world. This was the result of the latest analysis of scientific publications by the Clarivate Analytics company.

The "Highly Cited Researchers" list, which is compiled annually, shows which publications in each discipline are among the most cited one percent. RESIST member Prof. Osterhaus is listed in the "Microbiology" category and the three RESIST members Prof. Manns, Prof. McHardy and Prof. Werfel are listed in the "Cross-Field" category, which includes researchers who have an impact on science beyond their actual field of work.

Prof. Manns is a founding member of RESIST and currently serves in an advisory capacity on the RESIST Research Management Board as President of the MHH. Prof. McHardy, Prof. Werfel and Prof. Osterhaus are also founding members and they are involved in various RESIST projects.

The complete list of "Highly Cited Researchers 2021" and further information can be found on the Web of Science website at www.clarivate.com.

MORE SAFETY FOR MEDICINES

PROFESSOR LACHMANN RECEIVES
"ERC PROOF OF CONCEPT GRANT"

Prof. Lachmann with a bottle of sodium chloride infusion solution.



Medicines that are injected must be continuously tested for impurities as part of their production and release, as these can cause fever or even blood poisoning. Until now, this has mostly been done using animal tests, animal products or the so-called monocyte activation test (MAT). But the use of animal tests and products must be avoided – because they do not adequately reflect human physiology in some cases and because the European authorities will no longer accept them from 2026.

The MAT based on donated blood cells reflects human physiology better, but is not sufficiently accepted by the industry as blood donations are scarce and blood cells vary greatly. So far, the only alternative is artificial cells derived from cancer tissue, but these cannot detect all impurities. Therefore, new approaches are urgently being sought. The solution could be to also use innovative cell products, which are being developed for novel therapies, for the safety assessment of drugs.

Prof. Lachmann, Department of Paediatric Pneumology, Allergy and Neonatology at the MHH and researcher in RESIST, is developing the so-called iPYRO method for these reasons. This involves the use of novel, artificially generated immune cells to detect impurities in medicines. For this, the European Research Council (ERC) has now awarded him the "ERC Proof of Concept Grant". "Our iPYRO method will revolutionise the safety of drugs that are adminis-

tered parenterally by injection – i.e. all injection solutions, infusions as well as vaccines," he says.

An "ERC Proof of Concept Grant" is intended to explore the commercial or societal innovation potential of an ERC research project. Only researchers who have previously been awarded ERC funding can receive the award. Professor Lachmann had received the prestigious "ERC Starting Grant" in 2019 and with it 1.5 million euros of funding over five years for his research on human macrophages.

Prof. Lachmann's method is based on human cells of the immune system, which can be fully defined and produced in the laboratory without a donor. These are macrophages (phagocytes), which are derived from so-called induced pluripotent stem cells (iPS cells) and are grown in bioreactors suitable for industrial use.

"The cells are already being used in the development of cell-based therapies and will now additionally benefit millions of people as they can be used to produce safe drugs," he says. The new immune cells also make it possible to develop further pioneering test procedures to advance health research in Germany. The innovation was able to be advanced thanks to the interdisciplinary cooperation of the fields of Regenerative Medicine (REBIRTH Research Centre for Translational and Regenerative Medicine) and RESIST at the MHH.

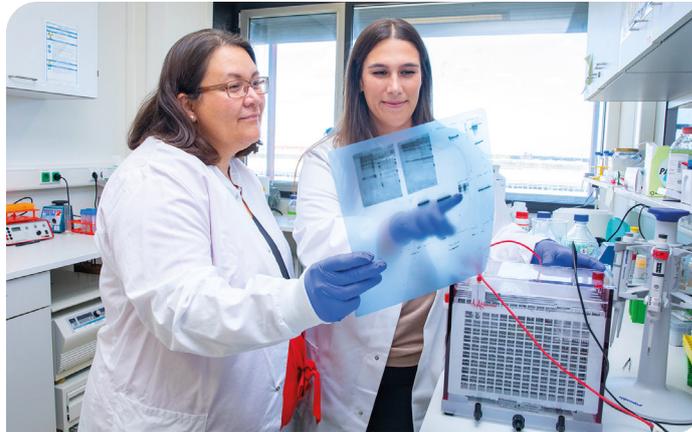
German courses

Within the framework of RESIST, "German as a foreign language" courses are offered again by the teacher Artur Sieg. Since November 2022, there has been an advanced course (A2/B1); this is the continuation of the basic course and takes place online on Wednesdays from 4.30 to 6.00 pm. And from January 2023 there will be a new basic course, also online, for one and a half hours once a week. The day and time have not yet been fixed. All interested RESIST members can take part, and do not have to pay for the courses. Currently, many (post-) doctoral students are taking these courses. RESIST researchers who would like to take part in a German language course are welcome to contact the RESIST office: (0511) 532-4107, e-mail: RESIST@mh-hannover.de.

The role of the six variants

NEW RESEARCH ON THE MULTIPLICATION OF ADENOVIRUSES

Prof. Schreiner (left) and Dr. Mai stand in front of a "wet tank" with which they perform the "Western blot procedure" to detect proteins with specific antibodies. Afterwards, the proteins can be visualised on X-ray films.



Inflammation of the gastrointestinal tract and conjunctiva, but also of the liver, brain, urinary tract and lungs – the list of diseases that an infection with human adenoviruses can cause is long. In addition, the viruses are common worldwide; these infections are becoming more frequent and can also become latent. Then they persist in the cells, temporarily have no detectable effect, but can reactivate again.

In healthy adults, adenovirus infections usually proceed without symptoms or with mild symptoms. But in people with a weakened immune system, they can become life-threatening and, not infrequently, fatal. There are also certain types of adenoviruses that can lead to life-threatening pneumonia even in healthy people. So far, there are neither specific antiviral therapies nor vaccination for the general population.

In the search for antiviral therapy approaches, the interdisciplinary team of RESIST researcher Prof. Schreiner from the MHH Institute of Virology – led by Dr. Mai – has now been able to show that certain factors in the cells of various human tissues are decisive in determining whether the viruses multiply there or not. The team also includes researchers from the Technical University of Munich and the Hannover-Glasgow Infection Strategy

(HAGIS) project of the MRC-University of Glasgow Centre for Virus Research. The results were published in the scientific journal [Microbiology Spectrum](#).

In their research, the team investigated the suspicion that the so-called PML nuclear bodies in human cells very likely counteract the multiplication of adenoviruses. The main component of the PML core bodies is the so-called PML protein, which is produced by the human cell in six different variants. Most studies to date have investigated the extent to which all PML variants act together on virus replication. "We have now examined what role the six individual PML variants play during adenovirus infection – and in different tissues and cell types," explains Prof. Schreiner. To do this, the team created cell lines from lung and liver tissue, each producing only one of the six PML variants. "In this way, we were able to identify exactly those PML variants in different tissues and cell types whose nuclear bodies can suppress the infection," continues Dr. Mai.

Based on the results of this study and through the better understanding of the host's own defence mechanisms, new treatment options against human adenoviruses can now be developed further within the framework of RESIST.

Consultant laboratory for adenoviruses

The German consultant laboratory for adenoviruses is located at the Institute of Virology of the MHH, headed by PD Dr. A. Heim. Here, all human adenovirus types can be detected, genomically sequenced and quantified in clinical samples. This plays a role in the diagnosis of life-threatening infections in immunosuppressed patients, especially in children after bone marrow transplantation. The laboratory team is also available to answer specialist questions and it provides cell cultures to support researchers in their work. Collaboration in epidemiological studies and advice on requirements for the study material and shipping conditions are also part of the repertoire.

Impressum

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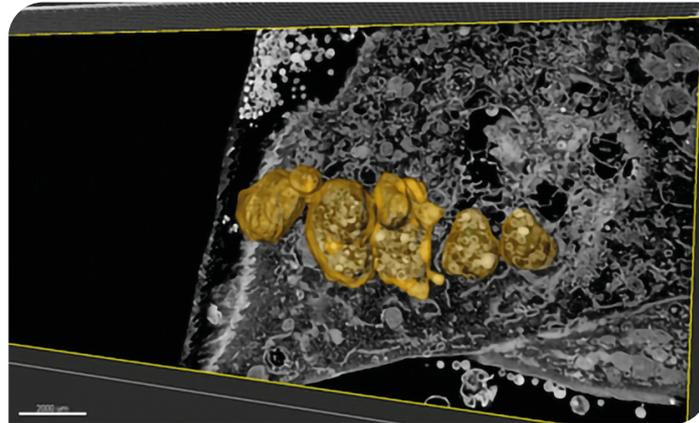
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Pulsating into freedom

CYTOMEGALOVIRUS: SPREAD OF INFECTION IN HUMAN CELLS FURTHER ELUCIDATED

The Prof. Bosse group has revealed a novel exit pathway used by the Human Cytomegalovirus (HCMV) to spread infection in human cells. The research study, published in *PLOS Pathogens*, shows that HCMV can release new virus particles in bulk pulses. According to the researchers, this new exit pathway contributes to the diversity of HCMV viral particles, which may explain the virus's ability to infect different cell types.

Viral infections begin when a virus penetrates a host cell and remodels the host cell's apparatus to enable the creation of new viral particles. For infection to spread, these new viral particles must find a way to break through the cell membrane and infect the next host cell. The journey that a new viral particle takes to leave the infected cell is known as an egress pathway.



An HCMV-infected cell imaged with serial block area scanning electron microscopy, multiviral bodies segmented and highlighted (yellow).

In the one known egress pathway for HCMV, single virus particles are enveloped into small transport vesicles and continuously ejected from the infected cell. "Several studies were, however, showing virus particles inside multivesicular structures, but no one could link them to an egress pathway," explains Prof. Jens Bosse. "We were intrigued and decided to investigate the dynamics of these structures in more detail."

Using an integrative approach based on volumetric live-cell imaging and three-dimensional correlative light and electron microscopy (3D-CLEM), the researchers were able to identify accumulations of enveloped virus particles in multivesicular bodies, which they dubbed multi-viral bodies (MViBs). "With live-cell imaging, we were able to demonstrate that the MViBs are transported and subsequently fused to the cellular membrane where they are then released

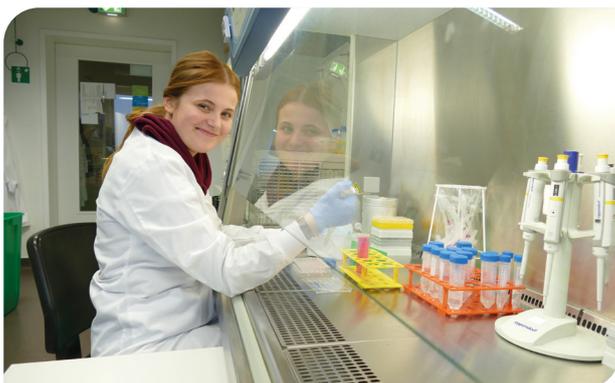
in pulses," explains the paper's first author Felix Flomm. "The infected cells are essentially spitting out viruses, and the neighboring cells are receiving 100 virus particles in their face." The existence of multiple egress pathways could explain the large diversity of HCMV viral particles.

HCMV causes a lifelong latent infection in most healthy individuals; however, in immunocompromised patients and newborns, it can lead to serious disease that affects different tissues and organs. "Understanding HCMV's egress pathways is essential for developing novel antiviral strategies for this clinically relevant pathogen," notes Bosse. The researchers will now look into how the bulk release of HCMV particles is triggered within the infected cell.

Prof. Bosse holds a RESIST professorship at the MHH and is a group leader at the Centre for Structural Systems Biology CSSB and at the Leibniz Institute of Virology (LIV) in Hamburg. *Melissa Prass, CSSB Hamburg*

A year in science

Emelie Dechant is doing a Voluntary Year in Science (FWJ) in the team of RESIST researcher Prof. Viemann.



"During my voluntary year in science (FWJ), I am getting a good insight into research – both in the lab and in documentation. This makes it easier for me to think about whether I want to do this later," says Emelie Dechant. The 19-year-old started her FWJ at MHH in September 2022 in the team of RESIST researcher Prof. Viemann after leaving the Tellkampfschule.

Emelie Dechant really likes her tasks. One of her jobs is to collect samples from the paediatric clinic that come from premature babies – these are breast milk, blood, throat swabs and stool – and prepares them so that they can be frozen and included in the Hannover Unified Biobank (HUB) at MHH. Another job is to assist with documentation: she transfers information from doctors' letters

Research of antiviral agents

TEAM LED BY PROF. PIETSCHMANN RECEIVES AROUND 700,000 EUROS FROM THE VOLKSWAGEN FOUNDATION FOR A RSV PROJECT

New approaches and new substances are needed in the fight against infectious diseases. This has been demonstrated by the coronavirus pandemic. In response to the emergence of SARS-CoV-2, the Volkswagen Foundation launched the "Innovative Approaches in Antiviral Drug Development" funding initiative back in 2020. Currently, the foundation has named more than ten projects that will be funded with a total of 6.6 million euros.

Prof. Pietschmann, Professor at the MHH and Director of the Institute of Experimental Virology at TWINCORE, is coordinating one of them. Together with Prof. Hirsch from the Helmholtz Institute of Pharmaceutical Research Saarland, Prof. Hansen from the MHH Clinic for Paediatric Pneumology, Allergology and Neonatology, and Prof. Krey from the Institute of Biochemistry at the University of Lübeck, he will be optimizing new inhibitors directed against the respiratory syncytial virus (RSV) over the next 15 months. The researchers are all in the RESIST team and they will receive a

total of about 700,000 euros for the project called OPTIS (Optimization of novel Respiratory Syncytial Virus-inhibitors by multi-parametric profiling).

RSV causes severe respiratory infections, especially in young children, and is the most common cause of hospitalization in the first two years of life. An effective antiviral therapy does not yet exist. In their own preliminary work, the research team has already identified some promising candidates for antiviral agents. Together with the company ENYO Pharma, these molecules and others discovered by ENYO Pharma, will now be structurally and chemically optimized, in order to make the development of resistance more difficult if virus mutations occur. Such industrial cooperation is an integral part of the funding initiative, and means that developability is factored in from the beginning unlike in purely basic projects.

"The new OPTIS project helps to find new active substances to treat seriously ill people. It thus complements



A stack of microtitre plates in the laboratory.

our RESIST project on RSV, in which we are investigating which genetic factors lead to severe RSV infection – with the long-term goal of using this knowledge to develop new diagnosis, prevention and treatment methods," says Prof. Pietschmann.

Jan Grabowski, TWINCORE

and questionnaires into lists. This involves, for example, the children's illnesses and the medication they receive. The young woman has not yet decided whether she wants to study medicine or whether she will choose another subject that has to do with research.

Prof. Viemann has had FWJ participants in her team several times in the past years. "What I like most about it is that the young people are highly motivated and learn very quickly. They are an essential support in establishing patient cohorts and are therefore a great help," she says.

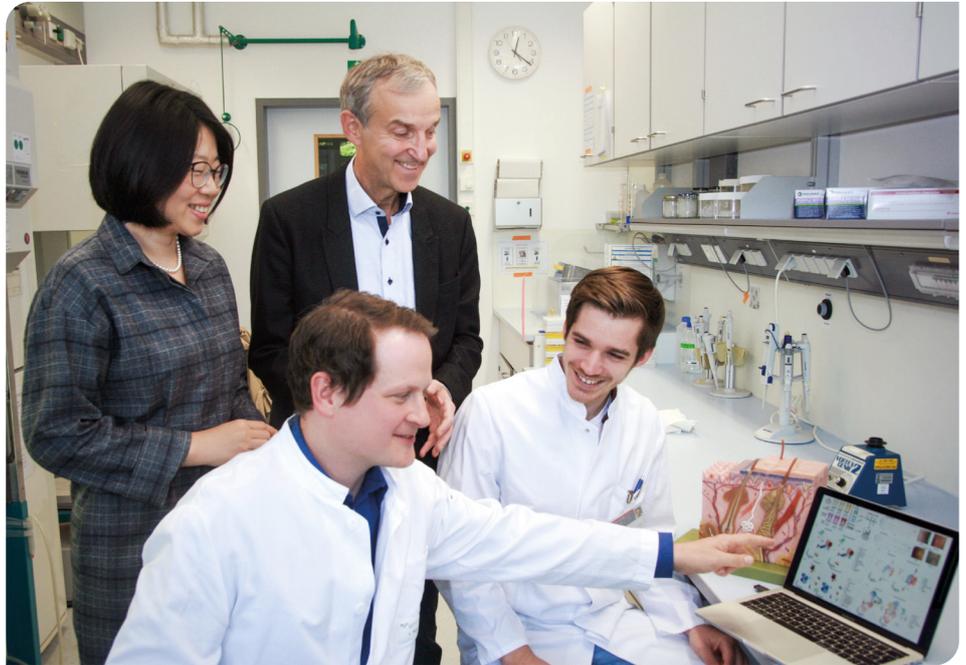
Voluntary year in science

You can apply until the end of January

A Voluntary Year in Science (FWJ) offers school leavers the opportunity to accompany a research project of their choice. It doesn't matter whether they are interested in the medical or natural sciences or in engineering. The application deadline for the next FWJ at the MHH, which starts in September 2023, is 31 January 2022 for students. Research teams that would like to host FWJers can apply at any time. More info and the list of projects you can participate in at MHH are on this homepage: <https://www.mhh.de/gb-i/freiwilligendienste/fwj>

When the skin hurts

ATOPIC DERMATITIS
AND PSORIASIS:
RESIST TEAM EXPLORES
LOCATION AND TYPE OF
IMMUNE CELL ACTIVITY



In the dermatology laboratory: Dr. Rösner (in the front) with Prof. Li, Prof. Werfel and Dr. Traidl (from left).

Many people suffer from neurodermatitis (atopic dermatitis) or psoriasis. These chronic inflammatory diseases, which have so far been incurable, can lead to a significant loss of quality of life in their severe forms due to the agonising itching and to stigmatisation.

Researchers in RESIST have now gained a number of new insights with potential clinical relevance using state-of-the-art technologies such as T-cell receptor and single-cell RNA sequencing based on skin biopsies and blood samples from patients. They have published these in the journal *Allergy*, currently the leading publication in the field of allergology, in two articles. The main authors include Dr. Bowen Zhang from the research group of Prof. Dr. Yang Li, Centre for Individualised Infection Medicine and TWINCORE, and Dr. Lennart Rösner and Dr. Stephan Traidl from the team of Prof. Dr. Thomas Werfel, MHH Clinic for Dermatology, Allergology and Venereology.

It was already known that in both psoriasis and atopic dermatitis, T-cells of the immune system migrate from the blood into the skin and drive the inflammation there. Detailed examination of T-cells in blood and skin has now led to evidence that in atopic dermatitis they migrate mainly into the skin, whereas in psoriasis they both drive inflammation in the skin and move from the blood into other tissues. Further findings suggested that the inflammatory factors produced by the T-cells in atopic dermatitis act primarily on skin cells, whereas in psoriasis they also activate circulating immune cells in the blood, potentially triggering or increasing inflammation elsewhere in the body. "This underlines that in psoriasis, possible disease symptoms must also be investigated beyond the skin. If necessary, the joints or the cardiovascular system may then also need to be treated, for example," says Dr. Stephan Traidl.

The team also found out that macrophages (phagocytes), which are also found in the skin in both diseases, develop differently and differ in terms of their inflammatory mediators. "This is very interesting with regard to atopic dermatitis. Because here, skin infections with pathogens such as staphylococci and herpes viruses can occur, which are directly fought by the macrophages," says Dr. Lennart Rösner.

Atopic Dermatitis and Psoriasis

Atopic dermatitis progresses in episodes and causes pronounced itchy eczema. In Germany, more than ten percent of children of preschool age are affected, but also about two percent of all adults. The disease begins with a defect in the skin barrier in conjunction with changes in the immune system. There are many triggers for a worsening of the disease – allergens, skin-irritating substances, mechanical stimuli, infections and psychological stress are among them.

Psoriasis is characterised by skin plaques on the extensor side. In Germany, about two to four percent of all adults are affected, mainly in the second and third decades of life. Both diseases may be treated externally and internally, depending on their severity. In recent years, there have been a number of effective new developments in this field. The MHH Clinic for Dermatology, Allergology and Venereology offers specialised consultations.

These links will take you to the publications:

<https://pubmed.ncbi.nlm.nih.gov/35255168/>

<https://pubmed.ncbi.nlm.nih.gov/35986602/>

Master's programme Start of the **second year**



The new students during the orientation week.

RESIST warmly welcomes the 18 students who started the Master's programme in Biomedical Data Science in October. The programme is part of RESIST and is now in its second year.

An orientation week was held at the MHH in October for the group of new students consisting of eleven bioscientists and seven medical doctors. The aim was to get to know the study programme as well as the other students and lecturers. In addition, there were

various other items on the programme. For example, RESIST researcher Prof. Meyer-Hermann gave a very exciting lecture on 6 October on the topic of "The need for more dynamism in medicine", which was very well suited to the study programme.

More information on the four-semester Master's programme can be found on the Internet at www.mhh.de/master-biomeddat.

Summer RESIST network meeting

At the end of August, the summer RESIST network meeting took place at the TWINCORE site. Around 50 researchers were there, some with their children, and so it was a friendly afternoon with interesting and fun conversations, tasty food and drink, and a quiz in which



the prizes included the rare RESIST mugs. Meanwhile, the younger guests could enjoy the bouncy castle. The summer weather supported the good mood and was only later replaced by a thunderstorm. There is already a plan to repeat this kind of gathering next summer and we are looking forward to numerous participants.

Convivial get-together in summer weather

RESIST Seminars 2023

The RESIST seminar series with interesting lectures by RESIST researchers and external guests will take place again in 2023 on Thursdays from 5 to 6 p.m. in Lecture Hall Q – with a video broadcast for external members. One member of the RESIST Research Management Board will be in charge of each seminar and new (post) doctoral researchers can introduce themselves before the respective lectures.

Further information on the dates can be found on the website www.RESIST-cluster.de.

12. January 2023	PROJECT B5
19. January 2023	PROJECT B8
26. January 2023	PROJECT B9
02. February 2023	GUEST LECTURE
16. February 2023	PROJECT B13
23. February 2023	PROJECT B14
02. March 2023	GUEST LECTURE
09. March 2023	PROJECT C4
16. March 2023	PROJECT D1
23. March 2023	PROJECT D2
13. April 2023	PROJECT D3
27. April 2023	PROJECT D4
04. May 2023	GUEST LECTURE
11. May 2023	Project D5

RESIST consultation hour

Do you have scientific questions, suggestions or criticism? Then you can come to the RESIST speaker trio's office hours. This takes place on the last Wednesday of every month from 5 to 6 pm. At these times, RESIST speaker Prof. Schulz, and co-speakers Prof. Hansen and Prof. Förster take turns in making themselves available to RESIST members for a discussion. You can find the dates and contact persons on the intranet at www.RESIST-cluster.de. If you are interested, please contact us by e-mail: RESIST@mh-hannover.de

RESIST Retreat

The second RESIST Retreat will take place from the 20th to the 21st of April 2023. On these two days, all RESIST researchers will be able to present their projects and their results, and there will also be an opportunity to exchange ideas and network even better. You will find more detailed information on the homepage www.resist-cluster.de under the heading "News/Events".

How researchers breed phagocytes

AROUND 200 GIRLS AND BOYS ATTENDED
PROF. LACHMANN'S KINDERUNI LECTURE

The children waited a long time to be able to enter the largest lecture hall of the MHH again. After a two-year break due to Corona, the time had finally come on 8 November 2022: around 200 inquisitive girls and boys aged eight to twelve came to the university to experience the lecture by RESIST Prof. Lachmann on the topic of "Medicine of tomorrow: How can phagocytes from the laboratory heal us?"

The lung expert is researching how to help young people whose immune systems are weakened to better defend themselves against bacteria and viruses. To do this, he has studied the "good" cells of the body's immune defence system, the phagocytes, in detail and discovered a way to multiply them in the laboratory. In this way, he and his team want to help patients whose immune system is not able to fight off bacteria and viruses well.

The children learned first-hand what these phagocytes are and how they

can be obtained and multiplied during his lecture. To this end, Prof. Lachmann first explained to the children with hands-on experiments how we breathe in not only oxygen but also viruses and bacteria through the air. The children were given balloons to inflate to see how much air they breathe in with one breath. "You breathe 30 times a minute, 40 bathtubs of air a day," added Prof. Lachmann, which amazed the children.

In healthy people, their own immune defence works: the phagocytes recognise bacteria and viruses that are inhaled with the air and enter the lungs, and eat them up – "like Pacman, you know him, don't you?" asked the 42-year-old researcher. The children agree. But what if children don't have these "good" cells in their blood, or too few of them? With a live transmission, Prof. Lachmann took the children virtually to a colleague in the laboratory. There was a cosy warm incubator where the phagocytes grow. "Later, the cells are shock-frozen," she



In the lecture hall: Prof. Lachmann shows children how much air they breathe in with one breath.

explained, "at minus 80 degrees. That's even colder than the North Pole."

The young students still had a lot of questions, which they asked their professor at the end of the lecture. "Is there a training for the phagocytes?" one boy wanted to know. There really is. Lachmann and his team give the useful cells food that makes them even fitter. Do phagocytes like viruses better than bacteria? "No, the other way

round," he answered. And can we strengthen the phagocytes ourselves, a girl asked. "Yes, if we eat a lot of fruit and drink Orange juice," Lachmann explained.

Bettina Dunker

The lecture can be viewed online via the following link: www.kinderuni-hannover.de. Further lecture dates are also listed there.



On 17 January 2023, Prof. Brinkmann and Prof. Förster will be on stage at the Volkswagen Foundation's "Herrenhausen Late" event at the Xplanato-

COVID-19: Pandemic and (no) end in sight?

rium Schloss Herrenhausen from 8.30 pm. They will draw conclusions from the course of the Corona pandemic so far and attempt to predict how we can protect our health even better against new virus variants in the future by looking into the pandemic crystal ball. Their talk will be in German.

"Herrenhausen Late – ScienceMusicFriends" is aimed at a young audience

interested in science. Original scientific topics are illuminated by experts from an entertaining perspective. The ballroom in the Herrenhausen Palace will be transformed into a lounge with seating areas, a small stage, music and drinks at the bar. Herrenhausen Late is a joint event series from the Volkswagen Foundation, the Leibniz University Hannover, the Hannover University of Music, Drama and

Media, the Hannover Medical School and the University of Veterinary Medicine Hannover.

Admission is free. Doors open 45 minutes before the start. Registration is not required. As a courtesy to the presenters, admission will be closed at the start of the event. More info is available at www.volkswagenstiftung.de/veranstaltungen.

RESIST – About us

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)**.

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