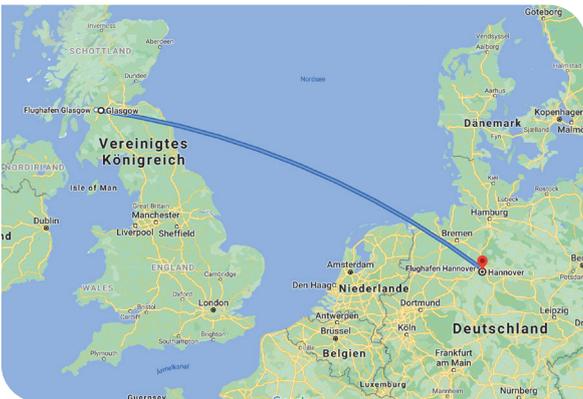


Successful launch of HAGIS

HANNOVER AND GLASGOW PLAN TO CONDUCT RESEARCH TOGETHER AND OFFER AN EXCELLENT TRAINING ENVIRONMENT



Scientists from the Cluster of Excellence RESIST and the [MRC-University of Glasgow Centre for Virus Research \(CVR\)](#) have launched the Hannover-Glasgow Infection Strategy (HAGIS) project. They aim to use their complementary strengths to advance the development of new therapies for infectious diseases – for example, in the areas of viral infections in susceptible individuals and emerging viral infections – and PhD students will benefit from the combined research strengths of the two sites. The Lower Saxony Ministry of Science and Culture is funding the launch of HAGIS with 42,000 euros.

To launch HAGIS, around 30 researchers from Hannover and Glasgow met in an online kick-off meeting on August 26, 2021, where RESIST speaker Prof. Dr. Thomas Schulz and CVR Director Prof. Dr. Massimo Palmarini introduced their institutions and HAGIS, followed by presentations of the work being done in their laboratories by some scien-

tists. For example, Dr. Alfredo Castello explained his research on the role of RNA-binding proteins in viral infection, and Prof. Dr. Abel Viejo-Borbolla and Prof. Dr. Daniel Depledge presented their research on varicella zoster virus latency and reactivation. The meeting also emphasized that in addition to virological projects, collaborations in the fields of immunology and microbiology will also be facilitated. Participants then discussed various research topics in groups before moving on to further action on HAGIS.

This first meeting will be followed by further video-conferences as well as a workshop, if possible in-person, to find research projects on which several PhD students can collaborate – for exchanges of a few months in the other country and institute. In doing so, the teams can build on existing collaborations between the researchers from Hannover and those from Glasgow. From the middle of 2023, a joint DFG proposal for an International Research Training Group will be developed, in which several „generations“ of doctoral students (ten to 15 per „generation“) could spend three to six months each in the laboratories of the other partner. If the proposal is successfully reviewed, the International Research Training Group could start at the beginning of 2024.

RESIST scientists who would like to host PhD students from Glasgow or send them to Glasgow are welcome to contact the RESIST office at: RESIST@mh-hannover.de.



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

Ready to go...

...HAGIS is the new duo between scientists from Hannover and Glasgow. Read more about this partnership here on the left.

...Prof. Depledge and Prof. Höglinger are our new RESIST members. Actually, we should write that they have already had a good start. You can read more about them on page 4.

...18 students will become the pioneers of the new Master's programme „Biomedical Data Analysis“ at the beginning of October – we report on page 6.

...and hopefully you are ready to read our RESIST newsletter. We wish you pleasant reading, your RESIST team.

Prof. Behrens (left) and Prof. Förster with AstraZeneca and Biontech/Pfizer vaccine vials held crosswise



Study on SARS-CoV-2: **Cross-vaccination** protects effectively – even with virus variants

A combination of the AstraZeneca and Biontech/Pfizer vaccines is more effective against SARS-CoV-2 infection than double vaccination with the AstraZeneca vaccine. It is also more effective against viral variants. This was the result of a study conducted by RESIST Co-Speaker Prof. Dr. Reinhold Förster, head of the MHH Institute of Immunology, and Prof. Dr. Georg Behrens from the MHH Department of Rheumatology and Immunology, and published in the scientific journal „[Nature Medicine](#)“. The study was carried out within the framework of the German Centre for Infection Research (DZIF) with financial support from RESIST, the State of Lower Saxony, the Federal Ministry of Education and Research (BMBF) and the Collaborative Research Centre 900.

The scientists compared immune responses in blood samples from 175 volunteers, all of whom had received the AstraZeneca vaccine for their first vaccination. One-third of the participants chose AstraZeneca again for the second vaccination and two-thirds chose Biontech/Pfizer the second time (so-called „cross-vaccination“). The volunteers were all MHH employees.

„Second vaccinations with the Biontech/Pfizer vaccine led to significantly stronger immune responses than second vaccinations with the AstraZeneca vaccine,“ reports Prof. Förster: After the second vaccine dose, there was an 11.5-fold increase in certain protective antibodies (anti-S IgG) in volunteers receiving cross-vaccination, whereas double AstraZeneca vaccination led to about a three-fold increase. There were similar changes in other antibodies (anti-S-IgA) and in T cells. The quality of antibodies

and T cells was also higher after cross-vaccination. Antibodies keep the virus from entering the cells. T cells destroy infected cells and trigger further immune reactions.

„The overall effect of the cross-vaccination was similar to that of people fully vaccinated with the Biontech/Pfizer vaccine,“ says Prof. Behrens. However, he adds, the immune response is still very high even after double AstraZeneca vaccination, and this vaccine remains very important in the fight against COVID-19.

Another key advantage of cross-vaccination is that – according to the values determined by the researchers in the laboratory – it also protects more strongly against the alpha, beta and gamma virus variants. In contrast, the immune response to these variants often remained weak after double AstraZeneca vaccination. Currently, the scientists are testing immune responses to the delta variant of the virus – first results indicate that cross-vaccination also protects more strongly against the delta variant than does double AstraZeneca vaccination. A double vaccination with the Biontech/Pfizer vaccine also protects very well against infections with these four virus variants, as is known from other studies.

„Our study, together with further work from other research institutes, forms a good basis for recommendations on the vaccination sequence. A different vaccine could be used specifically for a booster vaccination – also, for example, to be able to react to new mutations that could emerge at any time,“ says Prof. Behrens.

General Assembly

PLEASE SPEND MONEY AND SUBMIT REPORTS

The fourth RESIST general meeting took place on the 13th of July 2021 in lecture hall R. It was thus a rare opportunity to meet in person for once, although it was of course also possible to join online. RESIST speaker Prof. Schulz addressed numerous topics in his report on past and future plans, including the budget and the internal evaluation.

„Please spend your money on time,“ he said. If project funds from 2021 are transferred to 2022, it is very likely that the DFG will make budget cuts of up to 50 percent. To prevent funds from lapsing, unspent funds or those not planned to be used this year will be collected centrally again at the beginning of November.

The internal evaluation will be carried out to qualitatively assess the individual RESIST projects in order to decide on funding for the years 2022 to 2025 and to strategically align RESIST with a view to a follow-up application in 2025. For this purpose, all required information on existing as well as new projects must be entered into the reporting forms by 15 December 2021. These forms can be found on the RESIST intranet site. Further information is also available there – for example, on the timing of the internal evaluation. The subject areas of the seven new RESIST professors will also be evaluated. This is important for strategic orientation, but will not affect basic financial resources which remain secure.

At the end of the event, some of the RESIST members took advantage of the opportunity to exchange ideas over a snack in front of the lecture hall.

Every single cell counts – even before birth!

SOME IMMUNE CELLS ARE FORMED EARLY IN LIFE AND REMAIN LIFE-LONG

Some things are particularly deeply rooted: for example, some white blood cells of the adult immune system have already formed by the eighth week of pregnancy. These include gamma-delta T cells, more precisely the $V\gamma9V\delta2+$ T cells. These cells can recognise bacterial infections as well as tissue damage and changes such as cancer, or act as inflammation-enhancing cells in autoimmune diseases. They are found in the blood, but also in the intestine, skin, liver and lungs.

Prof. Dr. Sarina Ravens and Dr. Alina Fichtner from the MHH Institute of Immunology as well as Prof. Dr. Immo Prinz and Dr. Likai Tan from the Institute of Systems Immunology at the University Medical Center Hamburg-Eppendorf (UKE), who cooperate in RESIST, have been able to prove the early origin of these immune cells. They published their findings in the scientific journal „*Science Immunology*“.

Gamma-delta T cells are named after the proteins on their surface (the T cell receptors) with which they can recognise antigens. Each of these cells has an individual T cell receptor, resulting in a highly diverse T cell pool. „To study the diversity of gamma-delta T cells and their receptors, we developed an innovative high-throughput sequencing method based on the individual analysis of each cell,“ says Prof. Ravens.

Using this technology, the team studied gamma-delta T cells in umbilical cord blood samples as well as from adult blood samples. „Interestingly, certain human $V\gamma9V\delta2+$ T cells are generated exclusively in a very early phase of life to be ready for immediate use at the time of birth and subsequently persist as innate immune cells throughout life in humans,“ reports Dr. Fichtner.



Recently, the team was able to show that certain gamma-delta T cells proliferate expansively directly after birth and they are thus very likely to be important for the early childhood immune system. „Now we want to find out where these highly functional and innate gamma-delta T cells are found in the body and what role they play in immune defence and autoimmune diseases,“ adds Prof. Prinz. The scientists' long-term goal is to create a basis for optimised preventive measures, diagnoses and therapies.

At the MHH Institute of Immunology (from left): Prof. Prinz, Dr. Fichtner and Prof. Ravens



In the lab: Prof. Häußler (left) and Prof. Galardini

How do the hygiene and distance rules that were introduced due to the COVID 19 pandemic influence the transmission of multi-resistant pathogens in hospitals? Prof. Dr. Marco Galardini and Prof. Dr. Susanne

The sooner the better

Häußler are investigating this question in a new three-year project. The DFG is supporting them with 300,000 euros of funding.

„With this project we want to investigate which bacterial strains circulate in hospitals and with what frequency they occur there,“ explains Prof. Galardini. To do this, the research team will combine genetic and epidemiological data obtained through sequencing and digital tracking. „The goal is to be able to detect resistance as early as possible in order to prevent it from spreading,“ says Prof. Häußler. The team is focusing on bacterial strains of the species *Escherichia*

coli and *Klebsiella pneumoniae*, which are among the most important bacterial pathogens for hospital infections.

Prof. Galardini holds a RESIST professorship at the MHH and he collaborates in the RESIST projects in Research Area C, which focuses on bacteria. He heads the TWINCORE working group „Systems Biology of Microbial Communities“. Prof. Häußler heads the TWINCORE's working group „Molecular Bacteriology“ and she is a lead researcher of the RESIST projects C1 and C2.

New in our RESIST team



Prof. Depledge

Prof. Daniel P. Depledge, PhD, Professor of Systems Biology of Viruses within the DZIF since June 2021, is a new member of RESIST. "The opportunity to expand my research interests and engage in translational research led me to move from New York to Hannover to join the Institute of Virology at MHH. I am looking forward to collaborating closely with many excellent virologists, RNA biologists and immunologists here, while continuing to build new collaborations across Europe," says the 40-year-old.

Prof. Depledge investigates how herpesviruses survive and spread in people's bodies. To do this, he and his team apply computational biology, molecular biology and genomics/transcriptomics approaches to diverse model systems. "We want to identify and characterize key host and viral gene products that govern herpesvirus latency and reactivation across diverse cell types," he explains. In addition, he and his team explore the role of epitranscriptomic modifications on host and viral RNAs in regulating the outcome of infections.

After obtaining a PhD in Molecular Parasitology at the University of York in the UK, he began working on Herpesviruses at University College London, UK. Here he developed a new methodology for capturing and sequencing

viral genomes directly from clinical samples. He then focused his studies on the latency of the viruses varicella zoster and herpes simplex. To further these studies he worked at the New York University School of Medicine, USA, where he also established his own lab group as an Assistant Professor.

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Prof. Dr. Günter Höglinger, Director of the MHH Department of Neurology, joined RESIST in August 2021. His traditional scientific focus is on neurodegenerative Parkinson's syndromes, which result from chronic infection of nerve cells in the central nervous system with prion-like proteins.

As part of RESIST, he leads research centering on the influence of varicella zoster viruses on the nervous system. These viruses can cause shingles, among other things, and the brain and spinal cord can also be affected. As part of RESIST, Prof. Höglinger's team is exploring

the genetic factors that lead to such severe forms of the disease, and looking for biomarkers in brain and spinal cord fluids. This information is intended to form the basis of better therapies. Prof. Höglinger is pleased to now be associated with RESIST: „RESIST offers a unique environment in which to understand and foster resistance to chronic infections of the nervous system," he says.

Prof. Höglinger studied medicine in Regensburg and Würzburg. After professional appointments in Bern, Hong Kong, London, Paris, Marburg and Munich, he took over as



head of the MHH Department of Neurology Prof. Höglinger two years ago.

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Dr. Danica Bergmann joined the RESIST Management team in July 2021 in the area of administrative coordination as the parental leave replacement for Dr. Eugenia Faber. She is also project manager of the research area „Infections of the immunocompromised Host" of the German Center for Infection Research (DZIF). Dr. Bergmann has a PhD in virology from the Justus

Dr. Danica Bergmann

Liebig University in Giessen and has worked in industrial research and development of veterinary vaccines for the past eight years.

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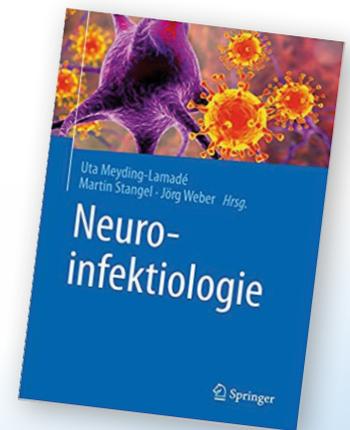
Professor Stangel breaks new ground

Prof. Dr. Martin Stangel moved to the Novartis Institute for Biomedical Research (NIBR) in Basel (Switzerland) in September 2021. The former head of the Clinical Neuroimmunology and Neurochemistry Section of the MHH Department of Neurology was jointly responsible for the RESIST projects A3 and A4, which centre on varicella zoster and herpes viruses. In addition, together with Professor Dr. Thomas Werfel, he established the „Zoster Cohort“ and the „HSV Cohort“ of patients with severe shingles and severe herpes infections, respectively – both groups also include neurologically affected patients.

Within the framework of an interdisciplinary RESIST team, Prof. Stangel also contributed to the establishment of a cohort of older people from Hanover, from whom neurological parameters and age-dependent changes in immune responses to infections are recorded. With the help of these cohorts, it is hoped that genetic factors linked to the occurrence of age-dependent severe courses of the disease can be

discovered, as well as new biomarkers with which the manifestation of the virus in the body as well as complications and secondary diseases can be predicted. On the Neurology side, PD Dr. Philipp Schwenkenbecher will continue to carry out the clinical work and PD Dr. Kurt-Wolfram Sühs the biomarker investigations – now under the direction of Prof. Dr. Günter Höglinger, Director of the MHH Department of Neurology.

„The collaboration with Prof. Stangel in connection with the establishment and management of the RESIST cohort projects was purposeful, efficient and always very pleasant, and contributed to the successful course of recruitment, and that partly under difficult pandemic conditions,“ says Prof. Werfel. „We regret his departure from our RESIST research group, but are of course delighted that he has been given this new responsible and interesting task at a renowned research institute,“ adds RESIST speaker Prof. Schulz.



New books

Prof. Dr. Martin Stangel has co-edited a book on clinical neuroinfectiology (currently only in German). Its title is „Neuroinfektiologie“, it has 500 pages and was published this year by Springer-Verlag (ISBN: 978-3-662-61668-0).

Further research in Würzburg – for the youngest

The immune system and intestinal flora of newborns and premature babies continues to be a focus of research by RESIST scientist Prof. Dr. Dorothee Viemann, who moved from the MHH Department of Paediatric Pulmonology, Allergology and Neonatology to the Medical Faculty of the University of Würzburg in July 2021. There she will devote herself to her W3 professorship in Translational Paediatrics. „I am continuing to research the topics of inflammatory medicine and infections in a clinic- and

patient-oriented manner, with my range of tasks expanding to include children of all ages,“ explains Prof. Viemann. She will remain on the management team of RESIST projects B1 and B3, which also revolve around the early development of the immune system and the fitness of immune cells.



Prof. Dr.
Dorothee
Viemann

Scientific writing

HOW DO YOU WRITE AND PUBLISH A RESEARCH OR REVIEW PAPER? WHAT ARE THE PROCEDURES FOR SUBMITTING A PUBLICATION AND FOR PEER REVIEW?

These and other questions are answered by editors who work for one of the prestigious „Nature“ journals in the online course „Scientific Writing and Publishing“.

RESIST bought a licence for one year for 15 people last year, thus enabling 15 RESIST doctoral students and postdocs to take part in the one-year course. A survey among them after the licence expired showed that this course was particularly suitable for doctoral students.

Due to the very high demand, RESIST will allow a further 18 people to participate in this course for one year starting in autumn 2021. They will now have access to the entire platform – including the „Writing a compelling grant proposal“ and „Networking for Researchers“ courses. This expands the range of courses for all career stages. More information about the platform is available on the homepage <https://masterclasses.nature.com/>.



RESIST Symposium

Participants in the second RESIST Symposium can look forward to interesting lectures and exciting discussions. It is planned to take place as a joint RESIST / SFB900 symposium from 4 to 5 October 2021 in the „Courtyard Hannover Maschsee“ hotel. Due to hygiene measures, only limited places will be available at the hotel; simultaneous

online participation will also be possible. Please visit the SFB900 homepage at www.sfb900.de for further information and the programme, which will, naturally, include current research on SARS-CoV-2 / COVID-19. If you have any questions or suggestions, please send an E-mail to: SFB900.Sekretariat@mh-hannover.de.



NEW Master's programme starts

On 4 October 2021, the first 18 students will start their studies in the new „Biomedical Data Analysis“ Master's programme, which has been developed within the framework of RESIST. Eleven women and seven men aged 22 to 34, including eleven graduates with bio-scientific bachelor's degrees and seven with medical degrees, will take the course.

In the new four-semester, interdisciplinary and multiprofessional degree programme, they will learn to generate and handle large, heterogeneous and complex datasets in a targeted manner and to develop and apply IT solutions – for disease prevention, precise diagnoses and treatment and therapy decisions.

At the official opening ceremony on 7 October 2021 from 2.30 p.m. to 4 p.m., MHH President Prof. Dr. Michael Manns and MHH Dean of Studies Prof. Dr. Ingo Just will welcome the new students. In addition, Prof. Dr. Rudi Balling, Director of the „Luxembourg Centre for Systems Biomedicine“ at the University of Luxembourg, will give a scientific keynote speech. Please check the homepage of the study programme at www.mhh.de/master-biomeddat for up-to-date information on the location of the event and for the required registration.

RESIST Seminars

The now well-established RESIST seminar series is continuing. On the following Thursdays, RESIST scientists will present their projects online from 5 to 6 pm:

- 16. Sept.** Prof. Hühn
- 23. Sept.** Prof. Messerle and Prof. Gerardy-Schahn or Prof. Routier
- 30. Sept.** Prof. Strowig and Prof. McHardy
- 14. Oct.** Prof. Sodeik
- 11. Nov.** Prof. Stiesch and PD Dr. Heidrich
- 18. Nov.** Prof. Viemann and PD Dr. Eschenburg
- 25. Nov.** Presentation of the RESIST cohort
- 09. Dec.** Prof. Manstein or PD Dr. Fedorov and Prof. Gerold
- 16. Dec.** Dr. Castell and Dr. Empting

If you are interested in participating by video and do not yet receive the announcements by E-mail, please contact RESIST@mh-hannover.de. As soon as the titles of the presentations are known, we will publish them on the homepage www.RESIST-cluster.de.

One health



Prof. Gerold at
"Schloss Herrenhausen"

At the fully booked "Herrenhausen Late" event on 15 July 2021, RESIST researcher Prof. Dr. Gisa Gerold and her colleague Prof. Dr. Asisa Volz presented the topic of zoonoses – the spread of viruses and bacteria from animals to humans – to an interested audience in the Xplatorium of the Herrenhausen Palace. The two scientists from the "Research Center for Emerging Infections and Zoonoses" of the TiHo explained ideas and strategies to detect such jumps early, to prevent them and to treat diseases arising from them.

"In principle, all infectious agents come from animals – many have developed together with the human species in the course of evolution," said Prof. Gerold, "animal and human health are closely related." The duo reported on current research into new vaccines against zoonoses, also emphasizing that many human diseases have occurred because humans have interfered directly or indirectly with ecosystems. "Global warming is an accelerator for epidemics whose pathogens are also transmitted by arthropods such as

mosquitoes or ticks," underlined Prof. Gerold, and she also noted that she believes targeting host cells is a promising therapeutic approach against future infectious diseases.

A report and a video of the event can be found on the Volkswagen Foundation website (www.volkswagenstiftung.de).

Impressum

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www.google.de/maps/ (1)
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Nico Herzog / Fokuspokus (1, 5)
Philip Bartz for VolkswagenStiftung and privat (6)
Carolin Korth and Bettina Bandel, MHH (8)



Maike Willers in front of the conference hotel

The TIS was able to take place in Potsdam

Top-class lectures from different fields of immunology, expert and career talks as well as poster presentations – all this was offered by the tenth Translational Immunology School (TIS) of the German Society of Immunology, which took place in Potsdam in June with about 60 participants. RESIST was a cooperation partner of the TIS and financed the participation of Maike Willers from the

team of RESIST researcher Prof. Dr. Dorothee Viemann. "It was great that a live event could finally take place again! It gave us an opportunity to learn more about basic principles and new findings in translational immunological research and also to talk directly with the other participants and speakers," Maike Willers said. The TIS was chaired by Prof. Dr. Bodo Grimbacher, also a RESIST researcher, and Prof. Dr. Birgit Sawitzki from Berlin.

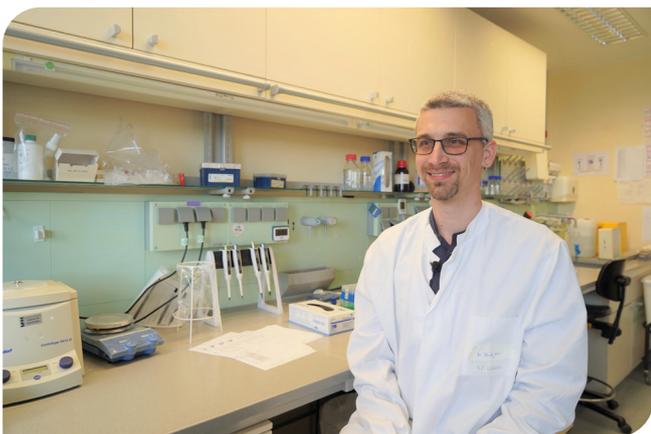
Videos for the RESIST homepage

Just like Prof. Dr. Thomas Pietschmann (photo), almost all RESIST researchers stood in front of the camera this summer to be interviewed and filmed for the RESIST homepage. They reported on the content of their research, but also on what fascinates them about their work and what opportunities arise from their participation in RESIST. Most of the videos were filmed by the company Science Relations at the MHH and the HZI, but some were also made at the HIPS, the CSSB and the CCI as well as at the University of Lübeck. The finished videos will soon be available on the respective pages of the RESIST members, which can be accessed via the RESIST homepage (www.RESIST-cluster.de).



An inhalable Corona vaccine

Dr. Berislav Bosnjak from the research group of RESIST co-speaker Prof. Dr. Reinhold Förster, MHH Institute of Immunology, reports in a new video about current research on a Corona vaccine that is not injected into the muscles but that can be inhaled. It is designed to protect the lungs directly from SARS-CoV-2 infection. The video can be seen on the RESIST homepage (in German language): www.RESIST-cluster.de.



Science moves

In a new video clip, Prof. Dr. Dorothee Viemann reports on the research of the RESIST project B1. It focuses on the immune defences of premature babies and in particular the question of what influence intestinal bacteria have on

the early development of the immune system and thus on susceptibility to infection. The video can be viewed in German on the RESIST homepage at: www.RESIST-cluster.de.

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, **Center for Structural Systems Biology (CSSB)** in Hamburg, **Centre for Chronic Immunodeficiency** in 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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