

Dr. Jasmin Zischke (left) uses the proteomics laboratory led by Professor Pich (right) for her research. PhD student Theresa Schweitzer (centre) shows an attachment of the new mass spectrometer.

Fast & Reliable

A NEW MASS SPECTROMETER – FUNDED BY RESIST AND THE MHH – SPEEDS UP RESEARCH

„It’s a real workhorse: fast and solid“. This is how Professor Dr. Andreas Pich describes the new mass spectrometer of the MHH research facility Proteomics: „We can now investigate the cell protein processes much more quickly. This new device is the fifth mass spectrometer in the lab, it can analyse samples about three times as fast as older models and it ideally complements the lab’s equipment,“ explains the Proteomics director. Another advantage: more measuring times are now available for the other mass spectrometers in the research facility, which can also be used for more specialised analyses.

The „Exploris240 Quadrupole-Orbitrap-Hybrid“, which costs around half a million euros, and its additional equipment were financed by the Cluster of Excellence RESIST and the MHH. The procurement was possible at very short notice: in September 2020, it was applied for at the RESIST Board, in December it was already on site and since February 2021 it has been in use. Since then, scientists have been able to use it to find out which proteins the cell extracts contain, and how they interact with other substances.

Wanted: Agents against herpes viruses

This is how Dr. Jasmin Zischke, for example, uses mass spectrometry. The postdoctoral researcher from the Institute of Virology is looking for new substances that are effective against the carcinogenic Kaposi Sarcoma Herpesvirus (KSHV). For this purpose, she „hooks“ various very small substances – which could possibly work against the viruses – and uses them to „fish“ in an extract from KSHV-infected cells for proteins that interact with these substances. These proteins are identified with the help of the mass spectrometer. „I am particularly interested in the mechanisms underlying the interactions between the low-molecular substances and the cell proteins,“ she explains.

The proteomics research facility is part of the MHH Institute of Toxicology. All MHH working groups and research association partners of the MHH can use the facility. In case of interest to use the facility, other academic organisations and companies can contact Professor Pich.

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Data

Generating, organising and interpreting data in infection biology: To become an expert in this field – this is possible with the new Master’s programme „Biomedical Data Science“, which was created within the framework of RESIST. Applications are open from the end of April (page 5).

The data always plays a fundamental role in research – for example, in finding cells that heal the body, developing a vaccine against the hepatitis C virus and studying our microbiome. You will learn more about RESIST research starting on page 2.

We have been highly successful with our research thanks to many people to whom we are grateful for their support (page 7).

Did you know that topics in infection biology fascinate many young people? (see page 8)

We hope you enjoy reading our newsletter,

your RESIST speaker team



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

Dr. Robert
Zweigerdt and
Professor Dr. Nico
Lachmann
(from left) with a
bioreactor in the
laboratory.



NEW COLLABORATION AIMS TO CURE LUNG INFECTIONS

Cells of the future

Healing the body with cells – this is the ambitious goal of RESIST-Professor Dr. Nico Lachmann and Dr. Robert Zweigerdt. They have initiated a research collaboration and license agreement with the pharmaceutical company Novo Nordisk A/S. The overall aim of the endeavor is to use special stem cells for developing advanced therapies to regenerate failing organs and cure diseases, for which no adequate treatment is currently available. The collaboration agreement was supported by the technology transfer agency Ascenion.

The project relies on so-called induced pluripotent stem cells (iPS cells), which can be obtained from patients' somatic cells by a technology known as "somatic cell reprogramming". The special feature of the resulting iPS cells is their ability to give rise to any functional cell type of the human body. Thus, iPS cells can be used to generate specific replacement cells in a dish, which subsequently can be returned to a patient as a cure.

MHH scientists have recently enabled continuous production of iPS cell-derived functional blood cells, including macrophages (phagocytes), by using special bioreactors. „Within the framework of the new research collaboration, we are now specifically developing this technique further, to enable a potential use of these macrophages therapeutically and eventually aiming for the first application in a clinical study. So far, there has been no clinical application of iPS cell progenies in Germany,“ explains Professor Lachmann.

Macrophages as a therapeutic agent for bacterial lung infections

The iPS cells-macrophages eliminate disease-causing bacteria. Therefore, they have the great potential, for example, for treating patients with severe bacterial infection of the lungs (pneumonia), which do not respond to antibiotics. „The concept of therapeutic application of iPS cell-derived progenies is already about 15 years old. I am very pleased that we can now advance this idea towards real therapies,“ says Dr. Zweigerdt.

Professor Lachmann holds a RESIST-professorship and conducts research at the MHH Clinic for Paediatric Pneumology, Allergy and Neonatology. The fundamental research work was originally performed at the MHH Institute for Experimental Haematology. His laboratory is part of the MHH REBIRTH Research Centre for Translational and Regenerative Medicine and a member of the German Centre for Lung Research (DZL).

Dr. Robert Zweigerdt is research group leader at the Leibniz Research Laboratories for Biotechnology and Artificial Organs (LEBAO) at the MHH Clinic for Cardiac, Thoracic, Transplantation and Vascular Surgery. His laboratory is also part of the REBIRTH Research Centre for Translational and Regenerative Medicine at the MHH and is specialized on developing the production of larger cell quantities in bioreactors.

A precise measure of protective immunity

NEW TOOL TO MAKE HCV VACCINE SEARCH EASIER



Dr. Dorothea Bankwitz (left) carried out the work in the laboratory. The data obtained was analysed by Akash Bahai (right) using bioinformatics.

No vaccine against the hepatitis C virus (HCV) has been found to date. This is also because there are numerous virus variants, which in some cases differ from each other by more than 30 percent. Professor Dr. Thomas Pietzschmann, TWINCORE Institute for Experimental Virology, and Professor Dr. Alice McHardy, Computational Biology of Infection Research (HZI), and their teams of researchers have now developed a testing system that precisely measures the protective immune response against the large spectrum of HCV pathogens. The results were published in the scientific journal *GUT*.

The researchers were initially interested if anti-HCV antibodies can neutralize as many different hepatitis C viruses as possible in HCV-pos-

itive patients. For this purpose, the blood samples of 104 patients were examined. „This is a central question for vaccine development. One does not know beforehand which virus one will have to deal with,“ says Dr. Dorothea Bankwitz, the first author of the study. „The vaccine therefore has to develop protective immunity against many different variants of the virus.“

Based on these findings, they used bioinformatics methods to divide the viruses into six different groups, known as clusters. „There is no obvious genetic correlation between the viruses of the same neutralisation clusters as we know it from the virus strains. However, they behave very similarly in terms of their susceptibility to antibodies,“ says Professor McHardy. „It is sufficient to use a test

virus from each of the clusters as an example to measure how well the antibodies protect against different HCV variants,“ says Akash Bahai, bioinformatician in McHardy’s team and also first author of the study. This is a substantial simplification and therefore a very effective method for assessing the efficacy of vaccine candidates in the future.

However, this discovery also has another special relevance for vaccine development: „Until now, it has been assumed that one has to vaccinate with genetically very different HCV variants in order to develop a broad protection. Now we have learned that the variants react differently to antibodies, regardless of their genetic background,“ says Professor Pietzschmann. „It is probably better to immunise against representatives of the virus clusters in order to build up a broadly protective immune response. The clusters we have found can now form a basis for this.“

The article is based on a press release of the TWINCORE.

www.twincore.de

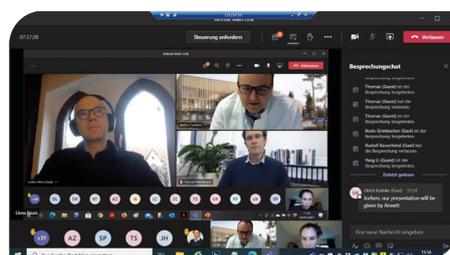
A bouquet of really good science

THE FIRST RESIST RETREAT TOOK PLACE

Presenting projects and their interim results, exchanging ideas and, above all, continuing to network with each other – that was the aim of the first RESIST Retreat, which took place online on 4 and 5 February 2021. Up to 160 listeners followed the 33 exciting presentations, some of them were given by two researchers.

The experts spoke about the projects and cohorts of our Cluster of Excellence, so raising new questions, perspectives and opportunities for cooperation. The talks of the professors who received a RESIST

professorship last year or who are newly associated with RESIST were met with a great deal of interest. „The quality of the presentations and research data was very high. Some of our projects have made a rapid progress. The overall results show that we have a bouquet of really good science in RESIST,“



said Professor Schulz summarizing his vision. The next RESIST retreat will certainly take place.

Moreover, the participants of the individual research areas A to D had an opportunity to exchange ideas in separate virtual meetings. As a result, a new networking was created. The scientists of the research Area D now meet by videoconference every two months, where each includes one keynote lecture. The first meeting has already taken place.

RESIST-Retreat:
The researchers met online.

The character of the **microbiome**

SCIENTIST IDENTIFIES THE CORE OF THE BACTERIAL IMMUNE SYSTEM



Professor
Dr. Alice McHardy

Billions of microorganisms – such as bacteria, viruses or fungi – colonize our skin, mouths and intestines. They are essential for the survival of human beings. However, what species are particularly common? How does the microbial community respond to disturbances, for example, to viral attack? Moreover, where are possible starting points for therapies?

Finding answers to such questions, Professor Dr. Alice McHardy, who is involved in several RESIST projects, and her HZI team collaborated with researchers at the Harvard School of Public Health in Boston (USA) to generate an extensive database containing the genetic information of the microbial community – the microbiome. The study is based on the data from the “Human Microbiome Project”, including the microbiota samples of healthy individuals.

“We analysed these sequence data from over 2000 samples for specific DNA segments which are of particular importance for characterising the microbiome and could also represent possible starting points for medical therapies in the future,” says Philipp Münch, a doctoral student in the McHardy work group and the first author of the study. In particular, the researchers have been looking for short frag-

ments in the genome of bacteria known as “CRISPR” or “spacers”, which form the core of the bacterial immune system and they provide evidence of viral attacks.

“In our study, we have now been able to identify more than 2.9 million new sequences. This is really enormous – it is more than ten times what has been saved in the CRISPR database of all microbial genomes to date,” says Professor McHardy. She heads the HZI Department of Computational Biology of Infection Research, coordinates the bioinformatics of the DZIF and is RESIST-scientist. Based on this extensive data collection, interactions between viruses and bacteria can now be better investigated. The study, funded by the DFG, is published in the journal *Cell Host & Microbe*.

The article is based on a press release by the HZI.

Particularly often cited



Professor Dr. Michael Manns

Professor Dr. Michael Manns and Professor Dr. Alice McHardy (Photo see top of this page) are among the most cited scientists in the world. This has been shown in the ranking „Highly Cited Researchers 2020“ by the US company Clarivate Analytics. The list includes around 6200 researchers from 22 disciplines, including 345 from Germany.

The basis for this list is the „Web of Science“, a collection of all citations of scientific research – namely from

2009 to 2019. This records how often colleagues from the scientific community cite the researchers' work in their publications. The reputation of the journal in which the work was published is also included in the evaluation.

Professor Manns, as president of the MHH, joins the research management board of RESIST as an adviser. Professor McHardy is involved in various RESIST projects with her work – the analysis of large biological and epidemiological data sets with computer-assisted methods. She heads the HZI Department of Computational Biology of Infection Research.

The complete list of the „Highly Cited Researchers 2020“ and further information can be found on the [Web of Science website](#).

Science Prize for RESIST research

Maike Willers, together with Dr. Thomas Ulas, has received the Nutricia Science Prize 2020, worth 10,000 euros, for their research on the influence of breast milk on the development of the immature immune system and intestinal flora.



Maike Willers

The team found that the alarmins contained in breast milk control the adaptation process that takes place after birth during the maturation of the intestinal immune system. In addition, these proteins are also produced in the baby's gut. „If newborns get too few alarmins through breast milk or produce them themselves, dietary supplementation with these proteins could promote the development of the immune system in newborns and protect against inflammatory bowel diseases and obesity in the long term,“ says Maike Willers.

She works in the team of RESIST researcher Professor Dr. Dorothee Viemann, MHH Clinic for Paediatric Pneumology, Allergology and Neonatology. Dr. Ulas works at the University of Bonn. Both share the first authorship of the paper published in the journal *Gastroenterology*. The prize money will be used for further research in this field. A more detailed article on the research entitled „*The Gold of Breast Milk*“ can be read on the RESIST homepage.



Leibniz Prize 2021 for Rolf Müller

Professor Dr. Rolf Müller

On 15 March 2021, Professor Dr. Rolf Müller received the Gottfried Wilhelm Leibniz Prize 2021 from the DFG for his outstanding research achievements – the most highly endowed award regularly presented to scientists in Germany. „I feel that this prize is a great recognition of the scientific achievements of the entire institution and especially of the Department of Microbial Natural Products,” says the Managing Director of the Helmholtz Institute for Pharmaceutical Research Saarland (HIPS) and RESIST scientist. Every year, the DFG awards up to ten Leibniz Prizes, each endowed with

prize money of up to 2.5 million euros. Professor Müller and his team will use the funding for antibiotic research to combat antimicrobial resistance in pathogens. In his search for new drug candidates, he primarily focuses on soil-dwelling myxobacteria, which produce biologically active substances to eliminate other microbial competitors or enemies.

Professor Müller co-leads the RESIST project C3, which focuses on severe lung diseases such as cystic fibrosis. In the lungs of affected patients, a healthy microflora balance has been lost, „good’ microorganisms have been replaced by disease-causing pathogens. The researchers of this RESIST project assume that the restoration of the healthy microbiome in lungs is essential for recovery.

Apply now...

... FOR THE MASTER'S PROGRAMME BIOMEDICAL
DATA SCIENCE

From 30 April to 15 July 2021, graduates of a bachelor's programme in bioscience or medicine can apply for the four-semester Master's programme „Biomedical Data Science”. This new RESIST-funded course at the interface between life science, medicine and informatics will be open to 20 students and will enable them to become experts in the field of big data analysis. The aim is to learn how to generate and handle large amounts of data. The main emphasis will be on the data from the field of infection biology. The master programme is scheduled to begin on 4 October 2021. The main language of instruction is German.

Prior to the application period, an informational event will take place on 28 April at 3 pm in lecture hall F at the MHH, where the new master programme will be presented. Regis-

tration takes place via the programme homepage www.mhh.de/master-biomeddat. In addition, further informational events will be held online on 27 May and 23 June. Information that is more detailed will be available on the homepage from May.

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RESIST research is funded

THE VOLKSWAGEN FOUNDATION AND THE STATE OF LOWER SAXONY ARE NOW SUPPORTING THE RESEARCH OF THE NEW W2-PROFESSORS WITH ONE MILLION EUROS FROM THE „NIEDERSÄCHSISCHES VORAB“.

Part of the support is given to Professor Ravens for her work. Her research includes an investigation to determine why some premature babies die from infections and what roles do infections and intestinal bacteria in early childhood play in lifelong susceptibility to infection. The scientist is focusing on certain white blood cells of the immune system (B and T cells). She is

also involved in a further RESIST project, which aims towards answering the question, why herpes viruses could become very dangerous for some people.

Professor Schreiner also receives part of the funding. Her research is dedicated to adenoviruses, which can cause conjunctivitis, gastrointestinal problems or pneumonia. These viruses are

particularly dangerous for people with a weakened immune system. In healthy people, however, they can also trigger pneumonia, which can be fatal. In order to find new starting points for the development of drugs and vaccines, Professor Schreiner at the MHH Institute of Virology is investigating how the virus multiplies in the cell.

Current scientific work of Professor Dr. Nico Lachmann, who also receives part of the funding, focuses also on pneumonia: he is researching certain immune cells that can eliminate bacteria and viruses – the so-called

phagocytic cells (macrophages). His aim is to cure lung infections using the macrophages grown from human stem cells in the laboratory. Professor Lachmann works in the MHH Clinic for Paediatric Pneumology, Allergology and Neonatology.

In the meantime, we know from SARS-CoV-2 that mutations can change the properties of viruses. However, this is also the case in bacteria. The influence of gene mutations on the pathogenicity of bacteria and on their resistance to antibiotics – is the research topic of Professor Dr. Marco Galardini from the Institute for Molecular Bacteriology of the TWINCORE. His research is also supported. Using bioinformatics and molecular biology methods, he aims to predict how the differences in the genome of pathogens will evolve.

Prof. Schreiner, Prof. Galardini, Prof. Ravens und Prof. Lachmann (from left).



RESIST Seminars

The well-established RESIST seminar series continues. RESIST scientists will present their projects online on the following Thursdays between 5 to 6 pm.

- 15 April:** Professor Grimbacher
- 22 April:** Professor Kalinke and Professor Witte
- 29 April:** Dr. Atsckekzei and Dr. Giulietta Saletti
- 20 May:** Professor Pietschmann and Professor Prinz
- 27 May:** Professor Viejo-Borbolla and Dr. Maximilian Schiek
- 10 June:** Professor Förster and Professor Meyer-Hermann
- 17 June:** Professor Tümmeler and Professor McHardy
- 24 June:** Professor Häußler and Professor Li
- 08 July:** Professor Ravens and Professor Cornberg
- 15 July:** Professor Sodeik and PD Dr. Bohne

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 we have the exact titles of the presentations are known, we will publish them on the homepage www.RESIST-cluster.de.

Warm welcome

On 15 January 2021, the President of the MHH Professor Dr. Michael Manns and the speaker of the Cluster of Excellence RESIST Professor Dr. Thomas Schulz welcomed the scientists who were offered the professorships at the MHH funded by RESIST in 2020.



In front of the Lecture Hall R (from left): Professors Proietti, Ravens, Bosse, Manns, Schulz, Schreiner, Lachmann and Galardini. Unfortunately, Professor Lauber was unable to be present.

Dr. Sabine Barlach, Johanne Davids-Schedler and Jenny Nayda (from left) are representative here for all those who support RESIST.



Looking behind the scenes

MANY MHH EMPLOYEES CONTRIBUTE TO THE SUCCESS OF RESIST

It is impossible to enumerate all people who have already helped RESIST, because there have been a lot. Some of them are permanently on the side of the Cluster of Excellence, others in certain phases. Without them, research and the infrastructure behind it could not succeed.

So not only money is indispensable for research, but also people who manage it. Dr. Eugenia Gripp and Dr. Eugenia Faber, who is currently being replaced by Dr. Olga Klimenkova during her parental leave, take care of the administrative management of the Cluster of Excellence. Jenny Nayda from the MHH-third-party funding department supports them. Together with the RESIST team this department controls the budget planning, maintains the costs in the company-wide database SAP, calls up the funds from the DFG and proves what they were used for. When it comes to spending the money, the MHH's central purchasing department often comes into play. This team supports RESIST, for example, in purchasing research equipment.

But managing money is not everything. RESIST has also benefited from help with other processes, for example last

year with the appointments of the seven new RESIST professors. Dr. Sabine Barlach in the MHH Presidential Office coordinated the many necessary steps in the appointment process, which were taken by the appointment committees, the RESIST team, but also by the MHH Presidential Board and Senate, as well as the Ministry of Science. This included, for example, setting up appointment committees, publishing calls for applications, screening applications, selecting candidates and conducting negotiations.

These negotiations had to become tangible employment contracts – a process for Marieke Flemming and Johanne Davids-Schedler from MHH Human Resources Management. Together with RESIST management and the department heads to whom the professorships are assigned, they worked out contracts tailored to the respective professor. Among other things, this involved remuneration, terms and possible civil servant status. Some of them had to come from another EU country and thus had to fulfil conditions that revolved around the topic that is moving the world: the Corona pandemic.

The new professors, as well as all the other scientists working in RESIST, can conduct research with their teams and thus help patients in the long term. This is only possible thanks to the people named in this article, but also thanks to many other people who have not been named here – because they are just as indispensable for RESIST.

Impressum

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Karin Kaiser, MHH (1 top, 2, 6)
Nico Herzog / Fokuspokus (1 below, 6)
TWINCORE (3)
Yamel Photography (4 top left)
Oliver Dietze (5 top)
Melina Celik (5 below)
Bettina Bandel (6 below, 7, 8)
Tom Figiel (4 below left)
private (below right)

Commitment on both sides

THE „BIG B4NG CHALLENGE“ COMPETITION HAS BEEN A TOTAL SUCCESS

Clever, detailed and differentiated – this is how the students answered the online competition „BIG B4NG Challenge“ of the Leibniz Universität Hannover (LUH), in which a RESIST team participated with commitment: Annett Ziegler from the TWINCORE Institute for Experimental Infection Research, Carla Seegers from the MHH Institute for Clinical Biochemistry, and Dr. Henrike Ahsendorf and PD Dr Jens Bohne from the MHH Institute for Virology. They came up with exciting tasks and experiments on infection research for

grades 9 to 12 and evaluated the answers of the 21 participating student groups.

The tasks were diverse and ranged from growing bacteria to epidemiological observations of SARS-CoV-2. Thus, they required material such as petri

dishes and potatoes, and above all will, concentration and voluntary commitment from the students – as well as from the RESIST team. „Setting the tasks and proofreading was time-consuming, but it was also a lot of fun. We will be happy to participate again next year,“ says Carla Seegers. „We were impressed by how many groups participated and how clever and detailed the answers were. Almost all of them scored full marks,“ adds Dr. Henrike Ahsendorf. The participants were rewarded with prizes in the form of money and book vouchers at the awards ceremony on 24 March 2021. On that day, Deutschlandfunk reported on this exciting school project and the dedicated RESIST team in a radio report on that day.

In action for „BIG B4NG“: Annett Ziegler, Carla Seegers, Dr. Henrike Ahsendorf and PD Dr Jens Bohne (from left).



Science in motion

In a new video clip, Professor Dr. Thomas Werfel reports on the research within the RESIST project A4, which focuses on the mechanisms underlying severe disease progression after herpes infection in patients with atopic dermatitis. He also explains the disease and its treatment with the help of one patient. This video will soon be available in German language on the RESIST homepage at: www.RESIST-cluster.de.



German **Virus** Madness

„German Virus Madness“ – this is the title of the 712th episode of the podcast „This Week in Virology“ (TWiV) from 28 January, in which Professor Dr. Gisa Gerold participated as a discussion partner. This podcast, in which Vincent Racaniello presents and discusses the results of current research in the field of virology, exists since 2008. Professor Gerold works at the

TiHo and she is also involved in the projects of the RESIST research area D, which revolves around viruses that manage to survive and multiply in the human body. In the podcast episode, the biochemist reported on the current status of the SARS-CoV-2 pandemic at the time. The podcast is available on the internet via microbe.tv.

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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