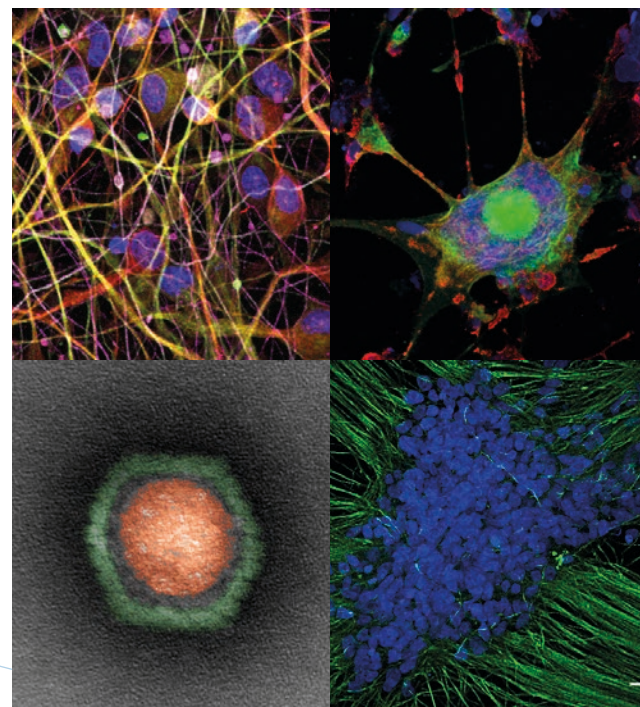


Chronic infections may also occur in the liver: these are chronic hepatitis C, B, D and E. Why do these diseases become chronic in some people whereas spontaneous healing occurs in others? In the case of hepatitis C, the outcome is already known to be partly dependent on certain components of the immune system, known as neutralizing antibodies, that prevent the virus entering the liver cells. This knowledge is a prerequisite for the development of a vaccine that offers protection against the hepatitis C viral infection. Ongoing work on chronic hepatitis B is investigating whether, by discontinuing (generally lifelong) treatment with antiviral drugs, the immune system can be stimulated and induced to eliminate the pathogen.

The RESIST team is also looking for ways to protect people from herpes viruses and their consequences. These viruses are easily transmitted and persist throughout the host's lifetime, including a dormant period during which there are no signs of illness. In susceptible individuals they may lead to serious skin conditions such as shingles or herpetic eczema, and can even damage the nervous system. They may also cause cancers such as lymphoma (affecting the lymphatic system), nasopharyngeal carcinoma and Kaposi's sarcoma. But how do herpes-viruses manage to survive and multiply in the human body? How can new, improved drugs be developed that complement already existing medications? The RESIST team is seeking answers to these questions. Its researchers want to make herpes viruses vulnerable to attack, especially during their dormant stage. The pathogens in question are the cytomegalovirus and the varicella zoster virus, Kaposi's sarcoma herpesvirus and herpes simplex virus.

“At the heart of RESIST are the patients. We want to help them more effectively – by closely integrating cutting-edge basic research and clinical science.”

RESIST-Sprecher: Professor Dr. Thomas Schulz



Das RESIST-Team erforscht unter anderem das Herpes-simplex-Virus (unten, links) und von Viren befallene Zellen (andere Abbildungen).

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RESIST

Resolving Infection Susceptibility



RESIST – research to help the most vulnerable

Scientific excellence for the people most vulnerable to infection

Some people become only mildly ill when they ‘catch’ viral or bacterial infections, whereas others are affected much more severely. But what are the reasons for these differences? And how can the course of a disease be predicted and personalized treatments developed? These questions are being addressed by the RESIST Cluster of Excellence team. This will enable them to help people with a weakened immune system, including newborn babies, the elderly, people with congenital immunodeficiency, those whose immune system is suppressed for therapeutic reasons, and implant users.

The new Cluster of Excellence called RESIST was launched on 1 January 2019 and, under the German Federal and Regional Governments’ Excellence Strategy, is being funded by the German Research Foundation (DFG) to the tune of some 32 million euros over a seven-year period. The Cluster is made up of 40 interdisciplinary teams. It enables clinical and scientific expertise to be combined in various different fields: infectious diseases in children and adults, primary immunodeficiency, immunology, virology, bacteriology, infection biology and bioinformatics.

Susceptibility to infection: what part do genes play?

What role does the human genome play in susceptibility to infection? How do genes influence the multiplication of viruses and our defences against them? The RESIST team is probing these questions – so that we can better predict how severe an infection is likely to be for a given individual and thus reach conclusions on the best treatment for them. Furthermore, people who are especially at risk of infection can be protected at an early stage – by vaccination, for example. This may even influence survival in (for example) those with the RSV cold virus, which can cause severe to life-threatening respiratory tract infections in young children.

Varicella zoster and herpes simplex viruses may also cause serious diseases, such as shingles or encephalitis.

RESIST will also explore the genetic causes of severe congenital immune deficiencies. For, in many cases, it remains unclear which genetic defects cause these deficiencies and why the immune system does not respond effectively. Bacteria and fungi may lead to severe infection in people with a genetically determined susceptibility to infection.

Susceptibility to infection: what part does the immune system play?

Newborn babies and the elderly are particularly susceptible to bacterial and viral infection. But why is this? How can we predict who will contract an infection – and how can they be optimally treated? To find answers to these questions, the RESIST team is also conducting research on the immune system in these vulnerable groups.

The focus of research involving newborns is on interaction with the microbiome (the entirety of the microorganisms that colonize the body) as it develops with the child. Why? These microorganisms ‘train’ the immune system and could potentially be used to promote immune maturation after birth so as to prevent the blood poisoning that typically results from bacteria and from life-threatening viral diseases. Interaction between the immune system and the microbiome is also being studied in relation to another medical condition affecting adults. This is spondyloarthritis, a class of rheumatic diseases that manifest as inflammation of the musculoskeletal system, and whose onset is triggered by an infection. RESIST will investigate the influence the gut microbiome has on whether the patient recovers from this condition or whether it becomes chronic.

In elderly people, the RESIST team will look at factors such as their vulnerability to flu viruses or the chicken pox virus, which causes shingles. Another focus of attention with this patient group is vaccination, since it remains unclear why this is often ineffective in individuals of advanced years.

Susceptibility to infection: how do bacteria and viruses manage to remain in the body?

Some pathogenic bacteria or viruses properly take hold in the human body: they persist in sites including the lung, liver or on implants.

Chronic infections of this nature represent significant medical challenges, as for example in people who suffer from cystic fibrosis. Biofilms form in their lungs; these are well organized communities with other microorganisms that protect them from the body’s immune defences and from antibiotics. They are home to numerous *Pseudomonas aeruginosa* bacteria, which cause pneumonia and ultimately compromise the lives of those affected. Dental and other implants, too, may be colonized by biofilms consisting of many different bacteria.

But how can the bacteria living in biofilms survive, and why are they so resistant to therapeutic agents? What part does the immune system play in this? Why are these infections mild in some people but severe in others? What connection is there with the human microbiome? The RESIST team will look at the underlying mechanisms – so that the severity of an infection can be gauged and antibiotic tolerance predicted, and to discover drugs that can target the bacteria.

