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### Focus on life-threatening fungal infections

Collaborative Research Center granted DFG funding for a further four years.

Jena/Würzburg. The German Research Foundation (DFG) will fund the Collaborative Research Center/Transregio (CRC/TR) "FungiNet" for four more years with approximately ten million Euro. In the only CRC studying human pathogenic fungi, scientists in Jena and Würzburg will investigate infection processes and novel therapeutic options.

Fungal infections are a major challenge for modern medicine. Elderly or immunocompromised patients, for example those with leukemia or requiring organ transplantation, are particularly at risk. These life-threatening infections are often diagnosed too late, treatment options are extremely limited, and the pathogens are increasingly resistant to available drugs. COVID-19 exacerbates the problem: "SARS-CoV-2 infected patients have a higher risk of developing fungal infections starting in the respiratory tract. The severity of the diseases also increases dramatically," warns Axel Brakhage, spokesman of the Collaborative Research Center. Hermann Einsele, Director of the Medical Clinic II at the University Hospital Würzburg and co-spokesperson of the CRC/TR adds: "The insights gained in basic research in recent years are increasingly enabling us to develop concrete applications in the diagnosis and treatment of severe fungal infections. In our hospital, we frequently treat affected patients and know very well where the deficits lie. The FungiNet projects in the new funding period therefore focus particularly on the translation of research results."

#### Understanding life-threatening fungal infections

Scientists and physicians from Jena and Würzburg have therefore joined forces to better understand life-threatening infections and to develop new, urgently needed therapeutic approaches. The Collaborative Research Center/Transregio 124 *Pathogenic Fungi and their Human Host: Networks of Interaction* - "FungiNet" for short – was established in 2013 and has been continuously funded by the DFG. Its research focus on human pathogenic fungi is unique in Europe. In the first two funding periods, experts from the fields of microbiology, immunology, clinical research, bioinformatics, and chemistry jointly conducted many fundamental studies on the two model pathogens *Aspergillus fumigatus* and *Candida albicans* which cause most severe fungal infections in Europe.

For example, the researchers developed a new microscopy method to study the spread of the mold *Aspergillus fumigatus* in the lungs. Using light sheet microscopy, the entire lung can be viewed and the interaction between immune cells and fungus mapped on a 3D map.

In addition, the FungiNet partners were able to gain important insights into infections caused by the yeast *Candida albicans*. For example, they elucidated how this fungus can be killed by certain immune cells and how the microbiome in the intestine influences the spread of the fungus.

#### Scientific contact

Prof. Dr. Axel A. Brakhage Spokesperson of the Collaborative Research Center/Transregio "FungiNet"

axel.brakhage@leibniz-hki.de

#### **Press contact**

Dr. Michael Ramm Public relations

03641 5321011 0176 54909562

presse@leibniz-hki.de

Leibniz Institute for Natural Product Research and Infection Biology - Hans Knöll Institute -

Adolf-Reichwein-Straße 23 07745 Jena

www.leibniz-hki.de





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#### **Developing clinical applications**

"In recent years, we have learned a lot about the mechanisms of infection. We have identified so-called virulence factors - i.e. the disease-causing properties of fungi - and now have a much better understanding of how the immune system reacts to them," sums up Brakhage, director of the Leibniz Institute for Natural Product Research and Infection Biology - Hans Knöll Institute - who also holds the chair for Microbiology and Molecular Biology at Friedrich Schiller University Jena.

"Our focus in the third funding phase is clearly on translation, the transfer of these findings into clinical applications to patients," the CRC spokesperson further emphasizes. Therefore, the FungiNet team will be strengthened by scientists from the clinical environment in the upcoming funding phase. The researchers want to identify so-called biomarkers to improve the difficult diagnosis of fungal infections. Furthermore, they will evaluate new therapeutic approaches in preclinical studies. Great expectations lie on certain cells of the immune system, such as T cells or natural killer cells. They are capable of learning and can be trained to fight invading fungal pathogens. This includes the evaluation of extracellular vesicles from immune cells as therapeutic option. The CRC FungiNet also aims to drive technological advances in bioinformatics and imaging and to develop virtual infection models.

#### The CRC at a glance

Since October 2013, more than 30 leading scientists from the University of Jena, the University Hospital Jena and the Leibniz-HKI have been working together with colleagues from the University of Würzburg and its hospital in 18 subprojects. In addition, more than 30 positions for doctoral and postdoctoral researchers will be created in Jena and Würzburg. The total funding for all three funding periods over a time period of twelve years is around 27 million euros.

In the second funding period from 2017 to 2021, the scientists were able to publish a total of 190 joint publications, including in journals such as Cell, Nature, Nature Communications, and Science Immunology.

Due to these scientific successes, FungiNet has made a major contribution to the development of both locations: For example, the CRC/TR was an important starting point for the Cluster of Excellence Balance of the Microverse in Jena.





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# LEIBN IZ:HKI

#### **Captions**

#### 21-07\_Brakhage\_Axel

Axel Brakhage, spokesperson of the Collaborative Research Center/Transregio (CRC/TR) FungiNet

Soruce: Leibniz-HKI, Photo: Anna Schroll



# FungiNet

#### 21-07\_Mikrobiologisches\_Arbeiten

Scientists of the CRC/TR FungiNet are investigating the pathogenicity factors of fungi.

Soruce: Leibniz-HKI, Photo: Anna Schroll



#### 21-07\_Bioinformatik

Researchers of the CRC/TR FungiNet drive technological advances in bioinformatics and simulate for example the interactions between fungal pathogens and human immune cells.

Soruce: Leibniz-HKI, Photo: Anna Schroll



#### 21-07\_pathogene\_Pilze

In order to study the disease-causing factors of a fungal pathogen, mutants are generated that in some cases already show differences in the appearance of the colonies.

Soruce: Leibniz-HKI, Photo: Anna Schroll





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# LEIBN IZ:HKI

#### The Leibniz-HKI

The Leibniz Institute for Natural Product Research and Infection Biology - Hans Knöll Institute - was founded in 1992 and has been part of the Leibniz Association since 2003. The scientists of the Leibniz-HKI study the infection biology of human-pathogenic fungi. They investigate the molecular mechanisms of disease initiation and the interaction with the human immune system. New natural products from microorganisms are screened for their biological activity and targeted for potential applications as active substances.

The Leibniz-HKI has seven scientific departments and four research groups, most of which are headed by appointed professors from Friedrich Schiller University (FSU) Jena. In addition, there are several junior research groups and cross-sectional units with an integrative function for the institute. Together with FSU, the Leibniz-HKI operates the Jena Microbial Resource Collection, a comprehensive collection of microorganisms and natural products. Currently, about 450 people work at the Leibniz-HKI, including 150 doctoral researchers.

The Leibniz-HKI is a core partner of large collaborative projects such as the Cluster of Excellence Balance of the Microverse, the Graduate School Jena School for Microbial Communication, the Collaborative Research Centers FungiNet (Transregio), ChemBioSys and PolyTarget, the Center for Innovation Competence Septomics, the Leibniz Center for Photonics in Infections Research as well as InfectControl, a consortium in the BMBF program "Zwanzig20 – Partnerschaft für Innovation". Leibniz-HKI is also the National Reference Center for Invasive Fungal Infections.

www.leibniz-hki.de



