PRESS RELEASE

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Candida albicans toxin plays a special role in the colonization of the digestive tract

By Alena Gold and Friederike Gawlik

Candida albicans is a fungus that occurs naturally in the digestive tract of most people. However, the fungus is not always harmless. It can cause mild to severe infections throughout the body. A toxin, Candidalysin, is involved in these infections. It appears to be of central importance in vaginal infections in particular. A team from the Leibniz Institute for Natural Product Research and Infection Biology (Leibniz-HKI), in collaboration with researchers from Brown University in the USA, has now discovered that the toxin also plays an important role in the colonization of the digestive tract. The study was published in the renowned scientific journal *Nature*.

“In our study, we focused on Candida albicans and the importance of its toxin Candidalysin. The fungus is a natural part of the human microbiome and coexists with numerous other microorganisms such as bacteria in our gastrointestinal tract,” says Richard Bennett, Professor at Brown University in Providence, Rhode Island, USA.

C. albicans multiplies in two different growth forms: a round yeast form and an elongated hyphae form. “Previous studies in mice indicated that the yeast form is advantageous for colonization of the intestine,” says Bernhard Hube. He leads a department at the Leibniz-HKI and is professor at the Friedrich Schiller University Jena. “The fungus develops its pathogenic effect primarily in the hyphal form. This form secretes Candidalysin and thus damages host cells,” explains Hube. “If C. albicans exists primarily as a colonizer of the intestine, i.e. as a round yeast form, why are almost all isolates of the fungus able to form hyphae?” asked Bennett and Hube. “What selection pressure ensures that the fungi do not lose the ability to form hyphae?”

Comparative studies on mice with a complete microbiome and a microbiome reduced by antibiotics now show that the previous assumption that the yeast form is better suited for colonization needs to be revised. As soon as a complex bacterial community is present, C. albicans uses both the yeast and the hyphae forms to colonize the intestine efficiently. But why is the hyphae form advantageous when bacteria are present?

“Only in the hyphal form does the fungus produce the toxin Candidalysin, which has an antibacterial effect. This enables the hyphae form to compete with bacteria in the gastrointestinal tract. The toxin inhibits the metabolism and thus the multiplication of the bacteria. This gives the fungus a competitive advantage. The release of Candidalysin associated with the formation of hyphae therefore probably contributes to the fact that the fungus is such a successful colonizer of humans. This may explain why the hyphal form of C. albicans is also so important during colonization of the intestine,” says Hube. If the formation of hyphae is blocked, the fungus is also less able to colonize the intestine.

“The fungus has therefore not developed the toxin primarily to damage human cells, but to be able to compete with bacteria on mucous membranes,” says Hube, summarizing the key message of the study. The researchers want to investigate the interaction between fungi and bacteria and their effects on the host in more detail. “The Cluster of Excellence ‘Balance of the Microverse’ at

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Leibniz Gemeinschaft

Friedrich Schiller University Jena, with its focus on microbial interactions, offers us an ideal environment for this," says Hube.

Participating institutions

Brown University, Providence, USA
New York University School of Medicine, New York City, USA
Leibniz Institute for Natural Product Research and Infection Biology, Jena, Germany
Friedrich Schiller University Jena, Jena, Germany
McGovern Medical School at the University of Texas Health Science Center, Houston, USA
Université Paris Cité, Paris, France

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Cluster of Excellence "Balance of the Microverse"

The Cluster of Excellence "Balance of the Microverse", within the framework of which the work was carried out, brings together researchers from various disciplines in Jena and unites a wide variety of different skills in the Thuringian university city. It is currently the only Cluster of Excellence in the Free State. Together, the scientists research the dynamics of microbial communities on Earth. Microorganisms are present practically everywhere and live in harmony with other large and small organisms. However, if this coexistence gets out of balance, this can have serious consequences: Weather extremes, crop failures or the spread of diseases are just some of the possible effects. The aim of the cluster is therefore to gain a deep understanding of the interactions of microorganisms with each other and with other living organisms. With this knowledge, the researchers want to determine the causes of a disturbed balance and find out how such a system can be brought back into equilibrium.

Original publication

Liang SH, Sircaik S, Dainis J, Kakade P, Penumutchu S, McDonough LD, Chen YH, Frazer C, Schille TB, Allert S, Elshafee O, Hänel M, Mogavero S, Vaishnava S, Cadwell K, Belenky P, Perez JC, Hube B, Ene IV, Bennett RJ (2024) The hyphal-specific toxin candidalysin promotes fungal gut commensalism. *Nature*, https://doi.org/10.1038/s41586-024-07142-4

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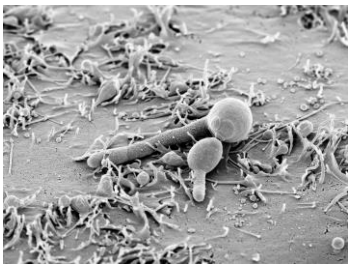
Captions

24_09_Candida-albicans.jpg

Candida albicans in the yeast and hyphae form on human epithelial cells.

Source: Gudrun Holland, Muhsin Özel, Katherina Zakikhany and Bernhard Hube / Leibniz-HKI



The Leibniz-HKI

The Leibniz Institute for Natural Product Research and Infection Biology was founded in 1992 and has been part of the Leibniz Association since 2003. The scientists at the Leibniz-HKI focus on 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 substances from microorganisms are examined for their biological activity and developed for potential applications as active substances.

The Leibniz-HKI has seven scientific departments and three research groups, most of whose heads are appointed professors at Friedrich Schiller University Jena. In addition, there are several junior research groups and cross-sectional facilities with an integrative function for the institute. Together with the University of Jena, the Leibniz-HKI operates the *Jena Microbial Resource Collection*, a comprehensive collection of microorganisms and natural products. Around 450 people currently work at the Leibniz-HKI, including 150 doctoral students.

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 and the Leibniz Center for Photonics in Infection Research. The Leibniz-HKI is also the National Reference Center for Invasive Fungal Infections.
www.leibniz-hki.de

The Leibniz Association

The Leibniz Association unites 96 independent research institutions. Its focus ranges from the natural, engineering and environmental sciences to economics, spatial and social sciences and the humanities.

Leibniz Institutes are dedicated to socially, economically and ecologically relevant issues. They conduct knowledge and application-oriented research, including in the overarching Leibniz Research Alliance, are or maintain scientific infrastructures and offer research-based services. The Leibniz Association focuses on knowledge transfer, especially with the Leibniz Research Museums. It advises and informs politics, science, business and the public.

Leibniz institutions maintain close cooperation with universities, including in the form of the Leibniz ScienceCampi, with industry and other partners in Germany and abroad. They are subject to a transparent and independent review process. Due to their national importance, the federal and state governments jointly fund the institutes of the Leibniz Association. The Leibniz Institutes employ almost 21,000 people, including almost 12,000 scientists. The total budget of the institutes is two billion euros.
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