

Healthcare industry BW

How Lactobacillus bacteria fight Candida albicans infections

Fungal infections of skin and mucous membranes are relatively common. Around 75 percent of the human population lives with Candida albicans, a fungus that has no harmful effects in people with an intact immune system that can fight off systemic infections. However, in people with immune systems that have been weakened by antibiotics or radiotherapy for example, C. albicans infections can lead to sepsis which may even be life-threatening. Prof. Dr. Martin Schaller and his group of researchers in the Department of Dermatology at Tübingen University Hospital have been studying the molecular pathogenesis of Candida infections for many years. The researchers have recently discovered that common probiotic bacteria are very effective against such infections.

Prof. Dr. Martin Schaller and his team in the Department of Dermatology at Tübingen University Hospital have been studying the interactions of the human immune system with the fungus Candida albicans (type of yeast) for many years. Candida albicans is commensal and a constituent of the normal skin and gut flora. It is also the most common cause of fungal infections, but only causes infections when a person's natural lines of defence are damaged and the immune system compromised.



"Under normal circumstances, Candida albicans is kept at bay and does not cause harmful effects," says Schaller. However, in people with a weakened immune system, systemic C. albicans infections are a major cause of mortality. "In immunocompromised patients, certain virulence factors help the fungus to survive on human body surfaces and also help it to penetrate into deeper tissues and organs, thus turning it into a dangerous pathogen," says Prof. Schaller.

C. albicans is becoming increasingly resistant to antimycotic drugs

Prof. Dr. med. Martin Schaller is chief consultant and assistant medical director of the Department of Dermatology at Tübingen University Hospital. Amongst other things, he studies the molecular processes underlying *Candida albicans* infections.

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People who need to take drugs that weaken their immune system, for example people with organ transplants or who are being treated for cancer, are at a particularly high risk of a *C. albicans* infection. Older patients, people with immunodeficiencies or diabetes also have an elevated risk of infection. On

top of that, the number of *C. albicans* infections have increased considerably over the last few years due to the increased application of immunosuppressive therapies. Invasive infections are a serious problem for hospitalised patients because the fungi are becoming increasingly resistant to common antimycotics. Therefore, there is currently no effective way of treating *C. albicans* infections (candidiasis).

Schaller and his team of researchers have been able to pinpoint which factors in the human immune system are involved in candidiasis. Normally, the human skin and mucous membranes produce peptides with an antimicrobial effect that prevent the excessive spread of the *C. albicans* fungus in the human body. The more aggressive the fungi, the more peptides are produced. The production of antimicrobial peptides is, amongst other things, regulated by Toll-like receptors, which are constituents of the innate immune defence system. The researchers' findings are based on a three-dimensional model consisting of epithelial cells of the human oral mucosa.

Probiotics provide relief without adverse effects

In order to develop other, much needed treatment options, Schaller and his team have recently tested the effect of probiotic bacteria on *C. albicans*. Many people have been consuming such probiotics for many years in the form of functional food and as capsules for the treatment of indigestion, and even as constituents of cosmetics.

In recent years, science and medicine have also become increasingly aware of the positive characteristics of the microorganisms, and have started to use and study probiotics as drugs or for disease prevention. *Lactobacillus* bacteria have long been used for the treatment of vaginal yeast infections. The doctoral thesis of Daniela Mailänder-Sánchez, a biologist in Schaller's team, specifically focused on the effectiveness of *Lactobacillus* bacteria for the treatment of infections of the oral mucosa. The motivation for undertaking this type of research was the increasing resistance of *C. albicans* to common antimycotic drugs that have traditionally been used for the treatment of oral candidiasis (thrush).

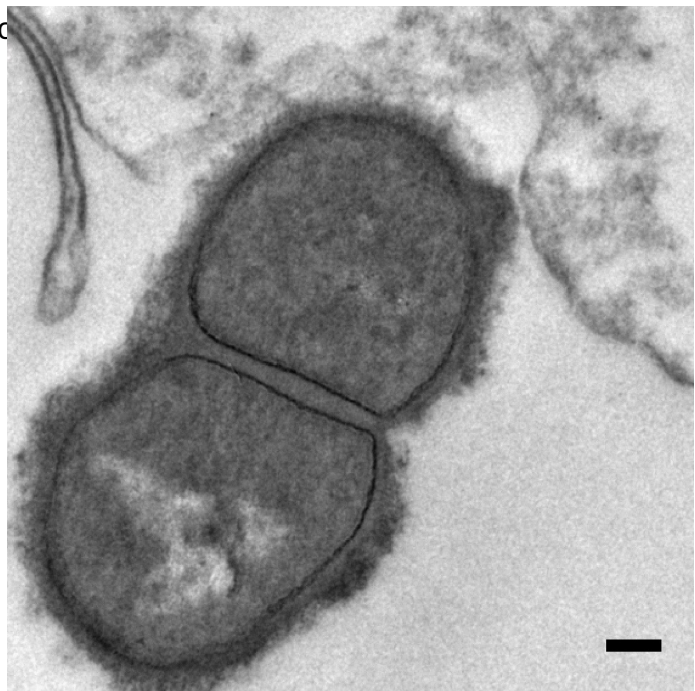
If antimycotic drugs no longer have an effect, harmless *C. albicans* infections can develop into life-threatening sepsis once the fungus manages to enter the bloodstream. In addition, these patients are often taking other drugs, some with serious adverse effects. The idea therefore was to develop an easy to use and effective therapy for the local treatment of candidiasis, which would prevent the spread of the fungus. At the same time, a therapy that was free of adverse effects had to be found.

Therapy in the form of yoghurt drinks

Lactobacillus bacteria are what the researchers were looking for, simple to use and with no harmful effects. *Lactobacillus* bacteria have been used by humans for many centuries without causing significant problems or adverse effects. Moreover, previous research has shown that probiotic *Lactobacillus* bacteria had a positive effect on treating vaginal yeast infections.

In order to find out whether the positive effect of Lactobacillus rhamnosus GG (LRGG) on oral mucosa cells, Tübingen researchers investigated Lactobacillus rhamnosus GG (LRGG) for its suitability as a probiotic. They wanted to find how protection can be achieved and whether LRGG bacteria are able to modulate the immune reaction of oral mucosa cells. The researchers established an oral candidiasis model consisting of a multi-layer epithelium made up of oral mucosa keratinocytes that were infected with and damaged by *Candida albicans* and subsequently responded with an inflammation.

The researchers tested a prophylactic approach in which the cells were treated with Lactobacillus bacteria before being exposed to *Candida* cells. They also investigated whether initiating treatment at the same time as or after infection made a difference.



Electron microscope image of a *Lactobacillus rhamnosus* bacterium that is in contact with a keratinocyte (measuring bar = 0.1).
© Schaller

Pretreatment with *Lactobacillus* bacteria protects against *C. albicans* infection

Using this model, Mailänder-Sánchez and her colleagues found that *Lactobacillus* bacteria were in fact able to protect human oral mucosa cells against damage caused by *C. albicans* infections: pretreatment of the model with probiotic *Lactobacillus* bacteria offered effective protection against the fungus, and inflammatory reactions were milder than without treatment. However, the researchers also found that the *Lactobacillus* bacteria were unable to directly inhibit the growth of the *Candida* cells.

"The *Lactobacillus* bacteria and *C. albicans* appear to compete for glucose; the bacteria thus deprive the fungus of the food it needs to form the hyphae that are crucial for its virulence," says Schaller explaining the effectiveness of the bacteria. "In addition, the bacteria occupy the docking sites that the fungus needs in order to attach to cells," says Schaller. The Tübingen researchers used molecular biology methods to find out how bacteria and *C. albicans* compete for food and space on human mucosa cells; they found that LRGG is able to affect important *C. albicans* virulence factors. The reduced ability to attach to and enter mucosal cells seems to be largely responsible for the greatly reduced damage to the mucosal cells.

Article

11-May-2015

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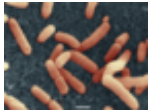
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Further information

Prof. Dr. med. Martin Schaller
Department of Dermatology
University of Tübingen
Liebermeisterstraße 25
72076 Tübingen
Phone: 07071/29-84555
E-Mail: martin.schaller(at)med.uni-tuebingen.de

► [University Department of Dermatology](#)

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