# How Candida albicans exploits lack of oxygen to cause disease

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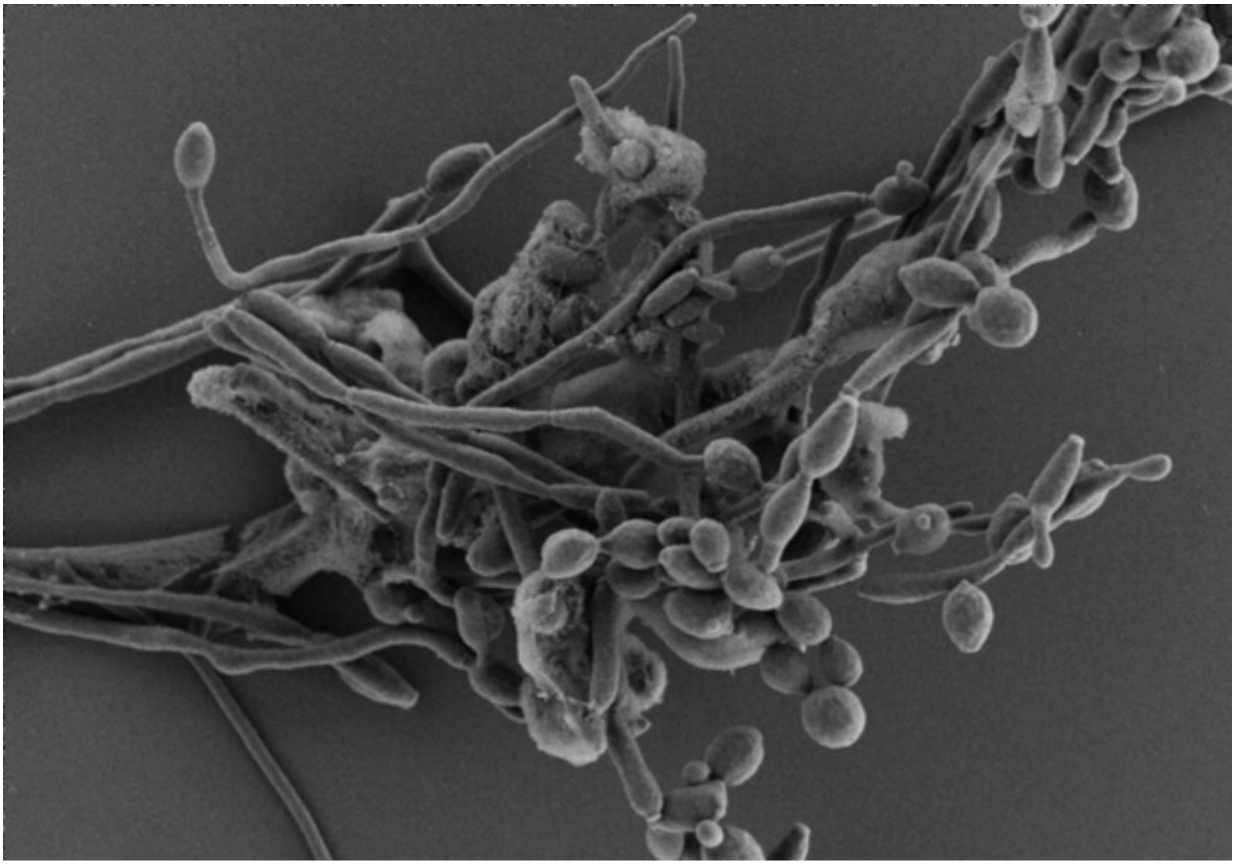

An electron micrograph of neutrophils interacting with a fungal biofilm in an anoxic environment. Neutrophils are not able to respond with their full antifungal potential. Credit: The image was acquired at the Umeå Core Facility for Electron Microscopy (UCEM)

Scientists from Umeå university have shown that the yeast Candida albicans can modulate and adapt to low oxygen levels in different body niches to cause infection and to harm the host. Studying adaption to hypoxic or anoxic niches is particularly fruitful for characterizing the pathogenicity of C. albicans toward the development of better therapeutic approaches. Details about the study are published in the journal *MBio*, a publication of the American Society of Microbiology.

"It was very surprising to see that the fungus does not require oxygen to cause disease. Unexpectedly, the microbial pathogen could even use low oxygen environments to evade immune attack and to become more virulent," says Constantin Urban, associate professor at the Department of Clinical Microbiology. The recent work of his group aims to elucidate how adaption of microbial fungi to low oxygen environments influences their recognition by immune cells and their ability to thrive and cause harmful infection within the host.

Interestingly, C. albicans is a commensal microbe of the gastrointestinal system, and when natural barriers fail due to immunosuppressive disease or treatment, C. albicans can spread from its natural reservoir and invade the body to cause life-threatening, systemic disease. "We now understand how C. albicans under these circumstances exploits the training from anoxic commensal niches to thrive in deep-seeded body sites which quickly induce inflammation and immune cell recruitment. Both processes rapidly exhaust oxygen and in turn create low oxygen milieus," says Dr. Urban.

Systemic infection, which often results in sepsis, can kill critically ill patients in a rapid manner, and comprises a global health threat. According to the World Health Organization, sepsis is estimated to affect more than 30 million people worldwide every year, potentially leading to 6 million deaths. Three-million are newborns, and 1.2 million are children. Candida albicans is the most common fungal pathogen and

a common cause of sepsis. While most individuals carry Candida albicans from birth, the infection causes serious illness or even death among those with a weakened immune system. The new study is a step toward the characterization of immune responses under low oxygen levels, a frequent stress condition during inflammation and infection. Neutrophils, the most abundant white blood cells and an essential defenceagainst fungal microbes, were hampered in their ability to attack and eradicate C. albicans under low oxygen conditions, whereas the neutrophils' metabolism and viability seemed unaffected.

This work is clinically relevant, since current fungal therapy is hampered by toxic side effects and ineffectiveness. The study provides insight into mechanisms that fungal pathogens use to circumvent immune surveillance in environments lacking oxygen. Hence, the study aims for identification of future therapeutic strategies to reduce premature deaths and to improve patients' life quality.

"But I always liked to think outside the box," explains Pedro Lopes, recently graduated Ph.D. student in the group and first author of the study. "Fungi are very versatile organisms, which can grow at almost any site. Interestingly, growing fungi were identified at the international space station (ISS). Ongoing research is attempting to elucidate how fungal microbes thrive under these conditions. Our investigations open up new avenues to study fungal adaptation to hypoxic environments, such as within our bodies or at space stations," says Dr. Lopes.

The report was published this month by the journal *MBio*, along with a complementary but independent study by researchers from Aberdeen University elegantly delineating the cellular processes of C. albicans that regulate fungal adaption to hypoxia. Both articles demonstrate the timeliness and importance of understanding adaption to hypoxia during infection.

**More information:** José Pedro Lopes et al, Evasion of Immune Surveillance in Low Oxygen Environments Enhances Candida albicans Virulence, *mBio* (2018). DOI: 10.1128/mBio.02120-18

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