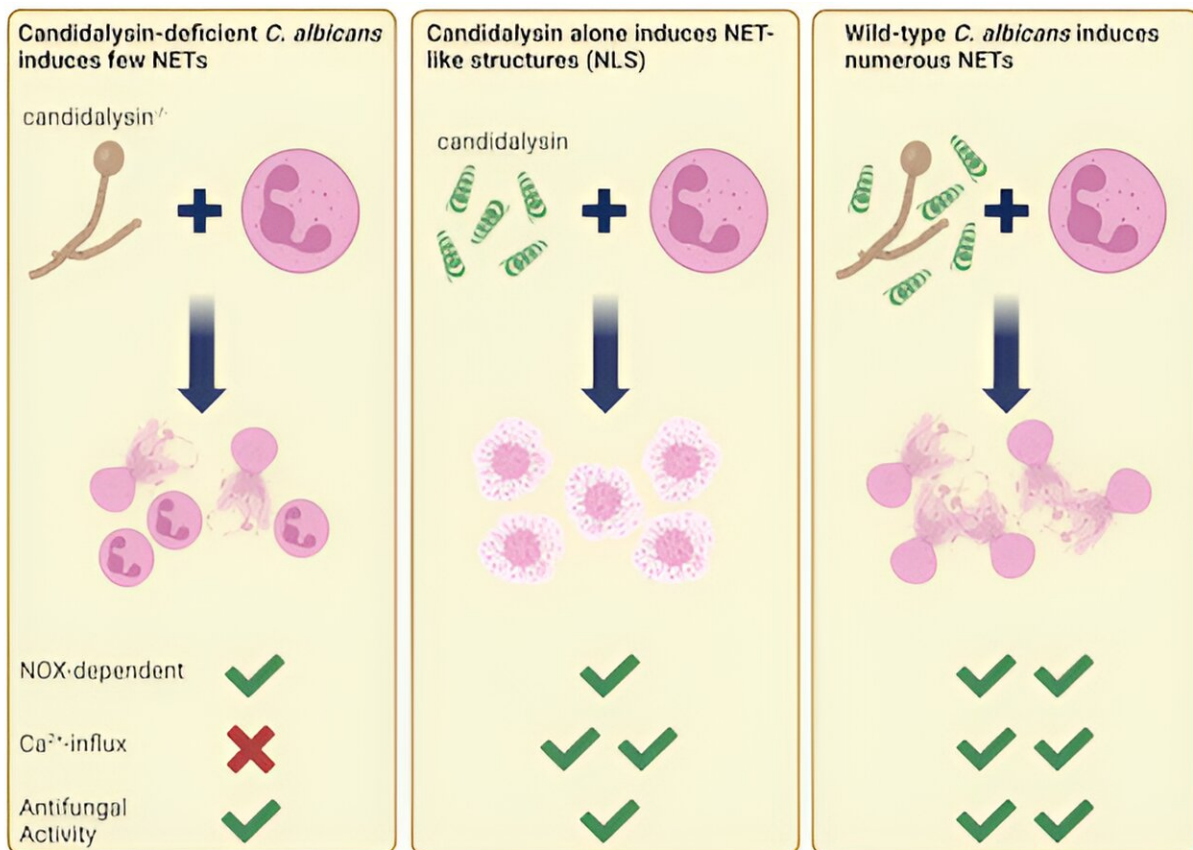


Fungal toxin triggers traps: Revealing the clever defense of white blood cells

October 5 2023



Credit: *EMBO Reports* (2023). <https://doi.org/10.15252/embr.202357571>

Researchers from Umeå University have unveiled how the most common white blood cells, neutrophils, counter *Candida albicans* toxin

and stop it in its tracks. [Their results](#) have been published in *EMBO Reports*.

"We found that when exposed to the toxin of the fungal pathogen, [neutrophils](#) trigger processes to release a chromatin meshwork which entangles and restrains *Candida albicans* hyphae," says Constantin Urban, Professor of Immunology at the Department of Clinical Microbiology at Umeå university, Sweden, and supervising investigator of the study.

Systemic infections caused by bacterial and fungal organisms frequently result in a clinical condition termed sepsis which is a leading cause of death of critically ill patients and hence, is considered a global threat. According to the World Health Organization, sepsis is estimated to affect more than 30 million people worldwide every year, leading to an estimated number of 6 million fatal cases. *C. albicans* is the most frequent human fungal pathogen and a common cause of invasive candidiasis which may result in sepsis.

A hallmark of *C. albicans*' virulence is the ability to reversibly switch from yeast forms to filamentous forms, hyphae. The organism uses the yeast form to rapidly increase biomass and the hyphae to invade and damage tissue.

While a large proportion of the world population is colonized by *C. albicans* since birth, those with a weakened immune system due to disease or [medical intervention](#) are at risk to develop severe or even life-threatening infections, including sepsis, caused by this fungal organism. Particularly neutrophils, the most abundant white blood cell, are an essential part in the defense against fungal microbes.

The newly published study sheds light on how neutrophils, respond to *C. albicans* hyphae, which release a peptide toxin called candidalysin.

Notably, candidalysin is exclusively secreted when *C. albicans* grows as hyphae and hence during invasive growth.

The researchers observed that neutrophils triggered cellular pathways which cumulated in the release of neutrophil extracellular traps (NETs). These chromatin fibers are formidable weapons against hyphae. NETs can entrap and inhibit the fungus with the help of large amounts of sticky and antimicrobial proteins located within the structures. The sticky nature of NET proteins efficiently binds microbes, such as fungal cells. The entangled fungus subsequently is attacked by the associated antimicrobial NET proteins.

"We were very surprised to see that neutrophils remained functional in the presence of candidalysin for such a long time. The [immune cells](#) continued to produce antimicrobial oxidants and continued to engulf fungal cells," says Urban.

In contrast, when neutrophils were infected with engineered strains of *C. albicans* lacking candidalysin, NET formation was virtually absent.

"Interestingly, candidalysin alone was not a sufficient stimulus to induce NET formation. It resulted in a more compact, less fibrous chromatin meshwork released by neutrophils, so-called NET-like structures, whereas only the combination of candidalysin exposure to and pattern recognition of *C. albicans* cells by neutrophils resulted in release of fibrous NETs," says Lucas Unger, research assistant at the Department of Clinical Microbiology at Umeå University at the time of the study, lead experimental researcher of the study.

The study unravels that candidalysin mainly contributes to chromatin swelling—an early step in the release of extracellular DNA structures—via calcium-dependent activation. Through effects upon neutrophil membranes calcium ions are allowed to enter the cells to start

these activation processes. The recognition of fungal [cells](#) via neutrophil receptor molecules triggers kinase activation and production of antimicrobial oxidants. Calcium influx, kinase activation and oxidant production in combination eventually induce the release of large amounts of NETs.

This work was only possible with engaged international collaborators located in Gothenburg in Sweden, Bristol and London in the United Kingdom, and Jena and Berlin in Germany.

"We are particularly grateful to clinicians from the Charité hospital in Berlin that allowed us access to neutrophils from patients with chronic granulomatous disease. The immunodeficiency renders neutrophils unable to produce antimicrobial oxidants and with the help of these we could thoroughly address the involvement of oxidants in candidalysin-triggered processes," says Urban.

More information: Lucas Unger et al, *Candida albicans* induces neutrophil extracellular traps and leucotoxic hypercitrullination via candidalysin, *EMBO Reports* (2023). [DOI: 10.15252/embr.202357571](https://doi.org/10.15252/embr.202357571). www.embopress.org/doi/full/10.15252/embr.202357571

Provided by Umea University

Citation: Fungal toxin triggers traps: Revealing the clever defense of white blood cells (2023, October 5) retrieved 29 April 2024 from <https://medicalxpress.com/news/2023-10-fungal-toxin-triggers-revealing-clever.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--