

Molecular causes for life-threatening fungal infections in case of sepsis unravelled

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(Medical Xpress) -- Pathogenic fungi cause infections with a high mortality rate in patients with weakened immune systems. At Karl Kuchler's CD Laboratory at the MedUni Vienna, the molecular causes of the life-threatening inflammatory reactions that are triggered by fungal infections are being deciphered.

With infectious diseases, it is often not the pathogen itself, but rather an excessive inflammatory immune response (= sepsis) that contributes to the patient's death, for instance as a result of organ damage. On intensive care units, sepsis is the second-most common cause of death worldwide. In patients with a severely compromised [immune system](#) specially, life-threatening candida fungal infections represent a high risk of sepsis.

The working group led by Karl Kuchler in the Christian Doppler Laboratory for Infection Biology (Max. F. Perutz Laboratories at the Vienna Biocenter Campus) has now deciphered the molecular causes of life-threatening inflammatory reactions that are triggered by fungal infections: two highly aggressive types of phagocytes in the immune system (neutrophils and inflammatory monocytes), which however also have a high

potential for collateral destruction, mediate the inflammatory reaction during an infection with candida. Certain interferons, the messenger substances used by the immune system, which are excreted during [fungal infections](#), stimulate the influx of immune cell types to infected organs and lead to sepsis.

Strategy: block the immune response

"We have been able to demonstrate for the first time that the targeted blockade of this immune response with inflammation-inhibiting drugs can significantly reduce candida sepsis and therefore mortality," says Karl Kuchler, who used an anti-inflammatory substance in the study that is also used as an active ingredient in the treatment of type 2 diabetes - namely pioglitazone.

When this medication was administered, the number and activity of neutrophils and inflammatory monocytes in the mouse model were specifically reduced, and the survival rate was increased for invasive candida infections. "The targeted blockade of excessive immune responses could therefore provide new therapeutic approaches to increase the chances of recovery from life-threatening fungal sepsis," says Kuchler.

Infectious diseases are the world's number 1 cause of death, with pathogenic fungi being responsible for extremely dangerous infections. Worldwide, more than 6 billion are spent each year on anti-fungal medications, and the total costs of the medical treatment of infectious diseases caused by [pathogenic fungi](#) is estimated at hundreds of billions of Euros.

More information: "[Type I Interferons Promote Fatal Immunopathology by Regulating Inflammatory Monocytes and Neutrophils during Candida Infections](#)", Olivia Majer, et al. *PLoS Pathog.* 2012 June.

Provided by Medical University of Vienna

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