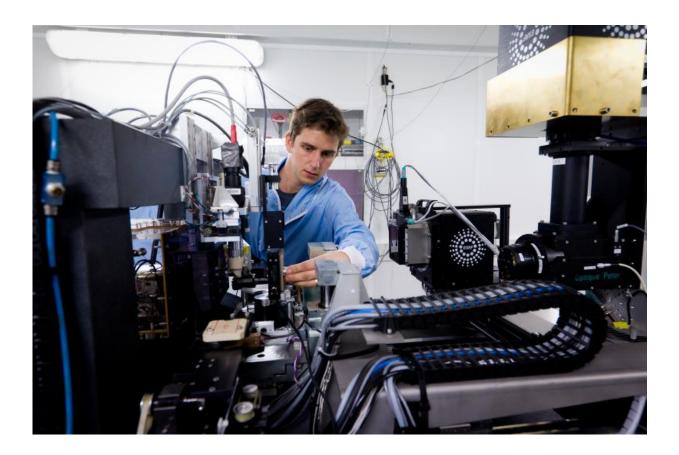


Neutrophils starve fungal invaders

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Björn De Samber from Ghent University placing the sample at the ID22NI beamline, ESRF, France. Credit: Jan Garrevoet

The most frequent immune cells in the human blood, so-called neutrophils, efficiently kill invading microorganisms and slowly starve microbes to death by removing crucial trace elements. This is shown by researchers from Umeå University in Sweden in a study published in a



special issue of Metallomics.

"Every infection is a battle for resources, most importantly trace elements which are comparably scarce in the host environment. We develop methods that allow us to decipher how these fights are fought on a molecular level," says Maria Joanna Niemiec, doctoral student at Umeå University and one of the researchers behind the new research findings.

While numbers of life-threatening infections by fungi are increasing, the risk is still widely underestimated and treatment strategies are limited. At Umeå University, the research group of Constantin Urban investigates the interplay of fungal pathogens and the human immune system.

In order to show how neutrophils withhold trace elements from fungal invaders, researchers at the Department of Clinical Microbiology and the Laboratory for Molecular Infection Medicine Sweden (MIMS) at Umeå University collaborated with a group at Ghent University in Belgium, which is one of the few groups world-wide with the expertise to analyse individual cells at sub-micrometre resolution. The method is called Synchrotron Radiation X-Ray Fluorescence (SR-XRF) and was performed at facilities in Grenoble, Switzerland, and Hamburg, Germany. Similar studies will soon be possible at the newly built synchrotron facilities MAX IV Laboratory near Lund in the south of Sweden.

Neutrophils defend the human body against <u>fungal pathogens</u>. They are best-known for their ability to track down and follow microbes in blood and tissue and to "swallow" and toxify them. More recently discovered, neutrophils release their DNA decorated with toxic proteins, so-called NETs, to entangle and deactivate microbes on the outside.

In their recent publication, the researchers show that the release of NETs dramatically decreases the availability of the key trace element for fungi:



zinc. And by combining XRF with live-cell microscopy, they reveal that zinc is actually hidden inside of the neutrophil long before NETs are released. This sophisticated strategy underlines the neutrophils' role as key players of the immune system, which remove invading microbes. The mechanism applied by neutrophils to retain trace elements, such as zinc and iron, from microbes has been coined as 'nutritional immunity' – a newly emerging exciting research field.

"We are very interested in translating our findings into future medications helping to cure fungal infections that are difficult to treat with the drugs available on the market today," says Constantin Urban, associate professor and research leader at the Department of Clinical Microbiology, and also responsible for the study.

More information: M. J. Niemiec et al. "Trace element landscape of resting and activated human neutrophils on the sub-micrometer level," *Metallomics* (2015). DOI: 10.1039/C4MT00346B

Provided by Umea University

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