Researchers discover new mechanism of microorganism resistance against free radicals

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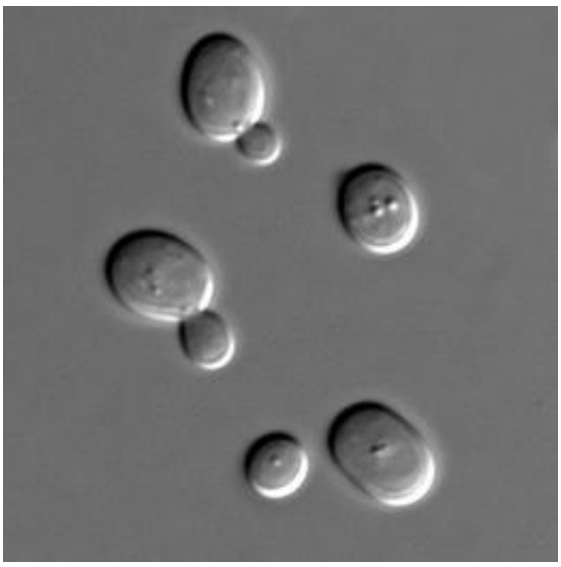

Sacharomyces cerevisiae cells in DIC microscopy. Credit: Wikipedia.

There are numerous different scenarios in which microorganisms are exposed to highly reactive molecules known as free radicals. These molecules are capable of damaging important cell components and may be generated during normal cell metabolism or in response to environmental factors. Free radicals play a significant role in antibiotic effectiveness, the development of diseases and the normal functioning of the human immune system. A team of researchers from Charité - Universitätsmedizin Berlin has discovered a previously unknown

mechanism which enables microorganisms to protect themselves against free radicals. Their findings may help improve the efficacy of antimicrobial substances. Results from this research have been published in *Nature*.

The term free oxygen radicals refers to highly reactive oxygen molecules which are capable of damaging a range of important cell structures such as proteins, DNA and cell membranes. While free radicals represent a destructive force, it is one which the human body has learned to exploit. Some cells of the human immune system produce free radicals as part of their fight against invading microorganisms. Metabolic processes also result in the production of free radicals when microbial cells come into contact with antibiotics. This is an important factor behind their activity. Microorganisms have developed various mechanisms to intercept and neutralize these highly reactive molecules in order to deflect an immune system attack. An international team of researchers led by Prof. Dr. Markus Ralser, Director of Charité's Institute of Biochemistry, has now been able to show that microorganisms also have another, previously unknown defensive strategy at their disposal. Compared with previously documented mechanisms, this strategy could prove particularly effective.

The researchers started their investigations using baker's yeast as the model organism, observing that yeast cells accumulate vast quantities of lysine, a building block used in the production of yeast proteins. After being absorbed from the environment, lysine was stored at levels 70 to 100 times higher than those necessary for normal growth. Using mathematical modeling and genetic analysis to determine the purpose of this 'lysine harvest," the researchers discovered that yeast cells use the accumulated lysine to alter their own metabolism. One of the consequences of this reconfiguration was the production of extraordinary amounts of glutathione, one of the most important radical scavenging molecules found in living organisms. Following lysine harvest, yeast cells were shown to have significantly increased resistance

against free radicals. This enabled them to break down quantities of free radicals which would normally have resulted in cell death. The researchers demonstrated that this resistance mechanism is used not only by different types of yeast, but also by bacteria.

"Our study shows that microorganisms absorb nutrients from their surroundings not only to enable growth, but also as a precautionary measure, to prepare against a potential attack by free radicals," explains Prof. Ralser. "This knowledge could prove useful in the future; if we succeeded in disrupting this resistance mechanism, we could potentially improve the efficacy of antimicrobial substances." The research group will continue its work with this aim in mind. "We will also search for other unknown resistance mechanisms. After all, an understanding of fundamental cellular processes is a prerequisite for the development of antimicrobial substances."

More information: Viridiana Olin-Sandoval et al, Lysine harvesting is an antioxidant strategy and triggers underground polyamine metabolism, *Nature* (2019). DOI: 10.1038/s41586-019-1442-6

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