How pathogens are controlled when tissue is deprived of adequate oxygen supply

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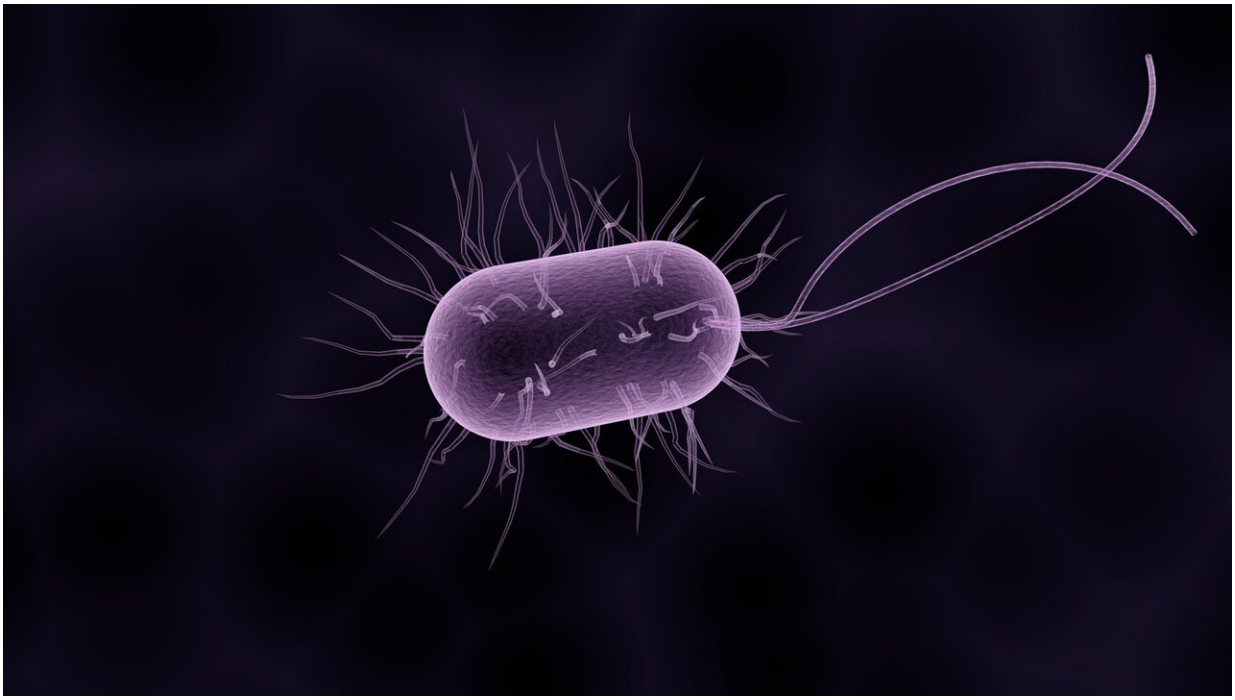

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Infected tissue has a low concentration of oxygen. The body's standard immune mechanisms, which rely on oxygen, can then only function to a limited extent. How does the immune system nevertheless manage to control bacteria under such conditions? The working groups led by PD Dr. Anja Lührmann and Prof. Dr. Jonathan Jantsch have investigated this question in collaboration with other groups from Erlangen,

Regensburg and Jena. The researchers discovered that fewer metabolites are produced in the citric acid cycle under hypoxic conditions, leading to a reduced rate of reproduction among bacteria in macrophages. The results have recently been published in the journal *Cell Reports*.

Macrophages are a type of phagocyte and belong to the congenital immune system, where they have a key role to play in defending against infection by intracellular pathogens such as those which cause tuberculosis, Legionnaires' disease or Q fever. The team of researchers observed changes in the mitochondrial metabolism of the macrophages caused by signaling pathways initiated by the lack of oxygen (hypoxia). This leads to a reduction in various metabolites in the citric acid cycle, especially citrate. This in turn prevents bacteria reproduction, as citrate is an essential growth factor for certain bacteria.

"Our results describe a method of pathogen control which does not depend on oxygen and which we were not aware of until now," explains Prof. Jantsch.

Dr. Lührmann adds, "The pharmacological influence of these signaling pathways opens up new opportunities for fighting infectious diseases."

More information: Inaya Hayek et al, Limitation of TCA Cycle Intermediates Represents an Oxygen-Independent Nutritional Antibacterial Effector Mechanism of Macrophages, *Cell Reports* (2019). DOI: 10.1016/j.celrep.2019.02.103

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