

Mitochondrial components are a possible trigger of auto-inflammatory illnesses

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(Medical Xpress)—Many illnesses, including psoriasis, include inflammatory responses that occur without an apparent infection and worsen with stress. In a study using cultured human mast cells in vitro and in rats, researchers from Tufts University School of Medicine and the Sackler School of Graduate Biomedical Sciences at Tufts University identified mitochondrial particles—secreted from live, activated mast cells—as a possible trigger of the inflammation that is common in such illnesses.

[Mast cells](#) are a part of the immune system and can secrete inflammatory molecules, such as [histamine](#), in response to allergens and other triggers. Generated in the [bone marrow](#), mast cells play vital roles in acquired and innate immunity within tissues in the body. Little is known about their secretory process except that energy generated by [mitochondria](#) is required.

When a person contracts an infection or has an allergic reaction, mast cells normally secrete molecules that alert the immune system to the presence of a foreign invader. These molecules trigger the body's responses in order to contain and eliminate the infection or alert the body to initiate an [inflammatory response](#). After this process, the mast cell regenerates. The research team sought to understand how inflammation could be triggered without the presence of an infection or [allergen](#).

In the study, mast cells were stimulated by triggers secreted from nerves,

rather than by infection or allergen. As a result, the mast cells secreted their inflammation-causing molecules, as well as some mitochondrial components. The mitochondrial components were secreted outside the cell into the extracellular fluid, but the mast cells retained their viability, indicating that the secretion of mitochondrial particles was not due to cell damage or death. The extracellular mitochondrial components then stimulated other [skin cells](#) to mount an auto-inflammatory response.

Purified human mitochondrial components were also injected into peripheral tissue of rats. Within four hours, they were detected in the blood, which suggests that mitochondrial components secreted in tissues can reach the systemic circulation, the part of the cardiovascular system that carries blood from the heart to the rest of the body.

"The immune system misread the mitochondrial components as an infectious agent, and there was inflammation as a result," said first author Bodi Zhang, M.D., M.P.H., Ph.D., graduate of the biochemistry program at the Sacker School. "Our study findings are different from a report last year suggesting that mitochondrial particles are released from damaged cells in patients with severe trauma. Additional studies are needed to gain a better understanding of this process."

"Our work provides a possible explanation for [inflammation](#) that arises without apparent disease or injury," said senior author Theoharis C. Theoharides, M.S., Ph.D., M.D., professor of molecular physiology and pharmacology at Tufts University School of Medicine and member of the Biochemistry, and Pharmacology & Experimental Therapeutics graduate program faculties at the Sackler School. "[Secretion](#) of mitochondrial components by immune cells may constitute an 'innate pathogen' that may stimulate self-response by the immune system."

"Although this study does not identify the inflammatory mechanism that is common among auto-inflammatory illnesses, the findings help to lay a

foundation for further research and may lead to new biomarkers and novel treatment targets," Theoharides added.

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Additional authors on the study are Shahrzad Asadi, Pharm.D., postdoctoral scholar in the Theoharides laboratory; Zuyi Weng, B.S., graduate student in the Pharmacology & Experimental Therapeutics program at the Sackler School working in Dr. Theoharides' laboratory; and Nikolaos Sismanopoulos, M.D., formerly a postdoctoral fellow in the Theoharides' laboratory and now at St. Elizabeth's Medical Center. The authors have declared that no competing interests exist.

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