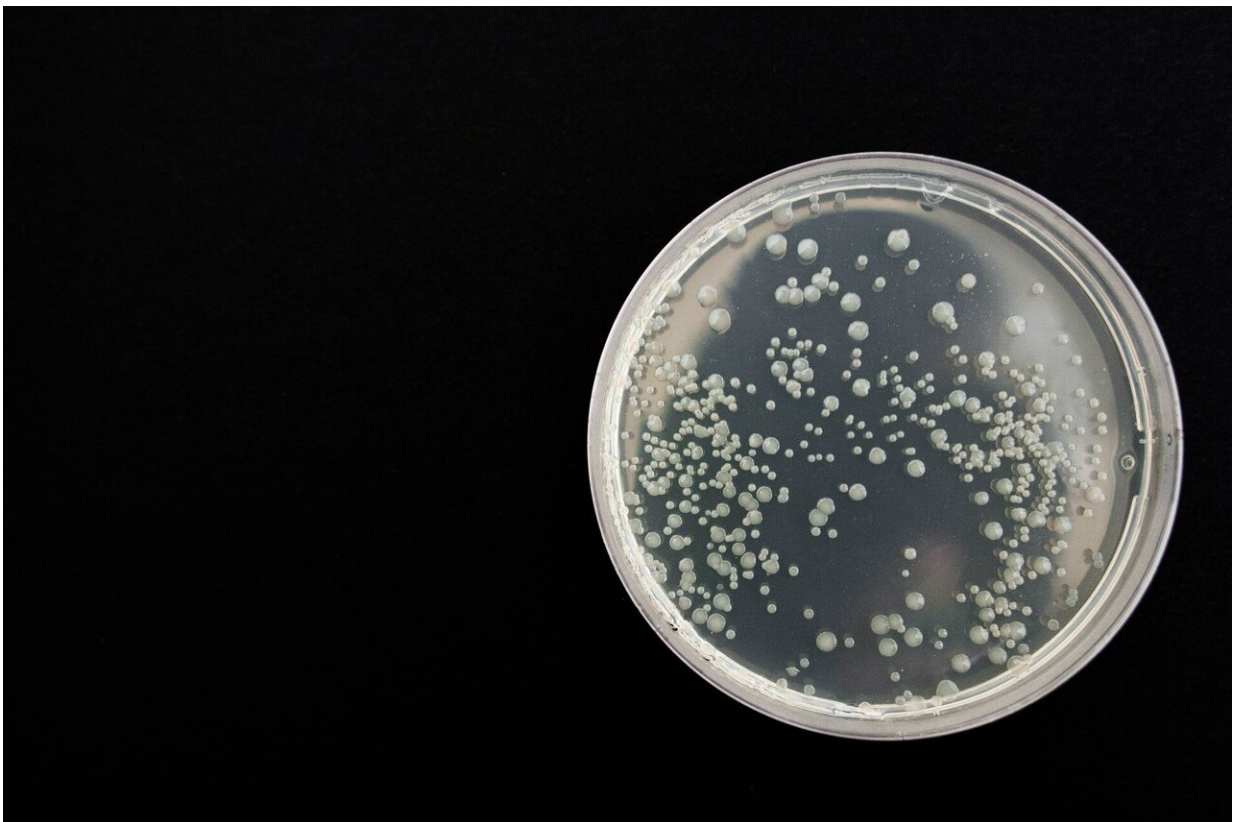


Protein produced in sepsis lowers blood pressure, treatment identified to reverse effects

April 23 2020



Credit: CC0 Public Domain

Overreaction is rarely useful, and in the case of the human immune system, it can be outright deadly. When the body overreacts to an

infection, the result is sepsis—a life-threatening condition that frequently leads to acute organ dysfunction, including deterioration of the heart and blood vessels, which make up the cardiovascular system. A major indication that the cardiovascular system is failing in sepsis is a drop in blood pressure, the only treatment for which is fluid replacement.

Now, in a new study published online April 23 in the journal *JCI Insight*, scientists at the Lewis Katz School of Medicine at Temple University (LKSOM) show that when a molecule known as c-Jun N-terminal kinase (JNK) becomes active in sepsis, it increases the production of a protein called B-type natriuretic peptide (BNP) - the more BNP that is produced in sepsis, the greater the deterioration of cardiovascular function. But perhaps more significantly, in mice, the researchers show that JNK and BNP activity can be halted, reversing cardiovascular damage and reducing the risk of death from sepsis.

"Low blood pressure is characteristic of the most severe form of sepsis, known as septic shock, in which fluid loss and decreased oxygen and nutrient delivery to tissues severely damages organ function," explained Konstantinos Drosatos, Ph.D., Assistant Professor of Pharmacology and Assistant Professor in the Center for Translational Medicine, the Center for Metabolic Disease Research, and the Alzheimer's Center at LKSOM and senior investigator on the new study.

In previous work, Dr. Drosatos's team found out why heart cells decrease their energy output in sepsis. They also knew from earlier studies that blocking JNK activation could correct cardiovascular dysfunction and lower BNP levels in an animal model of sepsis. The new study expands on this work and demonstrates how treatments aimed at improving cardiovascular function facilitate communication between the heart and [blood vessels](#), which circulate blood throughout the body.

The researchers carried out their investigation of JNK and BNP activation in heart cells and in a mouse model of sepsis. Their experiments revealed a direct relationship between the two molecules, in which a c-Jun activating protein attaches to the gene that encodes BNP. When this happens, the gene is switched on, resulting in the production of BNP. In sepsis, the BNP-encoding gene is always "on," explaining why BNP protein is secreted in excess by the heart.

In separate experiments, the researchers blocked either JNK activation, using a chemical inhibitor, or BNP activity, using an antibody against the protein that was developed in Dr. Drosatos's laboratory. Both approaches restored blood pressure in septic mice, though JNK inhibition yielded the most robust benefits. Inhibition of either molecule also led to improvements in survival from sepsis.

"At a clinical level, JNK or BNP inhibition could stabilize blood pressure and give other medications, such as antibiotics, time to work," Dr. Drosatos explained. "This strategy could be used alongside current supportive strategies, which attempt to slow or prevent fluid loss to stabilize [blood](#) pressure."

In follow-up research, Dr. Drosatos is working closely with Nina Gentile, MD, Professor of Emergency Medicine at LKSOM to explore potential clinical applications of BNP inhibition. "We hope to develop innovative treatments that will work in patients to combat [septic shock](#)," Dr. Drosatos said.

Another important next step is to explore whether the new monoclonal antibody against BNP can be used as an intervention to treat low [blood pressure](#) in sepsis patients. "In light of the ongoing COVID-19 global pandemic, the association of COVID mortality with viral [sepsis](#), and elevated BNP plasma levels in critical COVID-19 patients, the topic of BNP inhibition is very timely," Dr. Drosatos noted.

Provided by Temple University

Citation: Protein produced in sepsis lowers blood pressure, treatment identified to reverse effects (2020, April 23) retrieved 10 April 2024 from <https://medicalxpress.com/news/2020-04-protein-sepsis-lowers-blood-pressure.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.