New clues to sepsis may speed diagnosis

3 July 2018

Credit: public domain

Sepsis is an infection that kills as many Americans each year as stroke and Alzheimer's combined-about 250,000-but very little has changed in the treatment of this age-old scourge.

Now researchers at Columbia University Irving Medical Center have found a clue in understanding how an infection can spiral into sepsis by blunting the body's immune response. This research may also help doctors identify the patients who may need immediate intensive treatment to save their lives.

From Infection to Organ Failure

Sepsis can start with a simple infected cut. When the immune system fails to fight off the infection, sepsis occurs when inflammation spreads throughout the body, leaving patients vulnerable to organ damage, severe secondary infections, and death. While time is of the essence, doctors lack quick, efficient ways to diagnose this deadly condition.

"The best treatment for sepsis starts with rapid detection. Our results suggest that specific molecules called microRNAs may be potential biomarkers of poor prognosis, indicating the need for more aggressive treatment options," explains the study's senior leader Sankar Ghosh, Ph.D., the Silverstein and Hutt Family Professor of Microbiology & Immunology and chair of the Department of Microbiology & Immunology at Columbia University Vagelos College of Physicians and Surgeons (VP&S).

The immune system initially launches a vigorous attack against sepsis, but then the innate immune response shuts down. In a search to understand the underlying mechanism, Ghosh's team identified two microRNAs (miR-221 and miR-222) that are produced in immune cells during prolonged inflammation. These microRNAs silence inflammatory gene expression and in a mouse model of sepsis suppress the immune system at a time when the body desperately needs a full immune response.

Identifying Patients in Danger of Sepsis

Patients with suspected sepsis had a similar reaction. Among 30 hospitalized patients, those with evidence of organ failure exhibit higher levels of miR-221 and miR-222 in their blood samples. In septic patients, those with elevated miR-221 and miR-222 also exhibited evidence of immunosuppression.

The two microRNAs could be the basis of a test to help physicians classify patients into those with organ failure who are at high risk of sepsis and death and those patients with milder infections. With faster diagnosis, doctors could start antibiotics and fluids to control the infection more quickly before patients succumb to organ failure and secondary infections.

"When doctors face sepsis in the hospital, it is usually a mystery as to what is causing the infection, but they must act quickly. They can choose to use the broadest spectrum of antibiotics

for an aggressive approach to cover every bacterial cause of infection, but this may later cause antibiotic resistance, a growing problem," says study co-author Daniel Freedberg, MD, assistant professor of medicine at CUIMC. "Any test that can identify the cause of sepsis to guide treatment options is invaluable."

Clinical trials will be needed to validate the usefulness of testing patients for these microRNAs as a quick guide to prognosis and treatment. The research comes at a time when the number of sepsis cases per year has been on the rise in the United States, according to the National Institutes of Health. Creating better diagnostics may be able to help reverse this trend and save lives.

More information: John J. Seeley et al. Induction of innate immune memory via microRNA targeting of chromatin remodelling factors, *Nature* (2018). DOI: 10.1038/s41586-018-0253-5

Provided by Columbia University