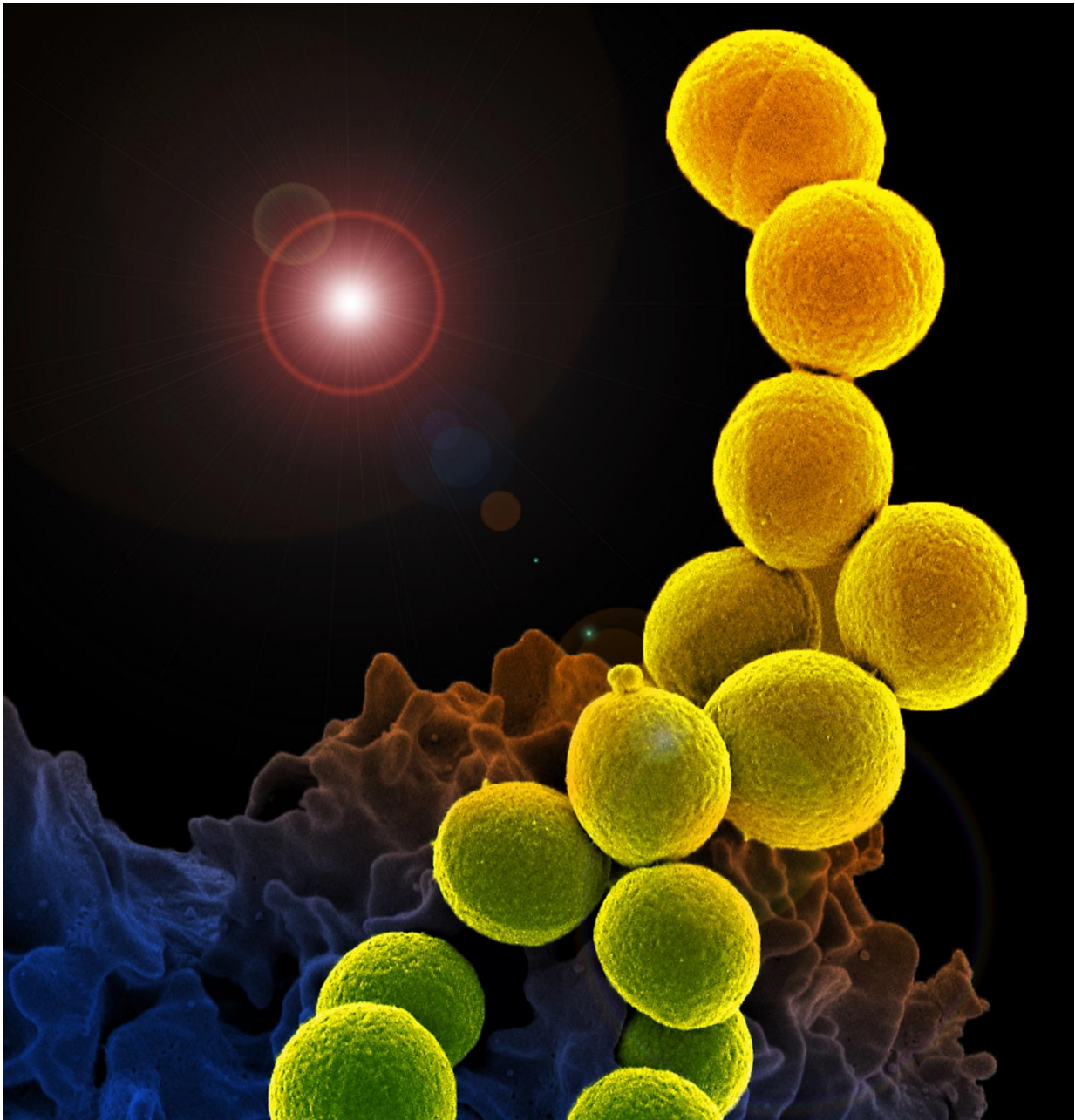# Researchers identify biomarker that predicts death in sepsis patients

March 8 2017

Bacteria (yellow) interact with a human white blood cell in this image from the National Institute of Allergy and Infectious Disease. If left unchecked, this encounter might develop into the runaway immune response to infection called sepsis, but a Duke team has now identified a chemical signal to predict which patients are most at risk of dying from sepsis. Credit: NIH-NIAID

Duke scientists have discovered a biomarker of the runaway immune response to infection called sepsis that could improve early diagnosis, prognosis, and treatment to save lives.

Sepsis is implicated in half of all hospital deaths and kills nearly a quarter of a million Americans every year.

Practically any type of pathogen—bacteria, fungi, parasites, and viruses—can provoke the life-threatening condition, which leads to the body's immune system overreacting and attacking its own tissues and organs. Sepsis is difficult to diagnose and even more difficult to treat.

The new biomarker, a molecule called methylthioadenosine or MTA, can predict which patients are most likely to die from the illness. The findings, which appear March 8 in the journal *Science Advances*, could also help determine whether patients could benefit from therapies that either enhance or suppress the immune system, paving the way for new treatments.

"This area has been a graveyard for the pharmaceutical industry, with more than 100 failed clinical trials of therapies that target the body's abnormal response to infection," said Dennis C. Ko, M.D., Ph.D., an assistant professor of molecular genetics and microbiology at Duke

University School of Medicine.

"It may be that these failed clinical trials are not actually failures of treatment, but rather failures of diagnosis," Ko said. "With better biomarkers, we may be able to group sepsis patients into more refined categories to more effectively test and possibly even resurrect old drugs."

People with sepsis are typically treated with a combination of antibiotics and supportive care, treatments that target the offending germs but do nothing to address the runaway immune response that, ironically, proves more deadly than the infection itself.

In the early stages of sepsis, the immune system churns out prodigious amounts of inflammatory proteins known as cytokines, some of which require activation through another class of proteins called caspases. Caspases can also trigger an explosive form of cell death aptly called pyroptosis (fire falling) that helps destroy pathogens but can exacerbate damage to the host if left unchecked.

In a study published five years ago in the *Proceedings of the National Academy of Sciences*, Ko searched for genetic variants that might predispose people to higher or lower levels of pyroptosis. His results pointed to some variation between patients in the components of an intracellular recycling system known as the "methionine salvage pathway."

In this study, Ko and his colleagues focused their search on a molecule called methylthioadenosine or MTA, which feeds into the methionine salvage pathway. They measured levels of MTA in sepsis survivors and sepsis non-survivors from two independent groups of patients, and found that those who died from the disease had elevated levels of the molecule.

They found that measurement of this single molecule was approximately 80% accurate in predicting death, which is comparable to the APACHE II (Acute Physiology and Chronic Health Evaluation II) score, a measurement that is now used in hospitals.

After Ko discovered that MTA could serve as a reliable biomarker of sepsis, he wondered whether he could change the course of infection by manipulating levels of the molecule. His lab found that mice infected with Salmonella lived longer when MTA was administered prior to infection, suggesting that manipulation of the methionine salvage pathway could be used to regulate the inflammatory response that leads to sepsis.

But Ko cautions that much more work needs to be done before a diagnostic or treatment based on MTA could make it into the clinic. It will be crucial to further examine the utility, dosing, pharmacodynamics, and mechanism of tweaking MTA levels in animal models, and if results are promising, to validate them in patients.

"It gets very complicated very fast," said Ko. "Some people might have too robust of an [inflammatory response](), some people might not have a robust enough response, and as a result their MTA levels will differ, both between individuals and within an individual over the course of an illness. Biomarkers could determine where individuals fall along that continuum, and what treatments might work."

  More information: "Human genetic and metabolite variation reveals that methylthioadenosine is a prognostic biomarker and an inflammatory regulator in sepsis," *Science Advances*, March 8, 2017. [advances.sciencemag.org/content/3/3/e1602096]()

Provided by Duke University

Citation: Researchers identify biomarker that predicts death in sepsis patients (2017, March 8) retrieved 8 May 2024 from https://medicalxpress.com/news/2017-03-biomarker-death-sepsis-patients.html