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# CALS researchers developing novel treatment for septic shock

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(Medical Xpress)—By the time doctors diagnose septic shock, patients often are on a knife's edge. At that point, for every hour that treatment is delayed, a person's risk of death rises an alarming six percent.

Time is of the essence. And CALS animal sciences professor Mark Cook was part of a team that developed a breath biomarker technology capable of detecting septic shock 12 to 48 hours earlier than standard methods. This powerful device, which was patented in 2008 and is making its way through clinical trials, creates an exciting opportunity for new, life-saving medical interventions.

"If you can detect septic shock earlier, then you can begin to explore ways of treating it earlier," says Cook, who already is in the process of developing a promising antibody-based treatment.

Septic shock—or severe sepsis—affects approximately 750,000 people in the United States each year, taking more than 200,000 lives and costing around $17 billion in treatment.

It occurs when a person's immune system, spurred by a bacterial infection or serious physical trauma, launches a massive inflammatory response that can lead to a drop in blood pressure, multiple organ failure and death.

The gastrointestinal tract is believed to be the primary site of this runaway response. Because of that, some scientists call the gut "the

motor for sepsis," says Cook. So it's no surprise that Cook looked to the gut for a solution.

With funding from a Robert Draper Technology Innovation Fund grant from the UW–Madison Graduate School, he began working to interfere with the activity of a protein called sPLA2, which is part of the chain of events in the gut that drives septic shock. It is a dual-purpose protein that can act as both an enzyme and a signaling molecule, so it wasn't initially clear which of the protein's roles—enzyme, signaling or both—were involved.

Cook and Jordan Sand, a scientist in Cook's lab, decided to first try blocking the gut protein's ability to signal, guessing that this would calm the immune response. So Sand made a series of antibodies that inhibited sPLA2's signaling function—but not its enzyme function—and then tested them in a mouse model of septic shock.

"We actually made it much worse," says Sand. "We absolutely failed. There's no other way to say it."

Sand went back and made antibodies that blocked only the protein's enzyme function. Those worked. "We had 100 percent survival across the board," says Sand.

If the antibody approach also works in people, this treatment could help patients with septic shock stay alive while they wait for antibiotics and other standard treatments to kick in.

Cook and Sand have filed a patent on the technology. But, Cook notes, "There are still a lot of steps to get this into human medicine."

Provided by University of Wisconsin-Madison