

Team improves its sepsis therapeutic device

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Last year, a Wyss Institute team of scientists described the development of a new device to treat sepsis that works by mimicking our spleen. It cleanses pathogens and toxins from blood circulating through a dialysis-like circuit. Now, the Wyss Institute team has developed an improved device that synergizes with conventional antibiotic therapies and that has been streamlined to better position it for near-term translation to the clinic. The improved design is described in the October volume 67 of *Biomaterials*.

Sepsis is a common and frequently fatal medical complication that can occur when a person's body attempts to fight off serious infection. Resulting widespread inflammation can cause organs to shut down, [blood pressure](#) to drop, and the heart to weaken. This can lead to septic shock, and more than 30 percent of septic patients in the United States eventually die. In most cases, the pathogen responsible for triggering the septic condition is never pinpointed, so clinicians blindly prescribe an antibiotic course in a blanket attempt to stave off infectious bacteria and halt the body's dangerous inflammatory response.

But sepsis can be caused by a wide-ranging variety of pathogens that are not susceptible to antibiotics, including viruses, fungi and parasites. What's more, even when antibiotics are effective at killing invading bacteria, the dead pathogens fragment and release toxins into the patient's bloodstream.

"The inflammatory cascade that leads to sepsis is triggered by pathogens, and specifically by the toxins they release," said Wyss Institute Founding Director Donald Ingber, M.D., Ph.D., who leads the Wyss team developing the [device](#) and is the Judah Folkman Professor of Vascular Biology at Boston Children's Hospital and Harvard Medical School and Professor of Bioengineering at the Harvard John A. Paulson School of Engineering and Applied Science. "Thus, the most effective strategy is to treat with the best antibiotics you can muster, while also removing the toxins and remaining

pathogens from the patient's blood as quickly as possible."

The Wyss team's blood-cleansing approach can be administered quickly, even without identifying the infectious agent. This is because it uses the Wyss Institute's proprietary pathogen-capturing agent, FcMBL, that binds all types of live and dead infectious microbes, including bacteria, fungi, viruses, as well as toxins they release. FcMBL is a genetically engineered blood protein inspired by a naturally-occurring human molecule called Mannose Binding Lectin (MBL), which is found in the innate immune system and binds to toxic invaders, marking them for capture by immune cells in the spleen.

The original device concept was similar to how a dialysis machine works: infected blood in an animal, or potentially one day in a patient, is flowed from one vein through catheters to the device where FcMBL-coated magnetic beads are added to the blood, and then the bead-bound pathogens are extracted from the circulating blood by magnets within the device before the cleansed blood is returned to the body through another vein.

The new and improved device removes the complexity, regulatory challenges and cost associated with the magnetic beads and microfluidic architecture of its predecessor, but it retains the ability of the FcMBL protein to bind to all different kinds of live or dead pathogens and toxins. The optimized system uses hollow fiber filters found in already-FDA-approved dialysis cartridges whose inner walls are coated with FcMBL protein to remove pathogens from circulating blood. In animal studies, treatment with this new pathogen-extracting device reduced the number of *E. coli*, *Staphylococcus aureus* and endotoxins circulating in the bloodstream by more than 99 percent.

"Using the device, alone or alongside antibiotics, we can quickly bring blood back to normal conditions, curtailing an inflammatory response rather than exacerbating it," said the paper's first

author Tohid Fatanat Didar, Ph.D., Postdoctoral Fellow at the Wyss Institute and Research Fellow at Boston Children's Hospital. "If all goes well, physicians will someday be able to use the device in tandem with standard antibiotic treatments to deliver a one-two punch to pathogens, synergistically killing and cleansing all live and dead invaders from the bloodstream."

With the new improved blood-cleansing therapeutic device proving extremely effective in small animal studies, the Wyss team is planning to move to large animal studies as a next step to demonstrate the proof-of-concept that is required before it could advance to human clinical trials.

"Seeing our system work in animal models gives us confidence that this could work in humans, because we are successfully treating animals infected with human [pathogens](#)," said Wyss Senior Staff Scientist Michael Super, Ph.D., who works on the Institute's Advanced Technology Team and is also an author on the new study.

"Since the development of earlier prototypes of the device, we've applied the Wyss model of de-risking the technology to prime it for commercialization," said Ingber. "Our goal is to see this move out of the lab and into hospitals as well as onto the battlefield, where it can save lives within years rather than decades."

Provided by Harvard University

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