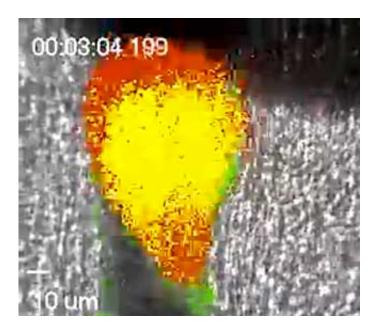


In surprise finding, blood clots absorb bacterial toxin

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Blood clots play an unexpected role in protecting the body from the deadly effects of bacteria by absorbing bacterial toxins, researchers at the University of California, Davis, have found. The research was published Dec. 2 in the journal *PLOS ONE*.

"It's a significant addition to the short list of defenses that animals use to protect themselves against toxin-induced sepsis," said Peter Armstrong, professor of molecular and cellular biology at UC Davis and senior



author on the paper.

Even with modern antibiotics, septic shock from bacterial infections afflicts about 300,000 people a year in the U.S., with a mortality rate of 30 to 50 percent. Septic shock is caused by Gram-negative bacteria, which release a toxin called lipopolysaccharide or endotoxin. In small amounts, lipopolysaccharide triggers inflammation. When infections with these bacteria get out of hand, lipopolysaccharide courses through the bloodstream, causing catastrophic damage to organs and tissues.

These toxins cause disease in a variety of animal species—lipopolysaccharide is also toxic to both <u>horseshoe crabs</u> and lobsters, separated from humans by hundreds of millions of years of evolution. In humans and other mammals, <u>blood clots</u> quickly form from a mix of specialized blood cells and protein fibers. Arthropods like horseshoe crabs and lobsters can also form clots in response to injury, with a different mix of cells and proteins.

Clots protect and help to seal wounds, prevent blood or body fluids from leaking out and form a physical barrier that entangles and blocks bacteria from entering the body. The new study shows that they also actively soak up lipopolysaccharide, reducing its release from the wound site into the body, where it could cause disease or even death.

Armstrong's laboratory had previously developed fluorescent labels to show that a lipopolysaccharide-like molecule is present in chloroplasts, structures inside cells of green plants that carry out photosynthesis and are thought to be descended from bacteria. As he also studies the role of blood clots in resisting infections, Armstrong decided to test the same techniques on blood clots that had been exposed to bacteria or to bacterial lipopolysaccharide. The fluorescent probes lit up the clots, showing that the clot fibers bound lipopolysaccharide to their surfaces.



"I was ecstatic," Armstrong said. "It was one of those moments that makes the rest of the slogging worthwhile."

Armstrong and colleagues Margaret Armstrong at UC Davis and Frederick Rickles at George Washington University looked at clots of blood, or its equivalent, from humans, mice, lobsters and horseshoe crabs. In all four species, they found that fluorescently tagged lipopolysaccharide was bound to the fibers of the blood clot. The toxin was too tightly attached to be readily removed by chemical treatments that remove weakly bound macromolecules from proteins.

During a sabbatical leave in the laboratory of Dr. Bruce Furie at Beth Deaconess Medical Center and Harvard University, Armstrong was also able to film clots in blood vessels of live mice and showed that these in vivo clots took up lipopolysaccharide in real time. These in vivo experiments, he said, confirm the bench-top observations and offer new insights into the pathology of sepsis.

One of the deadly consequences of <u>septic shock</u> is disseminated intravascular coagulation, when blood clots form rapidly throughout the body. But the new results suggest that on a small and local scale, this might be part of a protective mechanism against sepsis—these intravascular clots can soak up quantities of <u>lipopolysaccharide</u> from the blood. They also show that rather than being a simple physical barrier, blood clots play an active and dynamic role in protecting the body from infections.

Parts of the research were carried out at the Woods Hole Marine Biological Laboratory. The work was funded by a grant from the National Science Foundation.

Provided by UC Davis



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