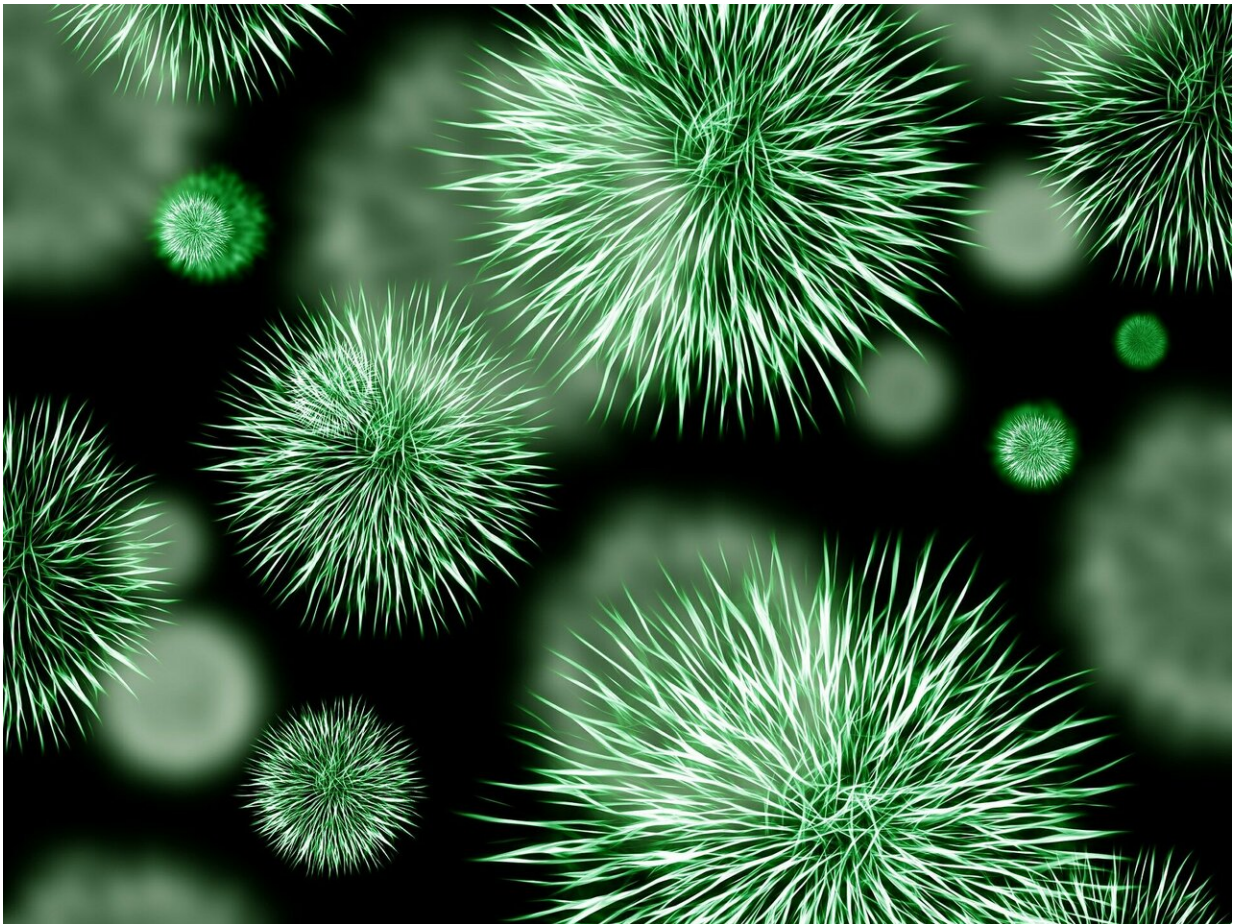


Blood clotting factors may help fight multi-drug resistant superbugs

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Coagulation factors, which are involved in blood clotting after injury,

may offer new strategies for fighting multidrug-resistant bacteria, according to a study published in *Cell Research*.

Infections caused by these [bacteria](#) pose an urgent public health risk, as effective drugs to combat them are lacking. A deficiency in blood [coagulation](#) factors—for example in patients with the blood clotting disorder haemophilia—has been associated with bacterial infection diseases such as sepsis and pneumonia, leading to the suggestion that these coagulation factors may have a role in anti-infection mechanisms as well as bloody clotting.

Now a group of researchers at Sichuan University, China, has shown that the factors VII, IX, and X—which are well known for their roles in blood coagulation—may act against Gram-negative bacteria, including extensively drug resistant pathogens such as *Pseudomonas aeruginosa* and *Acetivobacter baumannii*. Both bacteria were recently listed by the World Health Organisation among 12 bacteria that pose the greatest threat to human health because of their antibiotic resistance. Gram-negative bacteria are characterized by their cell envelopes, which are composed of an inner cell membrane, a thin cell wall and an [outer membrane](#) that make them harder to kill.

Xu Song, the corresponding author said: "In our study, we report a class of human antimicrobial proteins effective against some drug-resistant 'superbugs'. Unlike many [antibacterial agents](#) that target the cell metabolism or cytoplasmic membrane, these proteins act by breaking down the lipopolysaccharides of the bacterial outer membrane through hydrolysis. Lipopolysaccharides are crucial for the survival of Gram-negative bacteria."

The ability of bloody coagulation factors to hydrolyse essential lipopolysaccharides in the bacterial cell envelope, suggests they may potentially be used to combat Gram-negative bacteria. Examining the

mechanism further, the authors showed that the coagulation factors act on the bacteria via light chains—one of two domains of the proteins. The other domains (heavy chains) have no effect. In cells in the laboratory, the authors showed that treatment of cells of the bacteria *E. coli* with light chains led to clearly observable damage to the bacterial cell envelope initially and almost complete destruction of the cell within four hours.

The authors found that the light chain of coagulation factor VII was effective against all Gram-negative bacterial [cells](#) tested. The light chains, as well as the coagulation factors as a whole, were also shown to be effective in combating *Pseudomonas aruginosa* and *Acetivobacter baumannii* infections in mice. Heavy chains had no effect.

Xu Song said: "None of the known antibacterial agents has been reported to function by hydrolyzing lipopolysaccharides. Identification of the lipopolysaccharide hydrolysis-based antibacterial mechanism, combined with antibacterial features of blood coagulation factors, and the ability to manufacture them on a large scale at relatively low-cost, may offer new and cost-effective strategies for combating the urgent public-health crisis posed by drug-resistant Gram-negative pathogens."

More information: "Coagulation factors VII, IX and X are effective antibacterial proteins against drug-resistant Gram-negative bacteria," *Cell Research* (2019). [DOI: 10.1038/s41422-019-0202-3](https://doi.org/10.1038/s41422-019-0202-3)

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