

How bacteria exploit proteins to trigger potentially lethal infections

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New research by scientists at the University of York sheds light on how bacteria exploit human proteins during infections.

A research team led by Professor Jennifer Potts, a British Heart Foundation Senior Research Fellow in York's Department of Biology, studied how *Staphylococcus aureus*, which can cause life-threatening human infections, attach to two proteins fibronectin and fibrinogen found in human blood.

The human proteins play important roles in clot formation and wound healing and the bacteria appear to exploit them during the process of infection. Scientists had earlier shown that the binding sites for fibrinogen and fibronectin on the *S. aureus* protein FnBPA appear to "co-operate" in causing the dangerous [heart](#) infection infective endocarditis and the latest research suggest how the process occurs. The researchers, who included Vaclav Stemberk and Dr Richard Jones at York and Dr Ruth Massey, a microbiologist at the University of Bath, used X-ray crystallography, biophysical techniques and bacterial assays to investigate the process.

In research published in the *Journal of Biological Chemistry*, they solved the three dimensional structure of the bacterial protein FnBPA in complex with a small part of the human protein fibrinogen. This work showed that the fibrinogen binding site on FnBPA is close to, but not overlapping with, the binding site for fibronectin.

They then studied the binding of the two human proteins simultaneously to FnBPA and found that binding of fibronectin appears to block binding of fibrinogen to the bacterial protein. It appears that regulation of binding arises due to the close proximity of the fibrinogen and fibronectin binding sites on the [bacterial protein](#) and the large size of the human proteins. While the research provides the first biophysical evidence in support of the co-operation previously observed in the infection studies, it is still not clear how these two observations are linked. The scientists are planning further studies.

Professor Potts said: "Bacteria have evolved various mechanisms to exploit human proteins to cause infection. Understanding these mechanisms might not only lead to the development of new therapeutics but can also provide important information regarding the normal role of these human proteins in the body."

Dr Sanjay Thakrar, Research Advisor at the British Heart Foundation, which co-funded the study, said: "The bacteria studied can cause a wide range of infections including the potentially fatal heart [infection](#) known as infective endocarditis.

"This study showed how this bacterium interacts with proteins found in our blood, which may give us an insight into how these deadly heart infections occur. This is an important step towards developing new treatments, but more research is needed to fully understand this interaction."

More information: The paper 'Evidence for Steric Regulation of Fibrinogen Binding to Staphylococcus aureus Fibronectin-binding Protein A (FnBPA)' is published in the *Journal of Biological Chemistry*. www.jbc.org/content/early/2014/.../M113.543546.abstract

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