

## Instant immune booster dramatically improves outcome of bacterial meningitis and pneumonia

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Professor Wilhelm Schwaeble and team at University of Leicester. Credit: University of Leicester

A breakthrough study from University of Leicester shows low dose injections of artificial properdin provides substantial protection against septic diseases in mice.

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boosting the <u>innate immune</u> system can have a significant impact on the body's ability to defend itself against life-threatening infections" - Professor Wilhelm Schwaeble from the University of Leicester's Department of Infection, Immunity and Inflammation

Researchers at the University of Leicester have produced an artificial version of a naturally occurring protein, properdin, which has been found to successfully combat bacterial pneumonia and meningitis when tested in mice.

In the new study, published today (24 March) in the online early edition of the journal *Proceedings of the National Academy of Sciences (PNAS)*, the researchers have shown that a booster of the innate immune defence has a profound and immediate effect on the body's ability to clear infections, even when the bacteria have reached the bloodstream.

The study, funded by the Medical Research Council (MRC), found artificially produced properdin (Pn) to be 100 times more efficient at fighting infection than naturally occurring properdin, offering significant protection in mice against *Streptococcus pneumoniae* and *Neisseria meningitidis* infections.

Streptococcus pneumoniae is the leading cause of pneumonia and a major cause of septicaemia and meningitis, responsible for approximately 1.2 million deaths per year globally. *Neisseria meningitidis* causes epidemic bacterial meningitis and septicaemia with a high mortality in children and young adults.

Research lead Professor Wilhelm Schwaeble, Professor of Immunology and Royal Society-Wolfson Research Merit Award Holder from the University of Leicester, explained: "I am really excited about this landmark discovery. We demonstrate that boosting the innate immune system can have a significant impact on the body's ability to defend itself



against life-threatening infections."

An additional benefit of this treatment is that it was shown to effectively neutralise the harmful toxins released by bacteria when they are destroyed. There is a recognised problem with current treatments which can kill bacteria but do not combat the effects of toxic substances inside or released from bacteria, which often prove more harmful than the bacteria itself.

The artificial properdin was shown to kill bacteria by making them 'pop' like balloons in mouse and human blood with massive numbers of meningitis bacteria being directly destroyed following Pn treatment. This method was also tested by the researchers on human blood in the lab where it was found to have a similar combative effect.

Professor Schwaeble added: "What is especially exciting is that the infected mice continued to look healthy and normal after Pn treatment. We feared that the release of meningococcal debris into the bloodstream as a consequence of this treatment could prove to be fatal, however, the fact that treated mice looked healthy after infection indicates that the Pn also has a neutralising effect on the potentially toxic bacterial debris released.

"Next, we will expand our research to investigate other bacterial strains to assess which infectious diseases can be most effectively treated by Pn injections. We are also preparing the human Pn for toxicological studies and hope to see the first in-human trials within the next five years."

Professor David Wynford-Thomas, Pro-Vice Chancellor, Head of the College of Medicine, Biological Sciences and Psychology and Dean of Medicine at the University said: "This work is the latest in a series of high-profile research achievements by Professor Schwaeble's group. It represents an excellent example of what is now often called



'translational' research – the application of basic scientific knowledge to develop novel approaches to the treatment of human disease – which is a key priority of the College of Medicine, Biological Sciences and Psychology at the University of Leicester."

Dr Desmond Walsh, Head of Infections and Immunity at the Medical Research Council, added: "New treatments to combat bacterial infection are sorely needed. This study shows for the first time that enhancing the natural defence mechanisms to bacteria with artificial proteins may be a viable alternative in the fight against bacterial infection.

"The team in Leicester have taken the first steps in demonstrating this exciting approach in animal models and are planning to extend their experiments into humans. Their work is an excellent example of how the basic research the MRC funds can help in the development of new therapies, as well as demonstrating our commitment to tackling the challenges of infectious diseases."

More information: Youssif Mohammed Ali, Azam Hayat, Bayad Mawlood Saeed, Kashif S. Haleem, Saleh Alshamrani, Hany I. Kenawy, Viviana P. Ferreira, Gurpanna Saggu, Anna Buchberger, Peter J. Lachmann, Robert B. Sim, Dimitrios Goundis, Peter W. Andrew, Nicholas J. Lynch, and Wilhelm J. Schwaeble. 'Low-dose recombinant properdin provides substantial protection against Streptococcus pneumonia and Neisseria meningitidis infection' *Proceedings of the National Academy of Sciences* (PNAS):

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