Immunologists unearth key piece of MRSA vaccine puzzle

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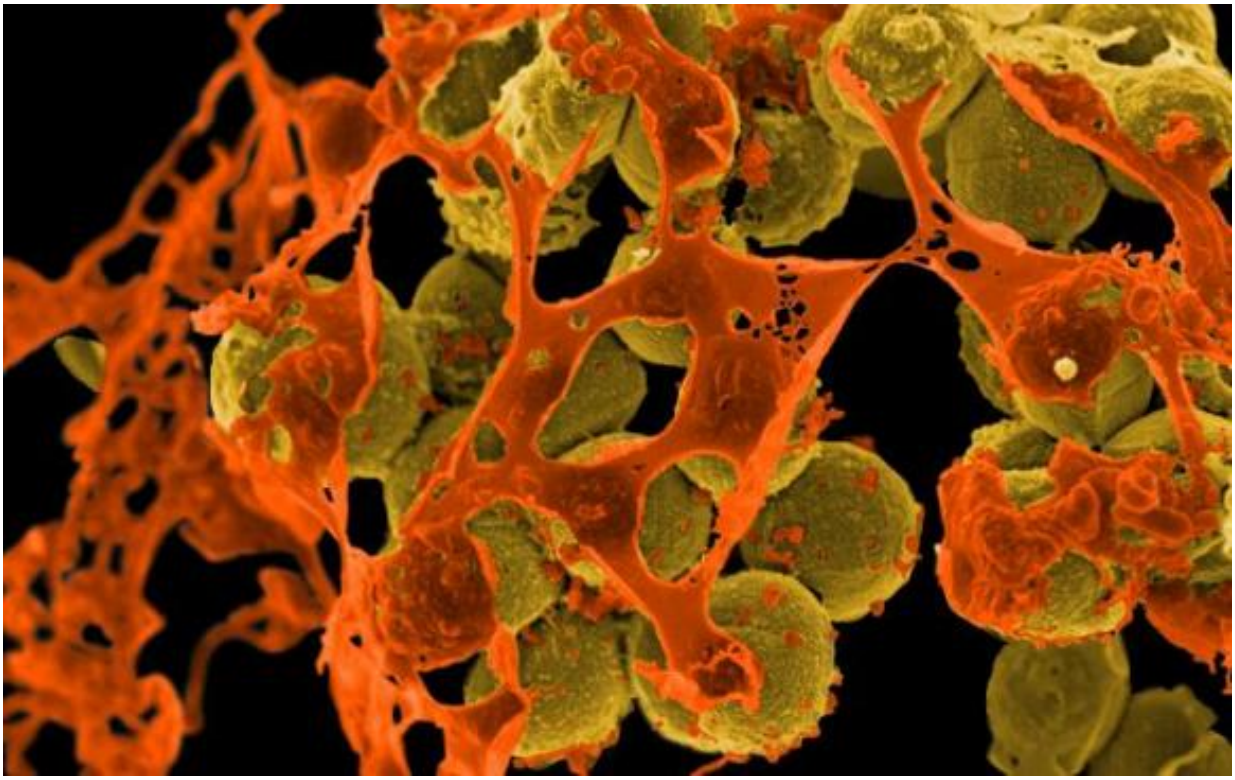

Methicillin-resistant *Staphylococcus aureus*. Credit: NIH/NIAID

Immunologists from Trinity College Dublin have unearthed a key piece of the MRSA vaccine puzzle by identifying specific 'helper' cells whose role in the immune response is critical in affecting infection outcomes.

The immunologists were able to develop a model vaccine, which targeted these 'T-helper type 1' cells, and then showed experimentally that its use led to improved infection outcomes.

Assistant Professor in Immunology at Trinity, Dr Rachel McLoughlin, said: "To design an effective vaccine it is imperative you know how a bacterium interacts with its host. By screening patients with *Staphylococcus aureus* blood stream infections we were able to isolate key players in the immune system that dealt with these infections and then designed a model vaccine that effectively sparked them into action."

The World Health Organisation (WHO) warns of an impending "post-antibiotic era," with the potential to undermine modern medicine. Anti-microbial resistance is a global crisis that demands the development of new antimicrobials, but developing alternatives to antibiotics such as vaccines would prevent infection in the first place.

The bacterium *S. aureus* is a major cause of healthcare-associated infections, and blood stream infections caused by *S. aureus* are associated with significant mortality. Resistance in *S. aureus* to the main antibiotic used for treatment, methicillin, was first reported in the 1960s and, over the past decades, antibiotic resistant *S. aureus*, or MRSA, has become endemic in hospitals throughout the world.

To date, around eight promising candidate vaccines have failed in clinical trials, despite showing promise in pre-clinical models. Traditional approaches to vaccine development have thus failed to develop an effective weapon against MRSA.

We now know that cellular immunity (involving 'T-cells') is vitally important in protection against *S. aureus* infection, because individual T-cell subsets are very important for activating phagocytes - the immune

cells that ingest and kill bacteria.

Dr McLoughlin and her colleagues found that 'T-helper type 1 cells' were elevated in patients following *S. aureus* infection. Their model vaccine, which jolted these cells into action, improved infection outcomes. The results therefore support the design of vaccines that specifically target these cells in humans.

Dr McLoughlin said: "This study demonstrates the importance of truly translational research. Using pre-clinical models we identified an immune mechanism important for protection against *S. aureus* infection, but it was via collaboration with clinicians at three Dublin teaching hospitals that we were able to translate these findings to show the same mechanism of immunity is relevant in human infection. Our findings will directly inform the design of next-gen anti *S. aureus* vaccines and could significantly increase our chances of realizing an effective vaccine to protect patients from MRSA."

More information: *PLOS Pathogens*, dx.plos.org/10.1371/journal.ppat.1005226

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