New tool helps scientist understand how MRSA superbug avoids immune detection

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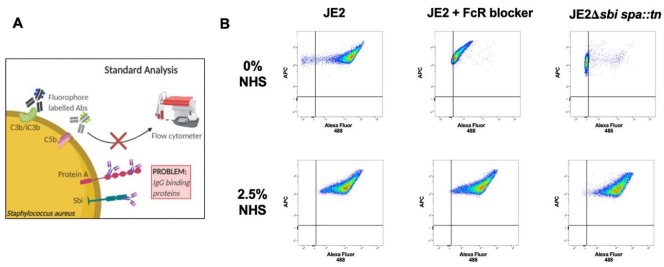

Non-specific binding of antibodies by S. aureus disrupts complement deposition detection by flow cytometry. (A) Schematic of Spa and Sbi interference with flow cytometry, figure created with permission using https://biorender.com/. (B) JE2 and JE2?sbi spa::Tn were grown to exponential phase, incubating with either normal human serum (2.5%) diluted in GVB^{++} buffer or buffer alone (0%). In addition, JE2 was incubated in 0% and 2.5% NHS in the presence of a commercial FcR blocking reagent (1:5). Opsonized bacteria were probed with polyclonal rabbit anti-human C3d and goat anti-rabbit AF488 and geometric mean fluorescence intensity (gMFI) was measured using a BD FACS Canto flow cytometer. Credit: *Scientific Reports* (2022). DOI: 10.1038/s41598-022-20098-7

A tool that promises to throw light on the strategies adopted by MRSA to avoid detection by the body's immune system has been developed at the University of Bath.

The MRSA superbug is notorious for going undetected by the body's immune system, but the mechanisms behind this evasion are poorly understood. Now scientists at the University of Bath have developed a tool that promises to throw light on the pathogen's tactics by tracking a protein produced by the host's body after the protein sticks to the microbe.

By measuring the levels of this protein on the microbe's surface, the tool—developed by Dr. Maisem Laabei and Professor Jean van den Elsen—promises to help researchers understand how the bacterium Staphylococcus aureus causes disease in humans. In time, it may also help them find new ways to boost a person's immune system against deadly Methicillin-resistant Staphylococcus aureus (MRSA) and other "staph" infections.

"Understanding how staph interferes with this protein, along with the immune system's ability to eliminate it from the body, may provide future targets for medical intervention," said Dr. Laabei.

The system that complements the activity of antibodies

The new tool, described in the journal *Scientific Reports*, measures C3—a protein belonging to a part of the immune system known as complement. Complement plays a central role in the body's defense against infection.

When all runs smoothly, the complement system (which includes a group of 50 proteins and protein fragments) springs into action when an invading microbe is first detected. The system enhances (or "complements") the rest of the immune system, surveying the body for intruders, rupturing the cell walls of bacteria and flagging microbes to immune cells, which then go on to eliminate the threat.

All successful pathogens have evolved mechanisms to resist complement, and the more skillful the pathogen is at evading this system, the more potential it has to cause harm to health. S. aureus owns a particularly extensive anti-complement arsenal. As a result, when actors from the complement system land on S. aureus, the cascade of disease-fighting reactions that is supposed to occur on the surface of the pathogen fails to be triggered.

Until now, unpacking the precise sequence of pathogen-led events that blocks complement has been hindered by a lack of tools to accurately

measure C3. The detection method developed in Bath is thought to be the first to give a reliably accurate measurement.

"C3 is essential for a successful immune response, so measuring how much is found on the surface of the microbe provides an important insight into the strategies used by the microbe to prevent complement activation," said Toska Wonfor, the Ph.D. student working on the project.

Damaged organs

A second potential application of the researchers' new tool involves detecting complement activation in people who have experienced organ damage. Complement is mobilized after the body has suffered an interruption of blood flow to an essential organ—say, as a result of an autoimmune disease (e.g. affecting the kidneys), a stroke or a heart attack.

Professor Van den Elsen said: "When the blood starts to flow again, complement is activated, and the damage to an organ can be understood by measuring the deposition of C3 to the tissue.

"As things stand today, you can only get a good indication of the status of a disease by taking an organ biopsy. We hope our tool will give experts a far less invasive way of exploring what has happened in the body."

He added, "We're very excited to see how we can use this tool as an application in the clinic for studying inflammation and autoimmune diseases."

More information: Toska Wonfor et al, Novel method for detecting complement C3 deposition on Staphylococcus aureus, *Scientific Reports* (2022). DOI: 10.1038/s41598-022-20098-7