# How drug-resistant staph paralyzes immune cells

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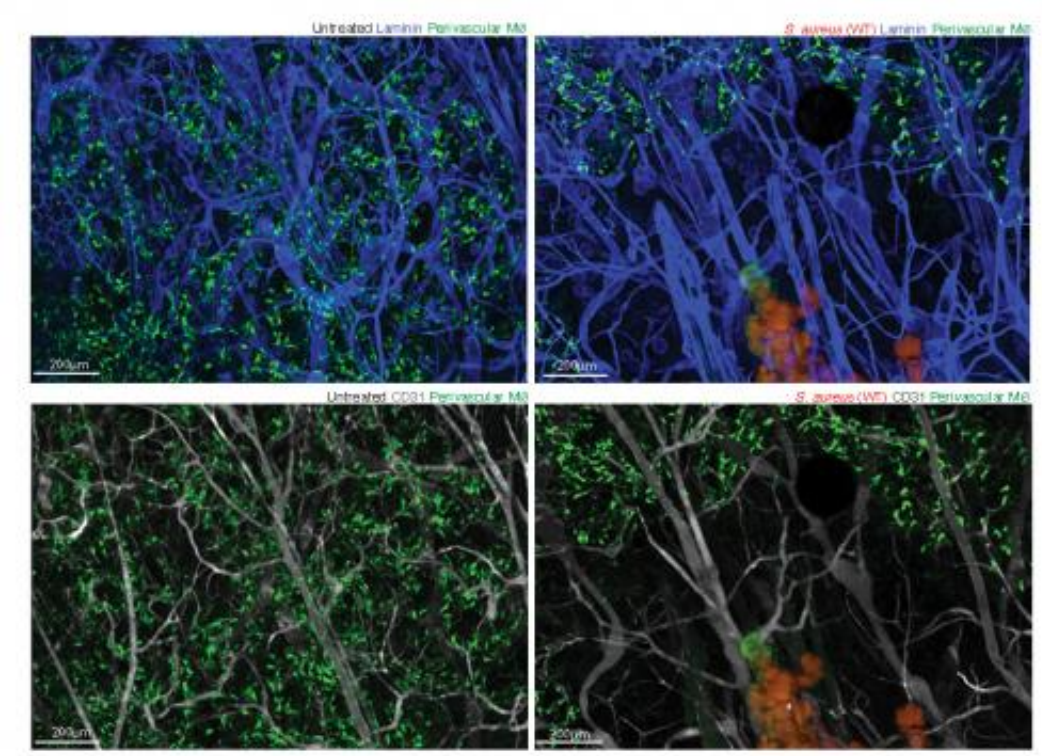


Depletion of macrophages (green cells) after injection of golden staph (orange-red material) into the skin. Credit: Centenary Institute/Nature Immunology

When golden staph enters our skin it can identify the key immune cells and 'nuke' our body's immune response.

Now we know how, thanks to an international research group led by

dermatologists from the Centenary Institute and the University of Sydney.

Using state-of-the art microscopy techniques, the team identified the key immune cells that orchestrate the body's defenders against invading golden staph, and also how the bacteria can target and destroy these cells, circumventing the body's immune response.

Golden staph (*Staphylococcus aureus*) is the multi-drug resistant bacterium that is the scourge of hospitals.

The details of the study have been published today in *Nature Immunology*. It also involved researchers from The Univeristy of Sydney School of Biological Sciences, Monash University, Singapore Immunology Network (A*STAR) and Harvard Medical School.

"Staphylococcus aureus kills many, many people around the world. In fact, more than tuberculosis and AIDS put together. And the skin is its primary entry point into the body, so it important to understand what happens in the skin," says Professor Wolfgang Weninger, Head of the Immune Imaging Research Program at Centenary and coordinator of the study.

Using techniques they have developed over the past decade, the research team was able to mark the different cells of the immune system with fluorescent tags of different colours. They then introduced bacteria labelled with similar coloured tags, and observed the unfolding battle live under a multiphoton microscope.

"We can use such imaging to visualise directly what happens under the skin. It allows us to see both invaders and immune cells at the same time, as well as all the structures in the skin, such as blood vessels, lymphatic vessels and hair follicles," says Professor Weninger.

The initial shock troops of the body's defence against the invading bacteria are immune cells known as neutrophils. They are stored in and launched from small blood vessels. Large immune cells called macrophages are positioned intermittently on the outside of these blood vessels.

The researchers were able to watch as clusters of neutrophils moved out from the blood vessels to fight against the bacteria. About 80 per cent emerged at points close to where macrophages were sitting. The macrophages released proteins which activate the neutrophils and guide them out of the blood vessels, the researchers say.

"But we also found that as soon as the bacteria enter the body, they release a compound called alpha-haemolysin which directly destroys the macrophages, thus disrupting the system that is marshalling the defence forces against them," says Professor Weninger.

This gives the golden staph time to breed up and overwhelm the immune system. In fact, by the time reinforcements arrive, the tissue surrounding the site of infection has begun to die, diverting the immune system into the task of cleaning up the debris.

This study and visualisation of the war against infection and the opening stages of inflammation builds upon earlier studies in which the research group was able to show how dendritic cells, the immune system's sentries, guard against invasion by the protozoan parasite, Leishmania.

Such visualisations are also being used to examine how the operation of the immune system changes over time as the body begins to wear out or age.

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