Staph's activation of blood clotting

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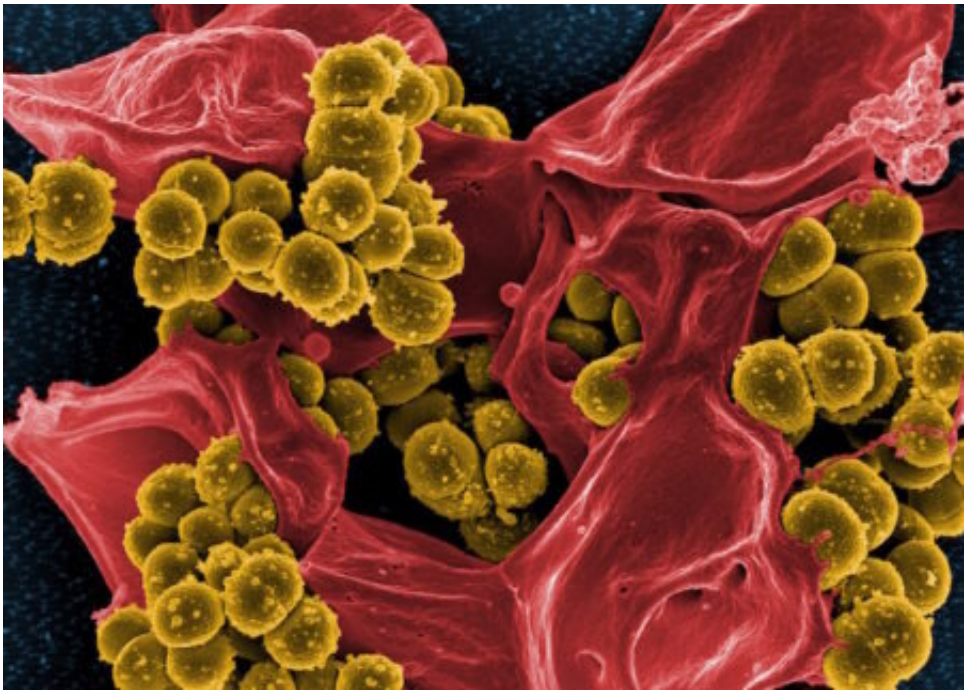

Scanning electron microscopic (SEM) image of Staphylococcus aureus bacteria, enmeshed in a human white blood cell. Credit: NIAID

Acute bacterial endocarditis—infection of the inner lining of the heart—is most often caused by the bacteria Staphylococcus aureus ("staph") and has up to a 40% mortality rate.

Staph bacteria circulating in the blood adhere to heart valves and secrete the virulence factor staphylocoagulase (SC), which activates the clotting factor prothrombin to build clot-like "vegetations" on the valves. A

previous structural study indicated that the first few N-terminal amino acids in the SC protein insert into a pocket of prothrombin.

Ashoka Maddur, Ph.D., Ingrid Verhamme, Ph.D., and colleagues have now characterized a series of SC fragments with changes in the N-terminal amino acids. They found SC variants that activated prothrombin with similar and higher efficiency compared to wild-type SC and defined the structural requirements of the prothrombin binding pocket.

The findings, reported in the *Journal of Biological Chemistry*, suggest that staph might change SC to evade the immune response and could guide efforts to develop antibody therapeutics targeted at SC.

More information: Ashoka A. Maddur et al. Specificity and affinity of the N-terminal residues in staphylocoagulase in binding to prothrombin, *Journal of Biological Chemistry* (2020). DOI: 10.1074/jbc.RA120.012588

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