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Antibody orientation at bacterial surfaces has implications for both mild and severe infections

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Abstract

Several of the most significant bacterial pathogens in humans, including *Streptococcus pyogenes*, express surface proteins that bind IgG antibodies via their fragment crystallizable (Fc) region, and the dogma is that this protects the bacteria against phagocytic killing in blood. However, analysis of samples from a patient with invasive S. pyogenes infection revealed dramatic differences in the presence and orientation of IgG antibodies at the surface of bacteria from different sites. In the throat, IgG was mostly bound to the bacterial surface via Fc, whereas in the blood IgG was mostly bound via fragment antigen-binding (Fab). In infected and necrotic tissue, the Fc-binding proteins were removed from the bacterial surface. Further investigation showed that efficient bacterial IgGFc-binding occurs only in IgG-poor environments, such as saliva. As a consequence, the bacteria are protected against phagocytic killing, whereas in blood plasma where the concentration of IgG is high, the antibodies preferentially bind via Fab, facilitating opsonization and bacterial killing. IgG-poor environments represent the natural habitat for IgGFc-binding bacteria, and IgGFc-binding proteins may have evolved to execute their function in such environments. The lack of protection in plasma also helps to explain why cases of severe invasive infections with IgGFc-binding bacteria are so rare compared with superficial and uncomplicated infections.

Biography

Pontus Nordenfelt has completed his Master of Chemical Engineering and Ph.D. in Biomedicine from Lund University in Sweden and is currently pursuing postdoctoral studies as a Research Fellow at Harvard Medical School in the United States. He has published 14 articles in reputed journals and has received the Nova Prize for best Master thesis and the Anna-Greta Crafoord Prize for best Doctoral thesis. Pontus Nordenfelt is currently holding Fellowships from the Swedish Research Council, the Blanceflor Foundation and the Swedish Society of Medicine.