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IMMUNE EVASION

Size does matter

Bacteria use numerous strategies to resist killing by the host immune system. Dalia and Weiser now add to this list of strategies by revealing that *Streptococcus pneumoniae* avoids complement-mediated killing by minimizing its size (chain length).

Control of *S. pneumoniae* infection involves opsonization of bacteria through the deposition of complement, leading to their recognition and phagocytosis by host neutrophils. *S. pneumoniae* resists this clearance mechanism through its polysaccharide capsule, which masks subcapsular antigens and decreases complement deposition on the bacterial surface. The authors sought to identify additional resistance mechanisms by screening for mutants that were more sensitive to opsonization-mediated killing. They observed that *S. pneumoniae*, which is normally a diplococcus, was more susceptible to killing when it displayed an increased bacterial chain length (which arises from incomplete peptidoglycan cleavage following cell division).

> “*Streptococcus pneumoniae* avoids complement-mediated killing by minimizing its size”

To further dissect the relationship between resistance to killing and bacterial chain length, the authors asked whether increased chain length leads to increased complement deposition and, as a result, increased phagocytosis by neutrophils. Indeed, long-chained mutants were more likely than diplococci to have complement component C3 deposited on their surface and to obtain a ‘focus’ of complement activation that could spread throughout the bacterial chain. As expected, this enhanced susceptibility to complement deposition resulted in increased neutrophil-mediated phagocytosis of long-chained mutants.

So, does the host have a mechanism to overcome this resistance strategy? Antibodies have also been shown to induce the formation of long bacterial chains through agglutination, so the authors examined whether this process can counteract complement evasion. Because antibodies can activate complement directly, the authors incubated bacteria with fragments that cannot interact with the complement system directly, to ensure that any killing observed was caused by agglutination. Fragments that agglutinate bacteria triggered complement deposition and phagocytosis of *S. pneumoniae* by neutrophils, an effect that was not observed with fragments that cannot induce agglutination. This indicates that antibody-mediated agglutination can promote complement-mediated killing of *S. pneumoniae* by increasing the size of bacterial targets.

Finally, the authors confirmed their findings using a mouse model of systemic *S. pneumoniae* infection. Wild-type bacteria (diplococci) significantly outcompeted long-chained mutants *in vivo*. This competitive advantage was dependent on complement activation, as long-chained mutants competed equally with the wild-type bacteria when mice were depleted of complement activity.

Together, these observations indicate that *S. pneumoniae* may minimize its size to resist complement-mediated killing, a finding that may apply to other pathogens that are tagged for clearance by complement. Interestingly, giant forms of other pathogens are also more resistant to phagocytosis, so it seems that, in this context at least, size really does matter.

Rachel David

ORIGINAL RESEARCH PAPER Dalia, A. B. & Weiser, J. N. Minimization of bacterial size allows for complement evasion and is overcome by the agglutinating effect of antibody. *Cell Host Microbe* **10**, 486–496 (2011)

FURTHER READING Serruto, D. *et al.* Molecular mechanisms of complement evasion: learning from staphylococci and meningococci. *Nature Reviews Microbiol.* **8**, 393–399 (2010)