Nature Reviews Microbiology | AOP, published online 21 July 2014; doi:10.1038/nrmicro3329

BACTERIAL PATHOGENESIS

Pneumococci find a sugar daddy in influenza

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Influenza infections are often associated with secondary bacterial pneumonia caused by *Streptococcus pneumoniae*; however, how influenza predisposes the host to pneumococcal colonization was not fully understood. Weiser and colleagues now show that the virus increases the availability of host sialylated mucins in the upper respiratory tract, which promotes pneumococcal growth and spread.

Compared to mice that were infected with pneumococci only, the authors found that prior infection with influenza resulted in increased pneumococcal colonization of the nasopharynx and promoted bacterial spread to the lungs.

> “pneumococcal growth is enhanced by sialic acid catabolism”

The availability of nutrients in the airway following influenza infection was then examined, and the levels of total and free sialic acid, a terminal saccharide on glycoconjugates, were increased. Thus, the authors reasoned that influenza-mediated release of this host metabolite promotes pneumococcal growth. Indeed, influenza-infected mice inoculated with pneumococci mutants that were unable to catabolize sialic acid showed a decrease in colonization compared with mice infected with wild-type bacteria. In addition, secretion of the sialylated airway mucin MUC5AC was increased in influenza-infected mice, and the observed influenza-mediated increase in bacterial replication was attenuated in animals depleted of MUC5AC or treated with a mucolytic agent. Together, these findings suggest that pneumococcal growth is enhanced by sialic acid catabolism and that the availability of host-derived sialylated mucins is promoted by co-infection with influenza.

So, how does influenza increase the availability of sialic acid? Using fluorescence microscopy, the authors showed that influenza desialylates the host mucosal surface, and that this effect was further enhanced following colonization with wild-type pneumococci but not with bacterial mutants lacking neuramidase, an enzyme that removes terminal sialic acid residues from host glycoconjugates. This suggests that both viral and bacterial neuramidases contribute to the desialylation of host substrates. Consistent with this, infection with pneumococci alone increased the levels of sialic acid in the nasopharynx of mice. In summary, these data suggest that pneumococci take advantage of the influenza-mediated increase in host-derived sialylated substrates to promote replication and spread to the lungs. An implication of this study is that, in addition to the antiviral effect, neuramidase inhibitors might have a beneficial effect on secondary bacterial infection.

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ORIGINAL RESEARCH PAPER Siegel, S. J., Roche, A. M. & Weiser, J. N. Influenza promotes pneumococcal growth during coinfection by providing host sialylated substrates as a nutrient source. *Cell Host Microbe* **16**, 55–67 (2014)
FURTHER READING McCullers J. The co-pathogenesis of influenza viruses with bacteria in the lung. *Nature Rev. Microbiol.* **12**, 252–262 (2014)