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Articles of Significant Interest in This Issue

The Obligate Intracellular Bacterium *Orientia tsutsugamushi* Targets NLRC5 To Modulate the Major Histocompatibility Complex Class I Pathway

Intracellular pathogens must counter adaptive immunity. The intracellular bacterium *Orientia tsutsugamushi* infects monocytic and endothelial cells to cause scrub typhus. Whereas monocytes aid in control and dissemination of the bacterium, endothelial cell infection can progress to severe sequelae. Rodino et al. (e00876-18) demonstrate that *O. tsutsugamushi* reduces levels of the major histocompatibility complex class I (MHC-I) transactivator NLRC5 to inhibit MHC-I biosynthesis. This novel strategy of adaptive immunity subversion is more effective in nonprofessional antigen-presenting HeLa and endothelial cells than in professional antigen-presenting monocytes. Therefore, host cell type influences the tug of war between *O. tsutsugamushi* and adaptive immunity, which could shape disease outcome.

Indole Is a ToxR-Dependent Environmental Cue in Toxigenic *Vibrio cholerae*

Indole is a bioactive molecule that is generated through the breakdown of tryptophan by tryptophanase. Many bacteria produce indole, including *Vibrio cholerae*, the etiological agent for the epidemic disease cholera. Although indole is widely distributed in nature, little is known about its biological functions. Howard et al. (e00776-18) demonstrate that indole signaled through the membrane-associated transcription factor ToxR to inversely regulate biofilm and virulence in toxigenic *V. cholerae*. Given that indole is produced at high cell density, these findings suggest that indole could function as a niche-specific signaling molecule that regulates responses during *V. cholerae* pathogenesis.

Subunit-Derived Peptides Inhibit Fimbrial Assembly

Porphyromonas gingivalis possesses adhesive fimbriae that mediate interactions with oral bacteria, abiotic surfaces, and host cells involved in periodontal disease pathogenesis. These fimbriae are assembled entirely on the bacterial surface by a poorly understood mechanism. Alaei et al. (e00750-18) present evidence supporting a donor strand-based assembly mechanism and show that subunit-derived C-terminal peptides can be used to inhibit polymerization and function of the *P. gingivalis* fimbriae. This work builds the foundation for developing highly specific and potent inhibitors of bacterial adhesion, targeting not only *P. gingivalis* but also other species of *Bacteroides* that possess type V fimbriae.

Novel Multiantigen Vaccine Approach for *Streptococcus pneumoniae*

Although the current *Streptococcus pneumoniae* conjugate vaccines based on capsular antigens linked to a carrier protein have been highly successful at reducing disease caused by vaccine serotypes, they are expensive and lead to increases in infections caused by nonvaccine serotypes. Chan et al. (e00846-18) have investigated in preclinical models an alternative vaccine approach based on bacterial lysates termed multiple-antigen vaccines (MAV). MAV lysates were prepared from *S. pneumoniae* cultured under conditions that induce expression of heat shock proteins and using a chromatography step to enrich for surface proteins. Vaccination of mice with MAV successfully induced robust antibody responses to multiple serotypes and protected against pneumonia. In addition, passive transfer of serum from MAV-vaccinated rabbits protected against sepsis caused by both homologous and heterologous *S. pneumoniae* strains. These data suggest that the MAV approach, which has previously completed a successful phase I trial in younger adults, may be able to prevent *S. pneumoniae* infections caused by multiple serotypes.

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