

## SPOTLIGHT

### Articles of Significant Interest Selected from This Issue by the Editors

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#### Gallbladder Bile Is a Nontoxic Environment for Bacterial Growth

Infection of the gallbladder represents a distinct phase of the infectious cycle in specific pathogens (including *Listeria monocytogenes* and *Salmonella enterica* serovar Typhi). Dowd et al. (p. 369–379) show that bile from porcine gallbladders is nontoxic and supports efficient growth of both pathogenic and nonpathogenic bacteria. The group shows that *L. monocytogenes* simply requires a range of common metabolic pathways to grow in this environment and that specific detoxification mechanisms are not required. The work suggests that many bacterial species have the capacity to grow in bile but that growth in the gallbladder is perhaps limited by the ability to reach this environment during infection.

#### The Epithelium Is Actively Involved in Scarring Trachoma

*Chlamydia trachomatis* causes blinding trachoma through a poorly characterized chronic immunofibrogenic process. Burton et al. (p. 499–511), using whole transcriptome analysis, show that the scarring complications of the disease are associated with a chronic inflammatory state characterized by factors likely arising from the epithelium, including *IL-1 $\beta$* , *CXCL5*, and psoriasin (*S100A7*). This supports the “cellular hypothesis” of chlamydial pathogenesis, which suggests that the sequelae are driven largely by the epithelial inflammatory response, with little evidence of T<sub>H</sub>2 response-mediated fibrosis as previously suggested.

#### Meningococcal Complement Factor H-Binding Protein Sequence Variants Differ in Factor H-Binding Affinity without Affecting Survival in Blood

Meningococcal factor H-binding protein (fHbp) binds the complement inhibitor factor H (fH), which enables the organism to evade host defenses. Dunphy et al. (p. 353–359) found large differences in fH-binding affinity of natural fHbp sequence variants expressed by invasive isolates. Isogenic mutants expressing fHbp variants with high or low fH binding showed similar rates of survival in human blood. Immune selection of fHbp variants may tolerate mutations that decrease fH binding without affecting fitness because of the high concentrations of fH in blood, which favor saturation of fH binding over a wide range of binding affinity.

#### Chronic Mold Spore Exposure Provokes a Mixed Th1/Th2/Th17 Response in the Lungs

*Aspergillus fumigatus* is a ubiquitous airborne fungus that can trigger allergic disease in a subset of otherwise healthy individuals. The study by Murdock et al. (p. 125–135) explores a critical gap in our understanding of how immune responses to repeated *Aspergillus* conidium exposure are regulated. The surprising finding in a murine model was that strict polarization of the T cell response in the lungs did not occur. Instead, robust Th1, Th2, and Th17 responses all developed simultaneously. However, as the challenges continued, the Th17 response began to dominate, while the Th2 response leveled off and began to wane.

#### High Throughput Method of Measuring Competitive Index *In Vivo* Using Quantitative PCR

Competitive index experiments compare growth of a parent and a mutant strain within the same infected host and are the most sensitive way to measure virulence, but they require at least one mouse for each strain tested. Yoon et al. (p. 360–368) developed a novel competitive index method that uses quantitative PCR (qPCR) to compare *in vivo* growth of numerous mutants in a single experiment by replacing the coding sequence of a given gene with a unique DNA barcode. This approach was applied to a mixture of 17 *Salmonella* mutants lacking key virulence regulators to compare growth in congenic Nramp1<sup>+/-</sup> mice.

**Novel Staphylococcal Surface Virulence Factor Promoting Resistance to Oxidative Killing and Endocarditis**

*Staphylococcus aureus* is a leading cause of nosocomial and community-associated infections and is implicated in incapacitating endocarditis, toxic shock syndrome, and septicemia. Malachowa et al. (p. 342–352) demonstrate that a novel surface virulence factor (SOK) contributes to the resistance to oxidative killing by neutrophils and vegetation formation at the aortic valve. SOK is a member of the myosin cross-reactive antigen family and is highly conserved in all sequenced *S. aureus* strains, suggesting that SOK plays an important role in cardiovascular and other staphylococcal infections.

**Glutamine Deprivation Debilitates Pathogenic *Streptococcus pneumoniae***

Pathogenic bacteria are highly adapted to their various ecological host niches. To exploit nutrients available in the host, such as carbohydrates, ions, and amino acids, bacteria express ABC transporters. Härtel et al. (p. 44–58) show a solid link between glutamine metabolism and virulence of *Streptococcus pneumoniae*. In spite of the fact that pneumococci express six glutamine uptake systems, a loss of function in GlnHPQ1098/1099 in D39 cannot be compensated by one of the other systems. This result illustrates that a fully avirulent strain is formed due to loss of fitness and that the putative redundant transporters are insufficient to overcome this defect.