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Articles of Significant Interest in This Issue

An Augmented Correlate for *Streptococcus pneumoniae* Serotype Profiling

The latter part of pneumococcal disease progression is accompanied by a shifting gene expression profile, which has been the basis for identifying novel antigenic targets in prophylactic treatment. Hill et al. (e00494-18) present the comparative characterization by RNA-seq and immunofluorescence of a target upregulated protein antigen (PncO), which has been proven effective in vaccine settings for pneumococcal disease. The strong correlation allowed for the adoption of immunofluorescence as a simple means of characterizing lots of biofilm-dispersed pneumococci. These results provide a rapid way to characterize pneumococcal subpopulations, which are gaining recognition in the emerging design of potent and broadly effective vaccines.

A Urine Cytokine and Chemokine Profile (High Interleukin-1β and CXCL1 with Low CCL2) Can Predict Likelihood of Progression from Bladder Colonization to Severe Disease

Urinary tract infections (UTIs) are common health care-associated infections, and prevalence varies with age. However, little is known about the impact of age on disease severity for different bacteria. Armbruster et al. (e00327-18) demonstrate that mature adult mice are better able to control *Proteus mirabilis* and *Escherichia coli* colonization than young or aged mice. Reduced disease severity was associated with high urine levels of interleukin-1β (IL-1β) and CXCL1 and low levels of CCL2, and this was independent of age, infecting bacterial species, or host genetics. This type of profile could contribute to more efficient antimicrobial stewardship by identifying individuals who may not need aggressive treatment.

Limits of Immunotherapy: Checkpoint Blockades Do Not Cure Secondary Infections with Virulent *Toxoplasma gondii* Strains

Checkpoint blockade treatments have had great success reviving exhausted T cells to fight chronic viral infections and tumors. Splitt et al. (e00459-18) test the efficacy of several checkpoint blockade inhibitors in a *Toxoplasma gondii* secondary infection model. They show that such therapies do not significantly ameliorate T cell dysfunction or disease severity elicited by virulent *T. gondii* strains. The findings demonstrate that checkpoint blockade has limited viability as a treatment option for highly virulent *T. gondii* secondary infections.

Pyroptosis Restricts *Brucella* Infection

Canonically, *Brucella* is thought to inhibit host cell death in order to promote its own survival. However, Lacey et al. (e00361-18) show that inflammasomes, and in particular caspase-11, mediate pyroptosis *in vitro* and *in vivo* in response to *Brucella* and that this cell death restricts *Brucella* infection. In addition, while inflammasomes contributed to bacterial clearance, inflammasomes were also found to mediate inflammation at the site of infection. Therefore, a proper level of inflammasome activation which controls infection, while minimizing potentially deleterious inflammation, is likely critical to the outcome of brucellosis.

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Platelets and Dendritic Cells Team Up To Stop *Staphylococcus aureus*

While *Staphylococcus aureus* is typically commensal, once it becomes invasive it is able to effectively evade innate immunity with its ability to persist in neutrophils and macrophages. However, little is known about the contributions of dendritic cells (DCs) to immunity against *S. aureus*. Nishat et al. (e00186-18) demonstrate that release of platelet-derived soluble CD40L contributes to increased phagocytosis and intracellular killing of *S. aureus* by DCs. Stimulation with platelet-derived products also led to increased DC activation (expression of CD80 and release of tumor necrosis factor alpha, interleukin 12 [IL-12], and IL-6). These observations support the premise that platelets are necessary for mounting an effective immune response.

Oh, the Iron-y! Malaria Lends Two Helping Hands

In sub-Saharan Africa, nontyphoidal *Salmonella* (NTS) is a primary cause of bloodstream infections in young children. A strong clinical association between invasive NTS and *Plasmodium falciparum* malaria suggests that underlying malaria compromises control of systemic NTS infections. Lokken et al. (e00301-18) demonstrate that parasite-mediated induction of interleukin-10 (IL-10) dampens macrophage control of invasive NTS. Additionally, elevated circulating heme levels induce higher heme oxygenase-1 activity in macrophages during concurrent parasite infection, facilitating NTS growth by increasing iron availability. These data demonstrate that enhanced IL-10 production and redistribution of iron during parasite infection synergistically dampen control of NTS by macrophages.