Articles of Significant Interest in This Issue

MyD88-Dependent Changes in Host Metabolism Restrict Brucella Infection

While MyD88 signaling is protective against a number of pathogens, how MyD88 alters host metabolism to restrict bacterial infection has not been well studied. During Brucella infection, Lacey et al. (e00156-21) find that MyD88 signaling promotes macrophage glycolysis and that MyD88 deficiency results in an increased availability of glucose in vivo, which Brucella can exploit via the glucose transporter, GluP. MyD88 also promoted production of the metabolite itaconate, which in turn had antibacterial and immunomodulatory effects during Brucella infection.

Neonatal Fc Receptor-Dependent Delivery of IgG Protects against Clostridioides difficile

Amadou Amani and colleagues (e00274-21) use a murine model of Clostridioides difficile disease to demonstrate that subcutaneous vaccine-induced IgG utilizes the neonatal Fc receptor (FcRn) to reach the gut and protect against a live pathogen challenge. FcRn dependency has been debated because intraperitoneal delivery of an IgG bolus bypasses the FcRn and because C. difficile-induced tissue damage in the colon can increase paracellular IgG transport. This study establishes the requirement for FcRn prior to infection-induced tissue damage and may have implications for understanding immunity to C. difficile and for targeting therapeutic antibodies to the gut.

Transcriptomics to Treatments: Targeting TREM-1 in Pertussis

Bordetella pertussis causes the debilitating pulmonary infectious disease whooping cough (pertussis). Ineffective treatment options and increased disease incidence have necessitated the development of novel pertussis therapies. Here, Gallop et al. (e00126-21) identify the triggering receptor expressed on myeloid cells-1 (TREM-1), an amplifier of inflammatory cytokine production, as a checkpoint between beneficial and detrimental pertussis immune responses. TREM-1 inhibition prevented pulmonary immunopathology but did not reduce bacterial control. This work suggests TREM-1 inhibition may be a viable option for the treatment of pertussis disease.

Peroxynitrite Induces Persister Formation in Staphylococcus aureus

Antibiotic-tolerant persister cells contribute to high rates of antibiotic treatment failure during Staphylococcus aureus infection. Prior research suggests that macrophage-derived reactive oxygen species (ROS) stress drives the formation of persister cells during S. aureus bacteremia. Here, Beam et al. (e00286-21) show that peroxynitrite, the reactive product of superoxide and nitric oxide, strongly induces persister formation by collapsing central metabolism. Additionally, peroxynitrite-induced persister formation superseded previously reported bacterial mechanisms underlying antibiotic tolerance. These results suggest that persister formation should be studied in the context of the host environment and that host-targeted therapies to reduce peroxynitrite levels may improve antibiotic efficacy.
Interplay at the Vector-Pathogen-Host Interface Influences the Contribution of a Borrelia burgdorferi Gene to Disseminated Infection

*Borrelia burgdorferi,* the foremost vector-borne bacterial pathogen, is transmitted by the bite of an infected tick and causes Lyme disease, a debilitating multi-tissue infection. *B. burgdorferi* gene *bbk13* is important for spirochete population expansion in the skin driving disseminated infection. Aranjuez et al. (e00216-21) determine that tick bite transmission of *B. burgdorferi* overcame the *bbk13*-dependent defect in the skin. Nevertheless, *bbk13* remained important for productive disseminated infection, likely contributing to evasion of host immune defenses. This work cements the importance of *bbk13* in promoting infection and underscores the significance of the vector as a catalyst of vector-borne pathogen adaptation and pathogenesis.