AMERICAN SOCIETY FOR MICROBIOLOGY | Infection and Immunity

SPOTLIGHT

Articles of Significant Interest Selected from This Issue by the Editors

Cryptococcus Cycles through Multiple Host Cell Types on the Way to Dissemination

The human pathogen *Cryptococcus* usually causes unnoticed infections in the general population but can expand and disseminate to the brain in the immunocompromised host. Davis et al. (p. 3047–3062) used the recently introduced larval zebrafish model of cryptococcosis to track pathogenesis from initial phagocytosis to meningoencephalitis. Using transgenic and mutant zebrafish strains, they found that infecting cryptococcal cells reside within macrophages, neutrophils, and also endothelial cells in a cycle of host cell uptake and release. This cycle maintains a sustained, low-level fungemia that eventually results in infection of the central nervous system.

Experimental Evidence of Human Myocardial Muscle Colonization by *Neisseria meningitidis* following Septicemia

Meningococcal septic shock is associated with profound vasoplegia, early and severe myocardial dysfunction, and extended skin necrosis and represents 90% of fatal meningococcal infections. Associated myocardial septic dysfunction makes the prognosis of the disease. By modifying a previously described humanized mouse model, Bergounioux et al. (p. 3017–3023) demonstrate that, during septicemia, *Neisseria meningitidis* targets the human myocardial tissue vasculature, leading to the formation of blood thrombi, infectious vasculitis, vascular leakage, and myocardial tissue colonization by the bacteria. These results suggest a new mechanism of sepsis-induced cardiac dysfunction in *N. meningitidis* septicemia, a consequence of the direct interaction between the pathogen and the myocardial tissue.

Candida albicans Pathogenesis and Host Immune Response

The damage response framework (DRF) is a concept that defined host damage outcomes as a function of the microbe and the strength of the immune response, with active participation by host indigenous microbiota. *Candida albicans* is a highly adaptable fungal species able to cause an array of infections at various anatomical sites with equally diverse host responses. Based on its various clinical manifestations as a function of host immune status, *C. albicans* arguably fits under each of the classes outlined by the DRF (p. 2724–2739). Animal models have been crucial in highlighting the complexity of *C. albicans* infections and associated host immune responses.

Host Z-DNA Binding Protein Mediates Control of Parasitic Infection

One of the most abundant host transcripts during acute and chronic *Toxoplasma gondii* infection is Z-DNA binding protein 1 (ZBP1). Pittman et al. (p. 3063–3070) determined that *T. gondii* has an increased rate of replication and a decreased rate of degradation in activated macrophages isolated from ZBP1 deletion ($ZBP1^{-/-}$) mice. *T. gondii*-infected $ZBP1^{-/-}$ macrophages display increased proinflammatory cytokines and decreased nitric oxide. $ZBP1^{-/-}$ mice have increased susceptibility to oral challenge, higher cyst burdens during chronic infection, and elevated inflammatory cytokines. These results highlight a role for ZBP1 in assisting host control of *T. gondii* infection.

Anatomical Site-Specific Carbon Availability and Pneumococcal Glycosidase Activity Together Impact Biofilm Formation during Colonization

Blanchette et al. (p. 2922–2932) demonstrate that anatomical site-specific carbon availability, specifically glucose absence and galactose presence, promotes *Streptococcus pneumoniae* biofilm formation during colonization of the nasopharynx. Moreover, neuraminidase A and β-galactosidase A are required for biofilm formation *in vivo*. Biofilm formation *in vitro* was inhibited by sugars inducing carbon catabolite repression (CCR), e.g., glucose. Pyruvate oxidase activity, which drives acetyl coenzyme A (acetyl-CoA) metabolism, was also found to be critical for biofilm formation. Subsequent transcriptome analyses identified pathways downstream of acetyl-CoA metabolism not previously associated with biofilm growth. In summary, carbohydrates act as key environmental signals to *S. pneumoniae* and tie into growth phenotype.

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