



Articles of Significant Interest Selected from This Issue by the Editors

***Acanthamoeba castellanii* Induces Interleukin-12 (IL-12) and IL-6 through MyD88-Dependent, TRIF-Independent, Toll-Like Receptor-Induced Events**

Acanthamoeba castellanii causes severe ocular infections, mostly in contact lens wearers, as well as granulomatous encephalitis in immunocompromised individuals. Although macrophages are acknowledged as playing a role during *Acanthamoeba* infections, the mechanisms accounting for their activation have remained elusive. By using bone marrow-derived macrophages from a series of gene-deficient mice, Cano et al. (e01054-16) demonstrate that *Acanthamoeba* induces macrophage production of interleukin-12 (IL-12) and IL-6 through MyD88-dependent, TRIF-independent, Toll-like receptor 4-induced events. Modulation of these signaling events at the site of infection might not only help control infection but also mitigate exuberant inflammatory responses to this rare but insidious pathogen.

Iron Efflux as a Countermeasure against Oxidative Stress

During infection, group A *Streptococcus* (GAS) deploys orchestrated systems to achieve metal homeostasis, through use of metal-binding proteins, metal acquisition systems, and metal efflux pumps. Iron acquisition is critical for the pathogenesis of infectious microorganisms, including GAS, but the role of iron efflux is less well understood. Turner et al. (e00140-17) have identified PmtA as an iron efflux pump in GAS. PmtA is under the control of the hydrogen peroxide stress regulator PerR and, as such, functions to remove prooxidant ferrous iron from the cytosol during conditions of oxidative stress.

Iron Efflux by PmtA Aids Group A *Streptococcus* Survival during Oxidative Stress

Group A *Streptococcus* (GAS) is a human-only pathogen that causes a variety of disease conditions. Despite the lack of classical bacterial antioxidant defenses, GAS displays the ability to evade host-induced oxidative stress. To elucidate the molecular basis for GAS oxidative stress resistance, VanderWal et al. (e00091-17) investigated the role of PmtA in GAS pathogenesis. They discovered that PmtA is a P_{1B-4}-type ATPase that exports iron from the cytosol. Since the free iron in the cytosol reacts with and potentiates the toxicity of oxidative stressors, iron efflux by PmtA represents an antioxidant defense mechanism that is likely conserved among other streptococci.

Interleukin-10 Regulates Host Susceptibility to Experimental Cerebral Malaria in a *Plasmodium berghei* Infection Model

A balance between pro- and anti-inflammatory responses is fundamental for resolution of malaria infection. Interleukin-10 receptor (IL-10R) signaling is known to attenuate the production of proinflammatory responses, including gamma interferon (IFN- γ), which can induce immune pathology. Claser et al. (e00941-16) sought to test the effect of antibody-mediated blockade of IL-10R in experimental cerebral malaria (ECM)-resistant BALB/c mice during blood stage *Plasmodium berghei* infection. IL-10R blockade resulted in increased CD8⁺ T cell activation, parasite and leukocyte sequestration, brain hemorrhages, and ultimately ECM in susceptible mice. These results underscore the importance of IL-10R signaling in preventing T cell- and cytokine-mediated pathology during lethal malaria infections.