Articles of Significant Interest Selected from This Issue by the Editors

Could a Contraceptive Increase the Severity of Tuberculosis?

The injectable contraceptive depot medroxyprogesterone acetate (DMPA) is the most widely used form of family planning in developing countries, where tuberculosis (TB) is rife. To establish the immune modulatory effect of DMPA in the context of TB, Kleynhans et al. (p. 1234–1244) employ two different murine *Mycobacterium tuberculosis* models. DMPA suppressed cytokine production and led to a significantly higher bacterial burden in the lungs of C57BL/6 mice. The data are consistent with their previous finding in contraceptive users and show for the first time that DMPA can impact TB disease severity. This finding could have major implications for contraceptive policies in countries where TB is endemic.

Survival Tactics of *Candida glabrata* inside the Infected Host

Candida glabrata is the second most common cause of *Candida* bloodstream infections in humans. However, when injected intravenously into mice, it is slowly cleared over several weeks. Fukuda et al. (p. 1325–1333) examine how *C. glabrata* responds and survives within the host by measuring the transcriptional response inside human neutrophils and in infected mouse spleens. The highest responses reflected glucose deprivation and oxidative stress while conserving resources by autophagy and downregulating protein synthesis. While ergosterol synthesis was downregulated, the gene encoding sterol transport was upregulated by 45- to 61-fold in the mouse spleen. These results suggest that *C. glabrata* may be able to utilize mouse cholesterol to replace ergosterol.

Paradox of Resistance to a Pulmonary Fungal Infection

Resistance to paracoccidioidomycosis has been associated with proinflammatory adaptive immunity mediated by gamma interferon-secreting Th1 cells. Using a model of genetic resistance and susceptibility to paracoccidioidomycosis, Pina et al. (p. 1064–1077) demonstrate that resistance is linked to concomitant expansion of immunogenic and tolerogenic dendritic cells (DCs), which secrete high levels of transforming growth factor β and expand increased numbers of regulatory T cells. In contrast, susceptibility is associated with proinflammatory DCs secreting high levels of interleukin-12 and nitric oxide, which induce T cell anergy and severe disease. These data indicate that initial tolerance to a pulmonary fungal infection is less deleterious than excessive proinflammatory innate reactivity.

Enteroaggregative *Escherichia coli*—Not Only a Diarrheagenic Pathogen

Enteroaggregative *Escherichia coli*, an enteric pathogen well-known for causing diarrheal illness, was recently identified as a cause of an outbreak of urinary tract infections (UTIs). Boll and colleagues (p. 1164–1171) demonstrate that these extraintestinal properties are highly attributable to aggregative adherence fimbriae (AAF), as expression of these adhesins facilitates adherence to human bladder epithelial cells and formation of extensive biofilms on urinary tract catheters. Thus, enteroaggregative *E. coli* appears capable of colonizing the urinary tract and causing catheter-associated UTIs. These findings illustrate the need for including enteroaggregative *E. coli* virulence genes in future detection and characterization of uropathogenic *E. coli*.

Phase Variable Alterations in the Amount of Surface Protein Contribute to Immune Evasion

Surface determinants of many bacterial commensals and pathogens are subject to phase variation. Stochastic, high-frequency, and reversible generation of phase variants enables bacterial populations to survive fluctuating selection pressures. Tauseef and colleagues (p. 1374–1380) demonstrate how escape from killing by a bactericidal antibody specific for a major surface protein of *Neisseria meningitidis* is mediated by a mononucleotide repeat tract. This tract is present in the promoter, and alterations in repeat number cause small changes in the amount of this surface protein. These findings indicate how repeat-mediated phase variation could contribute to the ability of meningococci, and other bacterial pathogens, to survive both carriage- and vaccine-elicited immune responses.

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How Does Tissue Damage Contribute to Th2 Immunity during Worm Infection?

Trichinella spiralis is a highly destructive parasitic nematode that invades and destroys intestinal epithelial cells (IECs), injures many tissues during its migratory phase, and occupies and transforms myotubes during the final phase of its life cycle. The alarmin interleukin-33 (IL-33) is a cytokine released by necrotic cells. Scalfone and colleagues (p. 1354–1363) demonstrate that IL-33 concentrates in the nuclei of IECs that are in proximity to migrating worms, a process that occurs in the absence of adaptive immunity. Furthermore, the receptor for IL-33, ST-2, is required for robust Th2 responses during both intestinal and muscle stages of infection.