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Articles of Significant Interest in This Issue

Dynamic Transcriptional Response to Metabolites Maximizes *Salmonella* Fitness through Lactate Utilization

Infection by *Salmonella enterica* serovar Typhimurium is a common cause of bacterial gastroenteritis. *Salmonella* infection perturbs host metabolism with accumulation of L-lactate and oxygen in the lumen of the large intestine. Gillis et al. (e00773-18) found that L-lactate and oxygen induce transcription of the *lldPRD* operon, genes required for lactate utilization. The ArcAB two-component system represses transcription under anaerobic conditions. The transcriptional regulator LldR is required for optimal *lldPRD* transcription and for efficient colonization in mouse models of salmonellosis. This study highlights the necessity for enteric pathogens to sense and respond to changes in the metabolic environment of the host.

Human Enteroids, a Promising Model To Study *Shigella* Pathogenesis

Research efforts to study *Shigella* infection are hindered by the lack of a good model that accurately mimics human disease. Ranganathan et al. (e00740-18) show that infection of human enteroids with *Shigella flexneri* reproduces the established paradigms of infection such as efficient basolateral invasion, increased mucus production, and cytokine responses. Furthermore, they use this platform to investigate early pathogenesis processes such as apical invasion via microfold cells in a human-relevant system. This report details the utility and methodology for using human enteroids to study bacterial pathogenesis and host responses.

Using "Mini-Intestines" To Study *Shigella* Pathogenesis

Shigella species are intracellular pathogens of humans and a major cause of diarrheal disease worldwide. There is no approved *Shigella* vaccine, and *Shigella* studies have been limited by a lack of physiologically relevant host-pathogen model systems. Koestler et al. (e00733-18) demonstrate that many critical aspects of *Shigella* virulence and host response can be recapitulated in intestinal enteroids, which are "mini-intestines" generated through differentiation of stem cells derived from human intestinal biopsy specimens. This study shows that human intestinal enteroids are a viable new model system for investigating *Shigella* pathogenesis.

Titanization of the Fungal Pathogen *Cryptococcus neoformans* Triggers Capsular Rearrangement

The fungus *Cryptococcus neoformans* is a major cause of death among immunocompromised individuals. The elaborate polysaccharide capsule produced by this pathogen is essential for virulence. Probert et al. (e00731-18) use a novel antibody approach to identify a capsular epitope that is redistributed towards the capsule surface as yeast enlarge to form Titan cells, a unique "giant" morphotype believed to be essential for pathogenesis. While Titan cell capsules are known to be structurally distinct from capsules produced by canonical yeast cells, this study identifies a morphotype-specific capsule characteristic that may influence how Titan cells are perceived by the host immune system.

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Pathogenic Fungus *Talaromyces marneffei* Secretes Protein That Targets Arachidonic Acids To Dampen Host Immune Responses

Pathogenic *Talaromyces marneffei* is responsible for talaromycosis, a deadly opportunistic infection among AIDS patients in Southeast Asia during the late 1980s. Lam et al. (e00679-18) combined structural, biophysical, and cell-based methods to demonstrate that the galactomannoprotein antigen Mp1 protein (Mp1p) is a specialized protein that captures arachidonic acid released from the host by the inflammatory response to *T. marneffei* infection. This reduces downstream production of eicosanoids and proinflammatory cytokines. Both ligand-binding domains of Mp1p function independently to bind two arachidonic acid molecules each. These results suggest an intriguing virulence mechanism developed by certain fungi to target and dampen host immune responses.

Helicobacter pylori VacA and Cell Death: How the Extracellular Environment Affects Intracellular Toxin Activity

Helicobacter pylori secretes a pore-forming toxin, VacA, which disrupts host cell functions and contributes to the pathogenesis of gastric cancer and peptic ulceration. However, gastric epithelial cells are relatively resistant to VacA-induced cell death, which occurs only following cellular exposure to high toxin concentrations for long time periods. Foegeding et al. (e00783-18) reveal that gastric cells resist VacA-induced cell death by degrading the toxin and that ammonia, generated in the stomach by *H. pylori* enzymes, enhances VacA toxicity by inhibiting toxin degradation. This work emphasizes that the composition of the extracellular environment can influence the activity of an intracellular bacterial toxin.