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Editorial overview: Host-pathogen interactions: bacteria

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Dr. Karen M Ottemann earned a B.S. from UC Davis in Bacteriology and a Ph.D. in Microbiology and Molecular Genetics from Harvard University, where she studied *Vibrio cholerae* transcriptional regulation and pathogenesis with John Mekalanos. For her postdoctoral fellowship, she focused on *E. coli* and *Salmonella* chemoreceptor signaling with Daniel E. Koshland, Jr. at UC Berkeley. She is currently a Professor in the Department of Microbiology and Environmental Toxicology at UC Santa Cruz, where she has been since 1999. Dr. Ottemann's laboratory focuses *Helicobacter pylori* pathogenesis, bacterial chemotaxis, and the role of bacterial chemotaxis in mammalian colonization.

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This issue presents a series of articles around the topic of how bacteria experience host microenvironments, divided into how and what bacteria sense within hosts, how bacteria respond appropriately, how bacteria remodel and alter their microenvironments, and what factors characterize these microenvironments. This issue will freshly examine the host-pathogen interface with respect to some of the unique niches bacteria encounter, including intracellular vacuoles and tissue microdomains. When bacterial pathogens encounter a host environment, they experience a new signaling situation. We discuss how the host alters bacterial signaling and how bacterial pathogens alter host signaling. Throughout, we include information about new approaches and technologies that enable exciting ways of looking at host-pathogen interactions, allowing an enhanced view of downstream signaling events, as well as more defined information about host niches.

Kicking off the issue is a discussion of an important stress that *Salmonella* must deal with: acid stress. New technological approaches to this question are described by Linda Kenney in her article "**The role of acid stress in *Salmonella* pathogenesis**". A key sensing system is the EnvZ/OmpR two-component regulatory system, which represses the *cadC/BA*system, preventing neutralization of the bacterial cytoplasm. A surprising finding came from the use of single cell techniques to find that the bacterial cytoplasm does acidify, and acidification is used as a signal to drive pathogenesis.

In the cytosolic pathogens *Burkholderia pseudomallei* and *Listeria monocytogenes*, host glutathione regulates virulence. In their article "**Modulation of bacterial virulence and fitness by host glutathione**", Joanne Ku and Yunn-Hwen Gan describe how pathogens use host glutathione as a spatio-temporal cue to modulate virulence through modification of bacterial transcriptional regulators.

Brittany R. Ruhland, and Michelle L. Reniere describe how *L. monocytogenes* senses reactive oxygen species in their homage to Jane Austen's little-known microbiology interest entitled "**Sense and sensor ability: redox-responsive regulators in Listeria monocytogenes**". *L. monocytogenes* uses an impressive five redox-responsive regulators that senses a variety of redox stresses including organic hydroperoxides, peroxides), NAD+/NADH homeostasis, disulfide stress), and infection redox stress.

One key nutrient that bacterial pathogens must obtain is sulfur. Joshua Lensmire and Neal Hammer use their article "**Nutrient sulfur acquisition strategies employed by bacterial pathogens**" to discuss the impressive diversity of strategies pathogens use to scavenge both organic and inorganic sulfur-containing metabolites. They speculate that this range of sulfur gathering abilities will require sophisticated strategies to block as an antibiotic target.

Dr. Linda J Kenney received her PhD in Physiology from the University of Pennsylvania. After a post-doctoral fellowship at Yale University, she changed fields and began studying the EnvZ/OmpR two-component system in the Silhavy laboratory at Princeton University. She was an Assistant and Associate Professor at Oregon Health and Sciences University in Portland, OR. In 2003, she moved to the University of Illinois-Chicago and was promoted to Professor. She has spent the last ten years as a founding member of the Mechanobiology Institute in Singapore. The multi-disciplinary environment has driven the application of single molecule approaches with AFM, super-resolution microscopy, biophysics and biochemistry to the study of two-component signaling and *Salmonella* pathogenesis. At the MBI, she founded the first Women in Science focus group in Singapore and she remains very active in promoting the careers of scientists from under-represented groups.

Leou Ismael Banla, Nita H Salzman, Christopher J. Kristich focus on how *Enterococci* respond to the host environment. These bacteria colonize the mammalian gastrointestinal tract as, harmless inhabitants, but under certain conditions, such as, antibiotic-induced dysbiosis, can cause disease. In their review entitled "**Colonization of the mammalian intestinal tract by enterococci**", the authors describe our understanding of how *Enterococci* can colonize the gastrointestinal tract, including their use of transcriptional reprogramming, the contributions of specific genes, genome plasticity, roles for intra-species, inter-species interactions.

The BvgAS system in *Bordetella* directly activates a large number of virulence genes in response to environmental changes. In the article " **The BvgASR regulon of Bordetella pertussis**", Qing Chen and Scott Stibitz describe additional complexity in this otherwise paradigmatic system. The first is by the action of BvgR, a phosphodiesterase that reduces the levels of cyclic-diGMP. Reduced cyclic-diGMP levels represses a set of key virulence genes call the *vrg* genes. The *vrg* genes are additionally controlled by a non-canonical response regulator, RisAP, which oddly is not phosphorylated by its cognate kinase RisS. During evolution, phosphorylation of RisA has been enhanced by truncation of *risS* in *B. pertussis*, but not in the ancestor *B. bronchiseptica*. The ability to activate the *vrg* genes potentially enhances aerosol transmission of *B. pertussis*.

Once bacteria are inside hosts, they need myriad abilities to colonize and cause disease. Victoria Korolik describes one of these, the ability to carry out directed motility, in her article "**The role of chemotaxis during *Campylobacter jejuni* colonisation and pathogenesis**". Studies with *C. jejuni* have found that a loss of chemotaxis signaling and sometimes even a single chemosensory receptor, can dramatically reduce the ability of *C. jejuni* to colonise various animal hosts and to cause disease. Cutting edge approaches to chemoreceptor ligand identification are also described.

Amit Tuli and Mahak Sharma describe in their paper "**How to do business with lysosomes: *Salmonella* leads the way**" the many ways that *Salmonella* creates its perfect niche, the *Salmonella*-containing vacuole (SCV). The review describes how *Salmonella* effectors target host endocytic trafficking machinery and the factors involved in endosome-lysosome fusion that allow the bacteria to obtain critical nutrients and to replicate.

Tomoko Kubori, Tomoe Kitao, and Hiroki Nagai describe how diverse bacteria are able to modify host ubiquitination in their article "**Emerging insights into bacterial deubiquitinases**". They describe the recent finding that multiple aspects of the host ubiquitin system are targeted by bacterial effector proteins, acting as ubiquitin ligases and deubiquitinases. Bacteria that do this include *Salmonella*, *E. coli*, *Legionella*, *Chlamydia*, *Burkholderia*, and *Xanthomonas*, leading to outcomes such as altered NF-kB signaling and host autophagy.

One way that bacteria can modify their environments is through secretion of effector proteins via secretion systems such as the type three secretion system (T3SS). Kelly A. Miller, Katharine F. Tomberlin and Michelle Dziejman describe such work in their article "***Vibrio* variations on a type three theme**". They report the finding that *Vibrio* spp., including some strains of *V. cholerae*, use T3SSs to influence a variety of host pathways, including modulation of innate immune signaling pathways and actin dynamics, and highlight that there is much more to learn about this process.

Inaya Hayek, Christian Berens, and Anja Lührmann discuss how the bacterial type four secretion system (T4SS) can be used to manipulate host cell metabolism to gain access to nutrients and to regulate specific virulence programs. In their article "**Modulation of host cell metabolism by T4SS-encoding intracellular pathogens**", they discuss specific examples from *C. burnetii* and other intracellular pathogens utilizing a T4SS to gain amino acids, lipids, glucose, and glycerol.

Christina Yang and Karen Ottemann round out the issue by discussing what we know about important microniches in the gastrointestinal tract, the gastric glands and intestinal crypts. In their article "**Control of bacterial colonization in the glands and crypts**", they describe host processes that restrict bacterial colonization in these regions, including the immune system, acid, mucin, oxygen and reactive oxygen species, as well as bacterial adaptations that allow growth in these niches including: bacterial immunomodulatory molecules, chemotaxis, and the use of certain metabolites.