Ingenious strategies of microbial pathogens

Naomi S. Morrissette[a] and Matthias P. Machner[b]
[a]Molecular Biology and Biochemistry, University of California, Irvine, Irvine, CA 92697-3900; [b]Cell Biology and Metabolism Program, Eunice Kennedy Shriver National Institute of Child Health and Human Development, Bethesda, MD 20892

Presentations at the Minisymposium "Pathogens and Parasites" featured the unexpected ways in which pathogens have adapted to their parasitic lifestyles.

Silencing innate immunity

During infection, microbes traverse or invade a variety of biological niches in which they are challenged by the innate immune responses of host cells. **Katherine Owen** (Casanova lab, University of Virginia, Charlottesville) showed that intracellular *Salmonella* escape autophagosomal degradation by activating mTOR through the FAK/Akt kinase pathway. This process requires pathogenicity island 2 (SPI-2), a key virulence system in *Salmonella*. Interference with SPI-2 function or depletion of host cell FAK renders *Salmonella* less capable of evading autophagosomal degradation, protecting mice from otherwise lethal *Salmonella* infections. **Matthias Machner** (National Institutes of Health) described how *Legionella pneumophila* bypasses endolysosomal degradation. *Legionella* produces VipD, a phospholipase A1 that specifically localizes to early endosomes by binding to the host cell GTPase Rab5. The phospholipase activity of VipD alters the lipid and, consequently, protein composition of endosomal membranes, rendering them fusion-incompetent and protecting *Legionella* from degradation. **Andrew Woolery** (Orth lab, UT Southwestern) demonstrated that the *Vibrio parahaemolyticus* protein VopS covalently modifies host cell Rho GTPases with AMP not only to disable the actin cytoskeleton but also to inhibit downstream signaling through several host immune pathways, including NFκB, MAP kinase, the inhibitor of apoptosis proteins (IAP), and the phagocytic NADPH oxidase system (NOX2). All three talks illustrated the critical role of interference with innate immune mechanisms in survival of bacterial pathogens.

Making an entrance, exit, or just passing through

A mechanism that allows *Listeria monocytogenes* to cross the intestinal epithelium emerged from work by Cindy Fevre, presented by **Marc Lecuit** (Institut Pasteur). The authors exploited high-resolution confocal microscopy to study pathogen transit from the gut lumen, using an intestinal organoid model. They showed that *Listeria* translocates through goblet cells by "piggybacking" onto E-cadherin recycling that moves from the apical to the basolateral side of enterocytes. Blocking E-cadherin recycling by pharmacological inhibitors or using protein mutants traps *L. monocytogenes* within goblet cells and prevents its dissemination. **Prabuddha Sengupta** (Lippincott-Schwartz lab, National Institutes of Health) resolved the conundrum of how proteins are sorted and incorporated into budding HIV virus particles. Using state-of-the-art imaging techniques, he showed that the enrichment of host cell proteins within the nascent viral envelope occurs only after oligomerization of the HIV protein Gag at the plasma membrane. Gag oligomerization creates a specialized lipid microenvironment and provides the physical force, through membrane curvature induction, that drives proteins with affinity for an ordered lipid environment into the viral envelope while excluding proteins that prefer disordered membranes.

Doing double duty

The obligate intracellular bacterium *Chlamydia* resides within a membrane-bound vacuole (termed the inclusion body) that is surrounded by a filamentous actin cage believed to stabilize the inclusion. **Marcela Kokes** (Valdivia lab, Duke University) discovered that the protein InaC is necessary for actin assembly at the inclusion. Interestingly, InaC also recruits host Arf GTPases—important regulators of trafficking and organization at the Golgi—to the inclusion, and this process promotes fragmentation of the Golgi ribbon into ministacks that are arranged at the periphery of the inclusion. A second example of resource repurposing was presented by **Naomi Morrissette** (University of California, Irvine). She described the SAS6-like protein, which is similar to SAS6, an essential component of centrioles. SAS6-like is found in a variety of simple eukaryotes that also express SAS-6 and localizes at the base of the axoneme in trypanosomes. Surprisingly, SAS6-like is located at the conoid in *Toxoplasma gondii* zoites, which lack flagella. This suggests that the tubulin-based conoid evolved from flagellar apparatus components.

Diverse pathogens, similar strategies

Collectively, the talks presented in the 2014 "Pathogens and Parasites" Minisymposium illustrate how successful pathogens evade or inactivate innate defense mechanisms and alter pathways and environments to facilitate their growth and survival, often reusing or redirecting pre-existing machinery to best suit their needs.

DOI:10.1091/mbc.E15-01-0011
Molecular Biology of the Cell Volume 26 Page 1007
MBoC is pleased to publish this summary of the Minisymposium "Pathogens and Parasites" held at the 2014 ASCB/IFCB Meeting, Philadelphia, PA, December 7, 2014.
Address correspondence to: Matthias Machner (machnerm@mail.nih.gov).