Cell–pathogen interactions (viruses and bacteria)

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This was a diverse session reflecting the many different mechanisms utilized by viral and bacterial pathogens to modulate and affect host cell biology. The talks and the lively question and answer sessions that followed ranged from discussing the impact of pathogens on generating the optimal cellular milieu for replication and assembly to understanding the host cell antipathogenic response.

Scott Grieshaber (Florida State University) started off the session by describing how *Chlamydia trachomatis* promotes early exit from mitosis in infected cells. This obligate intracellular pathogen targets the spindle assembly checkpoint, which is necessary for organized cell division, by functionally inactivating cyclin B1 and cyclin-dependent kinase 1 via the activity of the chlamydial protease-like activity factor, or CPAF. Infected cells enter prematurely into anaphase, causing an increased rate of DNA tangles and failure of cytokinesis.

David Shifrin (Vanderbilt University) presented evidence for a novel mechanism for battling pathogenic enteric bacteria in which intestinal epithelial cells shed vesicles into the gut lumen. Vesicle shedding is up-regulated by the presence of enteropathogenic and other Gram-negative bacteria. The vesicles are loaded with intestinal alkaline phosphatase, which dephosphorylates and inactivates bacterial lipopolysaccharides. Shifrin also showed that these vesicles directly adhere to the bacterial surface, and this adherence may mediate the observed loss in bacterial adhesion to intestinal epithelial cells and bacterial growth.

Pascale Cossart (Institut Pasteur) showed that the intracellular pathogen *Listeria monocytogenes* causes transient fragmentation of the mitochondrial network early in infection. The secreted, pore-forming toxin listeriolysin O was identified as the main bacterial factor responsible for disruption of the mitochondrial network and for mitochondrial function modulation. Transient disruption of mitochondrial dynamics and function may represent a novel strategy used by pathogenic bacteria to interfere with cellular physiology.

Sandy Simon (Rockefeller University) demonstrated the power of live-cell microscopy in dissecting the assembly of single HIV virions at the plasma membrane. He demonstrated that HIV Gag molecules must be myristoylated for genome recruitment, and these Gag molecules only assemble after engaging the HIV genome. He also showed that budding of HIV from the plasma membrane is mediated by the contemporaneous recruitment of ESCRTIII and VPS4 ATPase, which then dissociate from the nascent virion.

Leigh Knodler (National Institute of Allergy and Infectious Diseases, National Institutes of Health) described a subpopulation of intracellular *Salmonella typhimurium* that hyperreplicates in the cytosol of epithelial cells. Unlike intravacuolar *Salmonella*, these cytosolic bacteria are induced for the invasion-associated type III secretion system and motility. Epithelial cells laden with cytosolic bacteria undergo inflammatory programmed cell death and are extruded out of the monolayer, releasing invasion-primed *Salmonella* and allowing for completion of the infectious cycle. Knodler described a drug-based assay capable of distinguishing cytosolic from vacuolar *Salmonella* that is being used to define bacterial factors that contribute to cytosolic replication.

Nihal Altan-Bonnet (Rutgers University) revealed that many pathogenic RNA viruses, including poliovirus, coxsackievirus, rhinovirus, and hepatitis C virus, rewire the host cell lipid metabolism to generate membrane-based replication platforms that are enriched in both phosphatidylinositol 4-phosphate (PI4P) and cholesterol lipids. She showed that these lipids likely help adhere and assemble the viral replication machinery on the membrane to carry out viral RNA synthesis. Notably, Altan-Bonnet found that these viruses all hijacked members of the host PI4 kinase family to create a pool of PI4P lipids at the replication platforms. In addition, she showed that the host endocytic pathways were rerouted to feed cholesterol to the platforms. Altan-Bonnet went on to discuss the potential of generating therapeutics to target host PI4 kinases as panviral inhibitors of viral replication.

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