

Keynote Presentation



Maria Gloria Dominguez-Bello
Henry Rutgers Professor of Microbiomes and Health, Departments of Biochemistry and Microbiology, and of Anthropology
Importance of the microbiota to infant development

Bacterial populations and communities have coevolved with all eukaryotic life forms on earth. The physiology of all organisms must be wired to develop, tolerate, and respond to microbes. In mammals, natural birth ensures that the infant undergoes a massive exposure to live microbial communities in the maternal vagina, before exposure to the microbes from the environment and from other body sites. Throughout mammalian evolution, the primordial microbes have been passed through generations in a matrilineal way, just like the mitochondria, also of bacterial origin

The last 70 years have witnessed an epidemic increase in immune and metabolic disorders - such as allergies, asthma, type1 diabetes, celiac disease, and obesity - beginning in industrial societies. These diseases are associated with abnormal responses by T- helper and T- regulatory immune

cells. T cells are programmed in early life, and are trained by bacteria. Modern life style is associated with reduced human gut microbiome diversity. Causal relations between the reduction of gut microbiota diversity and the concomitant increases in immune diseases and obesity has not been fully demonstrated, but there is some evidence that supports causality. Epidemiological evidence shows that infants born by C- section or that consume antibiotics early in life are at higher risk of the immune and metabolic diseases of modern societies. Work on mouse models shows that disruption of the early life microbiota increases body weight and fat deposition later in life, increases incidence of allergies, and impairs normal immune development.

The human microbiome is at the same time a “self” co-evolved human entity - consistent with its role in normal human development - and a “non self” composite of microbial genomes amenable to manipulation. We have shown that the abnormal primordial microbiome after C-section can be restored by exposure to the natural microbial compositions during labor and birth. If there is a microbial role in the development of modern diseases, early microbiome restoration would be expected to translate into health restoration; this has not yet been demonstrated.

Presentation Summaries



Katherine Dawson, Environmental Sciences, School of Environmental and Biological Sciences, New Brunswick
Integrating geochemical and molecular biological tools to explore microbial metabolism

While only a small portion of microbial species have been isolated and cultivated, the environment provides a natural laboratory for studying the complex biogeochemical relationships and metabolic networks. Here a transect of naturally occurring deep sea methane seeps are examined with a focus on methane and sulfur cycling. A combination of correlative, co-occurrence, and network analyses reveal several consistent relationships between microbial groups, as well as between microbial composition, geochemistry, and environmental proteome data.



Yana Bromberg, Biochemistry and Microbiology, School of Environmental and Biological Sciences, New Brunswick
Deeper understanding of microbiomes as a benefit of forgetting microbial names

Microbes run the world... but they don't use titles; we give those to them. Focusing on microbial molecular functionality, instead of species names, allows for a better description of microbial and microbiome-ial abilities and similarities. Our novel tools for microbial functional annotations from sequence data highlight the advantages of this approach.



Eric Klein, Biology, Rutgers University, Camden
Tissue stiffness is a physiological regulator of bacterial pathogenesis

Host-pathogen interactions are regulated by a wide variety of environmental factors. While most studies focus on chemical signals, our lab has an interest in how mechanical stimuli modulate bacterial pathogenesis. Using uropathogenic *E. coli* (UPEC) as a model system, I will present our data demonstrating that bladder tissue stiffness is a key physiological regulator of intracellular biofilm formation



Donald Kobayashi, Plant Biology, School of Environmental and Biological Sciences, New Brunswick
Bacterial leaf scorch of oak – emergence of a greater problem in the northeastern United States?

Xylella fastidiosa is a xylem-inhabiting plant pathogenic bacterium known to infect a broad range of host species worldwide. Notable diseases caused by the pathogen include Pierce's disease of grapevine, a continued threat to the wine industry in California; citrus variegated chlorosis, a disease that threatens the citrus industry in South America; and olive quick decline syndrome, a recent epidemic that destroyed ancient olive groves in southern Italy within a two-year period. *X. fastidiosa* has been known for several decades to cause bacterial leaf scorch of oak and other shade trees in the northeastern United States. To date, however, it has not been detected in economically important crops grown in the region, including grapevine, blueberry and peach, each of which serve as hosts for *Xylella*-based diseases in other parts of the country. To gain better insight into the pathogen and disease, we initiated a population genetics study, evaluating pathogen isolates across the northeastern region of the United States. In this presentation, I will discuss results of this study, and the implications of disease spread among current hosts and potential spread to other hosts.



Alvaro Toledo, Entomology, School of Environmental and Biological Sciences, New Brunswick
Cholesterol-rich microdomains in *Borrelia burgdorferi*

Lipid rafts are microdomains present in the membrane of eukaryotic organisms and bacterial pathogens. They are characterized by having tightly packed lipids and a subset of specific proteins. Lipid rafts are associated with a variety of important biological processes including signaling and lateral sorting of proteins. In *Borrelia burgdorferi*, we found that both the inner and outer membranes have cholesterol and cholesterol glycolipids. By fluorescence anisotropy and FRET we determined that lipids from both membranes can form rafts but have different abilities to do so. The analysis of the biochemically-defined proteome of lipid rafts from the inner membrane revealed a diverse set of proteins associated with trafficking, chemotaxis and signaling. The presence of lipid rafts in the inner membrane establishes another layer of biological complexity in fundamental biological processes that could exist in many Gram-negative and prokaryotes with double-membranes.



Daniel S. Pilch, Pharmacology, Rutgers Robert Wood Johnson Medical School, New Brunswick
Development of new antibiotics for the treatment of MRSA infections

Bacterial resistance has emerged as a significant threat to global public health. The World Health Organization (WHO) and the Centers for Disease Control and Prevention (CDC) have identified methicillin-resistant *Staphylococcus aureus* (MRSA) as multidrug-resistant pathogen of particular concern. MRSA results in >80,000 infections and >11,000 deaths per year in the US alone and is associated with billions of dollars in annual healthcare costs. In this talk, I will highlight our recent efforts to develop new antibiotics with a novel mechanisms of action that can be used for the treatment of MRSA infections, including those that have become resistant to current standard - of - care drugs. Our lead agent (TXA709) targets the essential bacterial cell division protein, FtsZ, and exhibits potent *in vivo* efficacy against MRSA when administered intravenously or orally. IND-enabling studies with TXA709 are presently underway.



Chaoyang Xue, The Public Health Research Institute, Rutgers NJ Medical School, Newark
A sugar-coated killer: Inositol utilization in *Cryptococcus* biology and virulence

The human fungal pathogen *Cryptococcus neoformans* is the most common cause of fungal meningitis. However, despite extensive efforts, the mechanism whereby *C. neoformans* crosses the blood-brain barrier (BBB) and causes meningitis remains poorly understood. Our data demonstrate that inositol, an abundant metabolite in the brain, promotes fungal traversal of the BBB and plays a critical role in host-pathogen interactions during infection of the central nervous system (CNS). We show that *C. neoformans* utilizes the inositol stores of its plant niches to complete its sexual cycle. *C. neoformans* is likely to be uniquely adapted to thrive in the inositol-rich environment of the CNS and to utilize inositol-dependent pathways for pathogenesis. Our preliminary results suggest that inositol can promote formation of a unique capsule structure enriched in an M3 mannosyl triad structure reporter group that can help the fungus evade the host immune response. We aim to define inositol sensing and metabolic pathways required for modifying fungal cell surface structure by employing fungal mutagenesis analysis, enzymatic assays, and polysaccharide structural analysis.



Valerie Carabetta, The Public Health Research Institute, Rutgers NJ Medical School, Newark
Does HBsu acetylation regulate nucleoid compaction in *Bacillus subtilis*?

Recently, N^ε-lysine acetylation was realized to be a prevalent bacterial post-translational modification (PTM), contrary to the historical notion that this was a rare occurrence. Acetylation can impact protein function in multiple ways, by modifying conformation, interactions, subcellular localization or activity. Our recent characterization of the *Bacillus subtilis* acetylome revealed hundreds of proteins that are modified by acetylation; these proteins are involved in a broad array of biological contexts, including essential processes such as DNA replication, nucleoid organization, translation, cell shape and central carbon metabolism. Despite the growing recognition that numerous proteins are acetylated, the biological significance of these modifications in *any bacteria* remains largely unknown. I have focused on the highly conserved, essential (in *B. subtilis*) histone-like protein HBsu, which contains seven acetylation sites *in vivo*. I will present evidence that acetylation of critical lysine residues is required for HBsu to control nucleoid compaction. Additionally, I will discuss novel enzymes that may be directly involved in the regulation of HBsu acetylation.



Wei Dai, Cell Biology and Neuroscience and Center for Integrative Proteomics Research, New Brunswick
Visualizing phage maturation by cryo-electron tomography

Cyanobacteria began to convert solar energy and carbon dioxide into bioenergy and oxygen more than two billion years ago. Cyanophages, which infect these bacteria, have an important role in regulating the marine ecosystem by controlling cyanobacteria community organization and mediating lateral gene transfer. I will discuss how we visualize the maturation process of cyanophage Syn5 inside its host cell, *Synechococcus*, using Zernike phase contrast cryo-electron tomography (cryoET). This imaging modality yields dramatic enhancement of image contrast over conventional cryoET and thus facilitates the direct identification of phage assembly intermediates inside the congested cytosol of the infected cell. By correlating the structural features and relative abundance of viral progeny within cells at different stages of infection, we have proposed a morphogenetic pathway that is highly conserved and was probably established long before that of double-stranded DNA viruses infecting more complex organisms.



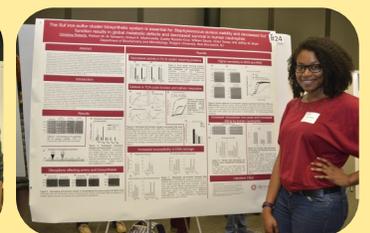
Konstantin Severinov, Waksman Institute of Microbiology, New Brunswick
Adaptive immunity in prokaryotes

CRISPR-Cas adaptive immunity systems are widespread in prokaryotes. Apart from their practical importance for genome editing, there exist interesting fundamental biological questions about the mechanism and evolution of these systems, their roles in shaping prokaryotic genomes and interactions with genetic parasites on a global scale. These questions will be discussed in my talk.



David Dubnau, The Public Health Research Institute, Rutgers NJ Medical School, Newark
How does *Bacillus subtilis* know if it is swimming and why does it care?

Bacterial flagella and the structurally very different eukaryotic cilia function as mechanosensors, often for the regulation of gene expression. In the Gram-positive bacterium *Bacillus subtilis*, the expression of competence for transformation is depressed in mutants with impaired flagella. This effect is mediated by enhanced phosphorylation of the transcription factor DegU and our evidence suggests that the initial signal is viscous load, sensed by rotating flagella. *B. subtilis* undergoes a motile-sessile switch in which the synthesis of flagella may be on or off. This switch may control the probability that a cell will enter the competent state.



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