Plenary Lecture

Dr. Nancy Freitag, University of Chicago, Illinois, USA

Dr. Freitag is a Professor of Microbiology and Immunology, the Associate Director of the Medical Scientist Training Program, and the Assistant Dean of M.D./Ph.D. Education at the University of Illinois at Chicago College of Medicine. Her continuously NIH-funded research focuses on understanding the molecular mechanisms by which pathogenic bacteria interact with mammalian hosts to cause disease as well as the host immune responses that limit infection. Her lab uses a combination of genetic, biochemical, structural, and cell biological techniques as well as animal models to understand the molecular physiology of bacteria inside and outside of the infected host. Dr. Freitag serves as an Editor for the journals *Infection* and *Immunity* and *mBio* and is a standing member of the 'Host Interactions with Bacterial Pathogens' NIH study section. She has mentored scientists at many stages of career development and has received multiple teaching awards. She is a member of the American Academy of Microbiology and has served as an ASM Distinguished Lecturer.

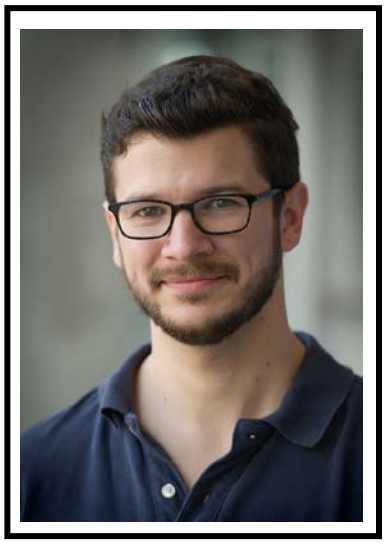
From soil to cytosol: the pathogenic transition of the environmental bacterium *Listeria monocytogenes*

Nancy FREITAG, University of Illinois at Chicago, Illinois, USA

Environmental pathogens are microorganisms that normally spend a substantial part of their lifecycle outside human hosts, but when introduced to humans are capable of causing disease. They exist in the water, soil, air, and food, and they affect almost every individual on the planet. *Listeria monocytogenes* is a ubiquitous bacterium that lives in the environment as a saprophyte but transitions into a pathogen upon ingestion by susceptible individuals. The transition from saprophyte to pathogen is controlled by a transcriptional activator known as PrfA that regulates the expression of multiple gene products required for host infection. PrfA activation influences not only the expression of virulence factors that promote bacterial replication within the cytosol but also serves to increase bacterial fitness within the host through alterations in bacterial physiology. We have recently identified two PrfA-dependent gene products that are essential for *L. monocytogenes* pathogenesis. PrsA2 is a secretion chaperone that regulates the folding and activity of multiple *L. monocytogenes* virulence factors and maintains cell wall integrity during host infection. pPplA is a small peptide pheromone that enables *L. monocytogenes* to sense the confines of host cell vacuoles and escape to the cytosol. These two PrfA-regulated gene products function together to facilitate *L. monocytogenes* adaptation to bacterial life within mammalian cells.

Thermo Fisher Award Recipient

Dr. Andrew Doxey, University of Waterloo, Waterloo, ON



My interests in bioinformatics and microbial genomics started in my undergraduate years (2003) in a summer research project with Drs. Brendan McConkey and Marilyn Griffith at the University of Waterloo. I was tasked with developing a method to predict proteins with ice-binding ("antifreeze") activity. This ultimately led to my Ph.D. work on the computational prediction of protein functions and evolutionary adaptations. I then completed an NSERC postdoctoral fellowship at Stanford University in the lab of Dr. Gill Bejerano, turning my attention to understanding non-coding regulatory sequences and how they work. Following my postdoc, I returned to the University of Waterloo in 2013 as an Assistant Professor to set up my laboratory. My lab's research merges my interests in protein biochemistry with computational genomics, and focuses on genomic data mining, unexplored molecular diversity, and protein function discovery. We have chosen microbial genomes and metagenomes as a central target for data-mining given the vast diversity of uncharacterized sequences (genes and genomes) that exist in the microbial world. We are particularly interested in the discovery of new protein domain families and domain combinations indicative of new biological functionality, and are currently focusing our efforts on bacterial toxins and degradative enzymes involved in bacterial biofilms and host tissue decomposition. My lab is supported by grants from NSERC, MITACs, and an Ontario Early Researcher Award.

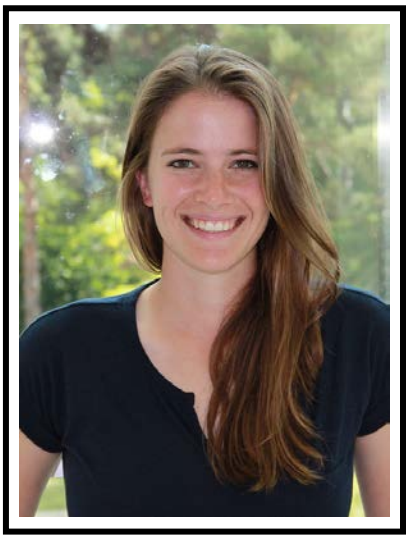
Searching for biological novelty in a sea of genomes: detecting the unexpected

Andrew C. DOXEY, Department of Biology and Cheriton School of Computer Science, University of Waterloo, Waterloo, ON

There are now hundreds of thousands of microbial genomes and metagenomes accessible to any researcher with a computer and internet connection. Encoded within these datasets is a plethora of novel sequences, but interpreting this novelty and placing it within a biological context remains a significant challenge. In this talk, I will describe our work in protein bioinformatics, and the application of function prediction methods to discover new protein families, pathways, and biological functions within public databases. I will highlight three examples of 'unexpected' data-driven predictions made by my lab, and how these predictions have shed light on three areas within microbiology: microbial vitamin B12 production, the evolution of bacterial toxins, and the functional plasticity of bacterial flagella. Key to our approach is the use of multiple bioinformatic methods, including remote homology detection, structural modeling, phylogenetics, and genomic context analysis. By integrating these methods, it is possible to sensitively and accurately predict functions for a substantial fraction of genomic and metagenomic sequences, including many marked as "orphans" or "hypothetical genes" of unknown function. With the further development of these methods, we will increasingly be able to mine genomes and metagenomes for not only known biological functions of interest, but for entirely novel ones as well.

Armand-Frappier Outstanding Student Award Recipient

Ms. Stephanie Jones, McMaster University, Hamilton, ON



Stephanie Jones completed her B.Sc. in Biology at Syracuse University in 2012, and is currently finishing her Ph.D. in the lab of Dr. Marie Elliot at McMaster University. Her research focuses on understanding the growth and development of *Streptomyces* bacteria, known for their antibiotic production capabilities and their complex life cycle. She discovered a novel form of *Streptomyces* development termed exploration, and has been working to characterize the genetic and biochemical factors underlying this form of development. Steph has found exploration involves the cooperation of two cellular growth mechanisms, and alters microbial community dynamics through various competition and communication strategies. Her work in the Elliot Lab has been supported by an NSERC Vanier scholarship. Steph will be starting a postdoc at the Massachusetts Institute for Technology in the lab of Dr. Mike Laub in September 2018, where she will be studying the evolution of chromosome dynamics and toxin-antitoxin systems in bacteria.

Exploring a new mode of bacterial development, communication and competition

Stephanie JONES, McMaster University, Hamilton, ON, MAE ELLIOT[1] [1]McMaster University

Streptomyces are filamentous soil bacteria best known for their antibiotic production capabilities, and their complex life cycle. It had always been thought *Streptomyces* grow solely as static colonies, until we discovered that *Streptomyces* can deviate from their classical life cycle via a novel mode of development termed 'exploration'. Explorer cells are motile and can rapidly transverse a wide range of surfaces, including rocks, plastics, and agar. We investigated the cellular mechanisms underlying this rapid form of colony growth, and discovered that two distinct forms of cell growth, governed by independent cytoskeletal proteins, drive different phases of exploration. Exploring colonies raise the pH of their surroundings using the airborne volatile compound trimethylamine (TMA). Remarkably, exploring colonies can promote exploration by more distantly growing *Streptomyces* using TMA. In addition to its role in *Streptomyces* communication and behaviour modulation, TMA can also act as a competitive tool by reducing the survival of other soil microbes. TMA raises the pH of the surrounding environment, and this impacts nutrient availability. In particular, a rise in pH leads to significantly reduced iron solubility. TMA release by exploring cultures therefore effectively starves other microbes of iron. At the same time, *Streptomyces* explorer cells thrive in this alkaline, iron-depleted environment by secreting iron chelators termed siderophores, and by upregulating siderophore transport clusters. Our work has revealed a novel mode of bacterial development, and has begun to define the molecular and environmental factors underlying this unique developmental system. We have demonstrated for the first time in bacteria, a switch in cell growth mechanisms, from typical growth at the cell poles, to lateral wall-mediated growth. We have further identified a pH-raising volatile compound capable of acting both as *Streptomyces* communication tool and as a weapon against other microbes. Finally, we have shown that volatile compounds can be used to modulate microbial community dynamics, and in the case of TMA, leads to the creation of an iron-depleted environment suitable for *Streptomyces* colonization, but detrimental for the growth of other microbes.

CSM Murray Award for Career Achievement Recipient

Dr. Gregor Reid, Western University and Lawson Health Research Institute, London, ON

Professor Reid is originally from Scotland where he received a BSc Honours in Microbiology at Glasgow University. Under a Rotary International Scholarship he obtained a PhD from Massey University in New Zealand studying *E. coli* pathogenesis in urinary tract infection. Latterly, he obtained an MBA from Monash University in Australia. He was recruited to Canada in 1982 for a post-doctoral fellowship by Dr. Bill Costerton, former student of Dr. Murray. The fellowship project was based in Toronto in collaboration with Dr. Andrew Bruce, Chair of Urology. It was through Dr. Bruce that he began to study the role of lactobacilli in preventing urogenital infection in women. This proved to be a prelude for the human microbiome era and probiotics, two research themes now at the forefront of microbiology. He joined the Department of Microbiology and Immunology, and Surgery at The University of Western Ontario in 1990, and became an Assistant Director at the Lawson Health Research Institute in 1996 where his lab currently resides. His research has so far resulted in 28 patents, 522 publications, over 600 talks in 54 countries, and a Google Scholar H index of 87 with more than 27,400 citations. He has helped create humanitarian programs in Uganda, Tanzania and Kenya that produce affordable probiotic yogurt for over 250,000 people. His efforts have also resulted in the use of probiotics to all but eradicate necrotizing enterocolitis in premature low birth weight babies in London ON. He has been the recipient of an Honorary Doctorate from Orebro University in Sweden, and is an inductee into the Royal Society of Canada and the Canadian Academy of Health Sciences.

Canadian Journal of Microbiology

The fourteen steps to relevance

Dr. Gregor REID, Western University and Lawson Health Research Institute, London, ON

In 1982, I made the decision to follow a different career path by joining a surgical research group in Toronto. The Chair, Dr. Andrew Bruce had observed in 1973 that women who had never suffered from urinary tract infection had lactobacilli as the dominant bacteria in the perineum and urethra, while *E. coli* were heavy colonizers of infected women. Having studied *E. coli* pathogenesis for my PhD, I expected to continue with this line of enquiry. Thankfully, I didn't. This presentation will cover the fourteen steps that I believe changed my scientific path, from the discovery and investigation of *Lactobacillus* species, to defining probiotics and ultimately helping to take the concept around the world. This incredible genus has been part of human evolution, with its fermentation ability utilized to preserve and produce foods of different sorts. But, its emergence as the main genus used as probiotics to confer a range of health benefits, with perhaps as many as one billion doses ingested each week, has placed it in a new light. The question facing us in 1982 was which strains could help prevent UTI and how could they do this? In conveying the answers, using examples from fourteen of my papers, I will feature fourteen colleagues and students whose contributions have been pivotal. The remarkably small 1.3kbp genome of *Lactobacillus iners* provides an example of the species ability to adapt to colonize the vaginal niche, while the capacity of probiotic strains *L. rhamnosus* GR-1 and *L. reuteri* RC-14 to modulate vaginal and intestinal immunity, inhibit pathogenic bacteria and fungi, and counter toxic compounds provides justification for their application to humans. In my view, such applications must reach people in most need, not only those with the financial means and healthcare access. Thus, our initiative in Africa that has empowered thousands of women, men and youth to make probiotic yogurt for over 250,000 people shows the importance of these lactic acid bacteria, and hopefully encourages others to reach out beyond their comfort zone. This includes going beyond science to define the term 'probiotics' for regulators, industry and policy makers, then perform stewardship so the term is not abused, and to educate consumers and healthcare professionals about the scientific and clinical levels of evidence. With a research focus on translation of microbiology to human health, the ultimate test of relevance is whether indeed the use of probiotic strains maintains health and/or prevents disease. Within the confines of limited funding for this field of science, I believe we have done this. When others confirm these findings and themselves create new applications for beneficial microbes, you realize that our wonderful discipline of microbiology is very relevant to life on our microbial planet.