Fisher Award Recipient:

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I first became fascinated with the world of bacteria during a summer work-study program at Ryerson University. Under the guidance of Dr. Debora Foster, I studied how pathogenic bacteria such as enteropathogenic and enterohemorrhagic *E. coli* causedisease in humans. I then obtained my Ph.D. at McGill University, where I elucidated the mechanisms of iron-uptake by Gram-negative bacteria under the supervision of Dr. James Coulton. Through this work I realized how visualizing molecular interactions using microscopy and high-resolution structural techniques could complement and greatly extend conclusions drawn from biochemical and molecular methods. This insight prompted me to become a Visiting Fellow in the lab of Dr. Sriram Subramaniam at the National Institutes of Health. Here we developed cutting-edge cryo-electron microscopy techniques, and combined these with molecular and biochemical methods, to investigate the architecture of receptor complexes involved in bacterial chemotaxis. In 2009 I set up my laboratory at the University of Guelph, where we continue to apply this multidisciplinary approach tostudythe structure and function of protein complexes involved in complex biological processes. We are particularly interested in the macromolecular assemblies that govern bacterial cell division, cell-to-cell interactions, biofilm formation, motility and chemotaxis. Moreover, with the emergence of a growing number of multidrug resistant bacteria there is a pressing need to identify new drug targets. Accordingly, these essential bacterial processes provide a number of exciting candidates.

Uncovering biofilm-specific virulence and antimicrobial resistance mechanisms in *Pseudomonas aeruginosa* using quantitative proteomics

Cezar KHURSIGARA, University of Guelph

Microbial biofilms are particularly resistant to antimicrobial therapies. These surface-attached communities are protected from host defenses and pharmacotherapy by a self-produced matrix.Recent evidence also suggests that some bacteria, including the opportunistic pathogen *Pseudomonas aeruginosa*, undergo modifications within a biofilm that make them uniquely resistant compared to their planktonic (free-living) counterparts. We recently completed a large-scale quantitative proteomics initiative comparing planktonic and biofilm *P. aeruginosa*PAO1 cultures to identify proteins that promote antimicrobial resistance and virulence. We identified 2443 and 1142 high-confidence proteins in *P. aeruginosa* whole cells and outer-membrane vesicles (OMVs), respectively, at three time points during biofilm development. Using this information, we have identified biofilm-dominant metabolic and virulence pathways, and investigated the expression of proteins related to antimicrobial resistance during biofilm development. Most recently, we have used this proteomics database to identify a series of putative β-lactamases that are predominantly expressed in PAO1 biofilms. Furthermore, we determined that many of these β-lactamase genes are conserved and present in multiple copies on the chromosomes of highly β-lactam-resistant clinical isolates, including isolates of the transmissible Liverpool epidemic strain (LES). These studies will increase our understanding of the mechanisms that drive intrinsic biofilm-specific antimicrobial resistance in *P. aeruginosa* and will helps us identify better ways to treat chronic infections.