UNIVERSITY of GUELPH

Graduate Student Opportunity in Microbiology or Biochemistry

ABOUT THE PROJECT

A MSc/PhD graduate student position is available in the laboratory of Dr. Rod Merrill in the Department of Molecular and Cellular Biology in the College of Biological Science

https://www.uoguelph.ca/mcb/people/dr-allan-rod-merrill

The proposed project is in the area of bacterial toxin research. Research in the Merrill laboratory concerns the characterization of the structure and function of bacterial toxins from the mono-ADP-ribosyltransferase (mART) family. The major research objectives in his laboratory are (i) to employ a bioinformatic strategy to discover new members of the mART toxin family that will be characterized both structurally and functionally with a biochemical/biophysical approach; (ii) to identify their biological targets in a yeast model system to provide new insights on host-pathogen interactions; and (iii) to develop potent active-site inhibitors against these toxins as tools for further study and as the basis for future drug discovery and development. A compelling, innovative and alternative approach to antibiotic therapy is the anti-virulence strategy that involves targeting virulence-associated rather than survival/fitness-relevant traits in the offending pathogen. Anti-virulence agents are compounds that disarm bacteria without killing them, thereby allowing the infected host to use its normal immune system defenses to control or remove the infection. The ability to discover and design therapeutics against mART toxins lies in the depth of our understanding of these toxin/enzymes' structures and reaction mechanism. He has developed a **Toxin-Discovery and Characterization Pipeline (TDCP)** strategy that features an initial *in silico* identification of new mART toxins from pathogenic bacteria by bacterial genomic data mining, followed by (1) cell-based validation of mART toxin toxicity against a model eukaryote (yeast), (2) cloning and expression in *E. coli*, followed by FPLC (affinity) purification, (3) target protein capture using biotin-NAD^+ substrate and streptavidin blotting assay coupled with mass spectrometry identification, (4) kinetic characterization of ADP-ribosyltransferase activity, including the mART toxin catalytic signature, (5) cytotoxicity assay for each mART toxin against the relevant mammalian target cell line, including the determination of the toxin LD_{50} against the target cells and (6) structural characterization by X-ray crystallography of each mART toxin with and without substrates and inhibitors complexed within the active-site. His **TDCP strategy** facilitates the discovery and characterization of new toxins as targets for therapeutic intervention to ultimately treat a wide-range of infectious bacterial diseases in plants, animals and man, and it provides a platform for anti-virulence drug discovery and development.

The position is available immediately available and will remain open until filled.

REQUIREMENTS

Independent and self-motivated applicants with strong background in biochemistry and/or microbiology are encouraged to apply. Past laboratory experience (undergraduate research project, volunteering or similar) is an asset.

Date posted: February 13, 2019

This position is open to Canadian citizens or permanent residents.

FUNDING

MSc students in the College of Biological Science are funded at a minimum of $21,259 per year, and the minimum guaranteed duration of support is 6 semesters. For more details regarding funding, see Student Stipend Information.

PhD students in the College of Biological Science are funded at a minimum of $25,259 per year, and the minimum guaranteed duration of support is 12 semesters. For more details regarding funding, see Student Stipend Information.

Depending on eligibility, students may also apply for a wide range of internal and external scholarships. See the full list of available Scholarships and Awards for more information.

INTERESTED in APPLYING?

Interested applicants should submit a CV, unofficial transcript, a letter describing their research interests and career goals, and contact information for two referees to Dr. Merrill (rmerrill@uoguelph.ca).

WHY CHOOSE GUELPH?

The University of Guelph is consistently ranked as one of Canada's top research universities and our faculty attract more research dollars per capita than any other comprehensive university in Canada.

The Department of Molecular & Cellular Biology resides within the College of Biological Sciences and provides a stimulating environment to pursue graduate studies in the molecular biosciences. The department's 40 faculty members direct research programs that involve multidisciplinary approaches to address novel biological questions at the level of organization of molecules to cells. Research in MCB spans a range of important eukaryotic and prokaryotic systems and addresses fundamental and applied research problems.

LOOKING FOR MORE INFORMATION?

Office of Graduate Studies

College of Biological Science

Living in Guelph