

Announcement: The Department of Molecular and Cellular Biology, in the College of Biological Science, invites all interested members of the university community to attend the Final Oral Examination for the degree of **Master of Science** of

BRONWYN LYONS, on Wednesday, July 26, 2017 at 1:00 p.m. in SSC 2315

(Advisor: Dr. Rod Merrill)

Thesis Title: A kinetic and structure-guided characterization of Scabin, a novel mono-ADP-ribosyltransferase produced by *Streptomyces scabies*

Examination Committee:

Dr. A. Nassuth, Dept. of Molecular and Cellular Biology (Chair)

Dr. R. Merrill, Dept. of Molecular and Cellular Biology

Dr. D. Josephy, Dept. of Molecular and Cellular Biology

Dr. S. Graether, Dept. of Molecular and Cellular Biology

Abstract: Mono-ADP-ribosyltransferase toxins are produced by pathogenic bacteria as virulence factors that target important macromolecules in host cells. In a few cases, the cellular target may be DNA. This family of enzymes transfers an ADP-ribose moiety from NAD⁺ to the target macromolecule, leading to an altered function of the target and ultimately host-cell death. A bioinformatics strategy was used to identify Scabin, a mono-ADP-ribosyltransferase from the plant pathogen *Streptomyces scabies*. A detailed kinetic analysis was performed on Scabin, revealing the target as genomic DNA. The crystal structure of Scabin with NADH as a substrate analog was determined, which provided important insights into the active site structure of the enzyme. Residues involved in activity and binding of DNA were identified. Hydrogen-deuterium exchange coupled with mass spectrometry was used to characterize the Scabin·DNA interface, revealing key interacting regions. Understanding the mechanism of Scabin will allow for a more targeted approach in the development of inhibitors against the potentially toxic activity of this enzyme.

Curriculum Vitae: Bronwyn obtained her Bachelor of Science (Honours) in Biochemistry at the University of Guelph in the summer of 2015, and then began her M.Sc. in the Merrill lab that fall.

Awards: NSERC-CGS-Master's (2016); CBS Arthur Richmond Memorial Scholarship (2016)

Publications: Lyons, B., Ravulapalli, R., Lanoue, J., Lugo, M.R., Dutta, D., Carlin, S., and Merrill, A.R. (2016) Scabin, a novel DNA-acting ADP-ribosyltransferase from *Streptomyces scabies*. J. Biol. Chem. **291**, 11198–11215.