UNIVERSITY of GUELPH

COLLEGE of BIOLOGICAL SCIENCE

DEPARTMENT OF MOLECULAR AND CELLULAR BIOLOGY

Announcement: All interested members of the university community are invited to attend the Final Oral Examination for the degree of **Master of Science** of

LISETTE VERZIJLENBERG, on Wed. August 23, 2017 at 9:00 a.m. in SSC 2315
(Advisor: Dr. D. Mosser)

Thesis Title: **Effect of hyperthermia and HSP70 protein overexpression on FOXO3a levels in Acute Lymphoblastic T-cells**

Examination Committee:

Dr. F. Brauer, Dept. of Molecular and Cellular Biology (Chair)
Dr. D. Mosser, Dept. of Molecular and Cellular Biology
Dr. T. Van Raay, Dept. of Molecular and Cellular Biology
Dr. R. Lu, Dept. of Molecular and Cellular Biology

Abstract: Cells that are damaged by hyperthermia are eliminated by apoptosis. Forkhead Box O3a (FoxO3a) is a transcription factor that triggers transcription of pro-apoptotic genes facilitating cell death. Normally FOXO3a associates with 14-3-3 proteins in the cytoplasm and is ubiquitinated and degraded by the proteasome. Turnover of FOXO3a is regulated by Akt-mediated phosphorylation at residues T32, S253, and S315. De-phosphorylation leads to nuclear translocation and transcriptional activation of the apoptotic program. Stress activates an evolutionarily conserved 'heat shock response' producing heat-shock proteins like HSP70, which act as a defense mechanism limiting protein damage and thereby allowing survival of cells exposed to proteotoxic stress. We demonstrated that hyperthermia causes nuclear translocation of FOXO3a which is inhibited in cells expressing HSP70. Additionally, hyperthermia targeted FOXO3a for proteasomal and caspase mediated degradation. Together, these results suggest a mechanism where HSP70 protects cells from cell stress by preventing the nuclear accumulation of FOXO3a and accelerating its destruction.

Curriculum Vitae: Lisette obtained her Bachelor of Science at Laurentian University in 2013. She then began her M.Sc. graduate studies in the lab of Dr. Richard Mosser in September 2014.