



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*

ZANE STEKEL

On Thursday, June 8, 2023 at 9:30 a.m. (online)

Thesis Title: The development of potent and specific inhibitors for Smurf1 and Smurf2

Examination Committee:

Dr. Michael Emes, Dept. of Molecular and Cellular Biology (Exam Chair)
Dr. Ray Lu, Dept. of Molecular and Cellular Biology
Dr. Marc Coppolino, Dept. of Molecular and Cellular Biology
Dr. Shaun Sanders, Dept. of Molecular and Cellular Biology

Advisory Committee:

Dr. Wei Zhang (Advisor)
Dr. Ray Lu

Abstract: E3 ubiquitin ligases catalyze protein ubiquitination by facilitating the transfer and subsequent covalent attachment of ubiquitin to a variety of target substrates. This process is essential for normal cellular functions, making E3s attractive therapeutic targets. The HECT subfamily of E3 ubiquitin ligases are involved in many important biological processes. Two E3 ligases, Smurf1 and Smurf2, are heavily involved in these crucial cellular processes, such as DNA damage response, gene expression, chromatin organization and cell migration/invasion. Developing synthetic modulators of Smurf proteins is of critical importance to better understand their roles in human health and disease.

Recently, a combinatorial structure-based protein engineering strategy has been used to produce ubiquitin variants (UbVs) to manipulate enzymes in the ubiquitination pathway. The goal of this work is to identify potent and specific UbVs to inhibit Smurf proteins. This research will lead to better understanding of Smurf proteins and potentially the development of small-molecule inhibitors and therapeutics targeting Smurf proteins.

Curriculum Vitae: Zane completed his Bachelor of Science (Hons.) in Molecular Biology and Genetics with a minor in Nutritional and Nutraceutical Sciences at the University of Guelph in April 2021. In September 2021, he began his Master of Science program in Molecular and Cellular Biology at the University of Guelph in the lab of Dr. Wei Zhang.

Publications: Stekel Z, Sheng Y, Zhang W. The Multifaceted Role of the Ubiquitin Proteasome System in Pathogenesis and Diseases. *Biomolecules*. 2022 Jul 1;12(7):925. doi: 10.3390/biom12070925.