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 ***Doctor of Philosophy*** *of*

ALEXANDRIA (LEXI) KELLINGTON

on Wednesday, April 24th, 2024 at 9:30 a.m. (SSC 3317)

Thesis Title: A bioinformatic assessment of oxygen-dependent 8-oxoGuanine placement in the human genome

Examination Committee:

Dr. Stephen Seah, Molecular and Cellular Biology (Exam Chair)
Dr. Jim Uniacke, Dept. of Molecular and Cellular Biology
Dr. Krassimir Yankulov, Dept. of Molecular and Cellular Biology
Dr. Lewis Lukens, Dept. of Plant Agriculture
Dr. Lori MacNeil, Dept. of Biological Sciences, Brock University (External Examiner)

Advisory Committee:
Dr. Jim Uniacke (Adv)
Dr. Krassimir Yankulov
Dr. Wei Zhang
Dr. Jonathan LaMarre

Abstract: Culturing cells in the ambient oxygen concentration of 21% (160 mmHg; normoxia) is common practice, despite the knowledge that most mammalian cells exist within the body in oxygen concentrations ranging from 2-12% (15-92 mmHg; physioxia). In tissue culture, cells have healthier physiology in the physioxic range in comparison to normoxia or the lack of oxygen at 1% oxygen (hypoxia). These alternate phenotypes caused by oxygen availability are a result of altered gene expression. One potential oxygen sensitive mechanism that impacts gene transcription does so through oxidized guanine nucleotides within DNA promoters. Recent studies have shown that the oxidization of guanines (8-oxoG) within gene promoters can increase gene expression through the recruitment of base excision repair (BER) proteins. When sequenced, 8-oxoG placement is non-random and promoters are differentially oxidized in normoxia compared to hypoxia. However, it is unclear how physioxia impacts 8-oxoG abundance and placement. Here, genome-wide DNA sequencing reveals that 8-oxoG is oxygen sensitive and that different promoters are oxidized in different oxygen environments. When compared to the epigenetic landscape, 8-oxoG is enriched in heterochromatin and highly correlated with histone modifications and transcription factors that promote heterochromatin formation. In contrast, the 8-oxoG containing promoters that lay outside of heterochromatic regions are correlated with high gene expression when oxidized and require BER proteins for their transcription. This study demonstrates how physioxic gene expression can differ from conventional normoxic cell culture and expands our knowledge of how oxygen regulates genes.

Continued…

Curriculum Vitae: Lexi completed her Bachelor of Science in Biological Sciences with a minor in Anthropology at MacEwan University in Edmonton, Alberta, in 2018. In Fall 2019, she joined the lab of Dr. Jim Uniacke in the MSc program and later in Fall 2020 transferred to the PhD program.

Publications: Judge, KA., Smith, BE., Ohlmann Chan, S., Steckler, D., Kellington, AT., Cade, WH. The evolution of weaponry and aggressive behaviour in field crickets. Evolution. In review.

Awards: Teaching and Career Development Fellowship (2022); DMR Memorial Scholarship (2020-2021).