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*

ANDREW DOLSON

On Thursday, July 18, 2024 at 9:00 a.m. (SSC 1511)

Thesis Title: **Impact of the Histone Chaperone FACT, Rif1p, and Tof1p on the Epigenetic Stability of Variegating Loci in *S. cerevisiae***

Examination Committee:

Dr. Terry Van Raay, Dept. of Molecular and Cellular Biology (Exam Chair)
Dr. Krassimir Yankulov, Dept. of Molecular and Cellular Biology
Dr. Rebecca Shapiro, Dept. of Molecular and Cellular Biology
Dr. George van der Merwe, Dept. of Molecular and Cellular Biology

Advisory Committee:

Dr. Krassimir Yankulov (Advisor)
Dr. Rebecca Shapiro

Abstract: Epigenetic regulation plays a central role in governing genomic integrity and cell fate. One of the main forms of epigenetic regulation is chromatin state, where the euchromatic or heterochromatic forms of chromatin determine the “on”/”off” state of genes. The heritable nature of chromatin ensures the transcription profile faithfully propagates through a cell’s lineage and remains intact over numerous generations. This heritability of transcription profiles maintains cell specialization and is critical in multicellular organisms to compartmentalize organ function and specialization. Conversions in epigenetic state allow for adaptation and diversity, increasing a populations overall fitness. In this thesis, I have examined the link between replication fork pausing and epigenetic conversions at three variegating loci by studying factors believed to be involved in the regulation of paused forks. I have acquired multiple strains with mutations in factors involved in replication-coupled chromatin reassembly and replication fork pausing. I tested the effect of these mutants on epigenetic conversions at the *VIIL t*elomere, *FLO11* and *HML* loci. My study revealed genetic interactions between FACT (Facilitates Chromatin Transcription), Tof1p (a component of the Fork Protection Complex, FPC), CAF-1(Chromatin Assembly Factor 1), and the DNA helicase Rrm3p. My results implicate FACT as a critical factor in epigenetic stability. My studies also showed Rif1p and DDK (Dbf4-Depenedent Kinase) genetically interact and influence gene silencing. These findings further develop our understanding of epigenetic conversions in the context of inherited histone epigenetic marks.

Curriculum Vitae: Andrew completed an Advanced Diploma in Biotechnology from Seneca College in 2019 after which he transferred to the B.Sc. (Hons.) in Molecular Biology and Genetics at the University of Guelph in Fall 2019. He began his M.Sc in Molecular and Cellular Biology in Fall 2022 under the supervision of Dr. Krassimir Yankulov.

Publications: Dolson A, Sauty SM, Shaban K, Yankulov K. Dbf4-Dependent Kinase: DDK-ated to post-initiation events in DNA replication. Cell Cycle. 2021 Nov;20(22):2348-2360. doi: 10.1080/15384101.2021.1986999

Shaban, K., Dolson, A., Fisher, A., Lessard, E., Sauty, S. M., & Yankulov, K. (2023). TOF1 and RRM3 reveal a link between gene silencing and the pausing of replication forks. Current Genetics, 69(4–6), 235–249. https://doi.org/10.1007/S00294-023-01273-3/FIGURES/6