



**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*

KHOLOUD SHABAN

on Wednesday, September 7, 2022 at 1:30 p.m. (online)

Thesis Title: **Replication Fork Pausing and Epigenetic conversions: Novel assays and new links with chromatin assembly factors CAF-1 and Asf1p**

Examination Committee:

Dr. Jaideep Mathur, Dept. of Molecular and Cellular Biology (Exam Chair)
Dr. Joseph Yankulov, Dept. of Molecular and Cellular Biology
Dr. George van der Merwe, Dept. of Molecular and Cellular Biology
Dr. Wei Zhang, Dept. of Molecular and Cellular Biology
Dr. Mark Currie, Dept. of Cell and Systems Biology, University of Toronto
(External Examiner)

Advisory Committee:

Dr. Joseph Yankulov (Advisor)
Dr. Rebecca Shapiro
Dr. George van der Merwe
Dr. Bernard Duncker

Abstract: The active or silent state of eukaryotic genes is controlled by heterochromatin or euchromatin structures, which are faithfully transmitted through multiple cycles of DNA replication. Such epigenetic mechanisms guarantee the continuity of tissue-specific gene expression over multiple cell divisions. On the other hand, conversions between the active and silent states of genes (epigenetic conversions) play important roles in cell differentiation or adaptation and are involved in multiple health disorders. We reasonably well understand the transmission and the maintenance of chromatin structure. However, the mechanisms of epigenetic conversions remain poorly understood. In my research, I have studied the link between DNA replication, and specifically the pausing of the replication fork, with gene silencing and epigenetic conversions.

I have generated a novel drug-free assay for measuring gene silencing and epigenetic conversions at the *VIII* telomere and *FLO11* loci. I have used this assay to study the genetic interactions between major factors involved in replication-coupled chromatin reassembly and replication fork pausing factors. I have also used another assay to study gene silencing at the *HML α* silent locus. My study revealed diverse genetic interactions between CAF-1 (Chromatin assembly factor), Asf1p histone chaperone, the component of the Replication fork Protection complex Top1p and the replicative helicase Rrm3p. These findings have expanded our understanding of the mechanisms of epigenetic conversions that work in the context of the mechanisms for inheritance of epigenetic marks.

My thesis provides strong evidence for the dependence of epigenetic change on the pausing of the replication forks. Continuation of these studies can lead to a major advance in our views on epigenetic inheritance. A solid understanding of epigenetic conversions in a model organism will appeal to the fields of fundamental epigenetics, but also to cancer epigenetics, cell differentiation, and epidemiology.

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Curriculum Vitae: Kholoud completed her B.Sc. (Hons.) with a major in Microbiology and minor in Biochemistry. She got her M.Sc. degree in Medical Microbiology from the University of Kuwait in 2011. She started her Ph.D. degree at the University of Guelph in Dr. Yankulov's lab in September 2017.

Publications: **Shaban K**, Dolson A, Sauty SM, Fisher A, Yankulov K. *TOF1* and *RRM3* reveal a link between gene silencing and the pausing of replication forks. *PLOS Genetics*. 2022. (submitted)

Shaban K, Sauty SM, Fisher A, Cheng A, Yankulov K. 2022. Evaluation of drug-free methods for the detection of gene silencing in *S. cerevisiae*. *Biochemistry and Cell Biology Journal*. 2022. (submitted)

Shaban K, Sauty SM, Yankulov K. Variation, Variegation and Heritable Gene Repression in *S. cerevisiae*. *Frontiers in Genetics*. 2021

Dolson A, Sauty SM, **Shaban K**, Yankulov K. Dbf4-Dependent Kinase: DDK-ated to post-initiation events in DNA replication. *Cell Cycle*. 2021

Sauty SM, **Shaban K**, Yankulov K. Gene repression in *S. cerevisiae*-looking beyond Sir-dependent gene silencing. *Current Genetics*. 2021

Rowlands H, **Shaban K**, Foster B, Proteau Y, Yankulov K. Histone chaperones and the Rrm3p helicase regulate flocculation in *S. cerevisiae*. *Epigenetics & Chromatin*. 2019

Rowlands H, **Shaban K**, Cheng A, Foster B, Yankulov K. Dysfunctional CAF-I reveals its role in cell cycle progression and differential regulation of gene silencing. *Cell Cycle*. 2019

Shaban K, Amoudy H, Mustafa AS. Cellular Immune Responses to Recombinant *Mycobacterium bovis* BCG Constructs Expressing Major Antigens of Region of Difference 1 of *Mycobacterium tuberculosis*. *Clinical and Vaccine Immunology*, 2013.