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*

SONIA EVAGELOU

on Monday, November 5, 2018 at 9:30 a.m. in SSC 3317

Thesis Title: **Investigating the role of DDX28 as a novel regulator of the hypoxic cap-dependent translation initiation complex.**

Examination Committee:

Dr. J. Vessey, Dept. of Molecular and Cellular Biology (Exam Chair)
Dr. J. Uniacke, Dept. of Molecular and Cellular Biology
Dr. R. Lu, Dept. of Molecular and Cellular Biology
Dr. D. Mosser, Dept. of Molecular and Cellular Biology

Advisory Committee:

Dr. J. Uniacke (Adv)
Dr. G. Bag
Dr. R. Lu

Abstract: The most common form of translation initiation in eukaryotes occurs in a cap-dependent manner, which requires the recruitment of the eukaryotic translation initiation factor 4F (eIF4F) to the m^7GTP cap located at the 5' end of all cellular mRNAs. eIF4F is a heterotrimeric protein complex composed of the cap binding factor eIF4E, the RNA helicase eIF4A and the scaffolding protein eIF4G, which together function to initiate cap-dependent translation. However, in response to low oxygen availability (hypoxia), a common feature of several physiological and pathological processes including embryogenesis and cancer, intricate signaling pathways are activated that culminate in eIF4E inhibition. Recently, it was discovered that hypoxic cells are able to utilize an alternate 5' cap binding mechanism, whereby cells switch to the use of the eIF4E homologue, eIF4E2, in order to maintain selective cap-dependent translation of a pool of critical hypoxic mRNAs. While there is currently some understanding of how this non-canonical hypoxic translation initiation complex, termed $eIF4F^H$, is functioning, there is still little known about its composition or its regulation. We have identified the DEAD-box protein family member DDX28 as a novel interactor and negative regulator of the $eIF4F^H$ translation initiation complex. We demonstrate that knocking-down DDX28 results in increased cap-retention of eIF4E2, corresponding with an overall increase in eIF4E2-mediated translation under hypoxia. Additionally, we report that depletion of DDX28 confers a proliferative advantage to cells grown in hypoxic conditions, which we suspect is a consequence of the translational upregulation of subset of hypoxic mRNAs.

Curriculum Vitae: Sonia obtained her Bachelor of Science (Hons.) at the University of Guelph in June 2016, and then began her M.Sc. in the lab of Dr. Jim Uniacke in the fall of the same year.

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SONIA EVAGELOU

Awards:

(2017-18) NSERC Canadian Graduate Scholarship - Masters
(2016-17) Ontario Graduate Scholarship
(2016-17) University of Guelph Graduate Excellence Entrance Scholarship

Publications:

Ho, J.J. D., M. Wang, T. E. Audas, D. Kwon, S. K. Carlsson, S. Timpano, **S. L. Evagelou**, S. Brothers, M. L. Gonzalgo, J. R. Krieger, S. Chen, J. Uniacke, and Stephen Lee. (2016). Systemic reprogramming of translation efficiencies on oxygen stimulus. Cell Reports. *14*, 1293-1300.

Timpano, S., G. Melanson, **S. L. Evagelou**, B. D. Guild, E. J. Specker, and J. Uniacke. (2016). Analysis of cap-binding proteins in human cells exposed to physiological oxygen conditions. J. Vis. Exp. *118*, e55112.