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*

GENYA GORSHTEIN

On Friday, December 17, 2021 at 9:30 a.m. (online)

Thesis Title: **Analysis of β3 integrin function during invadopodia based tumour cell invasion**

Examination Committee:

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

Advisory Committee:

Dr. Marc Coppolino (Advisor)
Dr. Wei Zhang
Dr. Jim Uniacke

Abstract: Invadopodia-based tumour cell invasion involves the formation of F-actin rich protrusions of the plasma membrane that mediate degradation of the extracellular matrix (ECM). Cell adhesion to the ECM is upregulated during the formation of invadopodia through the recruitment of integrins. Integrin attachment to the ECM elicits intracellular signaling pathways that facilitate actin polymerization, matrix metalloproteinase recruitment, cellular migration, and invasion. While β1 integrin has previously been shown to promote invadopodia-based cellular invasion, much remains unknown about the role of β3 integrin during this process. The goal of this study was to investigate the role of β3 integrin during invadopodia formation and cellular invasion. β3 integrin is required for invadopodia formation when β1 integrins are inhibited. Notably, β3 integrins showed high localization at invadopodia under conditions where β1 integrin was inhibited, and dual inhibition of β1 and β3 integrins significantly reduced cellular migration. β3 integrins function to phosphorylate and activate Src kinase and epidermal growth factor receptor (EGFR) to promote invadopodia formation, when β1 integrin is inhibited. The results of this study suggest that β3 integrin activity is upregulated in response to β1 integrin inhibition, and functions to promote invadopodia formation and cellular migration.

Curriculum Vitae: Genya completed her Bachelor of Science in Molecular Biology and Genetics at the University of Guelph in April of 2019 and started her MSc in the lab of Dr. Coppolino in the fall of the same year.

Publications: Gorshtein, G., Grafinger, O., & Coppolino, M. G. (2021). Targeting SNARE-Mediated Vesicle Transport to Block Invadopodium-Based Cancer Cell Invasion. *Frontiers in Oncology*, *11*. https://doi.org/10.3389/FONC.2021.679955

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Grafinger, O. R., Gorshtein, G., Stirling, T., Geddes-McAlister, J., & Coppolino, G. (2021). Inhibition of β1 integrin induces its association with MT1-MMP and decreases MT1-MMP internalization and cellular invasiveness. *Cellular Signalling*, *83*, 109984. https://doi.org/10.1016/j.cellsig.2021.109984

Brasher, MI., Chafe, SC., McDonald, PC., Nemirovsky, O., Gorshtein, G., Gerbec, ZJ., Brown, WS., Grafinger, OR., Marchment, M., Matus, E., Dedhar., S. *(Accepted).* Syntaxin4-Munc18c interaction promotes breast tumor invasion and metastasis by regulating MT1-MMP trafficking. *Molecular Cancer Research*.

Grafinger, O. R., Gorshtein, G., Stirling, T., Brasher, M. I., & Coppolino, M. G. (2020). β1 integrin-mediated signaling regulates MT1-MMP phosphorylation to promote tumor cell invasion. *Journal of Cell Science, 133*. https://doi.org/10.1242/jcs.239152