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*

GREGORY HIGGINS

On Tuesday, December 12, 2023 at 9:00 a.m. (SSC 1511)

Thesis Title: **Investigating the predatory capability of *Bdellovibrio bacteriovorus* towards colorectal cancer oncomicrobes *in vitro***

Examination Committee:

Dr. Melanie Alpaugh, Dept. of Molecular and Cellular Biology (Exam Chair)
Dr. Emma Allen-Vercoe, Dept. of Molecular and Cellular Biology
Dr. Terry Van Raay, Dept. of Molecular and Cellular Biology
Dr. Gisele LaPointe, Dept. of Food Science
Dr. Robert Mitchell, Dept. of Biological Sciences, Ulsan National Institute of Science and Technology (External Examiner)

Advisory Committee:
Dr. Emma Allen-Vercoe (Advisor)
Dr. Cezar Khursigara
Dr. Terry Van Raay
Dr. Kari Dunfield

Abstract: *Bdellovibrio bacteriovorus* is an aerobic bacterium with an obligately predatory lifestyle towards other Gram-negative bacteria. The use of *B. bacteriovorus* in a clinical context has recently been investigated as an alternative to treat infections caused by Gram-negative bacterial pathogens. An emerging hypothesis in colorectal cancer (CRC), one of the most prevalent cancers in Canada, is that certain 'oncomicrobes', including Gram-negative species such as *Fusobacterium nucleatum* and colibactin-producing *E. coli* (*pks*+) strains, may contribute to disease progression. Using *B. bacteriovorus* as a treatment strategy to reduce or eliminate oncomicrobes from the colon may aid in reducing incidence or progression of disease. This thesis aims to understand to what extent *B. bacteriovorus* can predate and interact with CRC oncomicrobes *in vitro*, using both rudimentary co-cultures and complex CRC-derived microbial communities. To expand the library of potential CRC oncomicrobe predators, *B. bacteriovorus* was isolated from geographically-distinct soil samples collected across Canada and assessed for differences in their genomes, morphologies, and predatory capabilities. These *B. bacteriovorus* isolates were largely capable of predating several strains of *F. nucleatum*, and *pks*+ *E. coli in vitro*, as detected by culture-based, electron microscopy, and optimized molecular methods. However, to truly understand *B. bacteriovorus*' applicability as a treatment modality for CRC, predation needs to be evaluated under similar physiological conditions to the human colon. This was conducted with chemostat bioreactor models supporting a defined but complex, CRC-derived microbial community. A *B. bacteriovorus* isolate was inoculated directly into the bioreactor vessel or into harvested bioreactor contents held in batch in an anaerobic chamber. Marker gene sequencing and cell counting were done to assess the abundances of ecosystem taxa. Although the impact of the *B. bacteriovorus* isolate on the composition of the CRC-derived microbial community was minimal, these results provide a foundation in how these experiments

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can be performed. Continuing to assess *B. bacteriovorus* predatory capabilities against *F. nucleatum*, and additional CRC oncomicrobes, in the context of a complex environment in this way will aid in determining the CRC therapeutic potential of *B. bacteriovorus*.

Curriculum Vitae: Gregory completed his Bachelor of Science (Honours) in Biochemistry with a minor in Microbiology, Co-op at the University of Guelph in Fall 2018. He began his Master of Science at the University of Guelph in the lab of Dr. Emma Allen-Vercoe in Summer 2019 and transferred to the PhD in Molecular and Cellular Biology program in Summer 2020.

Awards: Queen Elizabeth II Graduate Scholarship in Science and Technology (2019-2020; 2021-2022); Canada Graduate Scholarship – Master's, CIHR (2020-2021).

Publications: Culturing Human Gut Microbiomes in the Laboratory. Renwick S, Ganobis CM, Elder RA, Gianetto-Hill C, **Higgins G**, Robinson AV, Vancuren SJ, Wilde J, Allen-Vercoe E. Annu Rev Microbiol. 2021 Oct 8;75:49-69.