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*

JAMES GOETZ

On Tuesday, August 15, 2023 at 1:30 p.m. (SSC 2315)

Thesis Title: **Investigating functional interplay among *Escherichia coli* efflux pumps and their contributions to fitness**

Examination Committee:

Dr. Jasmin Lalonde, Dept. of Molecular and Cellular Biology (Exam Chair)
Dr. Georgina Cox, Dept. of Molecular and Cellular Biology
Dr. Stephen Seah, Dept. of Molecular and Cellular Biology
Dr. Matthew Sorbara, Dept. of Molecular and Cellular Biology

Advisory Committee:

Dr. Georgina Cox (Advisor)
Dr. Stephen Seah

Abstract: Bacterial efflux pumps are conserved, widespread active export proteins, many of which can provide multidrug resistance. In diderm bacteria, two different efflux pump structural types — single-component inner membrane efflux pumps and cell envelope-spanning multicomponent systems — cooperatively export antimicrobials with cytoplasmic targets from the cell. These efflux pumps also display a diverse range of physiological functions that have impacts on bacterial metabolism. Harnessing a recently developed efflux platform, which is built upon an extensively efflux-deficient strain of *Escherichia coli*, I explored functional interplay amongst a panel of diverse *E. coli* efflux pumps and investigated the effect of efflux pump gene expression on growth utilizing different sole carbon sources under nutrient-limited conditions. With regards to efflux pump interplay, the expression of two efflux pump-encoding genes from the same structural type did not enhance resistance levels regardless of the antimicrobial compound tested. In contrast, a combination of tripartite efflux systems with single-component pumps that share common substrates provided multiplicative increases to antimicrobial resistance levels. When studying the impact of efflux pumps on fitness under nutrient-limited conditions, efflux deficiency decreased growth when glycerol or fructose was used as the sole carbon source. This growth defect was mitigated by the expression of specific tripartite efflux pumps, but also by supplementation with zinc chloride, suggesting that efflux pumps may play a significant role in metallophore export under nutrient-restricted conditions. In summary, this research identified both interactions between specific efflux pumps and the effects of individual efflux pumps on fitness, suggesting that individual efflux pumps represent complex components of bacterial homeostasis.

Curriculum Vitae: James completed his Bachelor of Science (Hons.) in Microbiology (Co-op) at the University of Guelph in April 2021. He began his Master of Science program in Molecular and Cellular Biology in Dr. Cox's lab in September 2021.

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Awards: Queen Elizabeth II Graduate Scholarship (2022); Canada Graduate Scholarship - Master's (2021).

Publications: **Goetz, J. A**., Kuehfuss, N. M., Botschner, A. J., Zhu, S., Thompson, L. K., & Cox, G. (2022). Exploring functional interplay amongst Escherichia coli efflux pumps. *Microbiology*, *168*(11), 001261.

Teelucksingh, T., Thompson, L.K., Gilbert, S.E., MacNair, C.R., Kuehfuss, N.M., **Goetz, J.A.**, Geddes-McAlister, J., Brown, E.D., and Cox, G. (2022). A genetic platform to investigate the functions of bacterial drug efflux pumps. *Nature Chemical Biology*, *18*(12), 1399-1409.