



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

CAROLINE GANOBIS

On Wednesday, November 30, 2022 at 9:30 a.m. (online)

Thesis Title: Characterizing the mouse gut microbiome and improving mouse gut-derived microbial communities for mouse model studies

Examination Committee:

Dr. Joseph Yankulov, 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. Nina Jones, Dept. of Molecular and Cellular Biology
Dr. Aaron Ericsson, University of Missouri Metagenomics Center (MUMC)
(External Examiner)

Advisory Committee:

Dr. Emma Allen-Vercoe (Advisor)
Dr. Terry Van Raay
Dr. Tami Martino
Dr. Geoffrey Wood

Abstract: Reproducibility of mouse model studies remains a problem amongst researchers. Consequently, characterizing the mouse gut microbiota has become a necessary task. At present, the mouse gut microbiota is largely uncharacterized, both taxonomically and functionally. As such, shaping forces which may influence the gut microbial composition, such as environmental factors, like chow and housing, are not completely understood. In addition, existing mouse models do not completely capture the known complexity and diversity of the mouse gut microbiota. As such, this thesis sought to investigate the hypothesis that there are shared microorganisms within the gut microbiomes of SPF mice despite environmental factors and inclusion of these shared core microorganisms can improve current defined communities used in mouse model studies. To address this, three main objectives were outlined for mouse gut-derived microbial communities from various mouse samples, as well as for evaluating the inclusion of novel isolates within the commonly used defined mouse-derived microbial ecosystem Oligo-Mouse-Microbiota-12 (Oligo-MM¹²). A suitable model system, including the coupling of an *in vitro* bioreactor modeling the mouse colonic environment and microbial communities derived from mouse pellet samples enabled dissection of the microbial communities present within mice and determined which microorganisms are native to the mouse gut and their corresponding functionalities. Though a core microbiome was not uncovered in this study, additional species which were not previously characterized within the mouse gut were discovered. Additionally, *in vitro* investigation of the mouse gut metabolome presented findings highlighting differences in metabolite concentrations between genetic lines while uncovering lactate as a prevalent fermentative product. Finally, the addition of six novel *Muribaculaceae*

isolates to Oligo-MM¹² resulted in an altered metabolic signature that carried an increased number of anti-inflammatory metabolites compared to Oligo-MM¹² alone. Overall, the studies in this thesis have considerably expanded our knowledge of the taxonomic and metabolic profiles of the mouse gut microbiota, and provides groundwork that potentiates improvement of mouse gut-derived microbial communities to be used in mouse model studies.

Curriculum Vitae: Caroline completed her Bachelor of Science (Hons.) at Wilfrid Laurier University in 2015, specializing in Biochemistry. She then started her Master of Science in Molecular and Cellular Biology at the University of Guelph in Summer 2017 under the supervision of Dr. Emma Allen-Vercoe. She transferred to the Doctor of Philosophy program in Winter 2019.

Publications: MacNicol, J.L., Renwick, S., **Ganobis, C. M.**, Allen-Vercoe, E., Weese, J. S., Pearson, W. 2022. “A Comparison of Methods to Maintain the Equine Cecal Microbial Environment In Vitro Utilizing Cecal and Fecal Material.” *Animals*.

Renwick, S., **Ganobis, C. M.**, Elder, R., Gianetto-Hill, C., Higgins, G., Robinson, A., Vancuren, S., Wilde, J., and Allen-Vercoe, E. 2021. “Culturing Human Gut Microbiomes in the Laboratory.” *Annual Reviews in Microbiology*.

Ganobis, C. M., Bayer, G., Philpott, D., Allen-Vercoe, E. 2021. “Defined Gut Microbial Communities: Promising Tools to Understand and Combat Disease.” *Microbes and Infection*.

Ganobis, C. M., M. S. Al-Abdul-Wahid, Renwick, S., Yen, S., Carriero, C., Aucoin, M.G, and Allen-Vercoe, E. 2020. “1D 1H NMR as a Tool for Fecal Metabolomics.” *Current Protocols in Chemical Biology*.

Ganobis, C.M., and Allen-Vercoe, E. 2019. “Developing a Standard of the Murine Gut Microbiome for Murine Models.” Presented at the Anaerobe Virtual Congress, 23 July 2020.

Ganobis, C.M., and Allen-Vercoe, E. “Characterizing the Murine Gut Microbiota.” Presented at the Canadian Society of Microbiology Conference, Sherbrooke, QC, Canada, 12 June 2019.