



**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*

SIMONE RENWICK

on Tuesday, June 7, 2022 at 9:30 a.m. (online)

Thesis Title: **The impact of human milk oligosaccharides on the gut microbiota of infants at risk of type 1 diabetes**

Examination Committee:

Dr. Ray Lu, Dept. of Molecular and Cellular Biology (Exam Chair)
Dr. Emma Allen-Vercoe, Dept. of Molecular and Cellular Biology
Dr. Nina Jones, Dept. of Molecular and Cellular Biology
Dr. Matthew Sorbara, Dept. of Molecular and Cellular Biology
Dr. Steven Townsend, Dept. of Chemistry, Vanderbilt University
(External Examiner)

Advisory Committee:

Dr. Emma Allen-Vercoe (Advisor)
Dr. Nina Jones
Dr. Kevin McCann
Dr. Zeny Feng

Abstract: Shifts in gut microbiota composition have been widely associated with development of type 1 diabetes (T1D), although no specific T1D-promoting species have been consistently identified. Consequently, the functional output of the gut microbiota may be more predictive of T1D progression than its composition. Human milk oligosaccharides (HMOs), which are undigestible, complex carbohydrates, are suspected of having anti-diabetic properties. However, the ability of HMOs to modulate the T1D-associated infant gut microbiota has yet to be characterized. As such, this thesis sought to investigate two hypotheses: (1) the metabolic output of the gut microbiota of T1D-progressors can be distinguished from that of healthy controls; and (2) HMOs can be used to induce beneficial changes to the composition and function of the T1D-associated gut microbiota. To address these hypotheses, the composition and function of microbial communities representing the gut microbiota of three T1D-progressors and four healthy controls were characterized using multi-omics tools following single treatments with pooled HMOs (pHMOs) and 2'fucosyllactose (2'FL), the most common HMO structure used to fortify infant formula. The growth responses of pure cultures of 330 bacterial strains isolated from these communities were also assessed following exposure to pHMOs. Lastly, the HMO structure preferences of the communities and strains were determined. Several T1D-associated taxonomic and functional features were identified, including lower levels of several short-chain fatty acids (SCFAs) and increased secretion of *Alistipes*-derived lipopolysaccharide (LPS). Although communities treated with

pHMOs displayed only mild changes in composition compared to controls, significantly higher concentrations of health-associated metabolites, including various SCFAs, were observed. In contrast, 2'FL continuously yielded results similar to controls. HMOs interacted with a wider diversity of non-*Bifidobacterium* species grown axenically than was previously known. Tested strains displayed a range of HMO structure-based specificities, although a large amount of strain-level heterogeneity was observed in growth responses and HMO structure preferences. Furthermore, strains exhibited differing growth responses to pHMOs depending on culture conditions (monoculture vs. community). Finally, no significant differences were observed in the types of HMO structures utilized by T1D-progressor and healthy communities or strains. Overall, this study has considerably expanded our knowledge of the interactions between the T1D-associated gut microbiota and HMOs.

Curriculum Vitae: Simone completed her Bachelor of Science (Hons) in Biochemistry Co-op at the University of Guelph in Fall 2017. She then began her Doctor of Philosophy in Molecular and Cellular Biology in Summer 2018 under the supervision of Dr. Emma Allen-Vercoe.

Awards: Ontario Trillium Scholarship (2018)

Publications: Ruiz-Rico, M., **Renwick, S.**, Allen-Vercoe, E., Barat, J.M. 2022. *In vitro* susceptibility of human gut microbes to potential food preservatives based on immobilized phenolic compounds. *Food Chemistry*, 378, p.132136.

Renwick, S., Ganobis, C., Elder, R., Gianetto-Hill, C., Higgins, G., Robinson, A., Vancuren, S., Wilde J., Allen-Vercoe, E. 2021. Culturing human gut microbiomes in the laboratory. *Annual Reviews in Microbiology*, 75, pp.49-69.

Ganobis, C., Al-Abdul-Wahid, M.S., **Renwick, S.**, Yen, S., Carriero, C., Aucoin, M.G., Allen-Vercoe, E. 2020. 1D ¹H NMR as a tool for fecal metabolomics. *Current Protocols in Chemical Biology*, 12(3), p.e83

Renwick, S., Allen-Vercoe, E. 2020. Manipulating the gut microbiota. *The Developing Microbiome*, pp.195-215

Ramdath, D., Padhi, E., Sarfaraz, S., **Renwick, S.**, Duncan, A. 2017. Beyond the cholesterol-lowering effect of soy protein: a review of the effects of dietary soy and its constituents on risk factors for cardiovascular disease. *Nutrients*, 9(4), pp. 324

Ramdath, D., **Renwick, S.**, Duncan, A.M. 2016. The role of pulses in the dietary management of diabetes. *Canadian Journal of Diabetes*, 40(4), pp.355-363