Announcement:
All interested members of the university community are invited to attend
the Final Oral Examination for the degree of Doctor of Philosophy of

SANDI YEN

on Wednesday, September 25, 2019 at 1:30 p.m. in SSC 2315

Thesis Title:  Impact of parenteral antibiotic therapy on microbial and metabolic
relationships of the preterm gut microbiome as in vitro community cultures.

Examination Committee:
Dr. R. Lu, Molecular and Cellular Biology (Exam Chair)
Dr. E. Allen-Vercoe, Dept. of Molecular and Cellular Biology
Dr. C. Khursigara, Dept. of Molecular and Cellular Biology
Dr. G. Cox, Dept. of Molecular and Cellular Biology
Dr. K. Whiteson, Univ. of California, Irvine (external examiner)

Advisory Committee:
Dr. E. Allen-Vercoe, Co-Advisor
Dr. M. Aucoin, Co-Advisor
Dr. C. Khursigara.
Dr. H. Eberl

Abstract: The progression of preterm infant gut microbiome development is intricately linked with the
development of the infant, such that disruptions to the microbial system can manifest as neonatal
gastrointestinal (NEC) in the infant. Sadly, the urgency to develop treatment strategies for NEC
is driven by the fact that the idopathic disease has a high morbidity (2-7%) and mortality rate (20-50%)
when disease onset occurs. One of the proposed etiologies of NEC is that disease onset occurs when
microbiome development is challenged by an external perturbation, such as antibiotic treatment. The
research conducted in this thesis was motivated by the overarching hypothesis that infant health occurs
when homeostatic microbial relationships have been established. Conversely, when microbiome
development is disrupted, the preterm infant is susceptible to diseases such as NEC. Therefore, the driving
hypothesis of this thesis was that parenteral antibiotic treatment eliminates microbe-microbe
interactions which are imperative for fostering a gut microbiome that is resilient to external
perturbations. This hypothesis was tested using fecal microbiota from two preterm infants with different
antibiotic exposures while in hospital. Propagation of these preterm fecal microbiota in an in vitro
continuous culture system allowed for compositional, metabonomic, culture-based annotation of the
cosystems. Longitudinal analysis of each community revealed that the both communities reached a state of
equilibrium quickly, within the first 5 days. However, when the in vitro communities were challenged
with a course of in vitro antibiotic treatment, differences in each community’s functional capacity was
apparent. The Infant 1 community, which was antibiotic-naive, was able to restore that same steady-state
by 1-2 weeks after antibiotic treatment ended. In contrast, the Infant 2 community (had prior exposure to
antibiotics) was not able to re-gain the same compositional state after antibiotic treatment, nor was it able

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to carry out similar secondary metabolisms. The differences in the two communities’ resilience to antibiotic treatment was attributed to the microbial-microbial relationships in the *in vitro* communities. Strong microbial relationships were prevalent in the Infant 1 community, where examples of trophism were observed between genera. In contrast, the Infant 2 community exhibited very few inter-microbial interactions, and metabolic behaviour was heavily skewed towards protein degradation and fermentation resulting in volatile organic compounds. This work demonstrated that parenteral antibiotic therapy has the potential to disrupt microbe-microbe relationships such that the microbiome is hindered in its ability to function as a cohesive ecosystem. This work, which includes several other studies focused on examining the metabolic capacity of the early gut microbiome, provides groundwork that potentiates development of therapy alternatives that target endogenous microbial relationships to steer the preterm gut ecosystem towards a state of health.

**Curriculum Vitae:** Sandi obtained her Bachelor of Science (Honours) in 2012, and her Masters of Science in 2015, both from the University of Waterloo. In May of 2015, she entered into the Ph.D. program, in the department of Molecular and Cellular Biology, at the University of Guelph, under the supervision of Dr. Emma Allen-Vercoe and Dr. Marc Aucoin.

**Awards:** Ontario Graduate Scholarship for each of 2016, 2017, 2018 and 2019. University of Guelph.

**Publications: Peer-Reviewed**


