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*

ERIN ANDERSON

On Friday, December 9, 2022 at 1:30 p.m. (online)

Thesis Title: **Using peptidoglycomic methodology to examine peptidoglycan composition in *Pseudomonas aeruginosa***

Examination Committee:

Dr. Jaideep Mathur, Dept. of Molecular and Cellular Biology (Exam Chair)
Dr. Cezar Khursigara, Dept. of Molecular and Cellular Biology
Dr. Robert Mullen, Dept. of Molecular and Cellular Biology
Dr. Emma Allen-Vercoe, Dept. of Molecular and Cellular Biology
Dr. Frederic Veyrier, Armand-Frappier Sante Biotechnologie Research Centre (External Examiner)

Advisory Committee:
Dr. Cezar Khursigara (Advisor)
Dr. Robert Mullen
Dr. Anthony Clarke

Abstract: *Pseudomonas aeruginosa* is an opportunistic pathogen, which causes significant and difficult to eradicate infections that can become highly antimicrobial resistant. Understanding the cellular mechanisms behind the high-level resistance is critical for the future production of novel antimicrobial treatments. Peptidoglycan (PG) is an integral component of bacterial cell walls that participates in many cellular functions, is essential for survival, and is a common target for antimicrobials. Aspects of PG structure are fairly conserved across all bacteria. However, there is also considerable variation and numerous modifications in PG that can occur between species and in response to environmental stimuli. Examining a global overview of PG composition would help us understand this complex biopolymer and potentially identify unique mechanisms of antimicrobial resistance. However, conventional methods for analyzing PG composition are difficult and time-consuming. For this thesis, I applied modern bioinformatic techniques to develop a peptidoglycomics workflow and tested the sensitivity by examining two distinct growth morphologies, biofilm and planktonic, that differ in the overall resistance to antimicrobials. Then I used this methodology to examine the PG composition of the *P. aeruginosa* epidemic strains which are highly virulent with enhanced antimicrobial resistance. In addition, I examined the effect of nutritional conditions on PG composition. Overall, I demonstrate that my peptidoglycomics workflow produced a highly sensitive and detailed analysis of PG composition and I identified several modifications that have not been previously identified in *P. aeruginosa*. Further, my analyses show that *P. aeruginosa* can vary the composition of the PG significantly depending on the strain, nutrient condition, and growth morphology. Some of these changes may have implications for the virulence and antimicrobial

Continued…

resistance of *P. aeruginosa.* In addition, I provide an initial characterization of a PG modification that is likely important for the biofilm growth morphology. Together, this study has demonstrated the sensitivity of this peptidoglycomics methodology and has significantly advanced our understanding of the PG in *P. aeruginosa*. Future use of this methodology will facilitate further understanding of the dynamics of PG production and modification, as well as how it contributes to overall cellular functions.

Curriculum Vitae: Erin completed her Bachelor of Science (Hons.) at the University of Guelph in Winter 2001. In Fall 2003, she completed her Master of Science under the supervision of Dr. Robert Mullen with her thesis titled, "The evolutionary conservation of tail-anchored peroxisomal membrane protein targeting mechanisms among eukaryotes." Erin then began her Doctor of Philosophy in Molecular and Cellular Biology in Fall 2016 in the lab of Dr. Cezar Khursigara.

Awards: NSERC Canada Graduate Scholarship – Doctoral (2016 – 2019); Ontario Graduate Scholarship – Doctoral (2019 - 2020); University of Guelph CBS "best graduate student paper" award (2021)

Publications:

Anderson EM, Shaji Saji N, Anderson AC, Brewer D, Clarke AJ, Khursigara CM. 2022. Pseudomona aeruginosa alters peptidoglycan composition under nutrient conditions resembling cystic fibrosis lung infections. mSystems. 7(3): e0015622.

Anderson EM, Greenwood NA, Brewer D, Khursigara CM. 2020. Semi-Quantitative Analysis of Peptidoglycan by Liquid Chromatography Mass Spectrometry and Bioinformatics. J Vis Exp. 2020(164):1-20, e61799.

Anderson EM, Pũno-Sarmiento J, Park AJ, Khursigara CM, Barnett Foster DE. 2020. Potentiation of antibiotics by a novel antimicrobial peptide against Shiga toxin producing *E. coli* O157:H7. Sci Rep. 10(1):10029.

Anderson EM, Sychantha D, Brewer D, Clarke AJ, Geddes-McAlister J, Khursigara CM. 2020. Peptidoglycomics reveal compositional changes in peptidoglycan between biofilm- and planktonic-derived *Pseudomonas aeruginosa*. J Biol Chem. 295(2):504-516.

Article selected as a recommended read by JBC (2020 Jan), selected for JBC's 2020 issue of Methods Madness (2020 Mar), highlighted by Faculty Opinions as a good recommendation with a score of 4.7 (2020).