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*

DAVID SYCHANTHA

on Thursday, February 22, 2018 at 9:30 a.m. in SSC 2315

Thesis Title: **O-Acetylation of Cell Wall Glycans in Gram-Positive Bacteria**

Examination Committee:

Dr. A. Bendall, Dept. of Molecular and Cellular Biology (Exam Chair)
Dr. L. Howell, Molecular Medicine, Dept. of Biochemistry, SickKids
Dr. C. Whitfield, Dept. of Molecular and Cellular Biology
Dr. M. Kimber, Dept. of Molecular and Cellular Biology
Dr. A. Lovering, School of Biosciences, The University of Birmingham, (External)

Advisory Committee:

Dr. A. Clarke (Adv)
Dr. C. Whitfield
Dr. L. Howell

Abstract: The cell wall of Gram-Positive bacteria is vital for maintaining cell shape, integrity, and virulence. It is composed of a matrix of peptidoglycan (PG) and secondary cell wall polysaccharides (SCWP). These polymers are often modified through the process of O-acetylation, which mediates protein-carbohydrate interactions at the cell surface, and is responsible for pathogenicity. Little was known about the biochemistry of cell wall O-acetylation, and how these modified polymers affect protein-carbohydrate interactions. Hence, the primary purpose of this study was to examine the structure-function relationships of putative cell wall *O*-acetyltransferases and cell wall binding proteins. The crystal structures of polysaccharide *O*-acetyltransferase B and PG *O*-acetyltransferase A from *Bacillus cereus* and *Streptococcus pneumoniae* will be presented. A model for polysaccharide O-acetylation is proposed based on enzymatic analyses and structure guided mutagenesis of each enzyme. Additionally, a structure of a cell wall binding domain (Surface-layer homology domain) in complex with a modified SCWP unit from *Bacillus anthracis* will be presented. This structure provides insight into why modified SCWP are essential for the assembly of proteinaceous surface layers. The significance of this work is underpinned by the ongoing antimicrobial resistance crisis, as the findings described could guide the development of new strategies to overcome this major healthcare problem.

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Curriculum Vitae: David completed his Bachelor of Science (Hons.) in Microbiology in 2011, at the University of Guelph. He then completed his M.Sc. under the supervision of Dr. Anthony Clarke in 2013, and in January 2014 began his Ph.D. in the same lab.

Awards:

Canadian College of Microbiologists Student Symposium Award For Top Student Oral Presentation. 67th Annual Meeting of the Canadian Society of Microbiologists. Waterloo, ON. June 2017.

Outstanding Poster Award. Canadian Glycomics Symposium. Banff, AB. May 2017.

Outstanding Student Poster. 115th Annual Meeting of the American Society of Microbiologists, New Orleans, LA. May 2015

Publications:

Sychantha, D., Chapman, R.N., Bamford, N.C., Boons, G.J., Howell, P.L., Clarke, A.J. (2018) Molecular basis for the attachment of S-layer proteins to the cell wall of *Bacillus anthracis*. *Biochemistry*. (In review)

Sychantha, D., Little, D.J., Chapman, R.N., Boons, G.J., Robinson, H., Howell, P.L., Clarke, A.J. (2018) PatB1 is an *O*-acetyltransferase that decorates secondary cell wall polysaccharides. *Nature Chemical Biology*. 14, 79-85.

Sychantha, D., Jones, C., Little, D.J., Moynihan, P. J., Robinson, H., Galley, N.F., Roper, D.I., Dowson, C.G, Howell, P.L., Clarke, A.J. (2017) *In vitro* characterization of the antivirulence target of Gram-positive pathogens, peptidoglycan O-acetyltransferase A (OatA). *PLoS Pathogens*. 13 (10): e1006667.

Seepersaud, R., **Sychantha, D**., Bensing, B.A., Clarke, A.J., Sullam, P.M. (2017) O-Acetylation of the serine rich repeat glycoprotein GspB is coordinated with accessory Sec transport. *PLoS Pathogens* 13(8): e1006558.

Ha, R., Frirdich, E., **Sychantha, D.**, Biboy, J., Taveirne, M.E., Di Rita, V.J., Vollmer, W., Clarke, A.J., Gaynor, E.C. (2016) Accumulation of peptidoglycan O-acetylation leads to altered cell wall biochemistry and negatively impacts pathogenesis factors of *Campylobacter jejuni*. *Journal of Biological Chemistry* 291, 22686 - 22702.

Moynihan, P.J., **Sychantha, D.**, Clarke, A.J. 2014. Chemical biology of peptidoglycan O-acetylation and deacetylation. *Bioorganic Chemistry* 54, 44-50.