Notice of the Final Oral Examination
for the Degree of Master of Science

of

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BSc (Nottingham Trent University, 2012)

“Defining Molecular Mechanisms of Vector-Pathogen Interactions -Insights from the Tsetse-Trypanosome System”

Department of Biochemistry and Microbiology

Thursday, May 12, 2016
10:00 A.M.
Engineering and Computer Science Building
Room 130

Supervisory Committee:
Dr. Martin Boulanger, Department of Biochemistry and Microbiology, University of Victoria (Supervisor)
Dr. Alisdair Boraston, Department of Biochemistry and Microbiology, UVic (Member)
Dr. Steve Perlman, Department of Biology, UVic (Outside Member)

External Examiner:
Dr. Juergen Ehlting, Department of Biology, UVic

Chair of Oral Examination:
Dr. Leslee Pelton, Department of Curriculum and Instruction, UVic

Dr. David Capson, Dean, Faculty of Graduate Studies
Abstract

Vector-borne diseases such as malaria, leishmaniasis, and African trypanosomiasis are a major scourge to humans and animals in some of the most impoverished nations across the globe. Enabling the transmission of these disease-causing parasites is a highly sophisticated molecular arsenal of surface proteins. My research focuses on biophysical characterization of these proteins with the ultimate goal of deciphering the molecular crosstalk between pathogen and vector. In support of this goal, I have selected the tsetse fly-transmitted parasites of the genus Trypanosoma, the etiological agent of African sleeping sickness, as a model system. Before this study, GARP (Glutamic Acid Rich Protein from T. congolense), HbHpR (hemoglobin-haptoglobin receptor from T. congolense and T. brucei) and VSG (Variant Surface Glycoprotein from T. brucei) were the only structurally characterized surface proteins expressed by the trypanosome in the tsetse. Towards elucidating the molecular mechanism of transmission, I have attempted to characterize structurally three novel proteins; TbFam50.360, TbPSSA2, and TcCISSA and get insight into their functions.

Our structural analysis revealed that while the N-terminal region of TbFam50.360 adopted a three-helical structure similar to previously characterized trypanosome surface proteins, ectodomains of both TbPSSA2 and TcCISSA adopted a completely novel bilobed architecture. The structural analysis further identified putative ligand binding regions in TbFam50.360 and TcCISSA. However, in the absence of binding partners, the exact function of these proteins could not be established. Our lab in conjunction with our collaborators is investigating the binding partners of these proteins within the tsetse.

The structures of TbFam50.360, TbPSSA2, and TcCISSA can be added to the repertoire of structurally characterized surface proteins expressed by trypanosomes. The information gained from these first structures of trypanosome surface proteins will offer insight into their role in the trypanosome life cycle, promote strategies for transmission interference, and may, in the future, contribute to the control of African trypanosomiasis.