Notice of the Final Oral Examination
for the Degree of Doctor of Philosophy

of

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BSc (University of Victoria, 2011)

“Pannexin 1 Regulates Neuronal Development”

Division of Medical Sciences

Thursday, November 26, 2015
9:00 A.M.
Human and Social Development Building
Room A264

Supervisory Committee:
Dr. Leigh Anne Swayne, Division of Medical Sciences, University of Victoria (Supervisor)
Dr. Stephanie Willerth, Division of Medical Sciences, UVic (Member)
Dr. Craig Brown, Division of Medical Sciences, UVic (Member)
Dr. Chris Nelson, Department of Biochemistry and Microbiology, UVic (Outside Member)

External Examiner:
Dr. Tuan Trang, Department of Physiology and Pharmacology, University of Calgary

Chair of Oral Examination:
Dr. Laurence Coogan, School of Earth and Ocean Sciences, UVic

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

Neurons are generated from unspecialized neural progenitor cells (NPCs) in a process termed neurogenesis. This neuronal development continues throughout life in the ventricular zone (VZ) of the lateral ventricles, and the subgranular zone (SGZ) of the dentate gyrus in the hippocampus. NPCs undergo a complex and highly regulated set of behaviours in order to ultimately integrate into the existing brain circuitry as fully functional neurons. Recently the pannexin (Panx) large-pore channel proteins were discovered. One family member, Panx1 is expressed in the nervous system in mature neurons, and acts as an ATP release channel in other cell types throughout the body. Since post-natal NPCs are responsive to ATP via activation of purinergic receptors, I hypothesized that Panx1 was involved. In this dissertation I demonstrate that Panx1 is expressed in post-natal VZ NPCs, where it functions as an ATP release channel to promote NPC proliferation in vitro. Panx1 also positively regulates NPC migration and neurite outgrowth in vitro. Using an NPC-specific Panx1 knock-out strategy, I show that Panx1 expression is required for maintenance of a consistent population of VZ NPCs in vivo in both healthy and injured brain. Together these data indicate that Panx1 directs NPC behaviours associated with neuronal development both in vitro and in vivo. To further understand the molecular underpinnings of this regulation, I examine the Panx1 interactome, and uncover a novel association with collapsin response mediator protein 2 (Crmp2). Functional studies suggest that this interaction likely underlies Panx1’s negative impact on neurite outgrowth. Overall, my results represent important novel findings that contribute to our understanding of post-natal neuronal development, and the molecular function of Panx1 within the brain.