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

of

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BSc (University of Manitoba, 2010)

“Diabetes Impairs the Microglial Response to Cerebral Microbleeds”

Division of Medical Sciences

Thursday, January 12, 2017
10:00 A.M.
Medical Science Building
Room 210

Supervisory Committee:
Dr. Craig Brown, Division of Medical Sciences, University of Victoria (Supervisor)
Dr. Brian Christie, Division of Medical Sciences, UVic (Member)
Dr. Gautam Awatramani, Department of Biology, UVic (Outside Member)

External Examiner:
Dr. Patrick Nahirney, Department of Biology, UVic

Chair of Oral Examination:
Dr. Olaf Niemann, Department of Geography, UVic

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

Approximately 7-9% of the population are living with some form of diabetes. When poorly controlled (which is often the case), this disease is associated with cerebrovascular pathology such as microbleeds and impairments in cognitive function. The presence and burden of microbleeds in the brain has been strongly linked with cognitive decline and increased risk of dementia. Microglia, the resident immune cells of the central nervous system, dynamically respond to vascular insults by extending their processes to the site of injury. The rapid actions of microglia are thought to play a beneficial role in vascular repair since inhibiting these responses can exacerbate injury. Here, we hypothesized that diabetes, especially if not well controlled with insulin, will disrupt microglia responses to damaged microvessels in the brain which will lead to increased plasma leakage from damaged microvessels. Using 2-photon in vivo imaging, we show that chronic hyperglycemia in the streptozotocin model of type 1 diabetes leads to decreased microglial process accumulation around the site of microvascular injury and increased permeability of fluorescent dyes from the damaged vessel 30 minutes after induction of the bleed. Importantly, this impaired microglial and vascular response could be partially mitigated with tight control of blood glucose levels with insulin. These results indicate that chronic hyperglycemia disrupts microglial based repair of damaged microvessels, which may help explain why poorly controlled diabetes is associated with greater a risk of cerebrovascular dysfunction and cognitive decline.