



**University
of Victoria**

Graduate Studies

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

of

ANDREW AGBAY

BSc (University of Victoria, 2010)

**“Development of Guggulsterone-Releasing Microspheres for Directing
the Differentiation of Human Induced Pluripotent Stem Cells into
Neutral Phenotypes”**

Division of Medical Sciences

Monday, June 5, 2017
10:30 A.M.
Medical Sciences Building
Room 210

Supervisory Committee:

Dr. Stephanie Willerth, Division of Medical Sciences, University of Victoria (Supervisor)
Dr. Leigh Anne Swayne, Division of Medical Sciences, UVic (Member)
Dr. Brian Christie, Division of Medical Sciences, UVic (Member)

External Examiner:

Dr. Bob Chow, Department of Biology, UVic

Chair of Oral Examination:

Dr. Kim Juniper, School of Earth and Ocean Sciences, UVic

Dr. David Capson, Dean, Faculty of Graduate Studies

Abstract

In the case of Parkinson's disease, a common neurodegenerative disorder, the loss of motor function is characterized by the loss of dopaminergic neurons (DNs) in the brain. A more complete concept of rehabilitation to improve on current treatments requires the production of DNs to replace those that have been lost. Although the use of pluripotent stem cells (PSCs) is a promising candidate for the source of these replacement neurons, current protocols for the terminal differentiation of DNs requires a complicated cocktail of factors. Recently, a naturally occurring steroid called guggulsterone has been shown to be an effective terminal differentiator of DNs and can simplify the method for the production of such neurons. I therefore investigated the potential of long-term guggulsterone release from drug delivery particles in order to provide a proof of concept for producing DNs in a more economical and effective way. Throughout my study I was able to successfully encapsulate guggulsterone in Poly- ϵ -caprolactone (PCL)-based microspheres and I showed that the drug was capable of being released over 44 days *in vitro*. These guggulsterone-releasing microspheres were also successfully incorporated in human induced pluripotent stem cell (hiPSC)-derived neural aggregates (NAs), providing a preliminary study to continue investigating their effectiveness in producing functional and mature DNs. Together, these data suggest that guggulsterone delivery from microspheres may be a promising approach for improving the production of implantable DNs from hiPSCs.