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

of

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BSc (University of Guelph, 2016)

“Gold Nanoparticle Uptake in Synchronized Cell Populations and the Effect on Radiation Sensitization”

Department of Physics and Astronomy

Tuesday, December 11, 2018
11:00 A.M.
Elliott Building
Room 162

Supervisory Committee:
Dr. Devika Chithrani, Department of Physics and Astronomy, University of Victoria (Supervisor)
Dr. Wayne Beckham, Department of Physics and Astronomy, UVic (Member)
Dr. Isabelle Gagne, Department of Physics and Astronomy, UVic (Member)

External Examiner:
Dr. Julian Lum, Department of Biochemistry and Microbiology, UVic

Chair of Oral Examination:
Dr. Scott McIndoe, Department of Chemistry, UVic

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

To overcome the challenge in radiation therapy of delivering the prescribed dose to cancer cells while sparing normal tissue, preferential introduction of high Z material to tumour cells works as a method of radiation sensitization. Gold nanoparticles (GNPs) are very useful in this respect. It has been shown that the size, shape, and surface properties of GNPs affect their cellular uptake. Manipulation of the cell cycle to arrest cells at different stages offers a unique strategy to study the molecular and structural events as the cell cycle progresses. To optimize delivery of GNPs into tumour cells and enhance the effect of radiosensitization, nanoparticle (NP) uptake in synchronized populations of MDA-MB-231 breast cancer cells was investigated.

Populations of MDA-MB-231 cells were first synchronized in S-phase using double-thymidine block, and allowed the cells to progress through cell cycle in synchronization. Synchronized cells were incubated with 5 nm GNP, 15 nm GNP, 46 nm GNPs and two formulations of lipid NP encapsulated 5 nm GNPs. Uptake of NPs is visualized using hyperspectral optical imaging and quantified with ICP-MS (Inductively Coupled Plasma Mass Spectrometry). Following internalization of GNPs, cells were irradiated with 6 MV photon beams from linear accelerator, and the survival fraction and induced deoxyribonucleic acid (DNA) damage were studied.

Cell cycle analysis after a double-thymidine block showed that the cell population was well synchronized. Uptake of NPs was 1.5–2 times higher in synchronized cell population compared to the control where cells were at different stages of the cell cycle. We used clonogenic studies to evaluate the damage due to a radiation treatment. After a dose of 2 Gy, there was a decrease in cell survival fraction in synchronized cells treated with GNPs prior to radiation treatment compared to unsynchronized cells (control) indicating GNP-mediated dose-enhancement. We also used γ-H2AX immunofluorescent staining to probe DNA double strand breaks due to the radiation treatment. Our results show more DNA double strand breaks in cells treated with GNPs prior to radiation. Interaction of ionization radiation with GNPs inside of cells produces secondary electrons. These secondary electrons can interact with water molecules and produce additional free radicals. We believe that these low energy electrons and free radicals could cause cellular damage. Hence, optimizing uptake of GNPs is important to fully take advantage of their radiosensitizer properties and the cell cycle is a factor to consider.