MSc DEFENCE – Tuesday, December 15th, 2015
Student: Emma Conway
Title: **CISPLATIN PARTIALLY IMPEDES LUNG ADENOCARCINOMA-MEDIATED M2 MACROPHAGE POLARIZATION**
Time and Location: 12:00 pm, Ken Berry Reading Room, Pathology Education Centre at VGH, 3200, 910 West 10th Avenue, Vancouver, BC
Supervisor: Dr. Wan Lam

ABSTRACT
Lung cancer is the leading cause of cancer mortality and at 18%, has one of the lowest five-year survival rates of all malignancies. The majority of patients (>80%) are diagnosed with locally advanced or metastatic disease for which the standard of care is platinum-based doublet chemotherapy. However, chemotherapy has modest effects on overall survival, highlighting the need for novel and more effective treatments.
Within the past decade, the role of the immune system in tumorigenesis has become increasingly appreciated. Targeting the immune cells within the tumor microenvironment is a growing field of study that holds exciting therapeutic potential. Macrophages are a prominent immune cell type in the lung and lung tumors. It is widely accepted that a spectrum of macrophage activation states exists, with the exact phenotype dependent upon the precise composition of signals within the microenvironment. At opposite ends of this spectrum there exist M1 macrophages which are pro-inflammatory and have antitumor functions, and M2 macrophages which are anti-inflammatory and act in wound healing and thus promote tumorigenesis.
I hypothesized that macrophage differentiation is skewed by lung adenocarcinoma cells to an M2 phenotype and that cisplatin, a commonly prescribed chemotherapeutic, affects macrophage polarity. I co-cultured human monocytes with human lung adenocarcinoma cells in the absence and presence of physiologically relevant concentrations of cisplatin. Co-cultured macrophages displayed increased differentiation and an M2 polarity, in part potentially through IL-6 secretion by tumor cells. Cisplatin impeded macrophage differentiation, with treated macrophages displaying decreased size, granularity, and surface marker expression; however, CD206 expression, an M2 marker, remained elevated, suggesting a role for CD206 in response to treatment. Additionally, I optimized single cell analysis of clinical specimens in preparation for future projects, specifically ex vivo analysis of the effect of standard first line chemotherapy on macrophage polarity and other immune cells in advanced non small cell lung cancer.
Collectively, this work has demonstrated that macrophage polarity is affected by lung adenocarcinoma cells and by cisplatin. Moreover, the optimization of single cell analysis has prepared for the study of the effect of chemotherapy on macrophage polarity over the course of treatment using more physiologically representative specimens.