PhD DEFENCE – Tuesday, April 28th, 2015
Student: Jennifer Won
Title: **CLINICAL PERFORMANCE OF DIAGNOSTIC, PROGNOSTIC AND PREDICTIVE IMMUNOHISTOCHEMICAL BIOMARKERS FOR HORMONE RECEPTOR-NEGATIVE BREAST CANCER**
Time and Location: 9:00am, Room 200, Graduate Student Centre, UBC Campus
Supervisor: Dr. Torsten Nielsen

ABSTRACT
Gene expression profiling of breast cancer delineates a particularly aggressive subtype referred to as "basal-like", which comprises ~15% of all cases, afflicts younger women and is refractory to endocrine and anti-HER2 therapies. Immunohistochemical surrogate definitions for basal-like breast cancer, such as the ER/PR/HER2 triple negative phenotype and models incorporating positive expression of cytokeratin 5 (CK5/6) and/or epidermal growth factor receptor are more amenable to implementation in a clinical setting. Despite this and the fact that basal-like breast carcinomas are being increasingly recognized as a distinct clinical entity, there is no diagnostic method used and reported in routine practice. Without a reproducible test to identify this aggressive subtype in the clinic there will be no ability to establish clearly defined intake criteria for subtype-specific clinical trials, translating to no progress in the management of this form of the disease and little change in breast cancer survival rates for the foreseeable future.
A first evaluation of performance of the triple negative definition and various surrogate immunopanels for basal-like breast cancer in clinical laboratories is described in the initial chapters of this dissertation. Considerable staining variability of individual biomarkers included in immunopanels typically led to only moderate concordance with a gene expression gold standard for identification of basal-like breast carcinomas. Lack of standardization was the underlying reason for all of the observed variability, supporting the notion that further standardization efforts through continual participation in external quality assurance programs are needed before routine diagnosis of basal-like breast carcinomas could be made in a clinical setting.
In light of this, we sought to identify more easy-to-interpret and robust biomarkers for this disproportionately deadly type of breast cancer. A parallel comparison of 46 proposed immunohistochemical biomarkers of basal-like breast cancer was performed against a gene expression profile gold standard. Results from that survey determined that loss of expression of INPP4B and positive expression of nestin had the strongest associations with this aggressive subtype. Paving the way for further studies, this comprehensive immunohistochemical biomarker survey is a necessary step to determine an optimized surrogate immunopanel that best defines basal-like breast cancer in a practical and clinically-accessible way.