MSc DEFENCE Tuesday, December 12th, 2017
Student: Thyrza May Toledo
Title: OPTIMIZATION OF THE DETECTION OF CIRCULATING DNA IN PEDIATRIC SOLID TUMOR PATIENTS TREATED WITH GRANULOCYTE COLONY STIMULATING FACTOR
Time and location: 3:00pm PST; Room 3113, BC Children's Hospital Research Institute, 950 W 28th Avenue, Vancouver, BC
Supervisor: Dr. Suzanne Vercauteren

ABSTRACT

Solid tumor patients are often administered with a drug called Granulocyte-Colony Stimulating Factor (G-CSF). This drug is used to treat chemotherapy-induced neutropenia and/or to mobilize hematopoietic stem cells from the bone marrow into the blood for ease of collection. Previous in vivo studies in mice showed, that G-CSF can increase tumor growth and promote metastasis. As such, this study investigated whether G-CSF can promote tumor growth in children with solid tumors by non-invasively quantifying tumor derived circulating cell-free DNA (cfDNA) in the plasma. I also investigated whether tumor-derived cfDNA levels in the plasma correlate with tumor-derived genomic DNA (gDNA) levels in the stem cell product, on the day of stem cell collection procedure.

Tumor cfDNA was measured in the plasma of fourteen children with solid tumors, before and after G-CSF treatment, using methylation specific qPCR against the promoter region of the RASSF1a gene. Nine children [three rhabdomyosarcoma, five neuroblastoma and one rhabdoid tumor] had detectable tumor cfDNA in their plasma, which was suggestive of poor clinical outcome. In addition, paired plasma and stem cell products from the day of stem cell harvest were collected from nine children (four neuroblastoma, one glioblastoma, one rhabdoid tumor, two Hodgkin lymphoma and one choroid plexus carcinoma). At the time of stem cell harvest (post G-CSF administration), I found no evidence of tumor gDNA contamination in the stem cell product from all nine children. However, there was evidence of tumor cfDNA in the plasma product from six children, four of whom had known bone marrow involvement. Overall, four of the seven children with no detectable tumor cfDNA in the plasma had a diagnosis of brain cancer.

Altogether, tumor cfDNA levels in children with solid tumors can be detected but the current study did not show that levels increased upon G-CSF administration. The presence of tumor cfDNA in the plasma of children with pediatric cancer at the time of stem cell harvest was not consistent with tumor contamination of the stem cell product.