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Math you tem pel

**Presenting Author Category**

PhD Student

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**GBD Audio File**

IMG\_9774.mp3

**Headshot**

IMG\_8620.jpg

**Short Bio (100 words)**

Being a PhD student in the Tremblay lab researching T-cell Acute Lymphoblastic Leukaemia keeps me quite busy but I still find time to shred some guitar with my band Missing Treasure. My passion for discovery and desire for challenge has led me to academia where I gained a special interest in Immunology, leukaemia, and pediatric oncology. I believe that improving health care for children is an utmost priority as they are the future. What would we be without a future?

**Research Category**

Basic Science

**Abstract Title**

Investigating the role of the integrated stress response in chemotherapy resistance in T-cell acute lymphoblastic leukaemia

## Authors

| Name              | Role              | Profession          |
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## **Background**

Treatment for T-cell acute lymphoblastic leukemia (T-ALL) is limited to an aggressive chemotherapy regimen of vincristine, dexamethasone and L-asparaginase (VXL) that causes long-term side effects. Improvements to T-ALL treatment are needed but challenging due to the limited knowledge on how T-ALL cells respond and adapt to chemotherapy. Protein synthesis has emerged as a promising targetable pathway given its importance for cell function in homeostatic and stress conditions.

## **Objective**

To define the effects of chemotherapy on T-ALL cell function, informing novel therapeutic strategies.

## **Methods**

I determined the lethal concentration (LC50) of VXL by assessing viability of T-ALL cell lines by flow cytometry. I also assessed cell cycle distribution and changes in phosphorylation of the ribosomal protein S6 (pS6), which is an established marker of protein synthesis. In addition, I measured pS6 in T-ALL samples harvested from patient-derived xenograft (PDX) models at diagnosis and 24 hours after VXL treatment. I will validate effects on protein synthesis using OP-Puromycin incorporation into nascent peptides in T-ALL cell lines as well as the human samples from PDX models of T-ALL.

## **Results**

Treatment of the T-ALL cell lines with LC50 of VXL caused a significant reduction in pS6 after only 1 hour of exposure, prior to any measurable changes in cell cycle distribution. Treatment of PDX models with a single dose of VXL also causes a reduction in pS6 in human T-ALL samples, suggesting decreased protein synthesis in response to chemotherapy-induced stress.

## **Conclusion**

My results suggest that protein synthesis is impaired in response to chemotherapy-induced stress rather than decreased proliferation which occurs later in T-ALL cells. Given these effects, targeting key components of this stress response might limit the capacity of T-ALL cells to adapt, thereby preventing resistance to chemotherapy and improving outcomes.