

Presenting Author Name

Ovini Amarasinghe

Phonetic spelling of your (full) name

oh-VEE-nee uh-muh-ruh-SIN-uh

Presenting Author Category

PhD Student

Supervisor Name

Cédric Tremblay

GBD Audio File

Amarasinghe_CHRD2026.mp4

Headshot

Amarasinghe_Headshot.jpg

Short Bio (100 words)

Ovini Amarasinghe is a PhD candidate in the Department of Immunology at the University of Manitoba, working in Dr. Cédric Tremblay's laboratory. Her research focuses on understanding how therapy-resistant leukemia cells survive chemotherapy and contribute to relapse in T-cell acute lymphoblastic leukemia (T-ALL). Ovini's doctoral research is supported by the Cancer Research Society (CRS) Doctoral Research Award.

Research Category

Basic Science

Abstract Title

Defining Adaptive Chemotherapy Resistance Mechanisms in High-Risk T-cell Acute Lymphoblastic Leukemia

Authors

Name	Role	Profession
Ovini Amarasinghe	Presenting Author	Graduate
Jay Kormish	Co Author	Graduate
Mathew Tempel	Co Author	Graduate
Johnathon Lucas	Co Author	Graduate
Lamisa Tahsin	Co Author	Graduate

Nivitha Bhaskar	Co Author	Graduate
Shokoufeh Abdollahi	Co Author	Graduate
Alex Yan	Co Author	Graduate
Joel Pearson	Co Author	Assistant Professor
René Zahedi	Co Author	Full Professor
David J Curtis	Co Author	Full Professor
Cédric S. Tremblay	Co Author	Assistant Professor

Background

T-cell Acute Lymphoblastic Leukemia (T-ALL) is an aggressive subtype of leukemia, which is the most common childhood cancer. Although most patients achieve complete remission, rare resistant cells remain after treatment and drive relapse in 25% of cases. LMO2 is expressed in ~40% of T-ALL cases and is associated with increased risk of relapse.

Objective

While relapse-promoting genetic mechanisms are well-characterized in T-ALL, adaptive non-genetic resistance mechanisms remain unknown. The objective of the study is to address this knowledge gap to inform the development of more effective therapies for T-ALL.

Methods

To investigate Lmo2-driven relapse mechanisms, we use the Lmo2 transgenic (Lmo2Tg) mouse model where relapse-initiating cells emerge within DN3 T-cell progenitors during the preleukemic phase. We have previously shown that Lmo2Tg DN3 cells are resistant to pediatric chemotherapy regimen of Vincristine, deXamethasone, and L-asparaginase (VXL). We performed longitudinal RNA-seq and proteomics profiling on purified DN3 thymocytes harvested 24 hours (Acute) and 2 weeks (Persistent) after treatment, as well as 3 weeks post-treatment (Recovery). Pathways transiently upregulated in Acute and Persistent datasets will uncover candidate non-genetic resistance mechanisms.

Results

RNA-seq data analysis revealed that Lmo2Tg DN3 cells display a distinctive transcriptional adaptive response to VXL treatment, compared to Wild-type DN3 cells. Pathway enrichment analysis of preleukemic Lmo2Tg DN3 cells revealed selective activation of several interferon-mediated inflammatory pathways following VXL treatment. Longitudinal analysis of shared genes across these inflammatory pathways revealed activation of Interferon-Related DNA damage resistance Signature (IRDS) programs, which is associated with therapy resistance across multiple cancers. Gene set enrichment analysis demonstrated transient IRDS upregulation following VXL treatment, which was exacerbated after prolonged exposure.

Conclusion

Together, these multi-omics data strongly support IRDS as the central component of the adaptive response to VXL in preleukemic Lmo2Tg DN3 cells. This chemotherapy-induced inflammatory adaptation

program represents a novel, non-genetic mechanism of therapy resistance in T-ALL.