

Presenting Author Name

Johnathon Lucas

Phonetic spelling of your (full) name

JON-uh-thuhn

Presenting Author Category

Masters Student

Supervisor Name

Cedric Tremblay

Research Category

Basic Science

Abstract Title

Investigating the aberrant STAT5 axis in therapy resistant T-ALL

Authors

Name	Role	Profession
Johnathon T Lucas	Presenting Author	Graduate
Ovini Amarasinghe	Co Author	Graduate
Mathew Tempel	Co Author	Graduate
Lamisa Tahsin	Co Author	Graduate
Cedric S Tremblay	Co Author	Assistant Professor

Background

T-cell Acute Lymphoblastic Leukemia (T-ALL) is an aggressive cancer in which abnormal Signal Transducer and Activator of Transcription 5 (STAT5) signaling promotes leukemia cell survival, growth, and treatment resistance. Despite initial response to chemotherapy, T-ALL relapse occurs in up to 20% of pediatric and 60% of adult cases.

Objective

Because direct STAT5 inhibition has shown limited benefit, this study investigates alternative ways to target the STAT5 pathway in high-risk T-ALL.

Methods

We used patient-derived xenograft models of early T-cell precursor-like and TAL1/LMO2 T-ALL to study cytokine-driven STAT5 activation. STAT5 signaling was measured by flow cytometry after Interleukin-7 (IL-7) stimulation, using Tyr694 phosphorylation as a marker of activation and IL-7 Receptor (IL-7R) as a marker of STAT5-associated signaling. To assess treatment effects, we examined PDX models treated in

vivo with standard chemotherapy and validated key findings in human T-ALL cell lines. Bulk RNA-seq and ATAC-seq, and protein interaction studies are being used to identify STAT5 targets and binding partners.

Results

IL-7 activated STAT5 in all early T-cell precursor-like samples, but in only about half of the TAL1/LMO2 samples. Chemotherapy increased both STAT5 activation and IL-7R expression in PDX models, suggesting that treatment may promote an abnormal IL-7/STAT5 signaling axis. In the CCRF-CEM cell line, chemotherapy also increased IL-7R expression, enhanced IL-7 responsiveness, and further increased STAT5 activation.

Conclusion

This study shows that chemotherapy may strengthen IL-7R/STAT5 signaling and contribute to therapy resistance in T-ALL. Identifying STAT5 partners may support new treatment strategies for high-risk disease. Currently, there is no Indigenous-specific T-ALL data. Therefore, my position as an Indigenous researcher allows for my lived experience to influence T-ALL research in Manitoba. More broadly, supporting Indigenous researchers in cancer research will strengthen health equity in Manitoba and across Canada by improving the voice of Indigenous communities and reach of future cancer therapies.