

Presenting Author Name

Lamisa Tahsin

Phonetic spelling of your (full) name

2049631615

Presenting Author Category

PhD Student

Supervisor Name

Dr. Cedric Tremblay

Research Category

Basic Science

Abstract Title

Investigating the Role of Interferon gamma (IFN γ) in LMO2-driven T-cell Acute Lymphoblastic Leukemia

Authors

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

Background

T-cell acute lymphoblastic leukemia (T-ALL) is an aggressive hematological malignancy in which treatment-resistant cells can persist as minimal residual disease (MRD) and contribute to relapse. Inflammatory programs are associated with poor outcomes in T-ALL, and preliminary data from an LMO2-driven T-ALL model identified type II interferon (IFN γ) as a potential contributor to chemotherapy resistance. However, its role in treatment response remains poorly understood.

Objective

To determine whether IFN γ signalling promotes chemoresistance in LMO2-driven T-ALL and define its association with therapy-resistant disease.

Methods

IFN γ signalling was investigated using human T-ALL cell lines, Lmo2Tg mouse models, patient-derived datasets, and patient-derived xenografts. Transcriptomic profiling, longitudinal diagnosis-MRD-relapse data, ChIP-seq/ATAC-seq integration, and multiparametric flow cytometry were used to characterize IFN γ -

associated features. Chemotherapy response was assessed using vincristine, dexamethasone, and L-asparaginase (VXL).

Results

In ETP-like LOUCY cells, IFN γ attenuated VXL-induced cytotoxicity, resulting in approximately two-fold more viable cells than VXL alone. Human T-ALL datasets showed positive associations between LMO2 and IFN γ R1/2, while longitudinal analyses identified increased IFN γ R1 expression in DN3 and immature DN1/ETP-like populations at MRD and relapse. ChIP-seq/ATAC-seq integration identified LMO2 occupancy at regulatory regions of IFN γ R1/2 in ETP-like T-ALL. RNA-seq of VXL-treated Lmo2Tg DN3 cells identified induction of IFN γ following chemotherapy.

Conclusion

These findings link LMO2-driven T-ALL with IFN γ responsiveness and demonstrate an IFN γ -mediated chemoprotective effect in vitro. Ongoing studies will determine whether targeting IFN γ signalling can improve chemotherapy response.