

Characterization of the IKZF1 Local Association Network in Single-Cell Transcriptomic Data of Pediatric B-ALL

Narges Chal Ashtari Makari

The thesis has been submitted to the Faculty on Natural Sciences and Medicine of Ilia State University following the requirements for obtaining the degree of Master of Science

Program: Applied Genetics

Research Supervisor: Vincenzo Lagani, Ph.D.

Ilia State University

Tbilisi 2026

Statement

To the Dean of Faculty of Natural Sciences and Medicine LEPL Ilia State University

Ms. Elene Zhuravliova

Faculty of Natural Sciences and Medicine

Program: Applied Genetics

Master's student: Narges Chal Ashtari Makari

As the author of the submitted thesis, I declare that the thesis is my original work and does not contain materials previously published, accepted, or defended by other authors, which are not mentioned or cited according to the citation rules.

Narges Chal Ashtari Makari

15.06.2026

Contents

Abstract	1
1 Introduction	2
1.1 Pediatric B-ALL	2
1.2 IKZF1 in B-ALL	3
1.3 Single-Cell Transcriptomics and Cellular Heterogeneity	4
1.4 Gene Regulatory Networks and Local Causal Discovery	5
2 Methods	9
2.1 Available B-ALL scRNA-seq Dataset	9
2.2 Data Preparation (Pre-processing)	10
2.3 Cell Type Identification	11
2.4 Local Network Reconstruction Using the PC Algorithm	12
2.5 Functional Interpretation of the IKZF1 Local Network	14
3 Results	15
3.1 Samples Composition	15
3.2 Cell-Type-Specific IKZF1 Local Networks Across Patients	18
4 Discussion	23
Appendix: Complete IKZF1 Local Network and Functional Enrichment Results	27
Appendix A. Complete IKZF1 Local Network Results	27
Appendix B. Complete Gene Ontology Enrichment Results	31
Appendix C. Summary Statistics of Reconstructed IKZF1 Local Networks	32

Abstract

Pediatric B-cell acute lymphoblastic leukemia (B-ALL) is a biologically and molecularly heterogeneous malignancy, posing significant challenges for the identification of the regulatory mechanisms underlying disease development and progression. The transcription factor IKZF1 (IKAROS) plays a central role in normal lymphoid differentiation, and genetic alterations affecting this gene have been consistently associated with high-risk disease and poor clinical outcome in pediatric B-ALL. Despite its recognized importance, the local molecular environment surrounding IKZF1 across different cellular populations remains incompletely understood.

The aim of this study was to reconstruct and characterize IKZF1-centered local gene association networks using single-cell transcriptomic data. Publicly available scRNA-seq data from the GSE241405 dataset were analyzed across annotated cellular populations from multiple independently analyzed patient-derived samples. For each cell type, genes showing the strongest association with IKZF1 were identified using Pearson correlation analysis, and local gene association networks were reconstructed using the PC algorithm, a constraint-based network inference method. Genes directly connected to IKZF1 in the inferred networks were subsequently extracted and functionally characterized through Gene Ontology (GO) Biological Process enrichment analysis. The reconstructed IKZF1-centered local networks exhibited substantial variability across cellular populations and patient-derived datasets, with both the number and identity of directly associated genes differing according to the biological context. Despite this network-level heterogeneity, functional enrichment analysis revealed recurrent biological themes, including immune regulation, cellular communication, cell adhesion, stress response, and developmental processes.

Overall, the findings support the hypothesis that IKZF1 functions as a context-dependent regulatory hub in pediatric B-ALL. Although the composition of its local interaction network varies across distinct cellular populations, different IKZF1-associated gene sets appear to converge on a relatively conserved repertoire of biological functions. This study demonstrates the value of integrating single-cell transcriptomics, local network reconstruction, and functional enrichment analysis for the investigation of transcription factor-centered regulatory landscapes in pediatric leukemia.

Keywords: Pediatric B-ALL; IKZF1; IKAROS; single-cell transcriptomics; local gene network; PC algorithm; Gene Ontology; functional enrichment.