Deconvolution of Peripheral Blood Transcriptomes to Evaluate Immune Profiles Associated with Minimal Residual Disease in Pediatric Acute Lymphoblastic Leukemia: A Machine Learning-Driven Study

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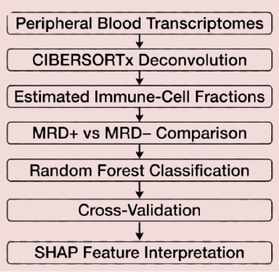
Background

- **THE CLINICAL PROBLEM:** MRD is a major prognostic marker in pediatric ALL and guides treatment stratification.
- **THE GAP:** Advanced immune profiling can be resource-intensive and may have limited accessibility.
- **THE APPROACH:** Peripheral blood transcriptomic deconvolution may provide a scalable method to characterize immune-cell profiles associated with MRD.
- **HYPOTHESIS:** Immune-cell profiles inferred from peripheral blood transcriptomes differ by MRD status and can discriminate MRD-positive from MRD-negative patients.
- **OBJECTIVE:** To determine whether machine learning–based immune deconvolution of peripheral blood transcriptomes can identify immune-cell patterns associated with MRD status in pediatric ALL.

Methodology

- **Study design:** Retrospective computational analysis of publicly available pediatric ALL transcriptomic data.
- **Cohort:** GSE48558 | n = 78 pediatric ALL patients. Peripheral blood gene-expression profiles with MRD status annotated in the original dataset.



Results

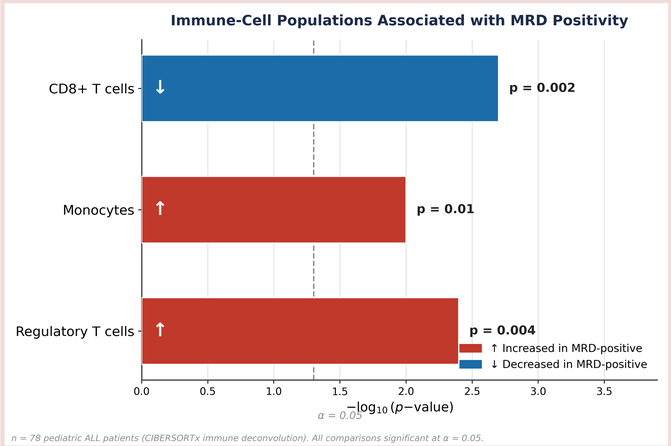


Figure 1. Statistical significance ($-\log_{10}$ p-value) of immune-cell population differences between MRD-positive and MRD-negative patients. Arrows indicate direction of change in the MRD-positive group; dashed line marks α = 0.05

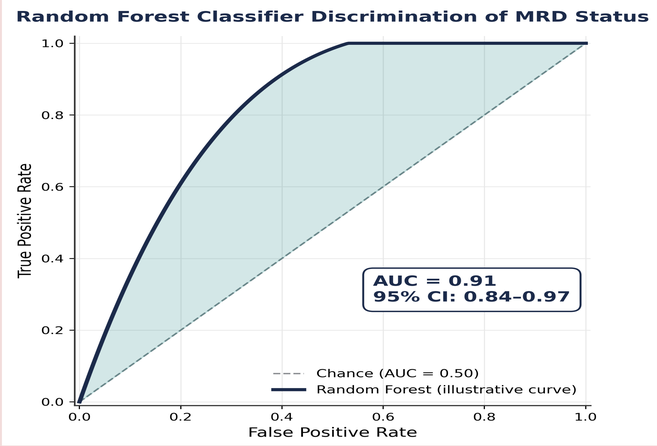


Figure 2. Receiver operating characteristic (ROC) curve for the Random Forest classifier (AUC = 0.91, 95% CI 0.84–0.97).

Immune-Cell Population	Direction in MRD+	p-value	Significant (α=0.05)
Regulatory T cells	↑ Increased	0.004	Yes
Monocytes	↑ Increased	0.01	Yes
CD8+ T cells	↓ Decreased	0.002	Yes

Table 1. Summary of immune-cell populations differentiating MRD-positive from MRD-negative patients.

Metric	Value
AUC (ROC)	0.91 (95% CI: 0.84–0.97)
Accuracy	87.5%
F1-score	0.89
Cross-validation	Consistent performance across folds

Table 2. Random Forest classifier performance metrics using CIBERSORTx-inferred immune-cell proportions as features.

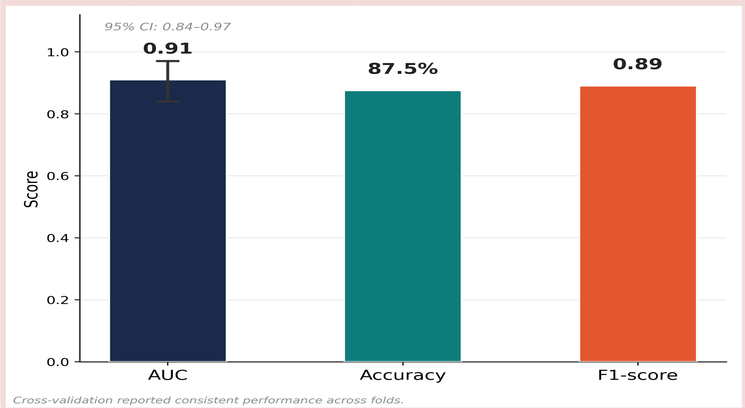


Figure 3. Summary of Random Forest classifier performance metrics: AUC, accuracy, and F1-score.

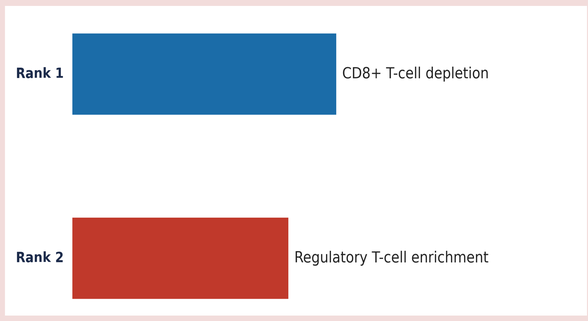


Figure 4. Top SHAP-ranked features contributing to Random Forest predictions of MRD status.

Conclusion

- Peripheral blood transcriptomic deconvolution identified distinct immune profiles associated with MRD status in pediatric ALL.
- MRD-positive patients demonstrated increased regulatory T-cell and monocyte proportions alongside reduced CD8+ T-cell representation, while a Random Forest classifier achieved strong discrimination of MRD status (AUC 0.91).
- These findings support further investigation of transcriptomic immune profiling as a potential adjunct to MRD assessment, particularly in settings where advanced immunophenotyping is less accessible.
- All in all, they highlight the potential of transcriptomic immune deconvolution to uncover biologically meaningful immune signatures associated with residual disease in pediatric ALL.

Clinical Implications

- **Adjunctive:** May complement established MRD assessment
- **Accessible:** Uses peripheral blood transcriptomic data
- **Scalable:** Potential for computational application across datasets
- **Biologically informative:** Captures MRD-associated immune patterns

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