



Characterizing the Tumor Microenvironment in CLL: The Role of NK Cells and Prognostic Gene Markers

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Background

1. Natural killer (NK) cells are critical regulators in the tumor immune microenvironment (TME) of chronic lymphocytic leukemia (CLL).

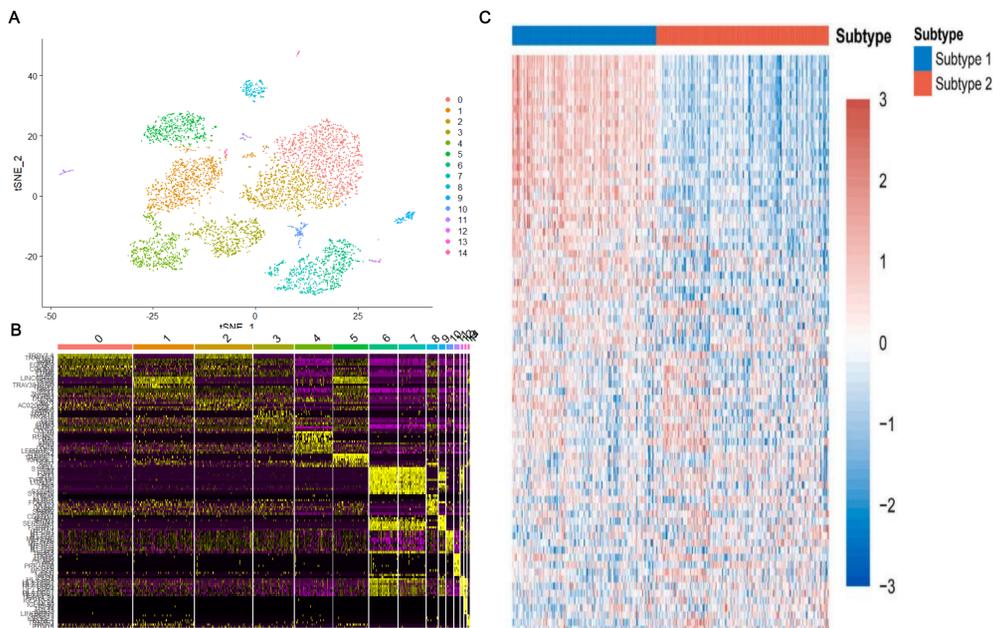
2. NK cells systematic profiling for clinical prediction has not been previously explored.

3. This study establishes an NK cell-centric framework to predict patient outcomes and therapeutic responses.

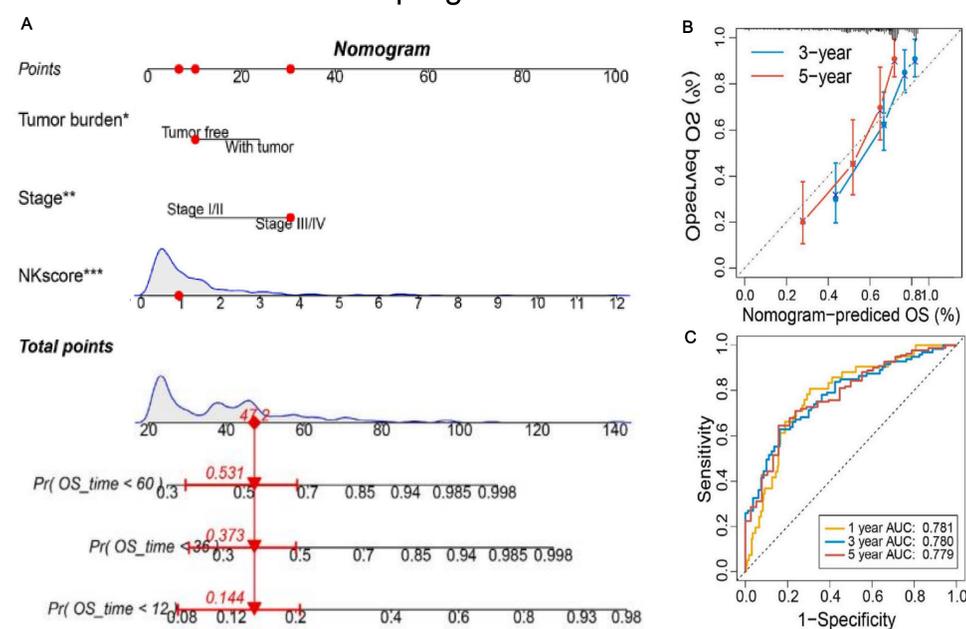
Results

NKscore Predicts Survival & Therapy Response:

Using scRNA-seq data from 52,784 CLL cells, we identified 265 NK cell marker genes (NKGs) through Seurat-based clustering and CellMarker annotation.

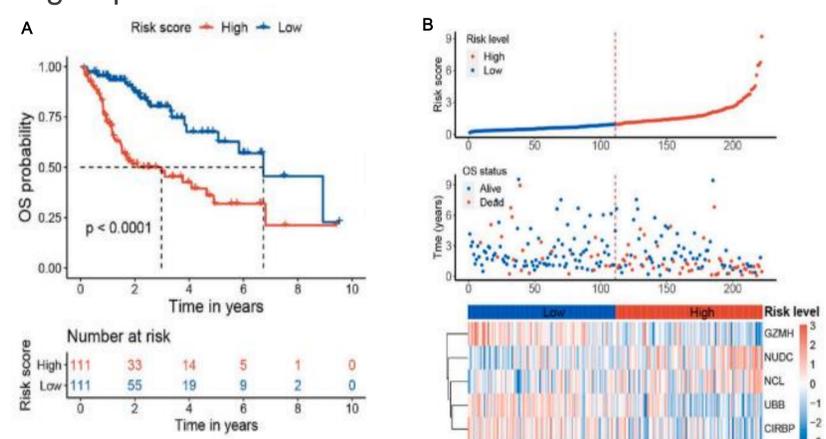


Aiming at establishing a reliable and accurate prognostic prediction tool based on NKGs, we adopted the ICGC training set and minimized overfitting and subsequently identified five hub NKGs to construct the prognostic NKscore.



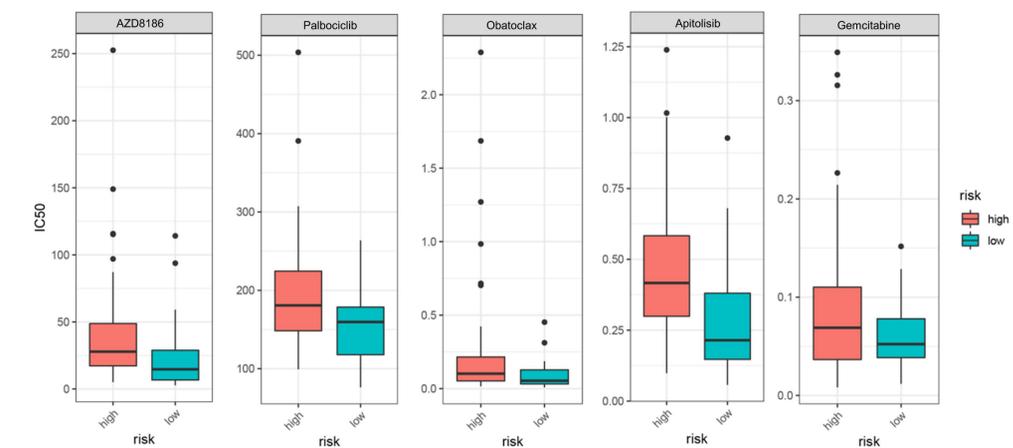
Clinical Utility:

Kaplan-Meier survival analysis showed that the patients in the low-risk group had better OS status.



Drug sensitivity prediction using the OncoPredict package:

The effects of 5 common chemo-/targeted therapeutic drugs were different in the two risk groups, which implied the potential of NKscore for the selection of chemo-/targeted drugs in clinical application.



Conclusion

1. We pioneer an NK cell-derived prognostic system that quantifies TME immunosuppression and predicts immunotherapy efficacy in CLL.

2. This study establishes NK cells as master regulators of CLL tumor evolution.

3. This study provides a clinically actionable tool for improved risk stratification and personalized therapy selection.