Poster #: 1603

Single-cell transcriptome analysis reveals molecular mechanism of stem-like cells in Richter Transformation

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INTRODUCTION

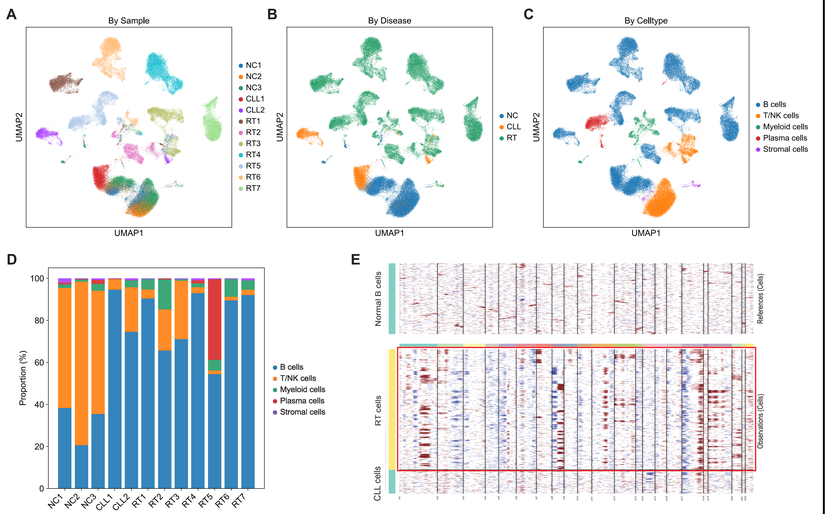
- Richter Transformation (RT) is a heterogeneous lymphoma defined as the histologic progression of chronic lymphocytic leukemia (CLL) into an aggressive subtype, associated with extremely poor prognosis.
- Although several molecular mechanism researches have been reported in RT, the key drivers remain incompletely understood.
- This study aims to construct the differentiation trajectory of RT cells and to identify key mechanisms driving RT by single-cell RNA sequencing (scRNA-seq).

METHODS

- scRNA-seq were performed for 12 lymph node (LN) tissue samples from 7 clonally related RT-DLBCL, 2 CLL, and 3 normal controls (NC) using the GEXSCOPE® platform (Singleron, China).

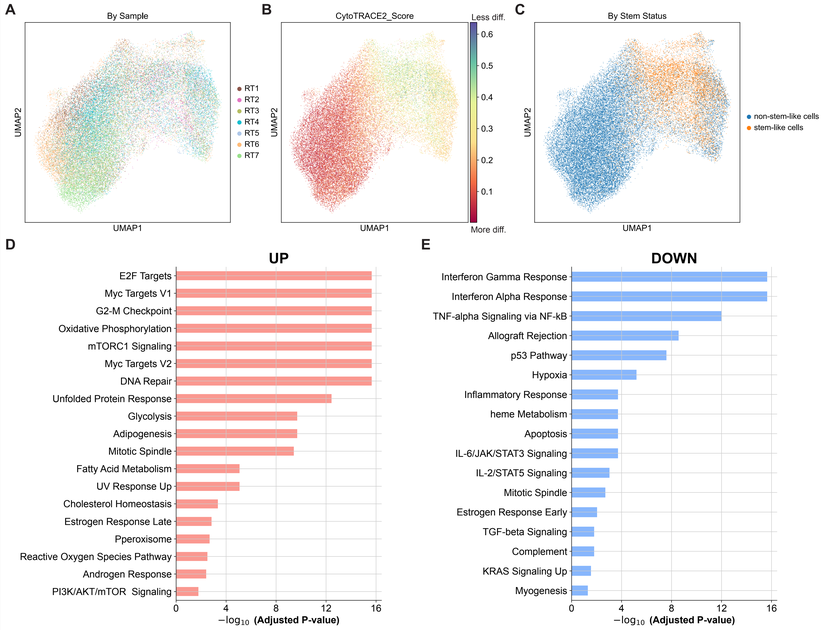
RESULTS

1. Single-cell analysis demonstrated high heterogeneity in CLL and RT tumor microenvironment (TME).



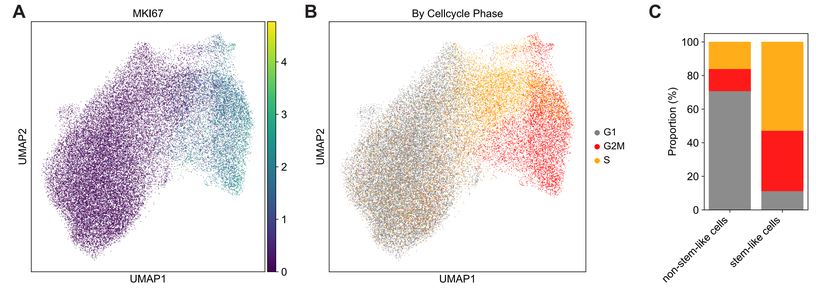
(A) The UMAP plot showing the cells colored by samples. (B) The UMAP plot showing the cells colored by disease subtypes. (C) The UMAP plot showing the cells colored by major cell types. (D) The stacked column chart of major cell type fractions in the TME of every sample. (E) The heatmap of the copy number variants (CNV) analysis inferred by *inferCNV* in CLL and RT cells. Normal B cells were used as references. The red rectangle highlights the complex alterations in RT cells.

2. Stem-like cells in RT exhibited upregulation of multiple tumor-related and metabolic pathways.



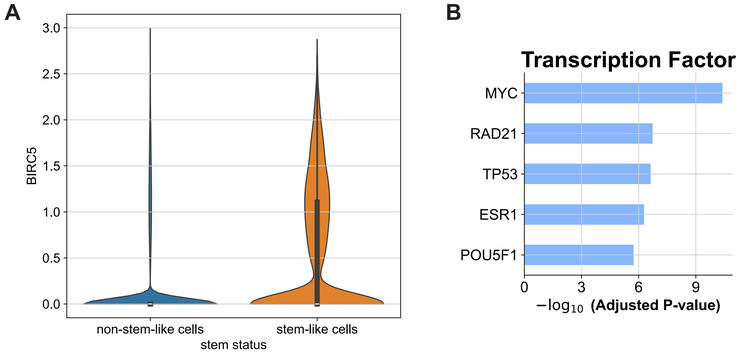
(A) The UMAP plot showing the RT cells colored by samples. (B) The UMAP plot showing the RT cells colored by CytoTRACE2_Score. (C) The UMAP plot showing the RT cells colored by stem status. (D) The bar plot of enriched MSigDB Hallmark pathways of upregulated genes in RT stem-like cells. (E) The bar plot of enriched MSigDB Hallmark pathways of downregulated genes in RT stem-like cells.

3. Stem-like cells in RT showed a strong association with cell cycle and proliferation markers.



(A) The UMAP plot showing expression of MKI67 in RT cells. (B) The UMAP plot showing the RT cells colored by cell cycle phase. (C) The stacked column chart of cell cycle phase fractions in different stem status cells in RT.

4. The overexpression of BIRC5 in stem-like RT cells may be regulated by MYC, promoting cell proliferation and inhibiting apoptosis.



(A) The violin plot of expression of BIRC5 in non-stem-like and stem-like RT cells. (B) The bar plot of transcription factors inferred upregulating BIRC5 expression.

CONCLUSION

- Stem-like cells, as the origin of cellular differentiation in RT, exhibit high proliferative potential and constitute a highly malignant subpopulation.
- BIRC5, which encodes an anti-apoptosis protein Survivin, is preferentially expressed in RT stem-like cells, linking enhanced proliferative capacity to their stem-like and potentially malignant phenotype.

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