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Inferring cell lineage differential gene expression analysis using single-cell RNA-seq

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Abstract

Backgrounds: Single-cell RNA sequencing (scRNA-seq) analysis can investigate gene expression at single-cell resolution and track the trajectories of distinct cell lineages. Intra-tumor heterogeneity (ITH) includes cellular differences in tumors and is associated with clinical outcomes such as drug resistance. Expression profiling of cells individually allows monitoring ITH and may unravel the dynamics of specific sub-population of tumoral cells. To identify differentially expressed genes in different lineages of Acute Lymphoblastic Leukemia (ALL), we utilized a scRNA approach to scrutinize the ETV6-RUNX role in promoting tumorigenesis.
Materials and Methods: We used the Seurat R package to analyze 3094 Pre-B t (12;21) [ETV6-RUNX1] ALL cells sequenced by 10x Genomics' scRNA-seq technology. Raw data retrieved from SRA public database (SRR9264343) and was processed to obtain count matrices using Cellranger count tools. UMAP algorithm and Slingshot was applied for dimensionality reduction and identifying branch-specific changes in gene expression respectively.
Results: We found 9 clusters and 2 lineages in our data. 12 genes were differentially expressed between 2 lineages, including TERF2, ID3, XRCC6, ATF4, and DDX17. We focused on ID3 and its biological networks. Our data not only showed a significant aberrant pattern of cellular heterogeneity between normal and tumoral cells but also ETV6-RUNX is intriguingly showed a distinguished cellular signature.
Conclusion: Based on our findings ID3 may be considered as a critical marker in ETV6-RUNX harboring cells. Its crucial biological roles in cell cycle, regulation of DNA replication and regulation of cell differentiation, may pave the way for generating of a new subtype of cells and should be considered as one of the key genes related to evolvability of lymphoblastic progenitors in ALL.

Keywords: scRNA-seq, Acute Lymphoblastic Leukemia (ALL), ID3, ETV6-RUNX1, Intra-tumor heterogeneity