



Dynamic Single-Cell RNA-Seq Reveals Mechanism of Selinexor-Resistance in Chronic Myeloid Leukemia

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INTRODUCTION

Chronic myeloid leukemia (CML) is a hematopoietic neoplasm caused by BCR-ABL chimeric oncogene.¹ Resistance to tyrosine kinase inhibitors (TKIs) brings subsequent treatment more challenges.² Selinexor is a small molecule inhibitor that targets a nuclear transporter called Exportin 1. Combined with TKIs, selinexor can effectively disrupt the nuclear-cytoplasmic transport signal of leukemia stem cells, resulting in reduced formation of clones.

AIM

We performed single cell dynamic transcriptome sequence to analysis intratumor heterogeneity of subpopulation of CML and identified key gene expression changes that occur as Selinexor-resistance.

CONCLUSIONS

Through single-cell dynamic transcriptome RNA-seq technology, this study revealed the the mechanism of drug resistance to selinexor in CML cell lines K562. We found differential expression patterns in genes between the parental and drug-resistant groups. Furthermore, we identified a subgroup exhibiting cancer stem cell properties, highlighting the potential involvement ferroptosis in drug resistance. Meanwhile, the combination of a ferroptosis inducer RSL3 might overcame drug resistance.

RESULTS

Fig 1. Single cell RNA-seq analysis of selinexor resistance K562 cell line.

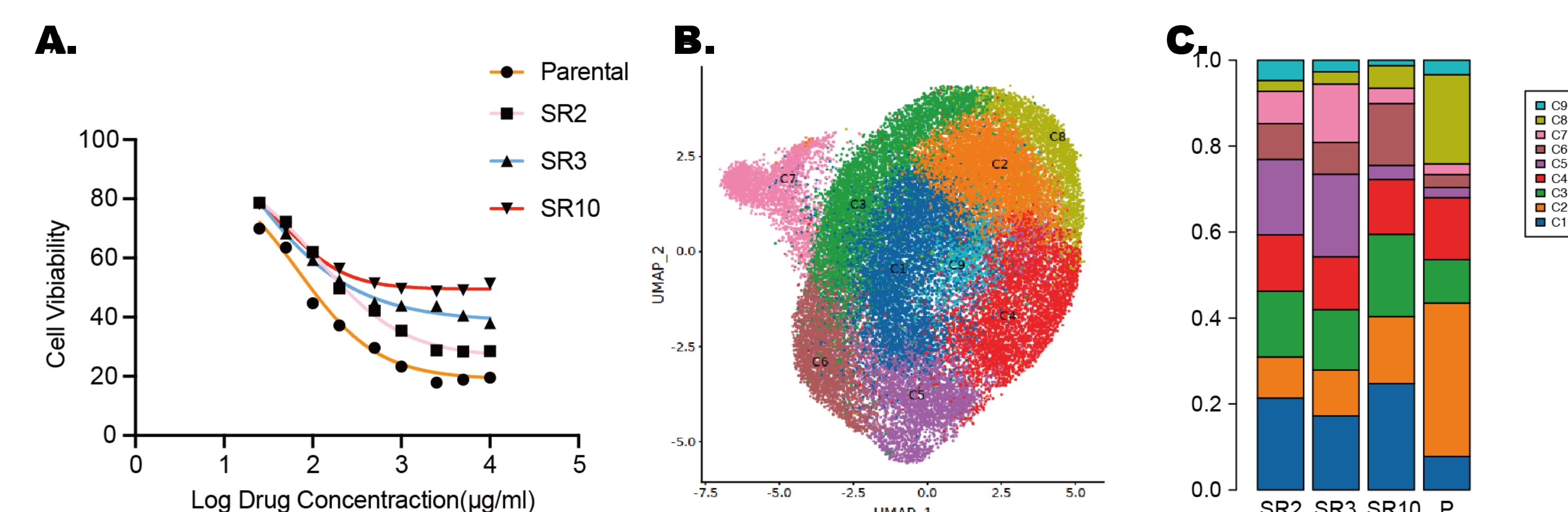


Fig 4. Reduction of ferroptosis within selinexor resistance

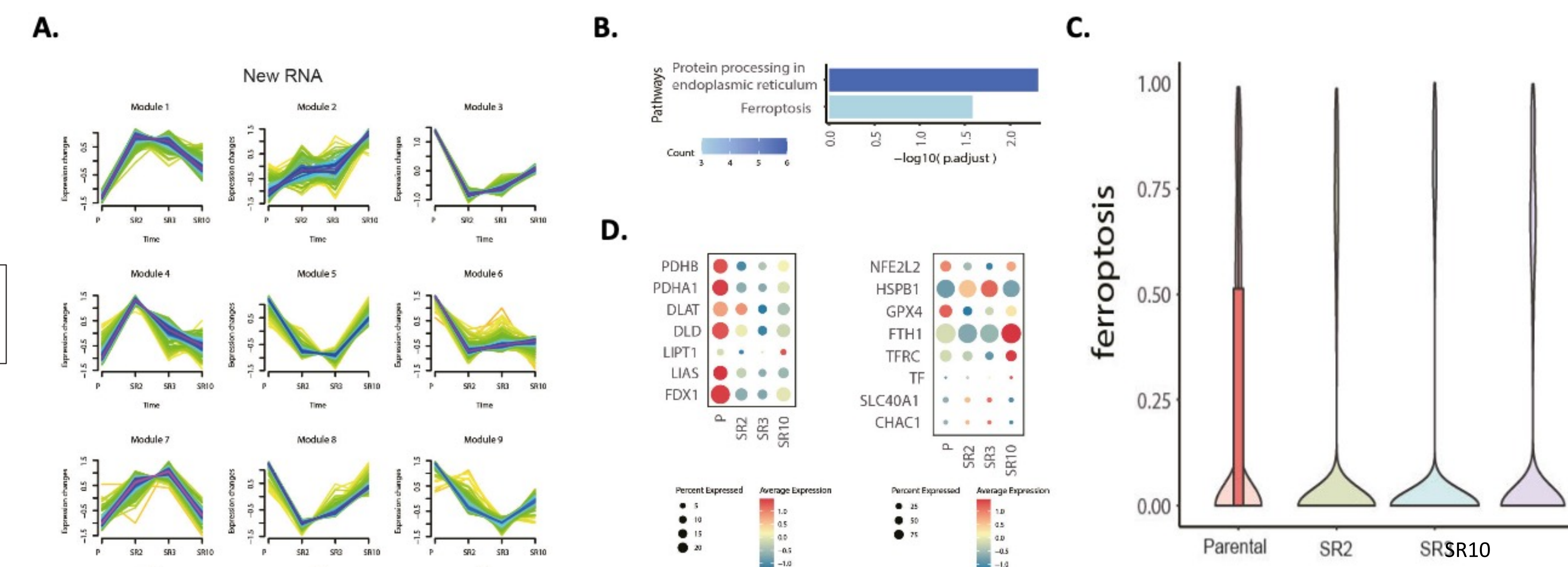


Fig 5. Combination of ferroptosis inducer RSL-3 improved resistance to selinexor

Fig 2. Differential gene expression between parental and SR groups.

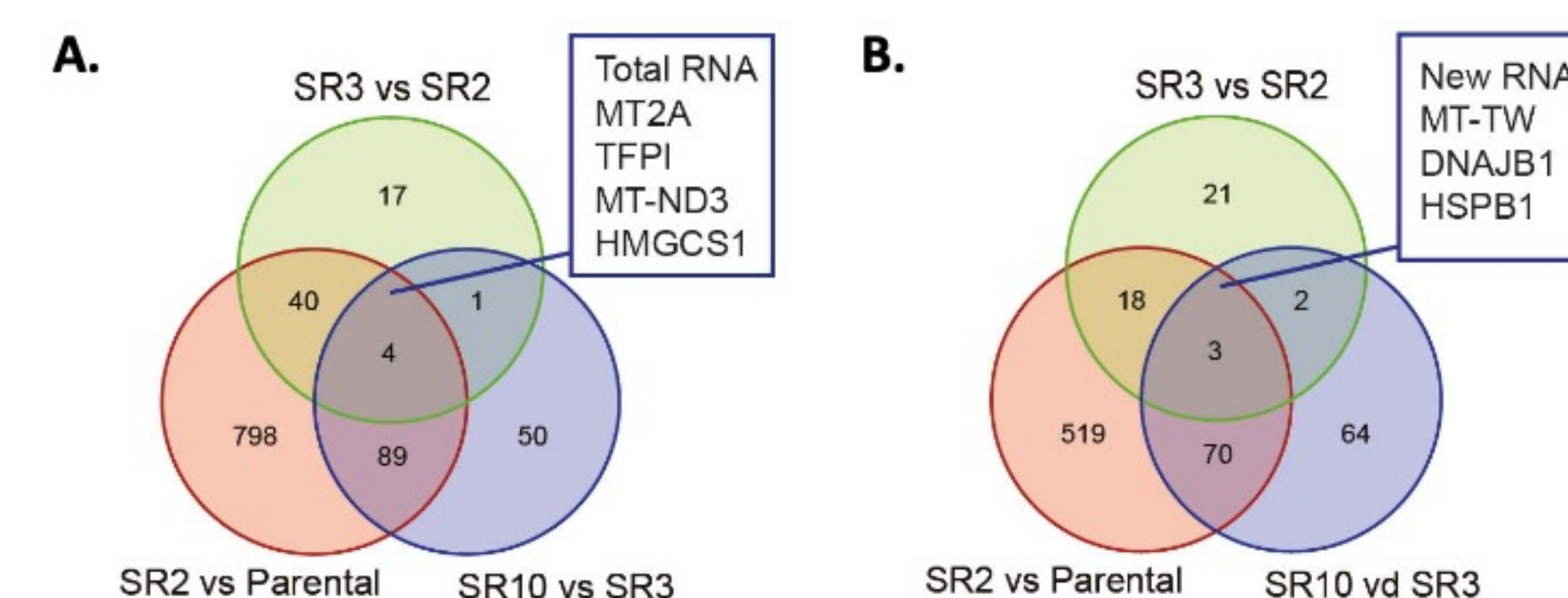
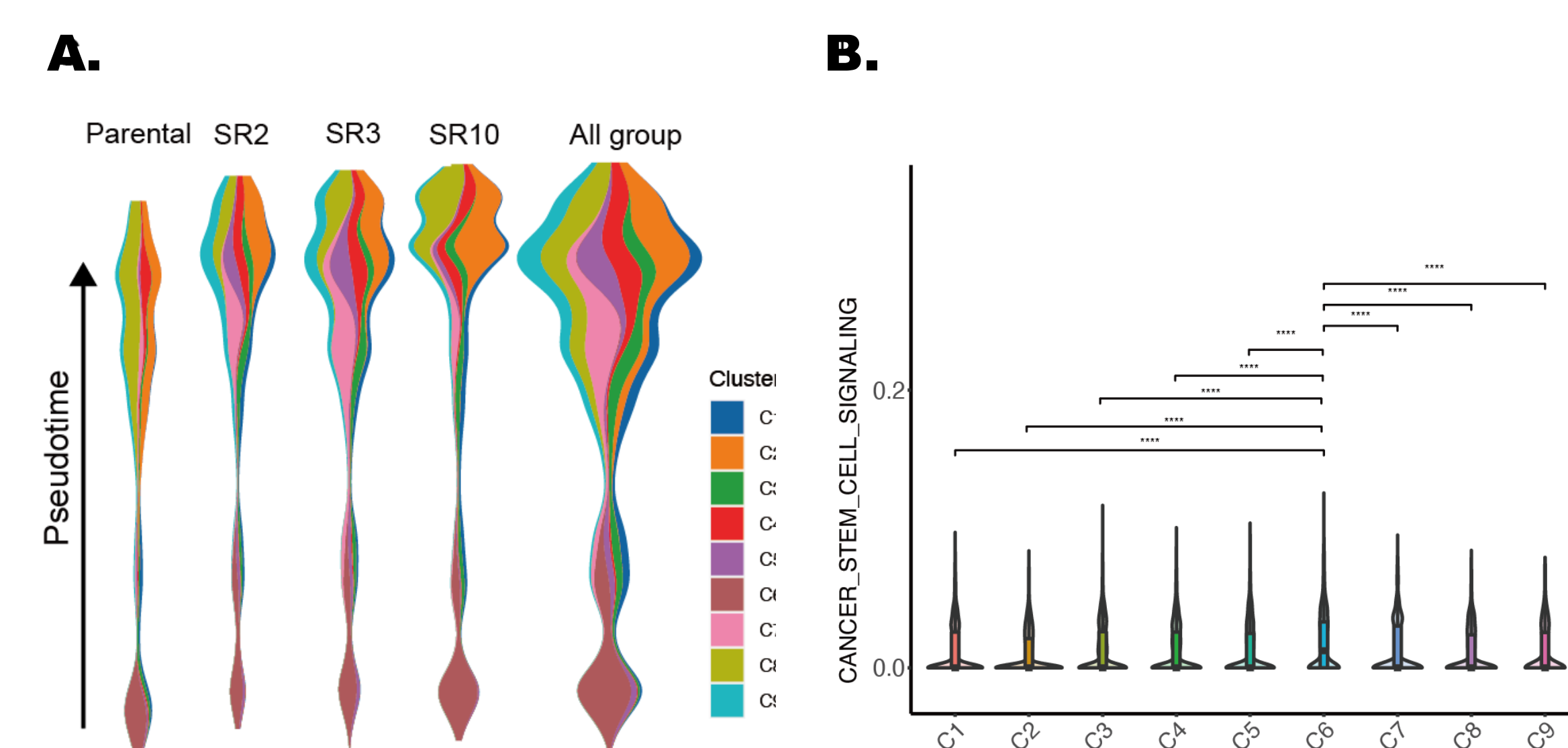


Fig 3 Characteristics of cancer stem cells in Cluster 6



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