**Single cell RNAseq analyses reveal the cellular heterogeneity and molecular changes of AML/MDS**

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[Introduction] Myelodysplastic Syndromes (MDS) represent a heterogeneous group of acquired bone marrow failure syndromes characterized by ineffective hematopoiesis and increased risk of progression to acute myeloid leukemia (AML). AML is an aggressive hematological cancer. The induction therapy can induce remission in 70-80% of patients, but the majority of patients eventually relapse. It is considered that heterogeneity within each patient is the cause of relapse. However, genetic and epigenetic heterogeneity of MDS/AML has not been investigated at high resolution until very recently, and many questions remain about the impact of these mutations and alterations and the divergent clinical response.

[Methods] We analyzed banked bone marrow samples of ten AML/MDS patients at two distinct time points by full-length single cell RNA-seq (scRNAseq) and whole genome sequencing (WGS). We inferred the cell types of each cell in hematopoiesis. We also predicted the activities of transcription factors (TF) based on gene regulatory network reconstructed from single cell gene expression profiles. In addition, we called variants from scRNAseq reads and compared to WGS.

[Results] The lineage inference showed distinct patterns between normal and AML/MDS bone marrows. Also interestingly the dominant cell types may change during the course of diseases indicating the changes in molecular characteristic of leukemic cell.

We compared mutant cell to wild type cells of one MDS patient. And we identified distinct TF activities in mutant cells. Mutant cells still remained at marrow complete remission (MCR). However, the mutant cells at MCR exhibited TF activities rather similar to wild type cells, which may suggest that the remaining mutant cells are benign clonal hematopoiesis population that existed before MDS was developed.

[Conclusion] Single cell data analyses revealed heterogeneity of cells, and molecular changes from two time points at unprecedented resolution. We demonstrated that single cell multi-omics data of mutation and expression could provide a deep insights into molecular mechanism of the disease.