



Genomic profiling of Chinese patients with acute myeloid leukemia and myelodysplastic syndrome

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Objective

In this study, we aimed to investigate the genomic difference of Chinese patients with myelodysplastic syndrome (MDS) and acute myeloid leukemia (AML), as well as the difference between Asian and Western.

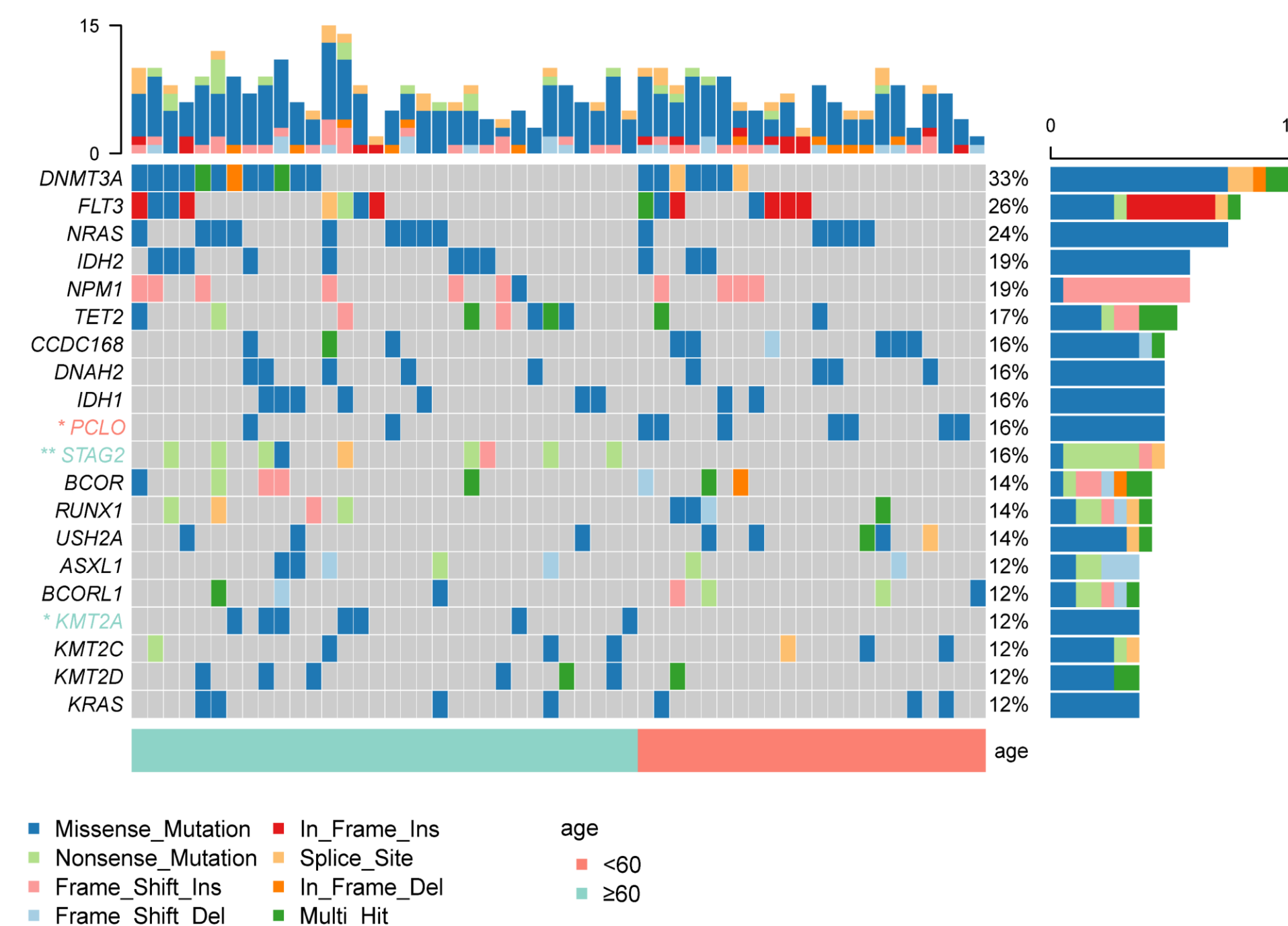
Methods

We systematically analyzed somatic alterations of the fresh bone marrow aspirate or peripheral blood specimens from 58 patients with AML and 26 patients with MDS with a hybridization capture-based Next-Generation Sequencing (NGS) panel including 196 genes known to be somatically altered in human hematological malignancies.

Results

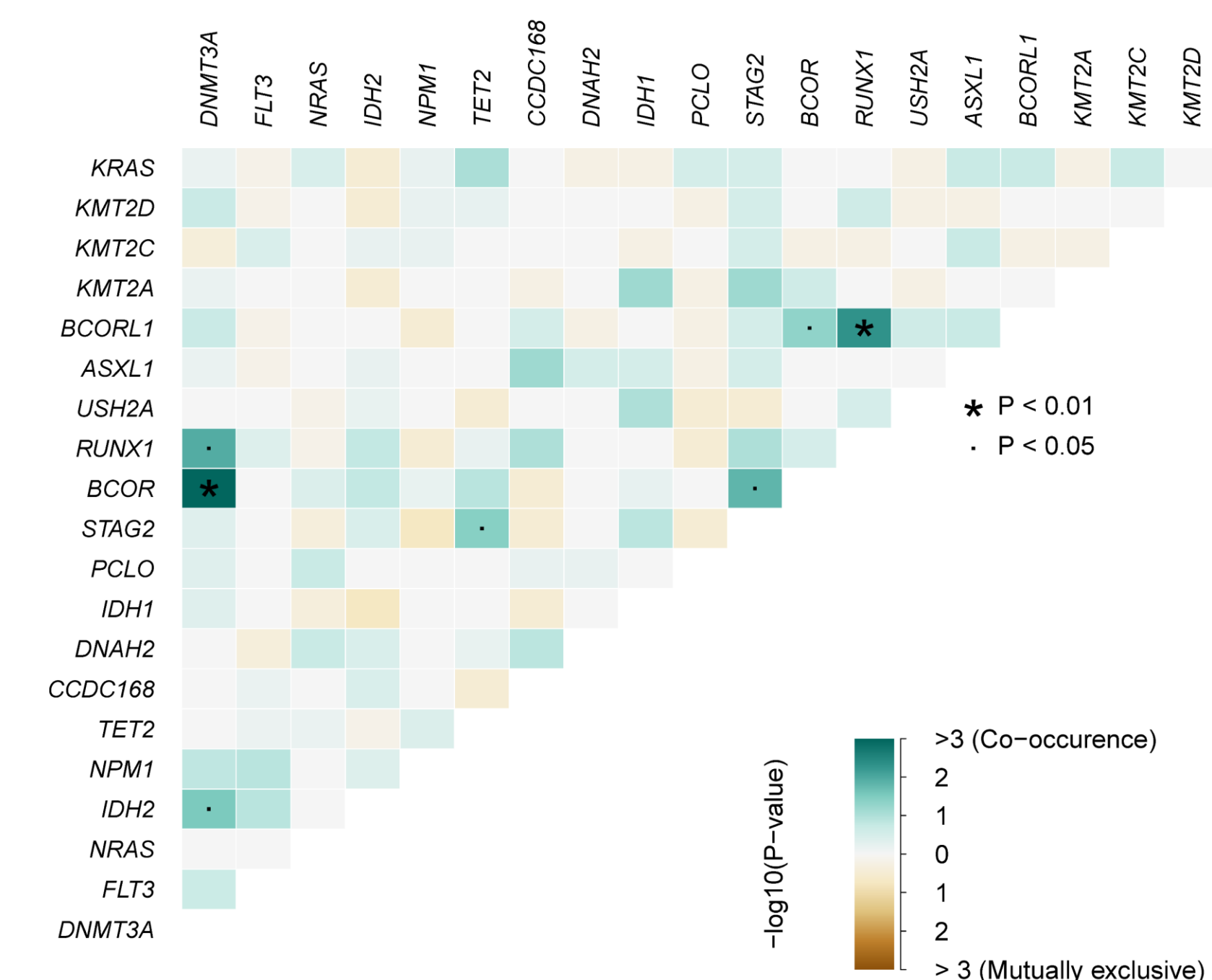
- At least one non-synonymous gene mutation was detected in 54 AML patients (93.1%) and 23 MDS patients (95.83%). Compared with AML patients aged < 60 years old, higher frequencies of *STAG2* (27.3% vs. 0%, $P < 0.01$) and *KMT2A* (21.2% vs. 0%, $P < 0.05$) mutations, and a lower frequency of *PCLO* (6.1% vs. 28%, $P < 0.05$) mutation was observed in patients ≥ 60 years, highlighting differences in the mutational landscape of AML between older and younger patients.

Age-based genomic landscape in AML patients

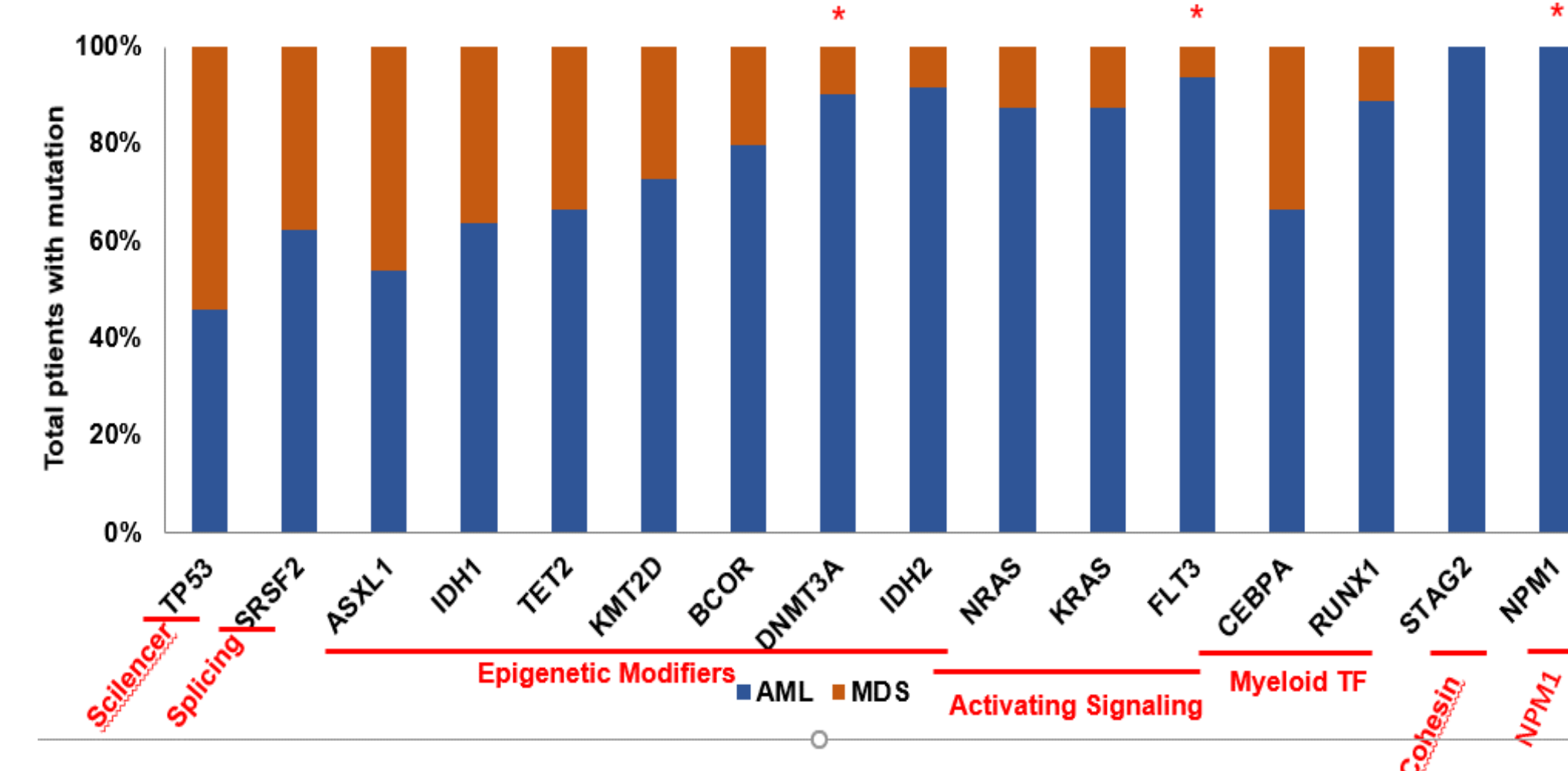


- Strong tendencies of co-occurring mutations were identified between *DNMT3A* and *IDH2*, *BCOR* and *RUNX1* in AML patients ($P < 0.05$, $P < 0.01$ and $P < 0.05$, respectively).
- Mutations of genes involved in major cellular pathways that were shared by MDS and AML, including spliceosome genes, epigenetic modifiers and *TP53*. By contrast, mutations in transcriptional deregulation (e.g., *RUNX1*, *CEBPA*) and activated signaling related genes (e.g., *NRAS*, *KRAS*, *FLT3*) are more common in AML, with *DNMT3A* (32.8% vs. 7.7%, $P < 0.05$), *FLT3* (25.9% vs. 3.8%, $P < 0.05$) and *NPM1* (19.0% vs. 0%, $P < 0.05$) mutations at significantly higher frequencies than MDS.

Epistatic interactions among driver genes in AML

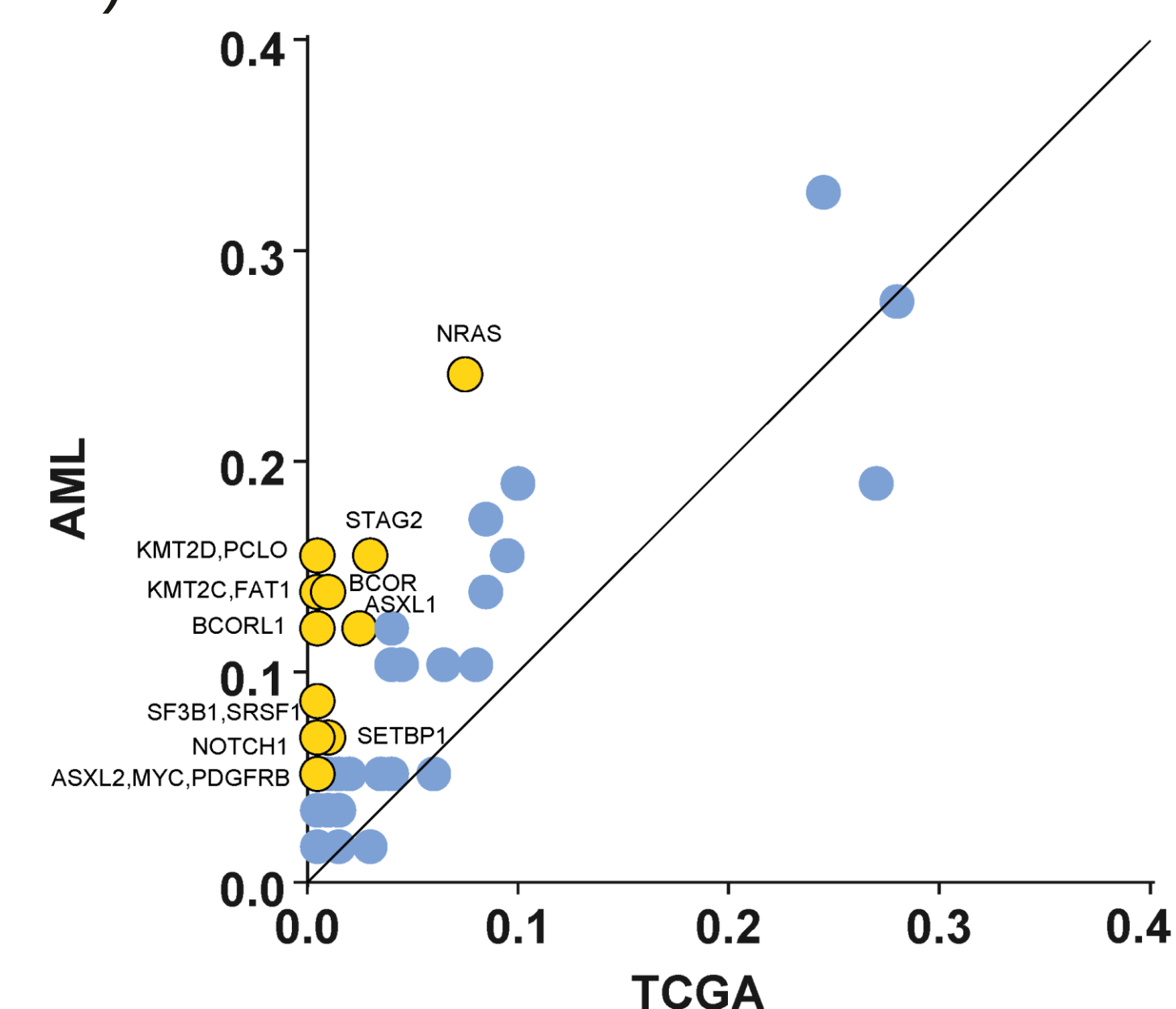


Signaling pathways of mutational genes



Mutational difference in AML and TCGA cohorts

- Compared with TCGA cohort of AML, 15 genes were found to mutate at higher frequencies in our cohort. They were mainly involved in RNA splicing (*SF3B1*, *SRSF2*), epigenetic modifiers (*ASXL1*, *ASXL2*, *BCORL1*, *BCOR*, *SETBP1*, *KMT2D* and *KMT2C*) and activated signaling (*NRAS*, *MYC*, *PDGFRB* and *NOTCH1*).



Conclusions

In this study, we elucidated the landscape of gene mutations in Chinese AML/MDS, and we further identified significant genomic differences between Asian and western patients, which should improve our understanding of pathogenesis and/or a better selection of targeted therapies.