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Low MS4A3 Expression Inhibits Differentiation of HSPCs in Patients with Myelodysplastic Syndromes

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INTRODUCTION

Impaired differentiation of bone marrow hematopoietic stem/progenitor cells (HSPCs), leading to haematopenia, is an important disease feature of MDS. Currently, first-line therapeutic agents are limited, so it is necessary to further research on the mechanisms of MDS cell differentiation disorder. The expression of MS4A3 in MDS-HSPCs is significantly decreased, which may be related to poor prognosis.

AIM

MS4A3 expression gradually increases during myeloid differentiation of normal bone marrow HSPCs cells, and the low expression of MS4A3 inhibits CML stem cell differentiation[1]. Our study shows that the low expression of MS4A3 in MDS may be related to the cell differentiation disorder and affects the prognosis of MDS, which may be a new target for therapy.

METHOD

Bone marrow from three healthy volunteers and three patients with newly diagnosed MDS were collected for single-cell sequencing, and the sequencing data were obtained and further analysed in conjunction with the GEO database datasets (GSE111085, GSE58831).

RESULTS

After dimensionality reduction clustering and annotation, from the scale graph（Figure a）, it could be seen that the proportion of HSC, MPP, and granulocytes increased, and the proportion of GMP, MDP and Pro-B decreased in the patient group. Among them, the expression of MS4A3 was significantly reduced in HSC, MPP, GMP and MDP cells (Figure b). Significant reduction in MS4A3 expression also occurred in patients with stable MDS (sMDS) in the GSE111085 dataset (Figure c), although there was no significant difference, compared with sMDS, the trend of MS4A3 expression was downward in patients who converted to AML within 12 months (Figure d). Clinical data from the GSE58831 showed that low expression of MS4A3 was associated with a poorer survival prognosis (Figure e).

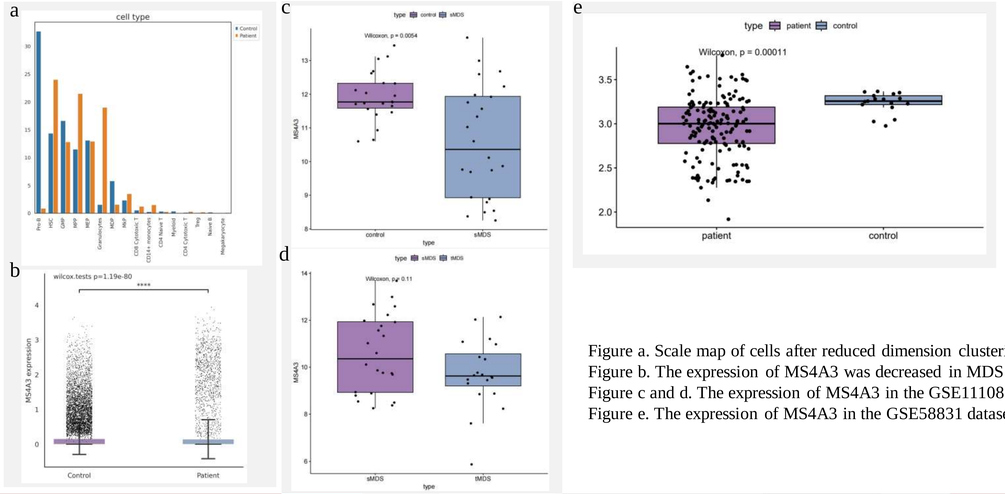


Figure a. Scale map of cells after reduced dimension clustering
Figure b. The expression of MS4A3 was decreased in MDS patients
Figure c and d. The expression of MS4A3 in the GSE111085 dataset.
Figure e. The expression of MS4A3 in the GSE58831 dataset.

CONCLUSIONS

HSPCs differentiation is impaired in MDS patients with increased HSC ratio and decreased GMP. The decreased expression of MS4A3 in bone marrow HSPCs of MDS patients may lead to the cell differentiation disorder of HSPCs, and is related to the poor survival prognosis of MDS. MS4A3 may become a new therapeutic target.

REFERENCES

1 Zhao H, Pomicter AD, Eiring AM, et al. MS4A3 promotes differentiation in chronic myeloid leukemia by enhancing common β-chain cytokine receptor endocytosis. *Blood*. 2022;139(5):761-778.

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