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617.ACUTE MYELOID LEUKEMIAS: BIOMARKERS, MOLECULAR MARKERS AND MINIMAL RESIDUAL DISEASE IN DIAGNOSIS AND PROGNOSIS

G Protein-Coupled Receptor 183 Plays a Prognostic Factor in Acute Myeloid Leukemia By Regulating Immune Regulation

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BACKGROUND G protein-coupled receptor 183 (GPR183) is a critical oligoheptameric transmembrane receptor that regulates cellular immune responses. Its malfunction causes a variety of immunological and inflammatory disorders. GPR183 overexpression enhances B cell migration from the germinal center and plays a significant role in the pathogenesis of Chronic myeloid leukemia. However, its prognostic value and regulatory role in AML are not clear. This study aimed to reveal the prognostic significance of GPR183 in AML and the mechanism of its regulatory role in AML.

METHODS The expression level of GPR183 in 300 *deno* AML patients was analyzed by RT-qPCR. Combined with the clinical characteristics and treatment response of patients, the expression characteristics and clinical prognostic significance of GPR183 in AML were analyzed. The regulatory function of GPR183 in AML was investigated using shRNA-targeted knockdown or over expression of GPR183 in AML, and the impact of knockdown of GPR183 on tumor burden and survival of AML mice was further confirmed in vivo using an AML mouse model. By using bioinformatics techniques, the potential regulatory mechanisms of GPR183's effects on AML cells were further examined and verified.

RESULTS The expression level of GPR183 in AML cells was higher than that in normal samples, and its expression was significantly higher in older AML patients than in younger ones. By univariate and multivariate analyses, it was found that the high expression of GPR183 was an independent poor prognostic factor in AML patients for overall survival(OS) and eventfree survival(EFS), and the knockdown of GPR183 in AML cells could inhibit the proliferation of AML cells, promote apoptosis, and inhibit the migration of AML cells, and the in vivo model of AML mice showed that the knockdown of GPR183 could reduce the tumor load and prolong the survival of AML mice. Overexpression of GPR183 in AML cells promoted the growth and increased the drug resistance of AML drug. Single-gene GESA revealed that AML patients with high GPR183 expression had HALLMARK_ALLOGRAFT_REJECTION, HALLMARK_TNFA_SIGNALING_VIA_NFKB, HALLMARK_INFLAMMATORY_RESPONSE, HALLMARK_COMPLEMENT, and HALLMARK_CLEARING_VIA_NFKB, and HALLMARK_INFLAMMATORY_RESPONSE. COMPLEMENT, HALLMARK_IL6_JAK_STAT3_SIGNALING, and HALLMARK_IL2_STAT5_SIGNALING pathways were activated, and all of these top 5 activated pathways were associated with immune regulation.

CONCLUSION GPR183 plays a prognostic factor in Acute Myeloid Leukemia by regulating immune regulation

Disclosures No relevant conflicts of interest to declare.

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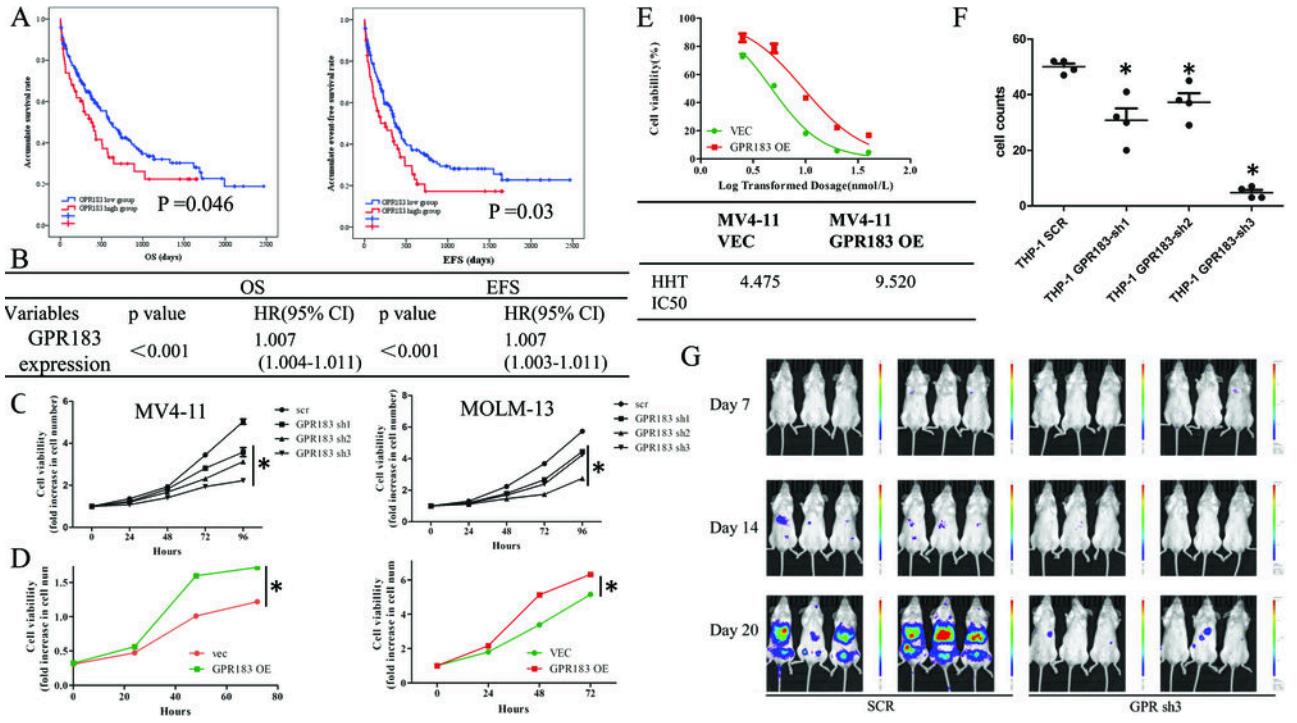

Figure 1

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