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PB1919 S100A9 DEFICIENCY ACCELERATES MDS ASSOCIATED TUMOR ESCAPE VIA PD-1/PD-L1 OVEREXPRESSION

Topic: 09. Myelodysplastic syndromes - Biology & Translational Research

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Background: MDS are mainly characterized by ineffective hematopoiesis contributed to inflammatory signaling or immune dysfunction. Our previous studies have shown that S100a9 expression was higher in low-risk MDS and lower in high-risk MDS.

Aims: In recent studies, the tolerable safety profile and positive BM response suggest a beneficial use of anti-PD-1 agents in the treatment of MDS, but the underlying mechanism is still unknown.

Methods: In this study, skm-1 cells and k562 cells co-cultured with S100a9 acquired apoptosis features. Moreover, we confirmed the inhibition effect S100a9 on PD-1/PD-L1. Importantly, PD-1/PD-L1 blockade and S100a9 can both activate the PI3K/Akt/mTOR signaling pathway. The cytotoxicity was higher in lower-risk MDS-lymphocytes than in high-risk MDS-lymphocytes, and S100a9 partially rescue the exhausted cytotoxicity in lymphocytes.

Results: Our study demonstrated that S100a9 may inhibit MDS associated tumor escape via PD-1/PD-L1 blockade through PI3K/Akt/mTOR signaling pathway activation.

Summary/Conclusion: Our findings indicated the possible mechanisms anti-PD-1 agents may contribute to the treatment of MDS. These insights may provide more accurate treatment as the supplementary therapy for MDS patients with high risk mutations, like TP53, N-RAS or other complex mutations.