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Total Flavonoids of Astragalus activate T cell anti-tumor immunity by reducing myeloidderived suppressor cells in 4T1 mammary tumor mice

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Abstract

Myeloid-derived suppressor cells (MDSCs) are a heterogeneous population of immature myeloid cells that increase in tumor-bearing hosts and suppress anti-tumor immunity to promote tumor growth and development. Thus, reducing the number or inhibiting the function of MDSCs may enhance anti-tumor immunity. Total flavonoids of Astragalus (TFA) are the main active components of Astragalus. The immunoregulatory effects of TFA have recently been extensively studied. However, the effect of TFA on MDSCs still remaines unknown. In the present study, we found that TFA treatment significantly alleviated the inhibitory effect of MDSCs on T cell proliferation in 4T1 mammary tumor mice. TFA decreased MDSCs accumulation in the bone marrow(BM), circulating blood, spleen, and tumor bed, whereas increased the percentage and activation of T cells in 4T1 mammary tumor mouse model. In addition, TFA treatment significantly reduced the number of MDSCs in BM cells induced by GM-CSF or the tumor burden in vitro. Mechanistically, the reduction of MDSCs was partially caused by increasing intracellular ROS level, which increased the apoptosis of Gr-1+ cells. In addition,TFA reduced the expression of iNOS and Arg-1 in both protein and transcription level. In conclusion,TFA could activate systemic T cell immunity by inducing apoptosis and inhibiting the function of MDSCs, suggesting that TFA has potential clinical benefits as it selectively attenuates MDSC-induced immunosuppression.

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