971 VISTA REGULATES THE DIFFERENTIATION AND FUNCTION OF MYELOID-DERIVED SUPPRESSOR CELLS

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Background Previous studies show that VISTA is a critical immune-checkpoint protein controlling the maturation of myeloid antigen-presenting cells in response to TLR signaling that in turn stimulates T cell activation. The role of VISTA in the differentiation and function of myeloid-derived suppressor cells (MDSCs) remains incompletely understood.

Methods Wild type and VISTA knockout mouse bone marrow monocytes were purified and myeloid-derived suppressor cells (MDSC) were cultured and purified. Total RNAs were isolated and cDNAs were made to examine the genes expression. Whole cell lysates were prepared and proteins level were determined by Western blot. MDSC cells were analysed in tumor models by flow cytometry.

Results Here, by studying BM-derived MDSCs and tumor-associated MDSCs, we have discovered that ablation of VISTA significantly reduces the expression of Arg1 and iNOS, as well as diminishing the inhibitory effects of MDSC on T cell activation. Mechanistically, VISTA directly controls the signaling of monocytes in response to inflammatory stimuli including GM-CSF and IL-6.

Conclusions Our studies uncover VISTA as an important regulator of MDSC differentiation and suggest that targeting VISTA may alleviate MDSC-mediated immunosuppression.

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