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Bone marrow -derived mesenchymal stem cells inhibiting CD8+ T cell immune responses via PD-1/PD-L1 pathway in multiple myeloma

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Abstract

High expression of the inhibitory receptor programmed death ligand 1 (PD-L1) on the surface of tumor cells have been found play a key role in tumor immune evasion in several human malignancies. However, the expression of PD-L1 on bone marrow mesenchymal stem cells (BMSCs) and whether the PD-1/PD-L1 axis is involved in the BMSCs versus T cell immune response in Multiple Myeloma (MM) remain poorly defined. In this study, we explored the expression of PD-L1 on BMSCs from MM patients and the role of PD-1/PD-L1 pathway in BMSCs-mediated regulation of CD8+T cells. We observed that the expression of PD-L1 on BMSCs was significantly higher in NDMM group, compared with the NC group (18.81±1.61% vs. 2.78±0.70 %; P<0.001). Furthermore, the expression of PD-1 on CD8+ T cells in NDMM group was significantly higher than that in control group (43.22±2.98% vs. 20.71±1.08%; P<0.001). However, there was no significant difference in PD-1 expression of CD4+ T cells and NK cells between NDMM group and NC group. Additionally, the co-culture assays revealed that BMSCs significantly promoted CD8+ T cell apoptosis and suppressed CD8+ T cell function. However, PD-L1 inhibitor effectively reversed BMSCs-mediated suppression in CD8+ T cells. We also found that the combination of PD-L1 inhibitor and pomalidomide can further enhance the killing effect of CD8+ T cells on MM cells. In summary, our findings demonstrated that BMSCs may induce apoptosis and functional imbalance of CD8+ T cells via PD-1/PD-L1 pathway and promote the immunity escape of MM.

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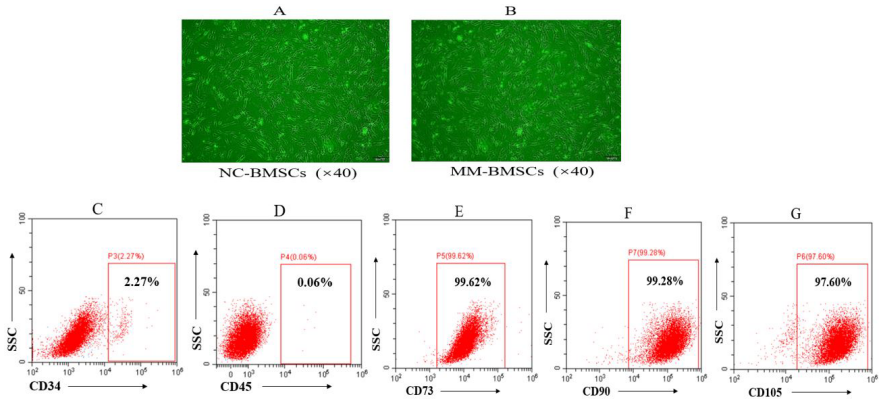

Figure 1: This is a caption

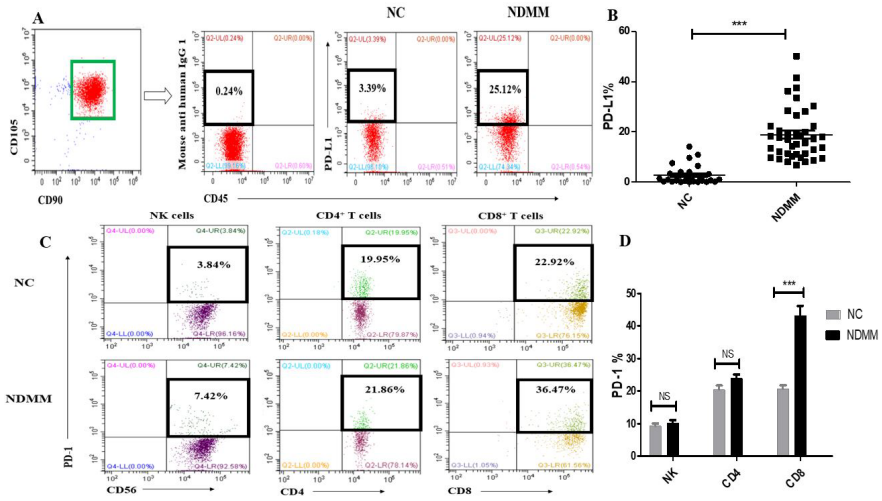

Figure 2: This is a caption

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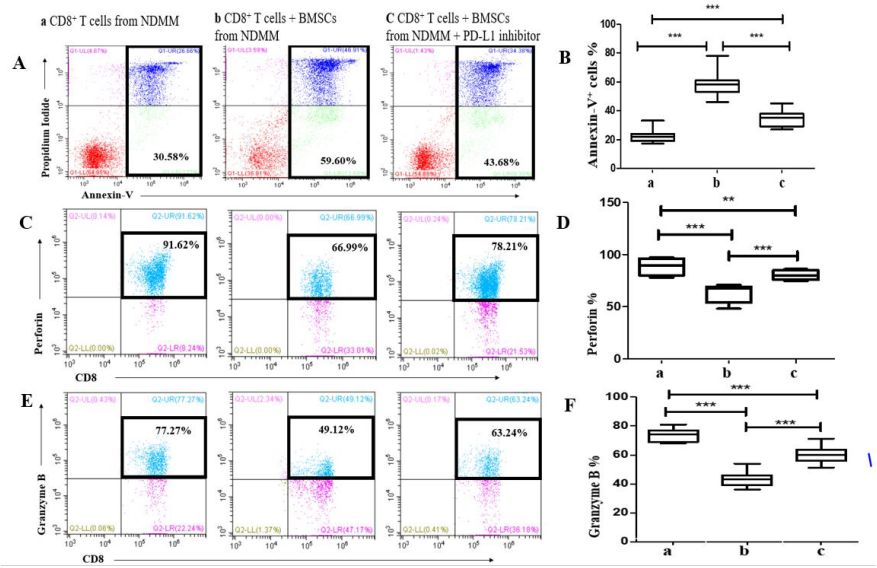

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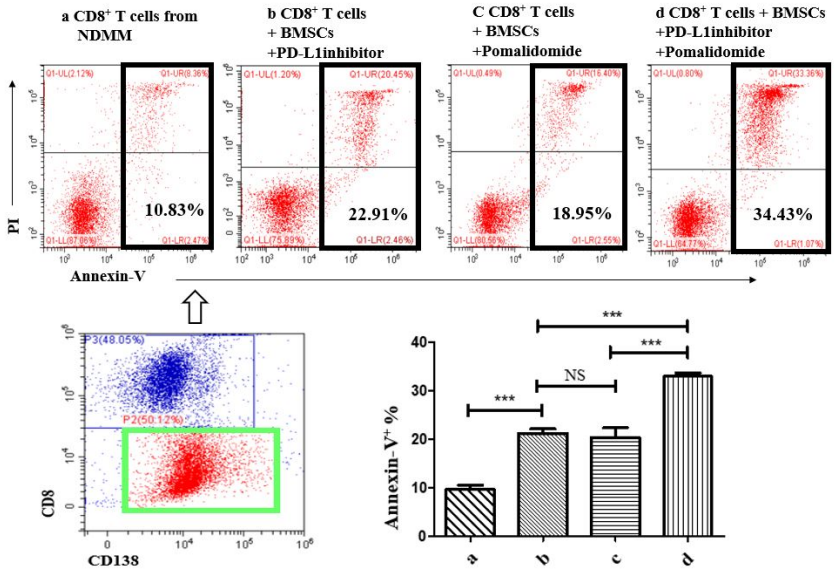

Figure 4: This is a caption

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Table 1 Baseline characteristics of patients with NDMM1.doc available at https://authorea.com/users/323220/articles/452026-bone-marrow-derived-mesenchymal-stem-cells-inhibiting-cd8-t-cell-immune-responses-via-pd-1-pd-l1-pathway-in-multiple-myeloma