Ex vivo Efficacy of Adoptive T cell Therapy using Autologous CD8+ T cells isolated by PD-1 Positivity from Peripheral Blood Mononuclear cells in Solid Tumors

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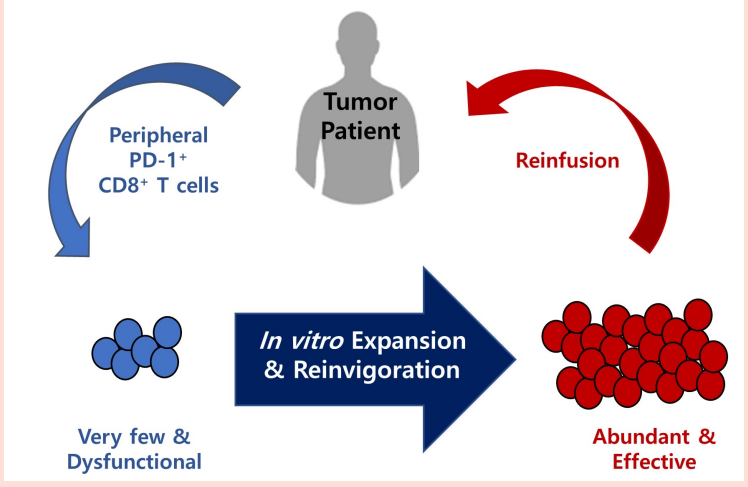
Abstract

Tumor-infiltrating lymphocytes have been shown to display an antitumor activity in solid tumors including melanoma. Previously the proof of concept was developed that CD8+ T cells isolated by programmed cell death-1 (PD-1) receptor positivity from peripheral blood mononuclear cells (PBMCs), recognized tumor-specific antigens and neoantigens, and thus were reactive to tumors. We evaluated ex vivo efficacy of autologous, tumor-reactive CD8+ T cells isolated by PD-1 positivity from PBMCs of breast cancer, ovarian cancer and leiomyosarcoma patients. Autologous PD-1+CD8+ T cells isolated from PBMCs of a few cancer patients displayed efficient antitumor activity in our established ex vivo models for adoptive cell therapy. Our results warrant further clinical development for adoptive T cell therapy in various types of cancers.

Introduction (A Therapeutic Model)



Results

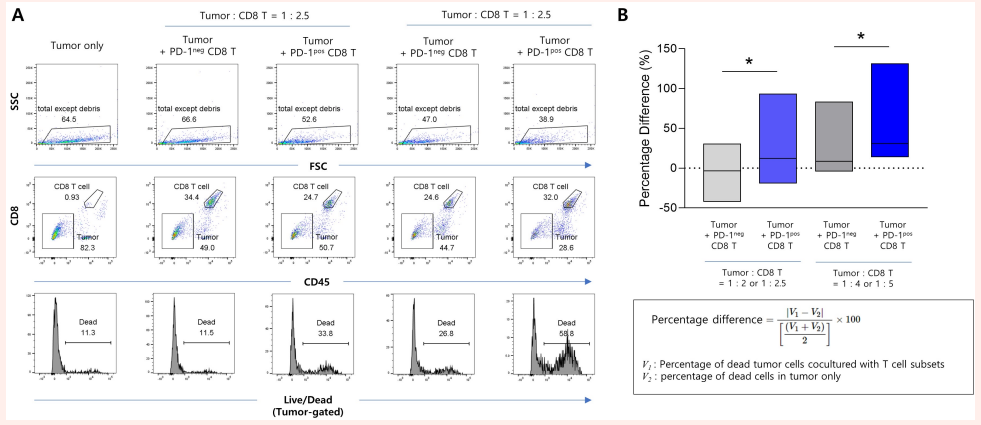


Figure 1. Autologous PD-1 positive CD8+ T cells from PBMC efficiently killed patient-derived tumor cells compared to PD-1 negative CD8+ T cells in the breast cancer (A and B) Flow cytometric analysis of the killing ability of autologous CD8 T cell subsets from PBMC against ex vivo cultured breast cancer cells. Representative FACS data are shown in A, and pooled data with mean ± sem from 6 independent experiments are shown in B. Statistical Analysis was performed using paired two-tailed t test (*p < 0.05)

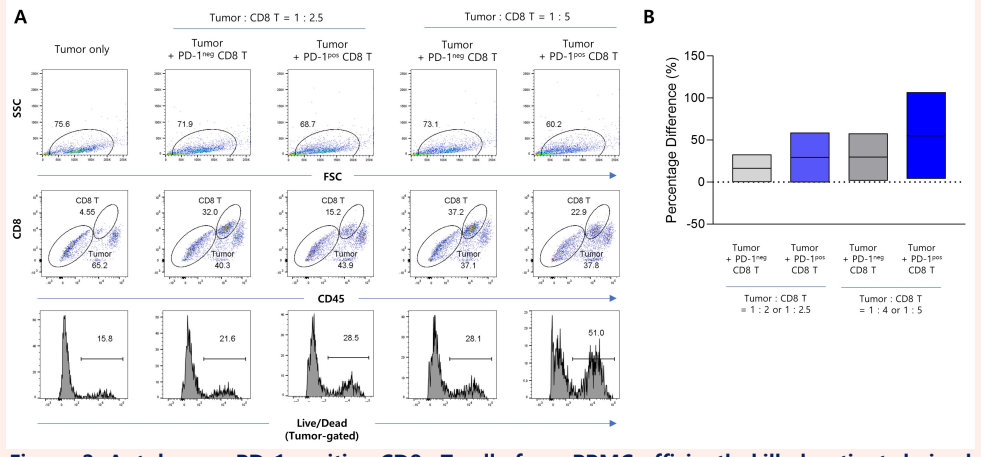


Figure 2. Autologous PD-1 positive CD8+ T cells from PBMC efficiently killed patient-derived tumor cells compared to PD-1 negative CD8+ T cells in the ovarian cancer (A and B) Flow cytometric analysis of the killing ability of autologous CD8 T cell subsets from PBMC against ex vivo cultured ovarian cancer cells. Representative FACS data are shown in A, and pooled data with mean ± sem from 2 independent experiments are shown in B.

Results

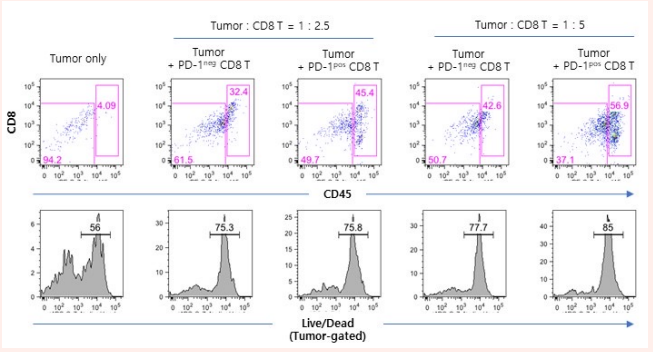


Figure 3. Autologous PD-1 positive CD8+ T cells from PBMC efficiently killed patient-derived tumor cells compared to PD-1 negative CD8+ T cells in leiomyosarcoma
Flow cytometric analysis of the killing ability of autologous CD8 T cell subsets from PBMC against ex vivo cultured leiomyosarcoma cells.

Conclusions

1. **We have successfully established ex vivo models for adoptive cell therapy using autologous PD-1 positive CD8+ T cells.**
2. **We demonstrated that circulating PD-1 positive CD8+ T cells from patients with breast cancer, ovarian cancer and leiomyosarcoma exhibit potent killing activity against autologous tumor cells compared to their PD-1 negative CD8+ T cell counterparts.**
3. **Adoptive T cell therapy using patient-derived peripheral blood PD-1 positive CD8+T cells can extend clinical application into varied types of solid tumors, which represents a promising strategy of personalized cancer immunotherapy.**