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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Background 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 and leiomyosarcoma patients.

Methods Fresh tumor tissues were cultured in RPMI supplemented with 20% FBS. PD-1 positive CD8+ T cells were isolated from PBMCs of the patients and expanded with Dynabeads human T-Activator CD3/CD28 in RPMI supplemented with 10% FBS and IL-2. Antitumor activity of PD-1-positive CD8+ T cells was tested by performing cytotoxic T lymphocyte (CTL) assay with the cultured autologous tumor cell targets. Specifically, the CTL assay was carried out by culturing tumor cells in multi-well plates overnight, and then adding the PD-1+CD8+ T cells to the plates. After 2 days, tumor cells were harvested from the wells and stained for CD45, CD8 and Live/Dead (ThermoFisher Scientific) to determine the killing activity of PD-1+CD8+ T cells. The results were compared to ones obtained with PD-1-CD8+ T cells.

Results We have successfully established ex vivo models for adoptive cell therapy using autologous PD-1+CD8+ T cells from three breast cancer and one leiomyosarcoma patients. Two breast cancer patients were hormone-receptor-positive and one was triple-negative. Stages were IA (n=1) or IIB (n=2). One leiomyosarcoma patient was in stage IV. All tumor and peripheral blood samples were obtained at chemotherapy-naïve status. CTL assays demonstrated that PD-1+CD8+ T cells efficiently killed target cells compared to PD-1-CD8+ T cells in all the breast cancer and leiomyosarcoma models. More and detailed results will be presented and discussed.

Conclusions 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.

<http://dx.doi.org/10.1136/jitc-2021-SITC2021.185>