by the antitumor immune-activating effect of HVJ-E itself with the inhibition of tumor PD-L1 molecule expression. We confirmed that intratumoral injection of HVJ-E containing siRNA targeting PD-L1 (siPDL1/HVJ-E) inhibited tumor PD-L1 protein expression in a mouse subcutaneous tumor model using TS, a mouse glioma stem-like cell. We conducted treatment experiments in the mouse brain tumor model in three groups: control group (PBS), siNC/HVJ-E group (negative control siRNA + HVJ-E), and siPDL1/HVJ-E group. We obtained a significant prolongation of overall survival in the siPDL1/HVJ-E group. Flow cytometric analyses of brain tumor models showed that the proportions of brain-infiltrating CD8+ T lymphocytes and NK cells were significantly increased after giving siPDL1/HVJ-E; in contrast, the rate of Treg/CD4+ lymphocytes was significantly decreased in HVJ-E-treated tumors (siNC/HVJ-E and siPDL1/HVJ-E). No difference was observed in the proportions of macrophages or M2 macrophages. CD8 depletion abrogated the therapeutic effect of siPDL1/HVJ-E, indicating that CD8+ T lymphocytes mainly mediated this therapeutic effect. We believe that this non-replicating immunovirotherapy may be a novel therapeutic alternative to treat patients with glioblastoma. The full article has been published (Cancer Science. 2021 Jan;112(1):81–90).

Key words: regulatory T lymphocyte | malignant glioma | PD-L1

IM-7

IDENTIFICATION OF NOVEL GLIOBLASTOMA SPECIFIC ANTIGEN USING PATIENT DERIVED TUMOR CELL FOR CAR-T CELL THERAPY

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Chimeric antigen receptor T (CAR-T) cell therapy is a newly developed antitumor immunotherapy presenting remarkable clinical response with leukemia, and is expected to be applied to other malignant solid tumors including glioblastoma (GBM). However, for development of CAR-T therapy against GBM, identification of novel and suitable tumor specific antigen is required to expect higher therapeutic efficacy. Herein, we developed our original method to detect novel GBM specific antigen using patient derived GBM (PD-GBM) cells. First, BALB/c mice were immunized by footpad injection of PD-GBM cells. B cells were extracted from lymph nodes of the mice, fused with murine myeloma cells, and then cultured to produce monoclonal antibodies for GBM cells. About 500 GBM binding monoclonal antibody lines were established, and then each antibody was again analyzed by flow cytometry with multiple PD-GBM cells and human non-tumor brain cells to find out GBM specific antibodies. Consequently, two GBM specific antibody lines were selected and genetically analyzed to identify the recognized antigen. CAR-T cells targeting the detected antigens were successfully generated, and the cytotoxicity against GBM cells was confirmed by chromium releasing assay and bioluminescent cytokine assay. Remarkably, one of the identified tumor specific antigens proved to be B7-H3, which is known pan-cancer antigen expected to be one CAR-T therapeutic target for malignant solid tumors, also expressed in most GBM cells. This result confirms that our experimental method using murine antigen-antibody reaction is feasible for detecting antigen as a novel CAR-T therapeutic target for GBM. Moreover, this method can also detect antigens derived from post-translational conformational changes such as glycosylation, which might have been overlooked by conventional methods. In addition, these results suggest our method using PD-GBM cells can identify potential targets of CAR-T therapy for each GBM patients respectively, thus leading to precision immunotherapy for GBM.

Key words: CAR T cell therapy | neurosphere | glioblastoma

IM-8

SIGNIFICANCE OF IL-1 PATHWAYS IN GLIOBLASTOMA

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Purpose: Previous studies have revealed that macrophages affect the prognosis of glioblastoma. However, there are still many unknown parts about the mechanism. In this study, we conducted an experiment with the aim of elucidating the mechanism by which tumor associated macrophages (TAM) work on tumors in the tumor microenvironment (TME). Method: Experiments were carried out using two glioblastoma cell strains, T98G, and U251. For clinical data, we analyzed it based on databases such as Protein Atlas, Ivy Glioblastoma Atlas, brain TIME database. Results: In 3D culture, we confirmed that IL-1β stimulation promoted glioblastoma cell proliferation and sphere formation. The addition of IL-1β increased mRNA expression of various cytokines such as IL-6 and CXCL8, and increased phosphorylation of STAT3 in arrays. When we administered IL-6 and CXCL8, the growth was significantly increased in cells administered with IL-6 and CXCL8. As a result, we speculated that STAT3 pathway and NFκB pathway via IL-6 and CXCL8 are involved in cell proliferation by IL-1β. In order to confirm these things, western blot was performed, and it was confirmed that phosphorylation of STAT3 and NFκB were increased. In addition, STAT3 inhibitors and NFκB inhibitors suppressed tumor growth. Clinically analysis was carried out based on the database, and it was found that IL-1β and macrophages were related. Furthermore, IL-1β was found in many cases around tumor necrosis. Discussion: This study clarifies some of the effects of IL-1β on glioblastoma. However, there are still many unknown points, and it is necessary to continue to consider them in the future.

Key words: Glioblastoma | Macrophage | IL-1β

BASIC OTHERS (BOT)

BOT-3

PROGNOSTIC FACTORS OF CNS GERM CELL TUMORS; MOLECULAR AND HISTOPATHOLOGICAL ANALYSES ON 154 CASES FROM THE IGCT CONSORTIUM

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