351 EXPANSION OF T CELLS FROM THE CEREBROSPINAL FLUID OF MELANOMA PATIENTS WITH LEPTOMENINGEAL DISEASE

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Background Leptomeningeal Disease (LMD) is a devastating complication from cancer, with a median survival of 6 to 8 weeks. The incidence of LMD is highest in melanoma patients (5–25%) and carries the worst prognosis, yet treatments and clinical trials are virtually lacking. Since adoptive cell therapy (ACT) using tumor-infiltrating lymphocytes (TIL) showed complete and durable responses in patients with advanced metastatic melanoma, TIL transfer may represent a novel therapeutic approach for patients with LMD from melanoma. The goal of this study is to isolate and expand T cells from the cerebrospinal fluid (CSF) obtained from patients with LMD from melanoma and to study their anti-tumor effect.

Methods CSF was collected from 6 melanoma patients with LMD via lumbar puncture or Ommaya tap. The initial volume was measured and the isolated cells were plated following established TIL culture protocols to determine optimal expansion conditions, including: 1) 6000 IU/mL of IL-2, 2) OKT3, and 3) anti-4–1BB agonistic antibody. CSF cultures were evaluated after the initial 4–6 weeks and T cells were further propagated via the rapid expansion protocol (REP), where available. The final T cell product was phenotyped for CD4+ and CD8+ T cells using flow cytometry.

Results An average of 6.31 mL of CSF was collected from patients with LMD, resulting in an average yield of 2.74e4 viable cells available for expansion (range: 1e3–2.43e6). After initial culture in IL-2, 75% demonstrated an increased cell yield, with an average of 271.79-fold expansion (range 3.85–1054). Phenotypic analysis of preREP TILs revealed approximately 67% of the samples were predominantly CD4+ T cells. Four samples subsequently underwent a REP, with a 100% success rate and average 231.99-fold expansion (Range 11.4–710.2). Post-REP products were analyzed by flow cytometry for the frequency of CD4+ and CD8+ T cells. Preliminary data from the postREP analysis revealed a similar result, with further expansion of CD4+ T cells. Ongoing experiments, analyzing the stimulatory effect of OKT3 and 4–1BB are producing similar expansion with a reduced T cell input requirement and final analysis will be revealed. Also, current efforts are focused on the evaluation of the tumor specificity of these expanded T cells with data forthcoming.

Conclusions Therapies for LMD patients are desperately needed. Results demonstrate successful expansion of T cells ex vivo from CSF from patients with melanoma LMD. Results raise potential to use TILs as a therapeutic strategy for patients with LMD in the future.

Ethics Approval This study was approved by the Ethics Committee and Internal Review Board (protocol MCC 19332). Tissue collected for analyses was performed after patient's approval and consent.

Consent This study does not require informed consent to participate or publish the study.

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