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Identifying biomarkers for predicting the response of MSC11FCD therapy to recurrent glioblastoma patients

Ju-Won Kim[1], JeongMin Sim[1], Jaejoon Lim[2,*], and Sohyun Hwang[3,4,*]

[1]*Department of Biomedical Science, CHA University*
[2]*Department of Neurosurgery, CHA Bundang Medical Center, CHA University School of Medicine*
[3]*Department of Pathology, CHA Bundang Medical Center, CHA University School of Medicine*
[4]*CHA Future Medicine Research Institute, CHA Bundang Medical Center*
*Corresponding author: coolppeng@chamc.co.kr (J.L.), blissfulwin@cha.ac.kr (S.H.)

Glioblastoma is an extremely aggressive malignant brain tumor and recurs in a short period of time. After recurrence, treatment options are very limited and challenging. Therefore, better treatment for recurrent glioblastoma is required. 5-Fluorouracil (5-FU) is one of the cytotoxic anti-cancer chemotherapy treatments, primarily for colorectal and stomach cancers. The conventional 5-FU treatment cannot be utilized in glioblastoma, because 5-FU cannot traverse the Blood-Brain Barrier. To address this issue, we conducted a Phase 1 clinical trial of MSC11FCD therapy in 10 patients (ClinicalTrials.gov identifier: NCT04657315). We directly injected MSC/CD (mesenchymal stem cell/cytosine deaminase) into the resection cavity of patients and administered 5-Fluorocytosine (5-FC) orally to them. We are expecting that cytosine deaminase could convert 5-FC into 5-FU in brain tumor area of patients. When we evaluated the treatment responses based on the RANO criteria, five patients responded the treatment well and left five would not. To understand the difference in treatment response, we performed RNA sequencing and identified differentially expressed genes (DEGs) based on patient response. And then, to understand the biological pathways associated with the DEGs, we performed pathway enrichment analysis. Pathways related to the cell cycle and resistance to 5-FU were enriched. Lastly, we identified genes that effectively discriminate treatment responses based on prognosis using Lasso-survival analysis. Through these findings, we could identify biologically important genes in 5-FU treatment as well as predicting the response to MSC11FCD therapy in patients with recurrent glioblastoma. These key genes could be very helpful for understanding molecular mechanisms of 5-FU treatment in recurred glioblastoma as well as for predicting the response to the treatment.