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Study of Sialic acid effect on the *HMGA1* and *HMGA2* gene expression in glioblastoma cell lines 1321N1

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Abstract

. Glioblastoma cancer is one of the most common and an aggressive cancer of the central nervous system, which is resistant to all types of cancer treatments such as surgery, radiotherapy, and chemotherapy, and has a poor prognosis. Its treatment is limited with low efficacy. The survival age of patients after high-efficiency treatment is less than one year, and about 2% of patients survive less than 3 years. The immunotherapy method shows better results for the use of peptide vaccines, dendritic tuberculosis vaccines, and chimeric receptors from T gene cells, treatment with architectures from cell cycle control genes and focus virus oncolytic treatment. One of the compounds that are abundant in cell membranes, especially nerve cells, is sialic acid. Research has shown its increase in cells related to colorectal cancer, breast, etc., which leads to the induction of tumor cell metastasis. According to the scientific reports about the induction effect of the cell microenvironment on the expression of metastasis factors in the cell, in the present research, in order to achieve a molecular definition of the effect of sialic acid on the signaling related to metastasis, it has sought to investigate the effect of this treatment on the expression of *HMGA2* and *HMGA1* genes. The *HMGA2* gene is a transcriptional mediator that mediates motility and self-renewal in normal and cancer stem cells. The *HMGA2* gene is considered as an invasion factor in glioblastoma cells. One of the things that cause diversity in glioblastoma cancer and its treatment resistance is the presence of stem cells in this cell. One of the important transcription factors that can work in this path is *HMGA1* through epigenetic and affects *Sox2* gene expression as the main stem cell marker. Increased expression of *HMGA1* increases proliferation, invasion and angiogenesis. First, the effective dose of sialic acid was determined by the MTT method on the glioblastoma cell line, and after the treatment of cells in different doses, RNA extraction and then cDNA synthesis were performed simultaneously in treated cells and untreated cells (as control) was done. Finally, a quantitative analysis of the expression changes of two *HMGA1-HMGA2* genes was done by real-time method and related analyzes were performed. Both genes showed a significant increase in the dose of 200 micro molar sialic acid, but in higher doses, there was a significant decrease. According to the past reports that have shown the inducing effect of sialic acid on the microenvironment of many cancers, it can be seen here that sialic acid in low concentrations increases the expression of genes that prevent the spread of tumor cells. But in high concentrations, it causes a severe reduction in the transcripts of the two target genes in this study, which will provide suitable conditions for tumor growth and expansion. Considering that sialic acid is produced as a natural sugar in many tissues of the body, we suggest to prevent the metastasis of cancer, especially glioblastoma, by suppressing and inhibiting sialic acid metabolism.

Keywords: Sialic acid, *HMGA1* gene, *HMGA2* gene, human Glioblastoma cell line