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Abstract

Changes in Gene Expression of Metalloproteinases-2 and -9 and Their Inhibitors TIMP2 and TIMP3 in Human Glioma Cells Exposed to Low Levels of Fluoride †

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Abstract: Introduction: Fluorine compounds are common environmental pollutants and may excessively penetrate the human body, especially the brain (fluoride penetrates the blood–brain barrier). Some of the latest studies have shown that fluoride may interfere with some of the metabolic pathways involved in the development of invasive potential in many types of cancer (e.g., Wnt/catenin or NF-κB). One of the stages of tumor invasion is the degradation of the extracellular matrix by metalloproteinases (MMP-2 and MMP-9), which allows for the migration and metastasis of cancer cells. Taking into account the above facts, we decided to check whether low concentrations of fluoride affect the expression level of genes encoding MMP-2 and MMP-9, as well as their TIMP-2 and TIMP-3 inhibitors, in human glioblastoma cells. Methods: U-87MG human glioblastoma cells were cultured with EMEM medium (10% FBS, 2 mM glutamine, 1% NEAA, 1 mM sodium pyruvate, 100 IU/mL penicillin, 10 µg/mL streptomycin) under optimal conditions (37 °C in an atmosphere of 5% CO_2 with 95% humidity). Cells were treated with sodium fluoride (NaF; 1–5 µM) for 24, 48, and 72 h. The analysis of the expression level of the MMP-2, MMP-9, Timp-2, and Timp-3 genes was carried out via RT-PCR. Results: The results indicate that NaF (0.1–5 µM) can disrupt the expression of MMP-2, MMP-9, Timp-2, and Timp-3. In the case of MMP-2, there was an approximately twofold increase in expression at 48 h (5 µM NaF) and about a 2.5-fold increase in expression at 72 h (0.1–5 µM NaF). For MMP-9, an approximately threefold increase in expression was observed at 24 h (0.1 µM NaF) and 48 h (5 µM NaF). Both Timp-2 and Timp-3 showed a significant increase in expression observed at all time points, especially at the highest concentration of NaF (5 µM). Conclusions: The obtained results suggest that even low concentrations of fluorine compounds may have an undesirable influence promoting the invasive potential of human glioblastoma cells.

Keywords: glioblastoma; fluoride; metalloproteinases; invasion

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