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Inhibition of U-87 human glioblastoma cell proliferation and formyl peptide receptor function by oligomer procyanidins (F2) isolated from grape seeds

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Abstract

Gliomas are the most common and lethal tumor type in the brain. The present study investigated the effect of oligomer procyanidins (F2) (F2, degree of polymerization 2–15), a natural fraction isolated from grape seeds on the biological behavior of glioblastoma cells. We found that F2 significantly inhibited the glioblastoma growth, with little cytotoxicity on normal cells, induced G2/M arrest and decreased mitochondrial membrane potential in U-87 cells. It also induced a non-apoptotic cell death phenotype resembling paraptosis in U-87 cells. In addition, it was found for the first time that F2 in non-cytotoxic concentrations selectively inhibited U-87 cell chemotaxis mediated by a G-protein coupled receptor formyl peptide receptor FPR, which is implicated in tumor cell invasion and metastasis. Further experiments indicated that F2 inhibited fMLF-induced U-87 cell calcium mobilization and MAP kinases ERK1/2 phosphorylation. Moreover, F2 attenuated the glioblastoma FPR expression, a new molecular target for glioma therapeutics, which has been shown to play important roles in glioma cells chemotaxis, proliferation and angiogenesis in addition to its promotion to tumor progression, but did not affect FPR mRNA expression in U-87 cells. Taken together, our results suggest that F2 may be a promising candidate for the development of novel anti-tumor therapeutics.

Keywords: Grape seed extract; Oligomer procyanidins; Glioma; Formyl peptide receptor; Chemotaxis; U-87

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