c-Fos over-expression promotes radioresistance and predicts poor prognosis in malignant glioma

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BACKGROUND: c-Fos is a major component of activator protein (AP)-1 complex. It has been implicated in cell differentiation, proliferation, angiogenesis, invasion, and metastasis. This study is designed to investigate the role of c-Fos in glioma radiosensitivity and to understand the underlying molecular mechanisms.

HYPOTHESIS: c-Fos over-expression would promote radioresistance and predicts poor prognosis in malignant glioma.

METHODS: we downregulated c-Fos gene expression by lentivirus-mediated shRNA in glioma cell lines and subsequently analyzed the radiosensitivity, DNA damage repair capacity, and cell cycle distribution. Finally, we explored its prognostic value in 41 malignant glioma patients by immunohistochemistry.

RESULTS: Our results showed that silencing c-Fos sensitized glioma cells to radiation by increasing radiation-induced DNA double strand breaks (DSBs), disturbing the DNA damage repair process, promoting G2/M cell cycle arrest, and enhancing apoptosis. c-Fos protein overexpression correlated with poor prognosis in malignant glioma patients treated with standard therapy. Our findings provide new insights into the mechanism of radioresistance in malignant glioma and identify c-Fos as a potentially novel therapeutic target for malignant glioma patients.