Investigating the Effect of Fibulin-2 on NF-kB Pathway Activity and Proliferation of Pediatric Gliomas

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The survival rate for patients diagnosed with gliomas (the most common type of brain tumor) is 5.6%. Gliomas are primarily driven by pathways like NF-kB signaling, which plays a key role in glioma proliferation. Fibulins are extracellular matrix (ECM) proteins, integral for cell adhesion. Some fibulins have been shown to have effects on the NF-kB pathway; however, Fibulin-2 has not been investigated in gliomas despite having inhibitory effects on other types of tumors. This project investigated the role of Fibulin-2 on cell proliferation and NF-kB pathway signaling, and it was hypothesized that Fibulin-2 would lead to decreased cell proliferation and decreased NF-kB signaling, indicative of tumor suppressors. The hypothesis was successfully tested and validated with a cell viability assay, which measured cell proliferation after addition of rhFibulin-2, as well as western blotting, which measured relative amounts of p65 and phospho-p65 after fibulin-2 treatment to determine NF-kB pathway activity. The cell viability assay showed that fibulin-2 led to a decrease in cell proliferation, as a 1000ng/ml treatment of fibulin-2 led to an 2% average decrease of cell proliferation across all four cell lines. This decrease was very significant, with a p-value of .0183 against the control in a two-tailed paired-t-test, and .0055 against fibulin-3 (a known tumor promoter). Western blotting showed that fibulin-2 led to a 45% decrease in NF-kB activity at a concentration of .5micrograms/ml. Overall, this investigation clearly demonstrates that targeting of ECM-proteins (important for cell structure and adhesion) is a possible novel mechanism for treatment of pediatric gliomas.

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