The Dominant Negative IQGAP1(IR-WW) Domain as a Potential Therapy in Brain Cancer

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Glioblastoma is a lethal brain tumor that currently has no effective treatment due to a lack of therapeutic targets. IQGAP1 is an oncoprotein that normally acts as a signaling scaffold that regulates diverse cellular functions which underlie cell dynamics, architecture, and proliferation. Genetic mutant analysis in breast cancer cells has shown that the various domains of IQGAP1 have distinct effects on cell proliferation. IQGAP1 is localized to the centrosome, and phosphorylation-cycling of IQGAP1 is important for its subcellular localization as well as its nucleocytoplasmic shuttling that regulates its role in cytokinesis. Research in our lab showed that expression of the dominant- negative (unphosphorylated) IQGAP1IR-WW fragment arrests cytokinesis and can serve as basis for potential future therapy in cancer. Our experiment tested this hypothesis in brain cancer cell lines.

Preliminary results showed that the overexpression of IQGAP1IR-WW in glioblastoma cells decreased cell proliferation and led to multinucleated cells. These results are consistent with our previous findings in cervical cancer cells and present IQGAP1 as a clinical target in oncology.

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