Using Zika Virus Proteins NS4A and NS4B to Investigate Oncolytic Virus Therapy against Glioblastoma Cancer

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Glioblastoma multiforme is the most aggressive form of brain cancer (<5% of people diagnosed survive for longer than 5 years), with no specific treatment or prevention. For many types of cancer, oncolytic virus therapy has shown potential by infectivity and mutability in a cancer cell's genome. Zika virus is a prospective treatment, because its proteins can kill glioblastoma stem cells using the same mechanism for inducing microcephaly. Viral vector based gene-therapies that deliver a protein that is only cytotoxic in brain-tumor cells could be a huge breakthrough for cancer prognosis. Therefore, ZIKV proteins NS4A and NS4B were identified and tested on glioblastoma cancer stem cells to design a safe and effective treatment for brain cancer. In the first stage of research, NS4A and NS4B plasmids were subcloning into a pLenti-GFP vector backbone using PCR amplification and restriction digestion. Plasmids (NS4A, NS4B, NS4A-NS4B, pLenti-GFP control) were transfected in glioblastoma cancer stem cells. Cytotoxicity was analyzed using a Trypan blue live/dead cell counting assay over the course of 10 days. Results showed that pLenti-GFP and NS4A-NS4B transfected cells had a growing ratio of dead cells when compared to live cells. ZIKV plasmids were capable of depleting glioblastoma stem cells, but not to a greater extent than the pLenti control plasmid. The control pLenti plasmid had greater metabolic activity against cancer stem cells, possibly due to the overexpression of GFP. Future research for novel treatments of cancer could involve creating a mutant form of GFP that selectively targets and kills cancer cells.

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