The Effect of UPP1, A Novel Metabolic Suppressor vs. Oncolytic Viruses on Pancreatic Cancers

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Pancreatic Cancer has the lowest survival rates of all cancers due to much diagnosis occurring in the later stages. Methods such as chemotherapy and drug treatments are effective but can lead to cell proliferation and affect surrounding cancer cells. The utilization of collagenase-eating viruses in tumors can help target the drug intake problems within the ECM matrix. UPP1, a newly discovered gene in pancreatic ductal adenocarcinoma, is activated in glucose-deprived environments within the ECM matrix. UPP1 enhances the cell's metabolism through metabolizing RNA. This project specifically suppressed UPP1 within PDACs by targeting them through a novel starvation-based viral approach. Not only did UPP1 shrink the tumors, but helped mark all PDACs that possessed UPP1. Furthermore, the efficiency of each of the oncolytic strains were determined to find the most efficient strain. First UPP1 plasmids were purified, then they were transfected within PDACs at differing concentrations. Then MTT Assay, GFP protein, Crystal Violet staining, and cell kinetics analysis were done for VMG, VSV, and MORV viruses. Overall all the combinations depicted higher cell viability than the control, but UPP1 with LENTICRISPR_sgRNA1 and pWPI-3xFLAG at and MOI of 10 depicted the least cell viability. Each of the Oncolytic Viruses also had significant results (P> 0.001**) when compared to control. VMG was the most effective on the Mia-Paca-2 cell lines. An ANOVA was conducted for UPP1 and found to be significant. Overall UPP1 demonstrated promising results as a novel gene that can suppress metabolism in PDACs and overall lead to less cell viability.

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