Investigating the Oncolytic and Immunomodulatory Effects of Herpes Simplex Virus in Pancreatic Ductal Adenocarcinoma

Iyer, Dev (School: Baton Rouge Magnet High School)

Pancreatic ductal adenocarcinoma (PDAC) is a highly aggressive cancer with poor prognosis, signifying a pressing need for novel therapeutic strategies. This study investigated the effect of the herpes simplex virus type 1 (HSV-1) VC2 strain on murine KPC and human MIA PaCa-2 cell lines. This study also evaluated HSV-1 VC2's overexpression of Granulocyte-Macrophage Colony-Stimulating Factor (GM-CSF) on cell morphology, viability, and the expression of genes related to cell proliferation, apoptosis, immunomodulation, inflammation, and angiogenesis. Cells were exposed to increasing multiplicities of infection (MOI) of oncolytic virus, and changes in cell morphology were assessed via light microscopy. Results showed dose-dependent cytotoxicity, with higher MOIs resulting in increased cell death and clustering, as well as a shift from adherent to free-floating cells. Quantitative PCR (qPCR) analysis of gene expression was performed on cells exposed to 0.1 MOI virus and no virus. Results showed that GM-CSF, IL-10, COX-2, FasL, and PD-L1 expression increased, while BAX, Ki-67, and FoxM1 expression decreased in both cell lines following treatment. IL-6 and TNF-alpha expression increased in MIA cells but decreased in KPC cells. These findings suggest that GM-CSF can alter PDAC cell behavior, promoting immune activation and modulating survival pathways. This study provides valuable insights into the oncolytic potential of HSV-1 (VC2) GM-CSF, highlighting its ability to serve as a potential alternative therapeutic agent in combating PDAC.

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