OPTIMAL OV-BORTEZOMIB INTERVENTION STRATEGIES AND NK CELL ADJUVANT THERAPY FOR TUMOR TREATMENT

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ABSTRACT

Proteasome inhibition and oncolytic virotherapy are two emerging targeted cancer therapies. Proteasome inhibition disrupts the degradation of proteins in the cell leading to accumulation of unfolded proteins which induces apoptosis. On the other hand, oncolytic virotherapy utilizes genetically modified viruses to infect cancer cells, induce cell lysis, and activate an antitumor response. The combination treatment with bortezomib (proteasome inhibitor) and oHSV (oncolytic virus) showed increased cancer cell killing through necroptosis and also led to NK cell activation. NK cells are innate components of the immune system and are essential to host immunity against cancer. In this work, we apply optimal control theory to a mathematical model that describes the dynamics of the cancer cells in oncolytic virus-bortezomib treatment and NK cell adjuvant therapy. We include isoperimetric constraints to describe the controls and identify optimal intervention strategies that maximize anti-tumor efficacy while minimizing treatment cost.

REFERENCES