

JEAN-EMMANUEL KOUADIO and QING WANG, Dept. of Computer Sciences, Mathematics and Engineering, Shepherd University, Shepherdstown, WV, 25443. Modeling the effect of a combinatorial anti-CTLA antibody and radiation therapy on metastatic melanoma.

Cytotoxic T-lymphocyte antigen 4 (CTLA-4) is an inhibitory receptor that is upregulated after T-cell activation, and transmits signals that suppress T-cell activation and proliferation. Antibodies targeting CTLA-4 can selectively deplete regulatory T cells by antibody-mediated cellular cytotoxicity mechanisms. Radiation therapy (RT) on the other hand is a longstanding pillar of cancer treatment, historically utilized to treat a discrete target and provide local tumor control. Recent preclinical studies demonstrated that RT is synergistic with anti-CTLA antibody and induces systemic anti-tumor responses. In order to better understand the effect of the combination therapy on metastatic melanoma, we developed a multi-scale mechanistic model using a system of impulsive differential equations. The objective of this study was to develop a predictive simulation platform to improve cancer management by manipulating dose and fractionation schedule of RT in the combination therapy. The project was supported by NIH Grant P20GM103434 to the West Virginia IDeA Network for Biomedical Research Excellence.