

1145-92-919

Trachette L Jackson* (tjacks@umich.edu), Department of Mathematics, University of Michigan, 530 Church St., Ann Arbor, MI 48109-1043. *Multiscale Modeling of Combined Traditional and Targeted Therapies Against Stem Cell Driven Cancers*. Preliminary report.

Targeting key regulators of the cancer stem cell phenotype to overcome their critical influence on tumor growth is a promising new strategy for cancer treatment. In this talk, a multi-scale mathematical model that operates at the intracellular, molecular, and tissue level is developed to investigate the impact of IL-6 signaling on crosstalk between cancer stem cells (CSCs) and vascular endothelial cells (ECs) during tumor growth. This EC-CSC model is used to study the therapeutic potential of Tocilizumab (TCZ), a competitive IL-6R inhibitor, on tumor growth and cancer stem cell fraction, alone and in combination with the traditional chemotherapeutic agent, Cisplatin. The approach is novel in that it includes full receptor occupancy dynamics between endothelial-cell produced IL-6, IL-6R, and TCZ. Validation is achieved by directly comparing model predictions to data generated by a series of in-vivo experiments. Simulations show excellent predictive agreement with the decrease in tumor volume, as well as a decrease in CSC fraction post therapy. This modeling framework can also be used to evaluate dosing strategies for IL-6 pathway modulation, as well as providing the basis for proposing combination treatments with IL-6 blockade and cytotoxic or other targeted therapies. (Received September 17, 2018)