

1145-92-238

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Modeling Tumor Immune Dynamics in Multiple Myeloma.

We propose a mathematical model that describes the dynamics of multiple myeloma and three distinct populations of the innate and adaptive immune system: cytotoxic T cells, natural killer cells, and regulatory T cells. The model includes significant biologically- and therapeutically-relevant pathways for inhibitory and stimulatory interactions between these populations. We focus on five main aspects: 1) obtaining and justifying parameter ranges and point estimates; 2) determining which parameters the model is most sensitive to; 3) determining which of the sensitive parameters could be uniquely estimated given various types of data; 4) exploring the model and updated parameter estimates numerically; and 5) analytically exploring the equilibria and stability of a reduced model. Using multiple sensitivity analysis techniques, we found that the model is generally most sensitive to parameters directly associated with M protein levels. This analysis provides the foundation for a future ultimate application of the model: prediction of optimal combination regimens in patients with multiple myeloma. (Received August 23, 2018)