

Tumor Dynamics under Immunotherapy: A Time-Delay Revised Predator-Prey Model

Krista Lotesto, Emma Turian

Abstract: Cancer remains a leading cause of death worldwide and traditional treatments such as surgical resection, chemotherapy, and radiotherapy may have limited benefits depending on the type of cancer and the stage at which it is diagnosed. Immunity is the state of protection against foreign pathogens or substances (i.e., antigens). Recent research into novel approaches to treatment has suggested that immunotherapy, which aims to optimize the body's own natural responses to combating disease through various mechanisms, may be a promising strategy that can improve prognosis for certain cancer types that are refractory to other treatment options. Quantitative models simulating the dynamics of tumor-immune system interaction, can facilitate both basic and clinical research efforts aimed at better understanding the impact of immunotherapy in the management of the disease. The presence of tumor cells stimulates the response of the natural killer (NK) cells. To destroy cancer cells, the NK cells must have the ability to bind to the cancerous cells through proteins. The binding process is successful only if the surfaces of the two cells types have features which make them compatible. Thus, there exists a time delay until immunotherapeutic effects are felt by the human body. Previous studies of these dynamics have been described by various versions of predator-prey models. The goal of this study is to expand on previous work by proposing an evolutionary revised predator-prey mathematical model that employs discrete delays. The discrete delay is incorporated in a logistic type rate-limiting recruitment term from the effector cell evolution equation. This model suggests that tumor cells decline sharply according to the effects of these characteristic delays. We analyze the system of differential equations using the steady state, stability techniques, and critical values relevant to explaining the impact of therapy on tumor reduction. A comparison between Michaelis-Menten and our modified logistic dynamics suggests that conclusions can be drawn from the oscillatory behavior of the latter model. Through sensitivity analysis, we determine that the most influential parameters that describe the model are the ones belonging to the effector cells evolution equation. Thus, our analysis suggests that under certain conditions it is possible not only to control tumor growth but also to reduce its size through the administration of immunotherapy.

Keywords: Immunotherapy, effector cells, delay, predator-prey