Mathematical model of STAT signaling pathways in cancer development and optimal control approaches

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ABSTRACT

In many diseases, STAT family displays various responses, such as cellular immunity, apoptosis, proliferation, and differentiation. In this study, we investigate how an intracellular signaling network (STAT1, STAT3, Bcl-2, and BAX) regulates an important cellular fate, either anti-apoptosis or apoptosis. We developed a mathematical model of a signaling network using a set of ordinary differential equations. We show that network can generate a bi-stability condition so that it will induce either apoptosis or anti-apoptosis status of tumor cells. Then, we use this model to develop several anti-tumor strategies including injection of IFN-beta and DDP. The model provides a visual display of the complex behavior of a population of STAT and tumor in response to various IFN-beta and JAK stimuli. The simulation results from the mathematical model were show agreement with experimental data.

In addition, the effect of anti-tumor drug administration is incorporated in the model in an effort to achieve optimal anti-tumor efficacy by optimal control theory.

REFERENCES