

An ERK/p38 ratio-structured mathematical model of cancer-immune dynamics

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Abstract

The ERK/p38 ratio regulates the level of dormancy of cancer cells. Most mathematical frameworks describing tumor-immune interactions do not account for varying levels of quiescence in a tumor. Here, we introduce a new mathematical model that captures the dynamic interactions between cancer and immune cells. In this model, tumor cells are structured for the first time according to the ERK/p38 signaling ratio. They are distributed along a continuum from fully dormant (low ERK/p38) to fully active (high ERK/p38), with transitions driven by epidermal growth factor (EGF) availability and immune surveillance. The model incorporates heterogeneity in proliferation, apoptosis, immune activation, and immunosuppression, all dependent on this ERK/p38 ratio. We validate the model against mice experiments showing the impact of p38 inhibitors on tumor growth. Then, we elucidate the impact of variations in cancer phenotype and interplay with immune cells on the efficacy of p38 inhibitors. Finally, we derive a simplified ODE model that yields the same results. Analysis of the simplified model provides the theoretical conditions for tumor elimination, cancer growth, and tumor-immune equilibrium.