Abstracts

Mathematical model of cancer and (CAR) T cells as structured populations. Cancer cells structured by damage and T cells by exhaustion

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The interactions between cancer and the immune system have been an area of intense interest and research in Mathematical Biology . These interactions play a central role in cancer progression, where the progressive exhaustion of immune cells significantly reduces their antitumor activity. To investigate this process, we focus on chimeric antigen receptor T-cell (CAR T) therapy and develop a mechanistic mathematical model that explicitly incorporates immune cell exhaustion into tumor dynamics. The model is initially formulated as a non-spatial structured system of partial differential equations (PDEs) describing the interactions between cancer cells and T cells. Cancer cells are structured according to the amount of accumulated damage, where each effective interaction with a T cell increases the damage level. A cancer cell is eliminated only when its accumulated damage exceeds a critical threshold, referred to as the apoptotic threshold. Conversely, T cells are structured according to their exhaustion level. To simplify the mathematical formulation while preserving its biological interpretation, the structured PDE model is reduced to a system of ordinary differential equations (ODEs). The reduced model describes the temporal evolution of the total tumor cell population, the average accumulated damage in tumor cells, and the mean exhaustion level of immune cells. A qualitative dynamical analysis is performed through the identification of equilibrium points, nullclines, and local stability properties, providing insight into the mechanisms governing tumor growth. The model was calibrated and validated using in vitro experimental tumor growth under Car T therapy data reported in previous studies. Model parameters were estimated through nonlinear optimization by minimizing the discrepancy between numerical simulations and experimental observations. The calibration procedure demonstrates that the proposed model accurately reproduces the observed tumor growth dynamics across all experimental datasets while maintaining biologically meaningful parameter values. The estimated parameters characterize key processes involved in immune exhaustion, tumor proliferation, and immune-mediated tumor cell elimination, providing quantitative insight into the underlying biological mechanisms. Overall, the proposed framework combines biologically structured modeling and data-driven parameter estimation into a unified mathematical approach. The close agreement between simulations and experimental data supports the predictive capability of the model and highlights its potential

as a quantitative tool for studying tumor–immune interactions and evaluating the impact of immune exhaustion on tumor progression.
