

Guiding Clinical Trials of Whole-cell Vaccination Therapy in Prostate Cancer by a Clinically Validated Mathematical Model of Antitumor immunity

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Prostate cancer (PCa) is the second most common malignancy in man. Patients are normally treated by androgen deprivation to control disease progression, yet cancer cells often become androgen-independent, leading to a relapse characterized by increased prostate-specific antigen (PSA) and bone metastasis. Attempts to treat this cancer indication by whole cell vaccination within a recent phase II clinical trial have been encouraging, yet designing effective immunotherapy for PCa is a difficult task. To help elucidate immune mechanisms in PCa, and gain insights into how it may be effectively modulated therapeutically, we formed a mathematical model describing the major players in the immune system-PCa interaction. The model, constructed and calibrated based on various preclinical and clinical data from the literature, was validated by its success in retrieving cancer progression, reflected in PSA levels, of vaccinated patients. By model-aided predictions of patient PSA levels, the efficacy of the applied treatments could be projected at each time within therapy, and precise dose modifications could be recommended. Our analysis also emphasized the importance of individualized therapy, as model simulations showed that each patient required different vaccination doses in order to control PSA escalation. We suggest a method for a collaborative interaction between modeling experts and clinicians, to carry out in-trial model-based calibration and treatment adjustment. This computational tool can help to plan better vaccination regimens and serve as the scaffold for patient-specific therapies.