The final exam seminar will take place online, through the ZOOM platform.
To get the access codes please contact the secretary office Roberta Coletti
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Mathematical Modeling of Prostate Cancer Immunotherapy

Abstract:
Immunotherapy, by enhancing the endogenous anti-tumor immune responses, is showing promising results for the treatment of numerous cancers refractory to conventional therapies. However, its effectiveness for advanced castration-resistant prostate cancer remains unsatisfactory and new therapeutic strategies need to be developed. To this end, mathematical modeling provides a quantitative framework for testing in silico the efficacy of new treatments and combination therapies, as well as understanding unknown biological mechanisms. In this dissertation we present two mathematical models of prostate cancer immunotherapy defined as systems of ordinary differential equations.
The first work, introduced in Chapter 2, provides a mathematical model of prostate cancer immunotherapy which has been calibrated using data from pre-clinical experiments in mice. This model describes the evolution of prostate cancer, key components of the immune system, and seven treatments. Numerous combination therapies were evaluated considering both the degree of tumor inhibition and the predicted synergistic effects, integrated into a decision tree. Our simulations predicted cancer vaccine combined with immune checkpoint blockade as the most effective dual-drug combination immunotherapy for subjects treated with androgen-deprivation therapy that developed resistance. Overall, this model serves as a computational framework to support drug development, by generating hypotheses that can be tested experimentally in pre-clinical models.
The Chapter 3 is devoted to the description of a human prostate cancer mathematical model. The potential effect of immunotherapies on castration-resistant form has been analyzed. In particular, the model includes the dendritic vaccine sipuleucel-T, the only currently available immunotherapy option for advanced prostate cancer, and the ipilimumab, a drug targeting the cytotoxic T-lymphocyte antigen 4, exposed on the CTLs membrane, currently under Phase II clinical trial. From a mathematical analysis of a simplified model, it seems likely that, under continuous administration of ipilimumab, the system lies in a bistable situation where both the no-tumor equilibrium and the high-tumor equilibrium are attractive. The schedule of periodic treatments could then determine the outcome, and mathematical models could help in deciding an optimal schedule.

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