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Chiara Fornari, Francesca Cordero, Marco Beccuti, Stefania Lanzardo, Laura Conti, Federica Cavallo, Gianfranco Balbo and Raffaele Calogero

1 Abstract

Recent studies have changed the traditional view of tumor progression, showing that the growth and evolution of many cancers are driven by a population of cells named Cancer Stem Cells (CSCs). The CSC model presents tumors as hierarchically structured and characterized by differentiated cell populations. This heterogeneity affects the choice of cancer therapies; indeed, CSCs resist to many current treatments, while these cures reveal a positive effect on the differentiated cell populations. In this paper we investigated the effect of vaccination on a cancer hierarchical structure, through a multi-level model that describes the inter-dependencies between population and genetic levels. In particular, the population level describes the cancer cell population's dynamics, while the molecular one details part of proliferation pathway. We adopt different formalisms for the two levels: population's dynamics are modeled by a system of Ordinary Differential Equations (ODEs), whereas the genetic level is designed using Petri Nets. Moreover, we propose a new methodology that exploits the solution obtained from the molecular level to parameterize the ODE system modeling population. Given the availability of molecular data on the cancer driving force, this multi-level model can be efficiently used to estimate the efficacy of drug and vaccine therapies in cancer models. Indeed, we use it to study the ErbB2-driven vaccination effect in breast cancer.