Title

A 3D multiscale model to explore the action of tyrosine kinase inhibitors during tumorigenesis

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Abstract

The epidermal growth factor receptor (EGFR) cascade plays an important role in the survival and division of tumor cells. Tyrosine kinase inhibitors (TKIs) are a set of drugs that inhibit both active and inactive epidermal growth factor receptors (EGFRs), hence prevents their binding to the epidermal growth factors (EGFs) and the subsequent transduction of the EGFR pathway. In this work, we extend a previously developed 3D model of tumor initiation by including tyrosine kinase inhibitors and their action on EGFRs and cancer cells. The model describes cells as individual objects that can move, divide, and die by apoptosis. The kinetics of intracellular and extracellular regulation are captured using the Brownian dynamics method. The focus of this work is to introduce the TKI drug molecules to this framework and to capture their competition with EGFs on EGFRs. After testing the effects of the treatment, we use numerical simulations to study the development of the tumor in the absence of the treatment and when the drug molecules are introduced. In particular, we compare the action of inhibitors which block the active EGFRs, the inactive ones and both. We conclude the talk by discussing the perspectives of the work. The high fidelity of the model makes it suitable to study the effect of fine-grained aspects influencing intracellular regulation which can be altered in cancer due to mutations.