Charles Morton
Center of Cancer Systems Biology - Tufts University School of Medicine
e-mail: charles.morton@tufts.edu

Tumor Growth Kinetics Modulated by Generational Lifespan of Non-Stem Cancer Cells

Numerous solid tumors are heterogeneous in composition. While growth is driven by cancer stem cells (CSCs), the reported relative frequencies of CSC versus non-stem cancer cells span wide ranges within tumors arising from a given tissue type. We have previously shown that tumor growth kinetics and composition can be studied through an agent-based cellular automaton model using minimal sets of biological assumptions and parameters. Herein we describe the pivotal role of the generational lifespan of non-stem cancer cells in modulating solid tumor progression. Although CSCs are necessary for expansion, tumor growth kinetics are surprisingly modulated by the dynamics of the non-stem cancer cells. Our findings suggest that variance in tumor growth curves and CSC content of solid tumors may be attributable to the proliferative capacity of the non-stem cancer cell population that arises during asymmetric division of CSCs. Remarkably, slight variations in proliferative capacity result in tumors with CSC fractions differing by multiple orders of magnitude. Larger proliferative capacities yield migration-limited tumors, as the emerging population of non-stem cancer cells spatially impedes expansion of the CSC compartment. Conversely, lower proliferative capacities yield persistence-limited tumors, with symmetric division frequency of CSCs determining tumor growth rate. Intermediate proliferative capacities give rise to fastest-growing tumors, indicating a between self-metastatic growth through symmetric CSC division and the availability of space facilitated by removal of senescent non-stem cancer cells. Our results offer novel explanations for the large variations in CSC ratio reported in the literature, and highlight the importance of non-stem cancer cell dynamics in the CSC hypothesis.