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Stochastic modeling and experimental analysis of phenotypic switching and survival of cancer cells under stress SEYED ALIREZA ZAMANI DAHAJ, NIRAJ KUMAR, BALA SUNDARAM, JONATHAN CELLI, RAHUL KULKARNI, Department of Physics, University of Massachusetts Boston
— The phenotypic heterogeneity of cancer cells is critical to their survival under stress. A significant contribution to heterogeneity of cancer calls derives from the epithelialmesenchymal transition (EMT), a conserved cellular program that is crucial for embryonic development. Several studies have investigated the role of EMT in growth of early stage tumors into invasive malignancies. Also, EMT has been closely associated with the acquisition of chemoresistance properties in cancer cells. Motivated by these studies, we analyze multi-phenotype stochastic models of the evolution of cancers cell populations under stress. We derive analytical results for time-dependent probability distributions that provide insights into the competing rates underlying phenotypic switching (e.g. during EMT) and the corresponding survival of cancer cells. Experimentally, we evaluate these model-based predictions by imaging human pancreatic cancer cell lines grown with and without cytotoxic agents and measure growth kinetics, survival, morphological changes and (terminal evaluation of) biomarkers withassociated epithelial and mesenchymal phenotypes. The results derived suggest approaches for distinguishing between adaptation and selection scenarios for survival in the presence of external stresses.

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