Impact of genetic dynamics and single-cell heterogeneity on development of nonstandard personalized medicine strategies for cancer

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Abstract

Cancers are heterogeneous and genetically unstable. Current practice of personalized medicine tailors therapy to heterogeneity between cancers of the same organ type. However, it does not yet systematically address heterogeneity within a single individual's cancer. We developed a mathematical model of personalized cancer therapy incorporating genetic evolutionary dynamics and single-cell heterogeneity, and examined simulated clinical outcomes. Analyses of an illustrative case and a virtual clinical trial of over 3 million evaluable "patients" demonstrate that augmented nonstandard personalized medicine strategies may lead to superior outcomes compared with the current personalized medicine approach. Current personalized medicine matches generally focuses on the average, static, and current properties of the sample. In contrast, nonstandard strategies also consider minor subclones, dynamics, and predicted future tumor states. Our methods allow systematic study and evaluation of nonstandard personalized medicine strategies. These findings may, in turn, suggest global adjustments and enhancements to translational oncology research paradigms.