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Virtual Combination Therapy in Virtual NSCLC Tumor Cells Supports Strategic Development and Treatment Decisions

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Combination therapy is the future of cancer treatment, but the combinatorics of exploring all combinations of treatment approaches in a range of cancer types and stages is daunting. To help inform development and treatment strategies, we created a high-level ODE-based computer model of the cancer cell lifecycle, focused on non-small cell lung cancer (NSCLC), and used it to explore the effects on tumor growth of different combinations of cytotoxic agents, targeted growth signal inhibitors, anti-angiogenic agents, and metabolic disruption. Further, we created a range of "virtual NSCLC cells" representing aspects of clinical variability in the mechanisms underlying tumor cell proliferation. This virtual testing of a variety of combinations in a range of virtual cells allowed us to identify synergistic regions of interest for combination therapy in a clinical setting, and to identify which combination approaches are most robust to clinical variability, i.e., most likely to be efficacious across a variety of patient types. We plan to extend this work by expanding to other cancer types, linking our virtual cells more explicitly to clinical patient states and eventually identifying biomarkers indicative of optimal treatment approaches at the individual patient level.