

***In Silico* Study of 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 number of *in vivo* studies required to explore all combinations of treatment approaches in a range of cancer types and stages is daunting. To inform development and treatment strategies, we created a dynamic mechanistic 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” to represent clinical variability in the mechanisms underlying tumor cell proliferation.

This *in silico* testing of a variety of combinations in a range of virtual cells allowed us to guide *in vivo* testing by identifying synergistic regions of interest for combination therapy in a clinical setting, and which combination approaches are most robust to clinical variability, i.e., most likely to be efficacious across a variety of patient types. We also show how this work can be extended to include other cancer types, link our virtual cells to clinical patient states, and identify biomarkers indicative of optimal treatment approaches at the individual patient level.