

Unconventional approaches to the treatment of cancer

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Synthetic lethal drug combinations have emerged as a powerful tool to treat cancers. A drawback from this synthetic lethality approach is that toxicity of a given synthetic lethal drug pair can be prohibitive in reaching an effective dose. We have therefore also focused on a new iteration of synthetic lethality in which we give drugs sequentially rather than simultaneously, but retain the strong synergy between the two drugs. I will discuss how we can use sequential drug treatment to deliver a lethal “one-two punch” to cancer cells.

In a second approach, we have explored the potential of a “paradoxical” activation of the MAPK pathway for cancer therapy that we have suggested recently as an unorthodox therapeutic rationale (PMID: 33955157). This approach is based on a deliberate further activation of an already activated signaling pathway, combined with inhibition of stress response pathways that help cancer cells survive in the presence of hyperactive oncogenic signaling.