Optimal targeted therapy for multiple cancers based on contrastive Notch signaling networks

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Over decades, cancer understanding has advanced significantly at molecular and cellular levels, leading to various therapies based on intra-/inter-cellular networks. Despite this, cancer still remains a leading cause of death globally.

The primary driver of cancer mortality is metastasis, responsible for about 90% of cancer deaths, due to unclear pathophysiological mechanisms that complicate treatment development.

The Notch signaling pathway, a crucial intercellular network in many cancers, has been extensively studied and therapies targeting the Notch pathway also have been well-studied based on inhibiting various stages of Notch activation.

On the other hand, Notch signaling's role varies between cancers; for instance, in non-small cell lung cancer, Notch1 and Notch2 have opposing effects compared to their roles in embryonal brain tumors.

In this study, we assumed a scenario of multiple cancers with contrasting Notch signaling pathways and explored optimal targeted therapies for reducing cancer cells by developing two mathematical models with contrasting Notch signaling pathways. The proposed therapies were compared with existing ones, and strategies were investigated to reduce cancer cell numbers for different stage of cancer.

We found that that multiple cancers with contrasting Notch networks can be controlled by a common targeted signal network. Combination therapy enhancing Notch production may be most effective in early-stage cancer, while cleavage therapies may be more effective in late-stage cancer. Our study also suggests that optimal treatment should consider the cancer stage, with careful selection and ordering of medication therapies.