Discovery of RAS-selective drugs to treat cancer

Columbia Technology Ventures

Cancer therapy to kill tumor cells

Many anti-cancer drugs currently in use are toxic compounds that cause significant side effects. These agents are often not particularly selective for tumor cells and can cause unwanted damage or death to normal cells. Furthermore, the high doses required to maintain the efficacy of many anti-cancer drugs results in increased toxicity in patients. Drug resistance is also an issue for cancer therapies: high doses and repeated treatments can produce tumors that are resistant to available classes of cancer drugs. Some tumors develop resistance to multiple classes of drugs, leaving few therapeutic options.

Targeted cancer therapies directed at specific oncogenic proteins or pathways are a promising alternative to agents that have a wide array of side affects. Combinatorial regimens of targeted therapies that are directed at two or more oncogenic pathways can be employed to improve treatment efficacy and improve treatment of drug resistant malignancies. Though targeted therapies are promising, developing and implementing them can be difficult. New approaches are needed to streamline the discovery and development of targeted cancer treatments that will be selectively lethal to tumors, highly efficient and therapeutically practical.

Small molecules that kill cancer tumor cells that expressing oncogenic RAS

This invention is a class of small-molecules capable of selectively killing tumor cells with oncogenic RAS signaling, which is mutated in 25-40% of tumors from a variety of origins. These molecules were identified using a synthetic lethal screen that was designed to isolate molecules that kill tumor cells that express oncogenic RAS. This invention also describes research tools for performing this small-molecule lethal screen for the identification and analysis of other potentially therapeutic tumoricidal compounds.

Applications:

• Novel tumoricidal class of cancer drugs targeting the RAS pathway
• Research tool for discovering new drug targets and novel pathways for cancer drugs
• Synthetic lethal screening method for isolating novel small molecules capable of specifically targeting and killing a variety of tumor cells

Advantages:

• Identified compounds selectively induce cytotoxicity of a variety of tumor cell types
• Potent tumoricidal activity
• Novel mechanism of inducing tumor-specific cell death by selectively targeting cells that activate the oncogenic RAS pathway
• Likely minimal in vivo toxicity due to the low doses required and specific targeting of tumor cells

• Synthetic lethal small-molecule screening method identifies compounds with high potency, specificity, and therapeutic potential

• Screens and small-molecules can be used to identify and develop combinatorial therapies to produce synergistic cytotoxicity of tumor cells and improve treatment efficacy

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