Loss-of-function mutations in KEAP1 drive lung cancer progression

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Video Byte

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Abstract

Lung cancer is the leading cause of cancer-related death worldwide. Although targeted therapy and immunotherapy have improved treatment, the 5-year survival rate of lung cancer patients remains low. New therapies are needed to target molecules that drive cancer progression. A new study examined the role of a common mutation in lung squamous cell carcinoma (LSCC). Loss-of-function mutations in KEAP1, an adapter protein that acts as a cellular sensor of oxidative stress, are present in over 25% of patients with LSCC. Researchers compared human lung cancer cell lines with and without KEAP1 mutations. They found that cells lacking KEAP1 function had increased proliferation, migration, and tumor growth and increased expression of NRF2, a transcription factor that regulates cellular protection against oxidative damage. Blocking NRF2 with a pharmaceutical inhibitor, ML385, inhibited proliferation of lung cancer cells with KEAP1 mutations. Although further study with primary patient cells is needed, the results suggest that NRF2 inhibitors may inhibit the proliferation of lung cancer cells with KEAP1 mutations, providing a new option for therapy in patients with LSCC carrying KEAP1 mutations.