Awakening genes that suppress tumors

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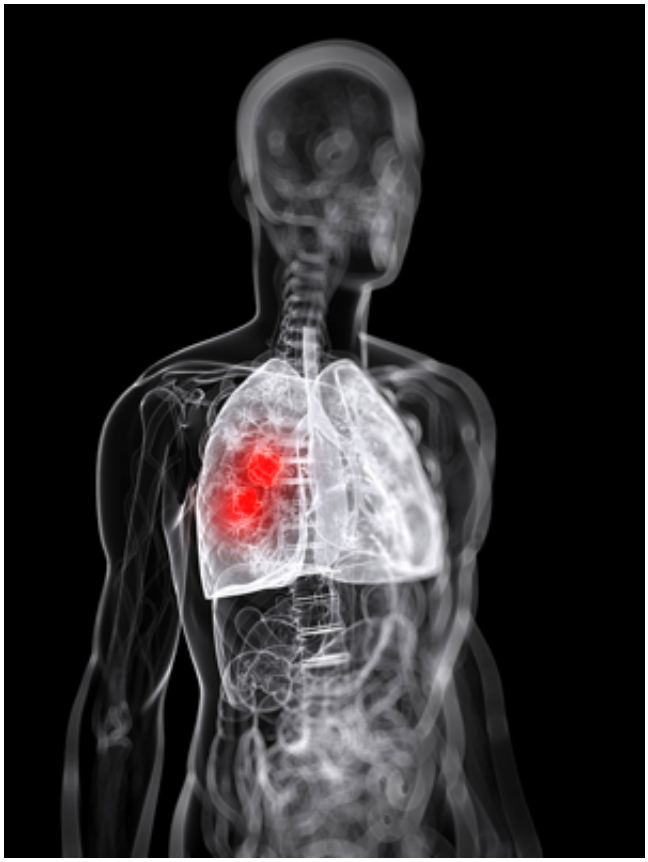

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(Medical Xpress)—When genes that normally suppress tumor growth are themselves suppressed, cancer cells can grow and proliferate uncontrollably. A new study led by a researcher at Yale University has uncovered the pathway through which some of these tumor suppressor genes are inactivated—a finding that could have implications for treatment of certain cancers. The study appears online in the journal *Genes and Development*, published by the Cold Spring Harbor Laboratory Press.

Focusing in mice on the RAS family of cell-signaling oncoproteins (genes that can turn normal cells into cancerous ones), the research team stopped the RNA transcription process that controls cell growth by either turning it on or off. In doing so, they found that RAS-led silencing occurs through a highly ordered genetic pathway that is continuously functioning, and dependent on many co-factors. They also discovered that the silencing action of this pathway is initiated by a specific DNA-binding protein called ZFP354B, and abetted by modified gene expression.

The team further found that all of these steps were required for the tumor suppressor genes to be silenced. This research could lead to development of therapies that interfere with the silencing in RAS-positive cancers, including pancreatic, colorectal, lung, and thyroid cancer.

"Oncogenic RAS mutations are found in about a third of all human cancers, but there are no current therapies that can effectively treat these cancers," said first author Narendra Wajapeyee, assistant professor of pathology at Yale School of Medicine and a member of Yale Cancer Center. "We have identified a RAS-regulated pathway that initiates and maintains the epigenetic silencing of tumor suppressor genes, and we are hopeful that many of the components of these pathways can be targeted for providing personalized therapy for RAS-mutant cancers."

Provided by Yale University