

Scientists detail critical role of gene in many lung cancer cases

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Scientists from the Florida campus of The Scripps Research Institute (TSRI) have shown that a well-known cancer-causing gene implicated in a number of malignancies plays a far more critical role in non-small cell lung cancer, the most common form of the disease, than previously thought.

These findings establish the gene as a critical regulator of lung cancer tumor growth. This new information could turn out to be vital for the design of potentially new therapeutic strategies for a group of patients who represent almost half of non-small cell lung cancer cases.

In the study, published online ahead of print by the journal *Cancer Research*, the scientists found that presence of known oncogene Notch 1 is required for survival of cancer cells. In both cell and animal model studies, disabling Notch 1 leads to a rise in cancer cell death.

"While Notch signaling has emerged as an important target in many types of cancer, current methodologies that target that pathway affect all members of the Notch family, and this has been associated with toxicity," said Joseph Kissil, a TSRI associate professor who led the study. "We were able to identify Notch 1 as the critical oncogene to target, at least in a common form of lung cancer."

The new findings show that Notch1 is required for initial tumor growth, as it represses p53, a well-known [tumor suppressor protein](#) that has been called the genome's guardian because of its role in preventing mutations. The [p53 protein](#) can repair damaged cells or force them to die through apoptosis—[programmed cell death](#).

Using animal models, the study shows that inhibition of Notch1 signaling results in a dramatic decrease in initial tumor growth. Moreover, disruption of Notch 1 induces apoptosis by

increasing p53 stability—substantially increasing its biological half-life, for example.

These findings provide important clinical insights into the correlation between Notch1 activity and the [poor prognosis](#) of non-small cell [lung cancer patients](#) who carry the non-mutated form of the p53 gene. "If you look at lung cancer patient populations, Notch signaling alone isn't a prognostic indicator, but if you look at p53-positive patients it is," Kissil said.

More information: "Notch1 is Required for Kras-Induced Lung Adenocarcinoma and Controls Tumor Cell Survival via P53" [DOI: 10.1158/0008-5472.CAN-13-1384](#)

Provided by The Scripps Research Institute

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