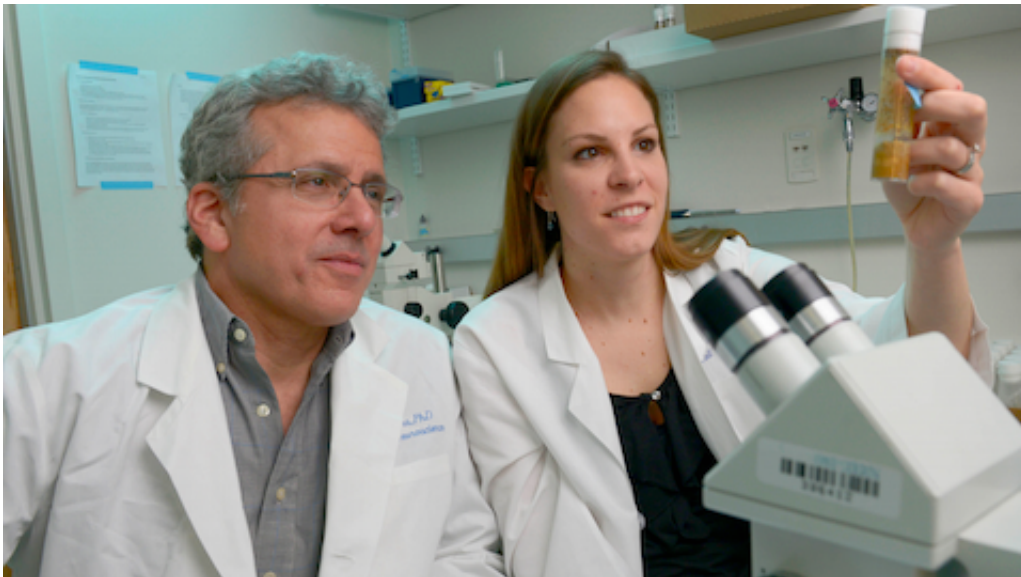


Tumor-suppressing gene restrains mobile elements that can lead to genomic instability

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Dr. John Abrams and Dr. Annika Wylie. Credit: UT Southwestern Medical Center

The most commonly mutated gene in cancer, p53, works to prevent tumor formation by keeping mobile elements in check that otherwise lead to genomic instability, UT Southwestern Medical Center researchers have found.

The [p53 gene](#) long has been known to suppress [tumor formation](#), but the mechanisms behind this function - and why disabling the gene allows tumors to form - were not fully understood.

Findings from the study, published recently in *Genes & Development*, answer some of these questions and could one day lead to new ways of diagnosing and treating [cancer](#), said the study's senior author, Dr. John Abrams, Professor of Cell Biology at UT Southwestern.

The investigators found that normal p53 gene action restrains transposons, mobile genetic elements called retroelements that can make copies of themselves and move to different positions on chromosomes. But, they discovered, when p53 is disabled by mutation, dramatic eruptions of these mobile elements occur. The study revealed that in mice with cancer and in human samples of two types of cancer (Wilms' tumors and colon tumors) disabled for p53, transposons became very active.

In a healthy state, certain mechanisms work to keep these retroelements quiet and inactive, explained Dr. Abrams. One of those mechanisms is p53 action. Conversely, when p53 is mutated, retroelements can erupt.

"If you take the gene away, transposons can wreak havoc throughout the genome by causing it to become highly dysregulated, which can lead to disease," Dr. Abrams said. "Our findings help explain why cancer genomes are so much more fluid and destabilized than normal genomes. They also provide a novel framework for understanding how normal cells become tumors."

Although much more research is needed, Dr. Abrams said, the potential clinical implications of the team's findings are significant.

"Understanding how p53 prevents tumors raises the prospect of therapeutic interventions to correct cases in which p53 is disabled," Dr. Abrams said. "If retroelements are at the heart of certain p53-driven cancers, finding ways to suppress them could potentially allow us to prevent those cancers or intervene to keep them from progressing."

This understanding also could lead to advances in diagnosing some cancers through biomarkers related to p53 and transposon activity.

"One possibility is that perhaps blood or urine tests could detect dysregulated retroelements that could be indicative of certain types of cancer," Dr. Abrams said.

Provided by UT Southwestern Medical Center

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