# Epigenetics can drive cancer, may be target for new treatments

For many of us, our medical education involved an inexorable link between mutations — changes in our very genes — and cancer. Yet over the last several years, evidence has accumulated that cancer is more than an inherited genetic disease; cancer patients often also display abnormalities in their epigenome. If your genes are words and your genome is a book, the epigenome is an overlay of notes that tells you how to read it.

A team from the Baylor College of Medicine has now shown that epigentic changes alone are enough to drive cancer without any mutations in the genome itself. The text of the book remains the same, but the reading is somehow corrupted.

The team, led by Lanlan Shen, used mice and the gene *p16* as their test subjects. They chose *p16* because of its normal function of regulating cell division — something that goes noticeably awry in cancers, in which tumors form from runaway cell division.

One of the most important mechanisms in the epigenome is methylation, a process by which a methyl group (a specific molecule) attaches itself to DNA and effective turns a gene on or off. Shen and her team raised two generations of mice: one set was engineered so that their *p16* gene would be turned off by abnormally high methylation, the other would have normal *p16* gene methylation.

The results were quite clear, as reported by The Scientist. Of the altered mice, "27 percent developed lung cancer, leukemia, or sarcomas, while wild-type controls did not develop tumors. Five percent of mice that inherited one copy of the transgene and one wild-type copy also developed tumors." The report elaborates:

> "For many years we've been very convinced that DNA methylation changes and epigenetic silencing contribute to human cancer, and there have been a lot of observations that support that concept,"Peter Jones, research director and head of the cancer epigenomics lab at Michigan's Van Andel Research Institute who was not involved in the work, told *The Scientist* . "What [this] paper does, which I think is very clever, is to selectively silence a tumor-suppressor gene—that's the *p16* gene—in a mouse model system and then show that those mice do develop cancers. This shows that epigenetic silencing can lead directly to the formation of cancer."

In other words, healthy genes, without proper epigenetic regulation, are perfectly capable of turning cancerous. Not everyone is convinced that genetics doesn't play at least some necessary role, even in this study, which used genetic modification (not of *p16* but of a nearby gene) as a way of influencing the epigenome. From The Scientist:

> Richard Meehan, who studies epigenetics in development and disease at the University of Edinburgh, argued that the paper does not directly demonstrate cause-and-effect. The authors […] did not expressly show that altered methylation—and not some other means of

transcriptional repression also associated with the transgene—initiated gene silencing.

Regardless, the study does demonstrate the importance of epigenetics in cancer formation and points toward a potentially rich vein of cancer research. Methylation is reversible, meaning if it's a major driver of cancer it can be targeted and treated. We don't yet have the means to un-mutate your genome easily, but epigenetic changes are within our grasp.

"This is not only the first in vivo evidence that epigenetic alteration alone can cause cancer," Shen said in a release. "This also has profound implications for future studies, because epigenetic changes are potentially reversible. Our findings therefore both provide hope for new epigenetic therapies and validate a novel approach for testing them."

Shen's study is part of a larger trend to pursue epigenetics as an important avenue of cancer research. A recent report on the state of epigenetics by Genetic & Bioengineering News found that of 100 open clinical trials with an epigenetic focus, nearly half are cancer-focused, noting that "the R&D pipeline is rich and will yield drugs over this decade."

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**Additional Resources:**

- 'Epigenetic' gene tweaks seem to trigger cancer, New Scientist
- Epigenetics Implicated In Mouse Cancer, Science 2.0
- No Nobel, but epigenetics finally gets the recognition it deserves, The Conversation