

# The ends of mRNAs may prevent the beginnings of cancer

August 20 2009

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The tail ends of cellular protein templates, regions often thought relatively inconsequential, may actually play a role in preventing normal cells from becoming cancerous.

The finding from scientists at Whitehead Institute for Biomedical research is reported in the August 20 edition of *Cell*.

Proteins are made from templates that are copied from a cell's DNA. These templates, called messenger RNAs (mRNAs), comprise three sections. The middle section codes for the actual protein, while the beginning and end sections are known as untranslated regions (UTRs) because they do not code for any portion of the protein. Instead, the beginning section gets [protein production](#) started, while the tail section, called the 3'UTR, appeared simply to be along for the ride.

"This end of the mRNA is often not considered that important because if you put the beginning and middle of the mRNA into a cell, you get the right protein," says Christine Mayr, first author of the *Cell* paper and a former postdoctoral researcher in the lab of Whitehead Member David Bartel. "But now we know that this end often has a protein production regulatory program and in some cases can play a role in cancer."

A cell uses proteins in almost all of its processes, from cell division, to transporting essential molecules, to providing the cell's structure. Because the cell's protein production profile is tightly controlled and specific to the cell's type and stage in its life cycle, the over- or under-

production of certain proteins can alter normal cellular function. These changes can include uncontrolled cell division and the ability to grow in the absence of a substrate—both defining traits of cancer cells.

When Mayr compared mRNAs produced in normal cells with those in [cancerous cells](#), she noticed that the tail end of the cancer cells' mRNAs were cut short. In some cases, nearly 95% of the 3'UTR was missing.

"So now, in the cancer cell, the same protein is being made, but a lot of regulatory sequences have been lost," says Mayr. "And in the beginning, I had no idea what this means. But then I found that those shorter mRNAs were making much more protein."

In fact, the shorter mRNAs were producing between two and 40 times more protein than their normal-length counterparts. When Mayr altered normal cells so they produced only shortened mRNAs for a specific gene, the cells again produced huge amounts of that mRNA's protein. And the copious proteins transformed normal cells into cancer-like cells.

"So, my theory is that in normal cells, genes are tightly regulated by their long 3'UTRs," says Mayr. "And the cancer cell somehow has the ability to express the shorter [mRNA](#) without those regulatory sequences. Without that regulation, it's able to express large quantities of [protein](#)."

Although Mayr has established a connection between short 3'UTRs and cancer cells, how the cells shorten their mRNAs remains a mystery.

"The next step is to try to explain this phenomenon mechanistically," says Bartel, who is also a professor of biology at MIT and a Howard Hughes Medical Institute investigator. "There has to be biochemical machinery that causes shortened 3'UTRs in cancer cells, something that the cancer cells have that normal cells don't have. Right now, the biochemical cause of this is not known."

More information: "Widespread shortening of 3'UTRs by alternative cleavage and polyadenylation activates oncogenes in cancer [cells](#)," *Cell*, published August 21, 2009; Christine Mayr and David P. Bartel.

Source: Whitehead Institute for Biomedical Research ([news](#) : [web](#))

Citation: The ends of mRNAs may prevent the beginnings of cancer (2009, August 20) retrieved 23 April 2024 from <https://medicalxpress.com/news/2009-08-mrnas-cancer.html>

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