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Researchers see helpful protein causing cancer

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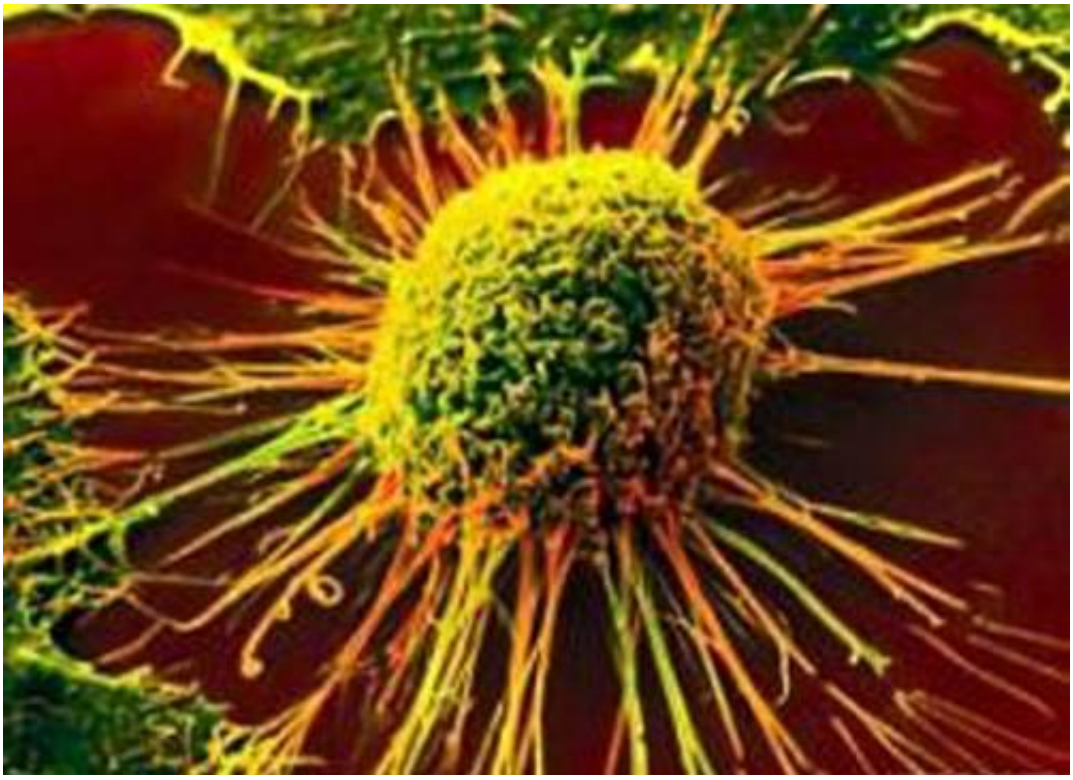

Washington State University researchers have determined how a protein that helps cells fight viruses can also cause genetic mutations that lead to cancer.

The research, published in the journal *Cell Reports*, shows how the

expression of a protein causes mutations to accumulate in actively replicating DNA. The work is complemented by studies from other researchers published in the *Proceedings of the National Academy of Sciences* and *Cell*, which indicate that similar phenomena occur in E. coli cells and sequenced human tumors.

"It makes the overall impact of the work greater when multiple research groups work together and come to similar conclusions using different techniques," said Steven Roberts, an assistant professor in the WSU School of Molecular Biosciences who coordinated publication with the other labs.

Roberts' lab introduced the protein, an enzyme with the shorthand name of APOBEC, into a laboratory strain of the baker's yeast Saccharomyces cerevisiae. He and his colleagues then documented how it mutated genetic sequences in a small region of just three nucleotides, the subunits of DNA.

The protein normally kills viruses by making changes to their genetic sequence, inactivating them. But the protein can also change the genetic sequence of a normal cell, altering the body's blueprint and making mutations that cause cancers.

"What we found is the way that the proteins are making these mutations in tumors is they actually take advantage of the fact that tumors are dividing a lot, so they're able to damage DNA that's being actively replicated," said Roberts.

As DNA replicates, it has moments in which single strands of its double helix are exposed. The APOBEC protein takes advantage of this vulnerability to cause damage. Prior studies have found that one in five human tumors have evidence of these enzyme-induced mutations.

In addition to causing tumors, the protein can continue to mutate tumor DNA, increasing a cancer's genetic diversity and giving it a wider tool kit with which to resist treatment.

A greater knowledge of how APOBEC works could lead to treatments that decrease its activity, said Roberts. Or a treatment could go in the other direction, creating so many mutations in a tumor that it self-destructs.

More information: James I. Hoopes et al. APOBEC3A and APOBEC3B Preferentially Deaminate the Lagging Strand Template during DNA Replication, *Cell Reports* (2016). DOI: 10.1016/j.celrep.2016.01.021

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