MedicalXpress

Antiviral enzyme contributes to several forms of cancer

July 14 2013

Researchers at the University of Minnesota have discovered that a human antiviral enzyme causes DNA mutations that lead to several forms of cancer.

The discovery, reported in the July 14 issue of *Nature Genetics*, follows the team's earlier finding that the enzyme, called APOBEC3B, is responsible for more than half of breast cancer cases. The previous study was published in Nature in February.

APOBEC3B is part of a family of antiviral proteins that Harris has studied for more than a decade. His effort to understand how these proteins work has led to these surprising discoveries that APOBEC3B is a broadly important cancer mutagen.

"We are very excited about this discovery because it indicates that a single enzyme is one of the largest known contributors to cancer mutation, possibly even eclipsing sources such as UV rays from the sun and chemicals from smoking," says Reuben Harris, a professor of biochemistry, molecular biology and biophysics based in the College of Biological Sciences. Harris, who led the study, is also a member of the Masonic Cancer Center, University of Minnesota.

For the current study, Harris, along with colleagues Michael Burns and Alpay Temiz, analyzed tumor samples from 19 different types of cancer for the presence of APOBEC3B and 10 related proteins. Results showed that APOBEC3B alone was significantly elevated in six types (bladder,

cervix, two forms of lung cancer, head & neck, and breast). Levels of the enzyme, which is present in low levels in most healthy tissues, were elevated in several other types of cancer as well.

A second key finding was that the mutational signature of APOBEC3B is a close match to the actual mutation pattern in these cancers. "Much like we each have unique written signatures, these enzymes each leave a unique mark," Harris says.

Findings from both studies are counterintuitive because the enzyme, which is produced by the immune system, is supposed to protect cells from HIV and other viruses, not harm our own genomic DNA.

While it's well known that sunlight and chemical carcinogens can mutate DNA, and that mutations are essential for cancer to develop, Harris is the first to discover that this human enzyme is a major cause mutation in cancer. He believes that APOBEC3B is a biological "double-edged sword" that protects some cells from viruses such as HIV and produces mutations that give rise to cancer in others.

Harris hopes to find a way to block APOBEC3B from mutating DNA, just as sunscreen blocks mutations that lead to melanoma. Many cancer mutations have been identified, but discovering a common source of mutation such as APOBEC3B is expected to help researchers to move "upstream" and look for a way to stop carcinogenesis closer to its source, he says, "like damming a river before it wreaks havoc on downstream areas." It's also possible that a simple test for APOBEC3B could be used to detect cancer earlier.

Harris is a professor in the Department of Biochemistry, Molecular Biology and Biophysics, which is a joint department of the College of Biological Sciences and the Medical School. He is also a member of the Masonic Cancer Center, University of Minnesota, which is part of the

National Cancer Institute's network of Comprehensive Cancer Centers. Harris and colleagues are grateful for support from the National Institutes of Health, the Department of Defense Breast Cancer Research Program, the Jimmy V Foundation, and the Minnesota Ovarian Cancer Alliance.

More information: Evidence for APOBEC3B mutagenesis in multiple human cancers, DOI: 10.1038/ng.2701