



DNA Shows Why Cancer Risk Rises the Longer You Live

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Written by Kristen Fischer

New research shows that small genetic changes, built up over time, increase a person's cancer risk. Scientists know that age is a risk factor for developing cancer, but they weren't sure why until now. A National Institutes of Health study published in *Carcinogenesis* shows that DNA methylation—when chemical tags known as methyl groups bind to DNA—could be the culprit. These methyl groups can either activate or silence genes by impacting their DNA.

Zongli Xu, Ph.D., and Jack Taylor, M.D., Ph.D., researchers from the National Institute of Environmental Health Sciences, examined DNA methylation sites throughout the human genome that change with age. They studied blood samples from people in the Sister Study, which involves more than 50,000 sisters of breast cancer patients.

They looked at samples from 1,000 women to show that those sites in the genome that become more methylated with age are also disproportionately methylated in a variety of cancers.

Of the 1,000 samples, about one-third showed more DNA methylation with age. Next, they examined three other data sets from smaller studies that used the same techniques and found 749 methylation sites that behaved consistently across all four data sets. They also studied methylation data from normal tissues and seven

types of cancerous tumors from the Cancer Genome Atlas.

Methylation Builds Up as We Age

Taylor explained that methylation is like dust settling on an unused switch—it effectively stops the cell from flipping on certain genes. If a cell can no longer turn on critical developmental programs, it might be easier for it to become a cancer cell, he said.

Taylor said that DNA methylation appears to be part of the normal aging process.

Researchers are used to seeing cancer cells with DNA methylation, but they were shocked when they found that 70 percent to 90 percent of sites linked to age showed significantly increased methylation across all seven cancer types.

The researchers also determined how fast methylation accumulates in cells. Methylation events occur at a rate of one per year, Xu said. The longer you live, the more methylation you will have.

“There is already a substantial research effort in using drugs that modify DNA methylation for cancer treatment, but we do not know whether the specific age-related sites would be particularly useful targets for therapy,” Taylor said.

Why Age Is Key

What impacts the methylation process, and what can people do to interrupt it? Taylor said that diet, chemical exposure, and lifestyle affect DNA methylation, but scientists don’t know whether those factors can reverse the effects of age on our DNA.

Samuel Waxman, M.D., a professor of medicine, hematology, medical oncology, and oncological sciences at Mount Sinai Hospital in New York, said part of the reason that cancer death rates are on the rise in people over 70 is due to a lifetime of toxic

exposure, inflammation, and dietary excess that cause a breakdown of controls that regulate gene function. Those patterns for abnormal gene control have been defined in the eight most common forms of cancer.

“This offers a road map to develop drugs to correct or reprogram gene function,” Waxman said.

The World Health Organization’s latest World Cancer Report says that the organization expects cancer cases across the globe to rise by 70 percent during the next two decades, which it calls a potential "human disaster." Since 2008, cancer has gone up from 12.7 million cases per year to 14.1 million cases in 2012. The report attributes this rise, in part, to increasing lifespans.

Taylor said the incidence of the most common cancers in adults—breast, prostate, colon, lung, and skin cancer—increases with age.

Certain viral infections may also increase the risk of specific cancers, such as the hepatitis B virus (HBV) and liver cancer or the human papillomavirus (HPV) and cervical cancer. Liver cancer incidence increases with age, whereas cervical cancer incidence peaks around the age of 35 and then decreases, so it's difficult to make a generalization, Taylor said.