

# Study finds smoking related to subset of colorectal cancers

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Smoking puts older women at significant risk for loss of DNA repair proteins that are critical for defending against development of some colorectal cancers, according to research from a team led by Mayo Clinic scientists.

In a study being presented at the annual meeting of the American Association for Cancer Research (AACR), the researchers found that women who smoked were at increased risk for developing colorectal tumors that lacked some or all of four proteins, known as DNA mismatch repair (MMR) proteins. These proteins keep cells lining the colon and rectum healthy because they recognize and repair genetic damage as well as mistakes that occur during cell division.

Researchers believe that, in this study population, few if any of the four proteins were absent because of an inherited genetic alteration. “We think that smoking induces a condition within intestinal cells that does not allow MMR genes to express their associated proteins, and this loss leads to formation of tumors in some women,” says the study’s lead author, Mayo gastroenterologist Paul Limburg, M.D.

The researchers also discovered a direct association between the number of cigarettes smoked daily by study participants and increased risk of developing these specific tumors. They say many previous studies have found only a very weak positive association between use of cigarettes and development of the cancer.

“Our findings suggest that tumors may form because cells can’t repair themselves from damage induced by smoking,” Dr. Limburg says.

“Tobacco toxins appear to block the DNA repair genes from producing their beneficial proteins.

“We are beginning to realize that there might be different risk factors for different subsets of colon and rectal cancers. Smoking is emerging as a potentially important, modifiable risk factor among postmenopausal women,” he says.

The findings also could have other clinical implications with respect to chemotherapy, as tumors that lack MMR proteins might respond differently to standard treatment regimens, Dr. Limburg says.

The research team examined data from the 41,836-participant Iowa Women’s Health Study and selected those 1,421 women who developed colorectal cancer since the study began in 1986. They then worked with the Iowa Cancer Registry and pathology laboratories around the state to collect tumor specimens from these patients. To date, they have retrieved about 50 percent of the samples. This study, a first analysis, includes 432 samples, or about 30 percent of the group.

They analyzed the tumors for presence of four DNA mismatch repair proteins known to be active in cells lining the colon and rectum. Samples that had all four were labeled MMR-positive. Tumors with less than four were tagged as MMR-negative.

The researchers then correlated information reported by the patients on whether they had ever smoked and how many cigarettes they used daily with MMR protein patterns in their tumors.

They found that smoking status was not significantly associated with development of colorectal cancer in the 432 patients in general.

However, when the scientists examined colorectal cancers in women smokers with the perspective of MMR-deficient gene involvement, there was a strong association between smoking and MMR-negative status. For example, former smokers had a 61 percent increase in relative risk for MMR-negative colorectal cancer compared to never smokers, and “current” smokers were more than twice as likely to develop colorectal tumors with absent mismatch repair proteins.

The association between smoking and MMR-negative colorectal cancer also steadily increased with the number of cigarettes a woman smoked per day, Dr. Limburg says. The relative risk for MMR-negative cancer increased 54 percent if a patient smoked 1–19 cigarettes daily, more than twofold for 20 cigarettes a day, and more than threefold for a woman who smoked more than 30 cigarettes daily.

He adds that the link between smoking with loss of MMR proteins and development of colorectal cancer may also occur in male smokers and in younger people, but that the researchers can’t make such associations because this study used data only from older women.

Source: Mayo Clinic

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