Study reveals cancer-linked epigenetic effects of smoking

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For the first time, UK scientists have reported direct evidence that taking up smoking results in epigenetic changes associated with the development of cancer.

The results were reported at the 35th Congress of the European Society for Medical Oncology (ESMO) in Milan, Italy.

The link between smoking and cancer has been established for decades, explained Dr Yuk Ting Ma from the Cancer Research UK Institute of Cancer Studies, Birmingham, who presented the results. Smoking is the single biggest cause of cancer in the world, and years of research have confirmed that carcinogenic substances in tobacco smoke can damage DNA.

Scientists have also suspected that smoking causes so-called epigenetic changes, such as methylation, which alter gene expression without causing changes to the actual DNA sequence.

"Until now, however, there has been no direct evidence that smoking induces DNA methylation in humans," Dr Ma said. "Cross-sectional surveys restricted to patients with cancer have revealed that aberrant methylation of several tumor suppressor genes is associated with smoking. But such surveys cannot distinguish those epigenetic changes that are a consequence of the disease process from those which are directly attributable to smoking."

In a study funded by Cancer Research UK, the British team set out to clarify the link between smoking and methylation in a cohort of 2,011 healthy young women aged 15-19 who were originally recruited as part of a study of pre-cancerous changes to cells of the cervix.

"For this particular study we have identified all the women from that cohort who had normal smears and who also tested negative for human papillomavirus throughout follow-up," Dr Ma explained. "In this subgroup of disease-free women we have then tested the cervical smears of all the women who first started to smoke following study entry for p16 methylation, and compared them to women who were never smokers."

The researchers selected this group of women to ensure there were no potential cofounding factors for the detection of p16 methylation in otherwise healthy young women.

The particular gene the researchers were studying was p16, a so-called tumor suppressor gene. When it is methylated, this gene's normal tumor-suppressing function is inactivated.

"DNA methylation is a type of epigenetic change that can result in tumor suppressor genes being inactivated," said Dr Ma. "Methylation of p16 has been frequently associated with the development of cancer in many parts of the body."

Because the women were all taking part in a study of cervical neoplasia, Dr Ma used cells from cervical smears to test for methylation of p16. Her group found that women who took up smoking during the study were more than three times as likely (odds ratio of 3.67) to acquire p16 methylation.

"Our study showed that compared with never-smokers, women who first started to smoke during follow-up had an increased risk of acquiring methylation of p16," Dr Ma said. "Our choice of study design and our study population allowed us to reveal, for the first time, the relationship between starting to smoke and the subsequent appearance of an epigenetic change."

The results provide evidence that smoking does induce DNA methylation, Dr Ma said. "The next step is now to show that women who acquire such smoking-induced methylation have an increased

risk of developing malignancy."

Provided by European Society for Medical Oncology