

Smoking turns on genes -- permanently

August 29 2007

Smoking tobacco is no longer considered sexy, but it may prove a permanent turn on for some genes. Research published today in the online open access journal *BMC Genomics* could help explain why former smokers are still more susceptible to lung cancer than those who have never smoked.

A Canadian team led by Wan L Lam and Stephen Lam from the BC Cancer Agency, took samples from the lungs of 24 current and former smokers, as well as from non-smokers who have never smoked. They used these lung samples to create libraries using a technique called serial analysis of gene expression (SAGE), which helps to identify patterns of gene activity.

Only about a fifth of the genes in a cell are switched on at any given time, but environmental changes such as smoking lead to changes in gene activity. The researchers found changes that were irreversible, and some changes that were reversed by stopping smoking. The reversible genes were particularly involved in xenobiotic functions (managing chemicals not produced in the body), nucleotide metabolism and mucus secretion. Some DNA repair genes are irreversibly damaged by smoking, and smoking also switched off genes that help combat lung cancer development.

The researchers identified a number of genes not previously associated with smoking that are switched on in active smokers. One example is CABYR, a gene involved in helping sperm to swim and associated with brain tumours, which may have a ciliary function.

The team also further investigated changes in genes involved in airway repair and regeneration, and within this group identified genes that fell into three categories following cessation of smoking: reversible (TFF3, encoding a structural component of mucus; CABYR, in it's newly discovered bronchial role), partially reversible (MUC5AC, a mucin gene) and irreversible (GSK3B, involved in COX2 regulation). These findings were tested against a second cohort of current, former and non-smokers.

"Those genes and functions which do not revert to normal levels upon smoking cessation may provide insight into why former smokers still maintain a risk of developing lung cancer," according to Raj Chari, first author of the study. The study is the largest human SAGE study reported to date, and also generated a large SAGE library for future research.

Tobacco smoking accounts for 85 percent of lung cancers, and former smokers account for half of those newly diagnosed with the disease.

Source: BioMed Central

Citation: Smoking turns on genes -- permanently (2007, August 29) retrieved 23 April 2024 from <https://medicalxpress.com/news/2007-08-genes-permanently.html>

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