Studying the metabolome of smokers, researchers find early signs of damage

November 7 2010

Examining the blood "metabolomics" profile of smokers immediately after they had a cigarette revealed activation of pathways involved in cell death, inflammation, and other forms of systemic damage, say researchers at Georgetown Lombardi Comprehensive Cancer Center, part of Georgetown University Medical Center.

They say their findings, presented at the Ninth AACR Frontiers in Cancer Prevention Research Meeting, is the best analysis for chemicals unequivocally produced by smoking and indicates the potential toll that carcinogens and toxins poise to smokers years before lung cancer, heart disease, or other smoking–related diseases appear.

"Our analysis uncovered hallmarks of liver, heart, and kidney toxicity in otherwise healthy patients," says the study's lead investigator, Ping-Ching Hsu, a doctoral student who works in the laboratory of oncology researcher Peter Shields, MD, who specializes in tobacco carcinogenesis. Shields is the senior author.

Shields says the findings could help in the development of new blood tests that will allow researchers to assess the harmfulness of one tobacco product compared to another. This could be useful to the federal Food and Drug Administration, the agency charged by Congress to begin controlling the contents of cigarettes.

The study presents a new way to evaluate the effect of cigarette smoking in humans, say the researchers. Previously, cigarette manufacturers were

only required to use machines that "smoked" cigarettes to derive the chemical content of potential carcinogens. "We have come up with an actual picture of what is happening in the body of smokers and the harm that is being produced," Hsu says.

In their pilot study, they analyzed the blood of 10 smokers before and after they smoked a cigarette, and then measured the effects again after a second cigarette smoked one hour later in a smoking laboratory. Because frequent tobacco users may metabolize smoking-related toxins differently, the study enrolled 5 light smokers (fewer than 12 cigarettes a day) and 5 heavy smokers (23 or more cigarettes smoked a day).

The researchers then analyzed the global metabolomic profile of about 3,000 chemicals in the blood of each smoker. A metabolite is produced when anything taken into the body – such as food, tobacco smoke, alcohol, medicine – is metabolized, or broken down into chemicals that produce a biological function via metabolic pathways. The global metabolome is the network of metabolic reactions, and metabolomics is analysis of the metabolome at any given time.

Using complicated tools, researchers can trace the metabolites in the context of relevant pathways that are affected by cigarette smoke including cell death, cell-cell interactions (a marker of inflammation), lipid metabolism, and gene expression In heavy smokers, they then traced metabolites that were being produced after smoking back to damage in multiple organs and to a breakdown in the phospholipids that make up a cell's membrane, and a change in production of bile acids.

The study is ongoing, and researchers also plan to compare changes in those smokers' metabolome to their transcriptome – all RNA molecules produced in the cells of the smokers, which was done in the lab few years ago. This would reflect the genes that are actively being expressed at a given time.

"One goal of our work is to identify new risk markers for lung cancer that can then enhance early detection of smoking-related disorders, and to do that we need to develop new biomarkers," Hsu says.

Provided by Georgetown University Medical Center