MedicalXpress

In lung cancer, smokers have 10 times more genetic damage than never-smokers

September 13 2012

Lung cancer patients with a history of smoking have 10 times more genetic mutations in their tumors than those with the disease who have never smoked, according to a new study from Washington University School of Medicine in St. Louis.

"None of us were surprised that the genomes of smokers had more mutations than the genomes of never-smokers with lung cancer," says senior author Richard K. Wilson, PhD, director of The Genome Institute at Washington University. "But it was surprising to see 10-fold more mutations. It does reinforce the old message – don't smoke."

The study appears online Sept. 13 in *Cell*.

Overall, the analysis identified about 3,700 mutations across all 17 patients with non-small cell lung cancer, the most common type. Twelve patients had a history of smoking and five did not. In each patient who never smoked, the researchers found at least one mutated gene that can be targeted with drugs currently on the market for other diseases or available through clinical trials. Across all patients, they identified 54 mutated genes already associated with existing drugs.

"Whether these drugs will actually work in patients with these DNA alterations still needs to be studied," says first author Ramaswamy Govindan, MD, an oncologist who treats patients at Siteman Cancer Center at Barnes-Jewish Hospital and Washington University. "But papers like this open up the landscape to understand what's happening.

Now we need to drill deeper and do studies to understand how these mutations cause and promote cancer, and how they can be targeted for therapy."

Lung cancer is divided into two types – small cell and non-small cell, the latter accounting for about 85 percent of all cases. Within non-small cell lung cancer are three further classifications. This current analysis included two of them. Sixteen patients had adenocarcinoma and one had large-cell carcinoma.

Govindan and Wilson also were involved in a larger genomic study of 178 patients with the third type, squamous cell carcinoma, recently reported in Nature. That study was part of The Cancer Genome Atlas project, a national effort to describe the genetics of common cancers.

"Over the next year or so, we will have studied nearly 1,000 genomes of patients with lung cancer, as part of The Cancer Genome Atlas," says Govindan, who serves as a national co-chair of the lung cancer group. "So we are moving in the right direction – toward future clinical trials that will focus on the specific molecular biology of the patient's cancer."

Indeed, based on the emerging body of genetic research demonstrating common mutations across disparate cancer types, Wilson speculates that the field may reach a point where doctors can label and treat a tumor based on the genes that are mutated rather than the affected organ. Instead of "lung cancer," for example, they might call it "EGFR cancer," after the mutated gene driving tumor growth. Mutations in EGFR have been found in multiple cancers, including lung, colon and breast.

This labeling is relevant, Wilson says, because today targeted therapies are approved based on the diseased organ or tissue. Herceptin®, for example, is essentially a breast cancer drug. But he has seen lung cancer patients with mutations in the same gene that Herceptin targets.

"For example, if genome sequencing revealed that a lung cancer patient has a mutation known to be sensitive to a drug that works in breast tumors with the same genetic alteration, you may want to use that agent in those lung cancer patients, ideally as part of a clinical trial," he says. "In the coming years, we hope to be treating cancer based more on the altered genetic make-up of the tumor than by the tissue of origin."

More information: Govindan R, Ding L, Griffith M, Subramanian J, Dees ND, Kanchi KL, Maher CA, Fulton R, Fulton L, Wallis J, Chen K, Walker J, McDonald S, Bose R, Ornitz D, Xiong D, You M, Dooling DJ, Watson M, Mardis ER, Wilson RK. Genomic landscape of non-small cell lung cancer in smokers and never-smokers. Cell. Sept. 13, 2012.

Provided by Washington University School of Medicine