# Study shows how cigarette smoke blocks cell repair

August 21 2006

Cigarette smoke can turn normal breast cells cancerous by blocking their ability to repair themselves, eventually triggering tumor development, University of Florida scientists report.

While some cells nonetheless rally and are able to fix their damaged DNA, many others become unable to access their own cellular first aid kit, according to findings from a UF study published today (Aug. 21) in the journal *Oncogene*. If they survive long enough to divide and multiply, they pass along their mutations, acquiring malignant properties.

Past research has been controversial. Tobacco smoke contains dozens of cancer-causing chemicals, but until more recently many studies found only weak correlations between smoking and breast cancer risk, or none at all. Those findings are increasingly being challenged by newer studies that are focusing on more than just single chemical components of tobacco, as past research often has done. In the UF study, researchers instead used a tar that contains all of the 4,000 chemicals found in cigarette smoke.

“Our study suggests the mechanism by which this may be happening,” said Satya Narayan, an associate professor of anatomy and cell biology at UF’s College of Medicine. “This is basically the important finding in our case: We are now describing how cigarette smoke condensate, which is a surrogate for cigarette smoke, can cause DNA damage and can block the DNA repair of a cell or compromise the DNA repair capacity of a cell. That can be detrimental for the cell and can lead to transformation or

carcinogenesis."

In their study, funded by the National Institutes of Health and the Miami-based Flight Attendant Medical Research Institute, UF researchers exposed normal breast epithelial cells to cigarette smoke condensate—a tar derived from a machine that literally "smokes" a cigarette in the laboratory—and found the cells acquired mutations characteristic of malignant cells.

The scientists say DNA repair appears to be compromised when chemical components of smoke activate a key gene. That gene interacts with an enzyme that plays a crucial role in repairing damaged DNA, preventing it from doing its job. The cell, despite its mutated form, can then multiply wildly.

A cell with damaged DNA has one of two fates, said Narayan, also a member of the UF Shands Cancer Center.

"Its DNA repair machinery can be enhanced and it can fix the damaged DNA and restore genomic stability, or if the DNA repair machinery becomes compromised within the cell, then it can lead to an accumulation of mutations because the DNA is not fixed before the cell begins to divide," he said. "The mutation then becomes a permanent part of the genome and causes genomic instability, and genomic instability can bring about several cellular dysfunctions, and one of them can lead to tumor formation."

Other UF research led by Dr. Xingming Deng, and published last month in the *Journal of Biological Chemistry* revealed that nicotine activates a protein in cancer cells that helps them live long, spread to new sites and grow resistant to chemotherapy.

Narayan's team has previously studied cells that were exposed to the

chemicals found in cigarette smoke yet did not die. In general, about two-thirds of these cells will be growth-retarded, and some actually acquire cancer-like characteristics, he said.

“Some of these cells that survive are really acquiring true mutagenic characteristics,” Narayan said. “A defect in only one cell is important for growth of a full-blown tumor. You don’t need 1,000 or 1 million cells to be affected. Only a single cell which may have genomic instability due to compromised DNA repair capacity of the cell can be sufficient for a tumor to develop. That has to be considered also when we do these kinds of studies.”

Narayan said the next step will be to find ways to manipulate cells’ capacity for DNA repair and to prevent tumor formation.

Meanwhile, he cautions people to avoid smoking, especially teenagers. A study last year found teenage smokers are at especially high risk of breast cancer development later in life, he said.

“Teenagers should realize they are inhaling 4,000 chemicals, and these chemicals can do so much harm in the body, not only posing a breast cancer risk but for so many other things,” Narayan said. “The consequence of these chemicals is not apparent in one day or two days or in months; it takes years and years for cancers to develop. Once the gene is damaged and sitting there it’s going to provide some harmful effect later on.”

Dr. Jose Russo, a researcher at the Fox Chase Cancer Center in Philadelphia who has studied how breast epithelial cells transform after exposure to the chemical benzo[a]pyrine, which is found in tobacco smoke, called the UF findings very interesting.

“We found significant alteration in many of the chromosomes in these

cells induced by the effect of benzo[a]pyrine," Russo said. "We were the first ones to demonstrate in normal-like epithelial cells this compound produced a transformation. Cigarette smoke condensate contains more than one compound, so the UF experiment is more similar to the way any human being would be exposed to the carcinogens. It mimics the human situation more closely."

Source: University of Florida