Mouth may tell the tale of lung damage caused by smoking

April 14 2008

Cells lining the mouth reflect the molecular damage that smoking does to the lining of the lungs, researchers at The University of Texas M. D. Anderson Cancer Center report today at the annual meeting of the American Association for Cancer Research.

Examining oral tissue lining the mouth to gauge cancer-inducing molecular alterations in the lungs could spare patients and those at risk of lung cancer from more invasive, uncomfortable procedures used now, said senior researcher Li Mao, M.D., professor in M. D. Anderson's Department of Thoracic/Head and Neck Medical Oncology.

"We are talking about just a brushing inside of the cheek to get the same information we would from lung brushings obtained through bronchoscopy," said study presenter and first author Manisha Bhutani, M.D., a post-doctoral fellow in Thoracic/Head and Neck Medical Oncology.

The team examined the oral and lung lining tissue - called the epithelium - in 125 chronic smokers enrolled in a large, prospective lung cancer chemoprevention study.

The status of two crucial tumor-suppressing genes was analyzed. The genes, p16 and FHIT, are known to be damaged or silenced very early in the process of cancer development. "There is substantial damage long before there is cancer," Mao said.

Study participants gave both an oral and lung sample initially and then another at three months. The researchers tracked whether either p16, FHIT or both had been silenced by methylation - the attachment of a chemical methyl group to crucial spots in a gene that shut down its function. Patterns of methylation were compared between the tissues.

The baseline tissue comparison showed methylation of p16 in the lungs of 23 percent of study participants, of FHIT in 17 percent and of either of the two genes in 35 percent. The percentages were similar in oral tissue, with p16 methylated in 19 percent, FHIT in 15 percent and one of the two in 31 percent.

Strong correlations were observed between methylation patterns in both tissues. When methylation of either gene was considered positive, 37 of the 39 individuals (95 percent) with p16 and/or FHIT promoter methylation in the oral samples had promoter methylation in at least one matched bronchial sample. This compared with only 59 of the 86 (69 percent) individuals without the promoter methylation in the oral samples. Similar correlations were seen at the three-month analysis.

"Our study provides the first systematic evidence that accessible tissue, the oral epithelium, can be used to monitor molecular events in less accessible tissue," Bhutani said. "This provides a convenient biomonitoring method to provide insight into the molecular events that take place in the lungs of chronic smokers."

One follow-up area of study is to find additional biomarkers in oral tissue. "We hope that our findings encourage researchers to test an increasing compendium of biomarkers to confirm the reliability of oral epithelium not only in lung cancer chemoprevention but also in therapeutic settings" said Ashutosh Kumar Pathak, M.D., another key study author and a post-doctoral fellow in Surgical Oncology.

"Our study opens the door to enhancing our ability to predict who has higher probability of getting tobacco-related cancers," Mao said. "Not only lung cancer, but pancreatic, bladder and head-and-neck cancers, which also are associated with tobacco use."

Source: University of Texas M. D. Anderson Cancer Center