

Researchers identify another potential biomarker

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Researchers from Boston University School of Medicine (BUSM) have demonstrated that a recently discovered class of molecule called microRNA (miRNAs), regulate the gene expression changes in airway cells that occur with smoking and lung cancer. These findings, which appear in the on-line early edition of journal *Proceedings of the National Academy of Sciences*, may lead to a new, relatively non-invasive biomarker for smoking-related lung diseases.

Approximately 1.3 billion people smoke cigarettes worldwide, which contributes to five million preventable deaths per year. Smoking is a significant risk factor for lung cancer, the leading cause of cancer death in the United States and the world, with more than one million deaths worldwide annually. Eighty-five to 90 percent of subjects with lung cancer in the United States are current or former smokers with 10 to 20 percent of heavy smokers developing this disease. Because of the lack of effective diagnostic biomarkers and the inability to identify which current and former smokers are at greatest risk, lung cancer is most often diagnosed at a late stage where current therapies are largely ineffective.

A previous study by the same researchers reported a gene expression biomarker capable of distinguishing cytologically normal bronchial airway epithelial cells from smokers with and without lung cancer, serving as an early diagnostic biomarker for lung cancer. The importance of this "field-of-injury" concept is that it allows for the detection of lung cancer in tissues that are more readily sampled than the diseased lung

tissue itself. In this study, the researchers profiled the miRNAs in these readily accessible airway epithelial cells and identified those that are differentially expressed with smoking.

Studying current and non-smokers, the researchers examined whole-genome miRNA and mRNA expression in bronchial airway epithelial brushings obtained at bronchoscopy and found 28 miRNAs to be differentially expressed in the majority of smokers. In addition, the researchers showed that by modulating the expression of one such miRNA (mir-218), it was sufficient to alter the expression of a subset of the mRNAs that are both predicted targets of this miRNA and altered by smoking in vivo.

"These studies suggest that smoking-dependent changes in miRNA expression levels mediate some of the smoking induced gene expression changes in airway epithelium and that miRNAs therefore play a role in the host response to environmental exposures and may contribute to the pathogenesis of smoking-related lung cancer," said senior author Avrum Spira, MD, an associate professor of medicine and pathology at BUSM.

According to the researchers, it is hoped that miRNA profiles obtained from these cells may serve as relatively non-invasive biomarkers for smoking-related lung diseases.

"These microRNA changes may serve as more robust biomarkers in clinical samples given their role as regulators of multiple mRNAs and their relative resistance to degradation," said first author Frank Schembri, MD, an assistant professor of medicine at BUSM.

Source: Boston University

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