Researchers identify molecule that could aid lung cancer detection, treatment

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Researchers at Boston University School of Medicine (BUSM) have discovered a molecule that could help lead to the non-invasive detection of lung cancer as well as its treatment. Using RNA sequencing, the team looked at airway epithelial cells and identified a regulatory molecule that was less abundant in people with lung cancer and inhibits lung cancer cell growth. The findings, which are published in the *Proceedings of the National Academy of Sciences*, suggest that this molecule may aid in diagnosing lung cancer in earlier stages and could potentially, when at healthy levels, aid in treating the disease.

According to the National Cancer Institute (NCI), lung cancer is the leading cause of cancer death among both men and women in the United States, and 90 percent of lung cancer deaths among men and approximately 80 percent of lung cancer deaths among women are due to smoking. The NCI also estimates that approximately 373,489 Americans are living with lung cancer and its treatment costs approximately $10.3 billion in the United States each year.

MicroRNA's are a new class of molecules classified as important regulators of the activity of other genes. In this study, the research team used a next-generation RNA sequencing technology and identified that a microRNA named miR-4423 in epithelial airway cells plays a major role in how these cells develop. In epithelial cells from the airway of smokers with lung cancer, levels of miR-4423 were decreased.

"These results suggest measuring the levels of microRNAs like

miR-4423 in cells that line the airway could aid in lung cancer detection through a relatively non-invasive procedure," said Avrum Spira, MD, MSc, the Alexander Graham Bell professor of medicine and chief of the division of computational biomedicine at BUSM, one of the study's senior authors.

Using experimental models in vitro and in vivo, the research team demonstrated that miR-4423 can both promote the development of the normal airway cells and suppress lung cancer cell growth. This suggests that miR-4423 plays a major regulatory role in cell fate decisions made by airway epithelial cells during maturation and low levels of miR-4423 contributes to lung cancer development. Interestingly, throughout the body, miR-4423 seems only to be present in high levels in the airway epithelium, suggesting this could be a very specific process occurring only in the lungs.

"Our findings open up the option to study whether returning miR-4423 levels to normal in the airway could help stop cancer growth and potentially be a way to treat lung cancer," said Catalina Perdomo, PhD, a researcher in the division of computational biomedicine at BUSM who is the paper's lead author.

"Interestingly, when we examined the genomes of other species for microRNAs that might function like miR-4423, we did not find anything in non-primates," said Marc Lenburg, PhD, an associate professor in computational medicine and bioinformatics at BUSM who is one the study's senior authors. "It makes us wonder what it is different about lung development in primates and excited that this could be a very specific process to target for lung cancer treatment."

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