New study provides insight in identifying, treating lung cancer at early stages

April 26 2021

Lung carcinomas are the leading cause of cancer-related deaths in the United States and worldwide. Lung squamous cell carcinomas (non-small cell lung cancers that arise in the bronchi of the lungs and make up

approximately 30 percent of all lung cancers) are poorly understood, particularly with respect to the cell type and signals that contribute to disease onset.

According to the researchers, treatments for lung squamous cell carcinomas are limited and research into the etiology of the disease is required to create new ways to treat it.

"Our study offers insight into how damage to the airways of the lung develops into lesions that can transition to cancer. Identifying and treating pre-cancer lesions would offer an opportunity for intercepting lung cancer development," said corresponding author Bob Varelas, Ph.D., associate professor of biochemistry at Boston University School of Medicine.

The study shows that disruption of proteins that control the shape of the lung epithelium drives signals that promote precancerous cellular growth in the airways of the lung. Using a combination of new experimental models, human tissues and bio-computational approaches, the researchers were able to show that damage to the architecture (polarity) of the lung epithelium drives signals that promote the formation of lesions that resemble human pre-cancer lesions that are known to progress to lung squamous cell carcinoma. The polarity damage can be caused in part by factors known to contribute to lung cancer, such as cigarette smoke exposure.

The researchers further identified factors that control a gene expression program associated with pre-cancer development and progression in human patients. From these genes they identified one factor, the growth factor Neuregulin-1, that is associated with pre-cancer cell growth that can be therapeutically targeted for treatment of pre-cancer lesions in experimental models. "Targeting these signals may allow us to prevent and treat the formation of pre-cancer lesions," explained Varelas.

The study is published in the *Proceedings of National Academy of Sciences*.

More information: Andrew Tilston-Lunel el al., "Aberrant epithelial polarity cues drive the development of precancerous airway lesions," *PNAS* (2021). www.pnas.org/cgi/doi/10.1073/pnas.2019282118

Provided by Boston University School of Medicine