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Researchers identify genes responsible for lung tumors

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The lung transcription factor Nkx2-1 is an important gene regulating lung formation and normal respiratory functions after birth. Alterations in the expression of this transcription factor can lead to diseases such as lung interstitial disease, post-natal respiratory distress and lung cancer.

Nkx2-1 expression is used to identify lung tumors of epithelial origin and to differentiate lung adenocarcinomas from squamous cell carcinoma. Researchers from Boston University School of Medicine (BUSM) have discovered new connections in the network of genes that control normal lung cells, and that may go awry in the formation of lung tumors and other lung diseases. The findings, which appear in the journal *Respiratory Research* may help control lung cell proliferation, tumor formation and progression.

Using miRNA array analyses of lung epithelial cell lines of an experimental model in which endogenous Nkx2-1 was reduced compared to cells with normal levels of Nkx2-1, the BUSM researchers identified numerous microRNAs that change their expression level in response to reduction of Nkx2-1. They also used experimental models lacking functional Nkx2-1 and showed similar effects. "We found that Nkx2-1 protein binds to regulatory regions of these miRNAs. In vitro studies indicated that miR-200c is inhibited by Nkx2-1, while miR-200c inhibits its predicted targets Nfib and Myb," explained corresponding author Jean-Bosco Tagne, PhD, assistant professor of medicine and molecular medicine at BUSM.

According to the researchers these transcription factors Nkx2-1, Myb and Nfib regulate lung cell proliferation in development, and in tumorigenesis acting as oncogenes. "The novel link we identified between NKX2-1, miR-200c and NFIB or MYB may participate in propagating fluctuations in the levels of Nkx2-1 in human lung tumors, adding substantial information to understanding lung tumorigenesis, for improvement of its prognosis, diagnosis and treatment," he added.

Tagne believes the regulatory network identified in this work addresses a mechanism of balancing the tumor suppressor miR-200c and the oncogenes Nkx2-1, Nfib and Myb. "This study adds new players to the regulatory mechanisms driven by Nkx2-1 in lung epithelial cells that may have implications in lung development and tumorigenesis," he said.

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