Taking aim at metastatic lung tumors

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A new study uses a sophisticated genomic analysis to unravel some of the complex cellular signals that drive the deadly invasive spread of lung cancer. The research, published by Cell Press in the June issue of the journal *Cancer Cell*, identifies specific molecules involved in the often fatal metastasis of a common type of non-small cell lung cancer (NSCLC) and uses this information to design effective therapeutic strategies.

"Previous cancer genomics studies have established a number of oncogene and tumor suppressor pathways as important for the initiation and maintenance of NSCLC," explains senior study author, Dr. Kwok-Kin Wong from the Dana-Farber Cancer Institute in Boston. "However, the molecular alterations necessary for invasion and metastases of NSCLC are less well-defined. Because metastasis causes much of the morbidity and incurability of cancer, there is an urgent need to elucidate the events underlying this biological process.

Dr. Wong and colleagues had recently shown that the loss of the Lkb1 tumor suppressor gene in a significant population of lung tumors results in metastasis in mice. Although the Lkb1 gene has also been linked with about 30% of human lung cancers, the pathways responsible for the metastatic effects had not been identified. To gain insight into the signaling pathways that underlie Lkb1-deficient lung tumors, the research team performed a comprehensive analysis of the genomic and signaling protein signatures of primary and metastatic lung tumors.

Loss of Lkb1 in mouse and human lung cancer cells was associated with an increase in the activity of proteins that are known to modulate cell motility and adhesion. Importantly, combined pharmacological inhibition of these key regulatory proteins in Lkb1-deficient cells decreased cell migration and induced tumor regression.

"Our analyses of primary and metastatic Lkb1-deficient mouse lung tumors have shown that progression to metastatic lung cancer is associated with unique gene and protein signatures," concludes Dr. Wong. "Importantly, our findings indicate that despite the complex transcriptional and signaling changes that occur in the setting of Lkb1 loss and progression of NSCLC, these tumors may still be addicted to isolated oncogenic events that can be successfully therapeutically targeted."

More information: Carretero et al.: “Integrative Genomic and Proteomic Analyses Identify Targets for Lkb1-Deficient Metastatic Lung Tumors.” Publishing in Cancer Cell 17, 547-559, June 15, 2010. DOI 10.1016/j.ccr.2010.04.026

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