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Researchers identify biomarker of early lung cancer that may increase survival

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Researchers in Taiwan have identified a biomarker that detects the most common lung cancer in its earliest stage. The discovery could one day change how long lung cancer patients live.

According to theNational Cancer Institute, lung cancer kills about 158,000 Americans each year—as many as the next 4 most deadly cancers combined. Non-small cell lung cancer (NSCLC) accounts for about 85 percent of all lung cancers.

"When NSCLC is detected early, patients have a 70 percent chance of being alive 5 years later. When NSCLC is detected at an advanced stage, 5-year survival drops to less than 10 percent," said senior investigator Pei-Jung Lu, PhD, professor of medicine at National Cheng-Kung University.

Lu and his colleagues tested Huntingtin interaction protein-1 (HIP1) as a potential new biomarker. They also investigated its role in lung cancer progression and metastasis, the cause of most lung cancer deaths. In addition to serving as a biomarker, the researchers found, HIP1 represses the mobility of lung cancer cells in laboratory studies and suppresses metastasis in a mouse model of the cancer.

Their findings were reported online ahead of print publication in the *American Journal of Respiratory and Critical Medicine*. Their study is the first to describe HIP1 involvement in the progression of adenocarcinoma, the most common type of NSCLC.

The researchers began by examining lung tissue from 121 patients. They found that those in the earliest stages of the diseases expressed more HIP1 than those in the later stages of the disease. They also studied the correlation between HIP1 expression in early stages of the disease (stage I-II), and found a significant correlation between those patients who expressed higher levels of HIP1 and longer survival, indicating that HIP1 was a prognostic biomarker.

The researchers also studied the correlation between HIP1 and cellular mobility in vitro and in a mouse model of adenocarcinoma. In the laboratory, they found that HIP1 expression was inversely associated with cancer cell mobility. They confirmed those results in their mouse model. High levels of HIP1 expression were significantly associated with fewer metastatic tumor cells.

The researchers then investigated the mechanisms behind HIP1's ability to suppress cellular mobility and metastasis. They found that HIP1 modulates Akt, a protein kinase that regulates the epithelial-mesenchymal transition, which in turn facilitates cell invasion and the beginning of metastasis.

"If we can restore HIP1 levels and functions, we may be able to stop or prevent human lung cancer metastasis in the early stage," Lu said. "To bring this discovery to clinical care, we now need to identify the regulatory factors of the HIP1 gene that are targetable through gene therapy or small molecule interventions."

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