Medical Xpress

Researchers discover blood proteins associated with early development of lung cancer

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A research team led by Fred Hutchinson Cancer Research Center has discovered proteins in the blood that are associated with early lung cancer development in mice and humans. The advance brings the reality of a blood test for the early detection and diagnosis of lung cancer a step closer.

The findings, by a team led by Samir Hanash, M.D., Ph.D., head of the Hutchinson Center's Molecular Diagnostics Program and member of its Public Health Sciences Division, are published online Sept. 12 ahead of the Sept. 13 print issue of *Cancer Cell*.

"A major feature of this study was that we were able to replicate findings from mouse models of lung cancer in blood samples from humans with lung cancer both at the time of diagnosis and, importantly, prior to the onset of symptoms and diagnosis," Hanash said. "Our data showed that the protein markers that were tested showed similar concordance between lung cancer in the mouse and lung cancer in humans. This means that developing a blood test to detect lung cancer is increasingly within reach."

The blood protein signatures discovered in the future may be used in a blood test to not only screen for lung cancer among high-risk individuals such as current and former smokers, but to aid in diagnosis, distinguishing between various subtypes of the disease, such as small-cell

lung cancer and lung adenocarcinoma.

Hanash envisions that such a test could be used together with imaging technologies such as CT screening to monitor people at high risk of developing the disease. "There is a substantial need for simple, non-invasive means to detect lung cancer. While imaging-based screening to detect lung cancer has shown promise, blood-based diagnostics provide a complementary means for detection, disease classification, and monitoring for cancer progression and regression," the authors wrote.

For the study, the researchers conducted in-depth blood protein analysis of three mouse models of lung adenocarcinoma and a genetically engineered mouse model of small-cell lung cancer. To further refine the results, they compared these lung cancer protein profiles to those from other well-established mouse models of pancreatic, ovarian, colon, prostate and breast cancer, as well as two mouse models of inflammation without the presence of cancer. Several protein signatures emerged that were specific to lung cancer:

- In models of lung adenocarcinoma, the researchers uncovered a set of elevated proteins that are regulated by the NKX2.1 transcription factor, which has been linked to lung development and function. They also discovered a network of dysregulated proteins linked to epidermal growth factor receptor which, when mutated in lung tissue, is associated with cancer development. Levels of these proteins returned to near normal upon treatment with a tyrosine kinase inhibitor, an anti-cancer drug.

- In a model of small-cell lung cancer, the researchers found a distinct blood protein signature that was associated with neuroendocrine development.

To determine whether these protein signatures in mice were relevant to human lung cancer, the researchers analyzed blood samples from 28 smokers who had been newly diagnosed with operable lung cancer and blood samples from 26 other subjects that were obtained up to a year before lung cancer was diagnosed. For comparison purposes they also analyzed blood from a similar number of matched, cancer-free controls.

The researchers found striking similarities between the protein signatures in mice and human. For example, in mice with small-cell lung cancer, they found elevated levels of a neural protein called Robo1. They also found significantly increased levels of this protein in patients with small-cell lung cancer as compared to matched human controls.

"Additional validation studies are in progress to further determine the sensitivity and specificity of the marker panels," Hanash said. Collaborators on the study included researchers from Memorial Sloan-Kettering Cancer Center, the National Human Genome Research Institute, Yale University School of Medicine, Stanford University, the University of Texas Southwestern Medical Center, and Brigham and Women's Hospital and Dana-Farber Cancer Institute, Harvard Medical School.

More information: Hanash et al.: "Lung Cancer Signatures in Plasma Based on Proteome Profiling of Mouse Tumor Models"

Provided by Fred Hutchinson Cancer Research Center

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