Predictive biomarkers for lung cancer reported in laboratory finding

by Mary Ruth Helms — last modified Mar 26, 2012 10:24 AM

A team of scientists, including several from UNC Lineberger, has identified predictive genetic biomarkers in pre-clinical models that affect response to therapy for non-small cell lung cancer (NSCLC). The study was done in parallel to an ongoing clinical trial among lung cancer patients at multiple institutions.

Their findings were reported in the March 18 online journal Nature.

Lung cancer is the leading cause of cancer deaths in women and men both in the United States and throughout the world. Non-small cell lung cancer makes up about 75 percent of all lung cancers diagnosed in the United States. According to the National Cancer Institute, only about 2 percent of those diagnosed with lung cancer that has spread to other areas of the body are alive five years after the diagnosis, although the survival rates for lung cancers diagnosed at the earliest stage are higher, with approximately 49 percent surviving for five years or longer.

Neil Hayes, MD, MPH, one of the UNC authors, says, " this finding has direct implications for the treatment of a significant proportion of lung cancer patients if the findings from the mice model are fully confirmed in human populations. Most cancers are a complex mix of multiple mutations rather than the result of a single altered gene. However, most of the progress in recent years has been in patients with the relatively rare alterations of single genes. The more common scenario of a patients with more complex tumors and multiple mutations has seen little insight into cancer treatment. In the current study we look at some of the most common combinations of tumors found in human lung cancer and show that targeting combinations of mutations in commonly altered genes, More importantly, we showed different results for different combinations of mutations. This provides a very specific recommendation as to the direction clinical strategies should be considered in human studies."

Hayes is an associate professor of medicine and a member of UNC Lineberger Comprehensive Cancer Center.

The study took samples from the tumors of human patients whose tumors exhibited a mutation of the KRAS gene, which occurs in 15-30 percent of all patients with NSCLC. The KRAS mutation is thought to be one of several genetic variables that are likely involved in the development of NSCLC.

The research team used those samples to create laboratory models to test whether an experimental drug called selumetinib increased the efficacy of the drug docetaxel, a standard of care chemotherapy, in cancers that carry a mutation in the KRAS gene and one of two tumor suppressors called p53 and Lkb1. Selumetinib blocks the activity of a protein (MEK), a critical component of a molecular pathway that is overactive in some non-small cell lung cancer tumors.

The study demonstrated that adding selumetinib provided substantial benefit for lung tumors carrying the KRAS and p53 mutation. However, tumors with KRAS and Lkb1 mutations were resistant to the combination therapy.

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Other institutions involved in the study are: Dana-Farber Cancer Institute, Massachusetts General Hospital; Beth Israel

Deaconess Cancer Center, Harvard School of Public Health, and Brigham and Women's Hospital, Boston, Massachusetts; Iowa State University, Ames, Iowa; Scripps Research Institute, Jupiter, Florida; Loyola University Chicago Stritch School of Medicine, Maywood, Illinois; Simmons Comprehensive Cancer Center, UT Southwest Medical Center, Dallas, Texas.

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