MedicalXpress

Genome-wide scan maps mutations in deadly lung cancers; reveals embryonic gene link

September 5 2012

Scientists have completed a comprehensive map of genetic mutations linked to an aggressive and lethal type of lung cancer.

Among the errors found in small cell lung cancers, the team of scientists, including those at the Johns Hopkins Kimmel Cancer Center, found an alteration in a gene called SOX2 associated with early embryonic development.

"Small cell lung cancers are very aggressive. Most are found late, when the cancer has spread and typical survival is less than a year after diagnosis," says Charles Rudin, M.D., Ph.D., professor of oncology at the Johns Hopkins Kimmel Cancer Center. "Our genomic studies may help identify genetic pathways responsible for the disease and give us new ideas on developing drugs to treat it."

The scientists found an increase in the copy number of the SOX2 gene in about 27 percent of small cell lung cancer samples. The resulting overproduction of proteins made by the SOX2 gene may play a role in igniting or sustaining abnormal cell growth in the lung. SOX2 offers a new target for scientists working to develop new drugs to combat this intractable cancer, say the investigators.

For the study, published online Sept. 2 in Nature Genetics, colleagues from Johns Hopkins, Genentech, the University of Texas Southwestern Medical Center and the University of Colorado Cancer Center scanned the genome's coding regions of 63 small cell lung cancers, including 42

with matching samples from patients' normal cells.

The scientific team scanned 56 of the samples for evidence of "amplification," a cellular process seen in cancer in which cancer cells acquire more than the typical two gene copies inherited from each parent. They found that one of the genes, SOX2, was amplified, in about 27 percent of the samples (15 of 56). SOX2 encodes a protein complex that binds to DNA and controls when and how genes are decoded to make other proteins. It has been linked to tissue and organ development in embryonic cells, and is one of the four genes used by scientists to convert adult cells into an embryonic state.

The scientists confirmed SOX2 amplification in an independent set of 110 small cell lung cancers. This amplification, they found, causes cells to overproduce SOX2 proteins and may promote growth that leads to cancer. Samples with amplified SOX2 also correlated with patients who had more advanced disease. "SOX2 is an important clue in finding new ways to treat small cell lung cancer," says Rudin. "We may be able to link a patient's outcome to this gene and develop a drug to target it or other genes it regulates." Rudin says his team will further explore the function of SOX2 and how to target it.

In addition to amplification, the study mapped errors in the genome's sequence and protein production levels.

In a second report appearing in the Sept. 2 issue of *Nature Genetics*, scientists from Germany and elsewhere completed another genome wide scan of small cell lung cancers and focused on changes in several genes, including FGFR1, a growth factor previously linked to cancer development. Rudin says FGFR1 may prove to be a rare but significant change among small cell lung cancers.

More information: *Nature Genetics* paper: