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Molecular tumor markers could reveal new therapeutic targets for lung cancer treatment

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Analysis of 607 small cell lung cancer (SCLC) lung tumors and neuroendocrine tumors (NET) identified common molecular markers among both groups that could reveal new therapeutic targets for patients with similar types of lung cancer, according to research presented today at the 2014 Chicago Multidisciplinary Symposium in Thoracic Oncology. The Symposium is sponsored by the American Society of Clinical Oncology (ASCO), the American Society for Radiation Oncology (ASTRO), the International Association for the Study of Lung Cancer (IASLC) and The University of Chicago Medicine.

This study examined the clinical specimens of 607 total cases of SCLC tumors (375) and lung NET (232), which included carcinoid, atypical carcinoid and large-cell neuroendocrine tumors. Biomarker testing was achieved through a combination of DNA sequencing (Next-Generation Sequencing (NGS) or Sanger-based); immunohistochemistry (IHC) to identify which proteins are present; and in situ hybridization (ISH) testing, a form of gene amplification, to determine if any of the markers that can cause cancer cells to grow or to become resistant to treatment are present.

Sequencing data were obtained from 201 total specimens (SCLC=115, NET=86). The 115 SCLC tumors harboured a wide spectrum of gene markers. Sequencing revealed mutations in p53 (57 percent), RB1 (11 percent), ATM, cMET (6 percent), PTEN (6 percent), BRAF (3 percent), SMAD4, KRAS (3 percent), ABL1, APB, CTNNB1, EGFR, FBXW7, FGFR2 (2 percent), HNF1A, HRAS, JAK3 (2 percent), MLH1

and PIK3CA (1 percent).

Multiple genes of interest were found in the NET group of 86 tumors, including 66 pulmonary neuroendocrine carcinomas and 20 carcinoid tumors. Among the neuroendocrine tumors, mutations were seen in p53 (44 percent), FGFR2 (9percent), ATM (9 percent), KRAS (6 percent) and PIK3CA (4 percent) as well as EGFR (2 percent) and BRAF (4 percent). Analysis of the carcinoid tumors revealed fewer markers, with notable mutations in p53 (11 percent), HRAS (11 percent), and BRAF (6 percent).

EGFR amplification was verified for 11 percent (5) of the 46 SCLC tumors tested. No SCLC tumors displayed amplification of cMET or HER2. The neuroendocrine tumors exhibited amplification of EGFR (13 percent), cMET (3 percent), and HER2 (4 percent) amplification, while the carcinoid tumors only showed amplification in EGFR (8 percent).

The overexpression of cKIT (64 percent vs. 37 percent), RRM1 (54 percent vs. 28 percent), TOP2A (91 percent vs. 48 percent), TOP01 (63 percent vs. 43 percent), and TS (46 percent vs. 25 percent) was found more frequently in SCLC tumors compared to lung NET, respectively (p=0.0001 for all). Low expression of PTEN was more often identified in SCLC tumors compared to lung NET (56 percent vs. 36 percent; p=0.001).

Molecular profiling of these lung cancer subtypes is not routinely performed, however, numerous mutations were found to be in common with non-small cell lung cancer tumors. Specifically, an EGFR mutation was noted in one small cell lung cancer specimen and one neuroendocrine specimen, an ALK rearrangement was detected in a neuroendocrine tumor, and HER2 amplification was seen in a neuroendocrine specimen.

"Even cancers that appear to be very similar can be dramatically different at the molecular level, and these differences may reflect unique vulnerabilities that could positively impact therapeutic options and decisions," said Stephen V. Liu, MD, senior study author and Assistant Professor of Medicine in the Division of Hematology/Oncology at Georgetown University's Lombardi Comprehensive Cancer Center in Washington, DC. "We are pleased that this research confirms these rarer subtypes; it calls for additional investigation on a larger scale. Once confirmed, molecular profiling of small cell tumors and NET could become standard, as it is currently for non-small cell lung cancers, which will be especially important as more molecularly targeted chemotherapy agents are developed."

More information: The abstract, "Molecular Profiling in Small Cell Lung Cancer and Lung Neuroendocrine Tumors," will be presented in detail during a poster session at 5:00 p.m. Central time on Thursday, October 30, 2014.

Provided by American Society for Radiation Oncology