

Novel therapeutic targets identified for small cell lung cancer

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Newly discovered molecular differences between small cell lung cancer and nonsmall cell lung cancer have revealed PARP1 and EZH2 as potential therapeutic targets for patients with small cell lung cancer, according to the results of a study published in *Cancer Discovery*, a journal of the American Association for Cancer Research.

Currently, small cell [lung cancer](#) accounts for about 15 percent of lung cancer diagnoses in the United States. Patients with the disease will initially respond to chemotherapy, but almost all will have [disease recurrence](#) within a couple of months, according to Lauren A. Byers, M.D., assistant professor of thoracic/head and neck [medical oncology](#) at The University of Texas MD Anderson Cancer Center in Houston.

"Unlike nonsmall cell lung cancer [NSCLC], where there have been new targeted drugs developed in the last ten years, the only currently approved treatments for small cell lung cancer are cytotoxic chemotherapies," Byers said. "Because most targeted therapies directly act on proteins, identifying if certain proteins are overexpressed in small cell lung cancer could have therapeutic applications."

In order to identify molecular differences between NSCLC and the more aggressive small cell lung cancer, Byers and colleagues used tools called reverse phase protein arrays. These allow the examination of the expression of about 200 proteins that are in key signaling pathways known to be involved in driving [cancer growth](#).

"We discovered that small cell lung cancer and NSCLC have dramatically different protein profiles in terms of which proteins are 'turned on' and are driving the behavior of these cancers," Byers said. "In small cell lung cancer, proteins that were present at higher levels included several DNA repair proteins such as PARP1 and a protein involved in cancer stem cell renewal, EZH2."

PARP1 was further evaluated as a target for treatment of small cell lung cancer because there are several PARP inhibitors in advanced-stage clinical trials for other tumor types such as breast and ovarian cancers. Moreover, small cell lung cancer is sensitive to platinum-based chemotherapy, and PARP inhibitors have shown increased activity when used on other platinum-sensitive tumors.

Two PARP inhibitors were tested on small cell lung cancer cell lines alone and in combination with standard frontline chemotherapeutics, cisplatin and etoposide, or another commonly used chemotherapeutic, irinotecan. The inhibitors slowed the growth of small cell lung cancer cells, but not non-neuroendocrine NSCLC cells, according to the study. In addition, levels of PARP1 expression directly correlated with PARP inhibitor sensitivity.

As with many targeted drugs, it is possible that combining PARP inhibitors with other targeted drugs may significantly improve efficacy, according to Byers.

"Our next step is to begin to examine the use of PARP inhibitors in combination with other drugs in preclinical and clinical investigations of small cell lung cancer," she said.

Provided by American Association for Cancer Research

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