Study identifies possible marker for lung cancer chemotherapy

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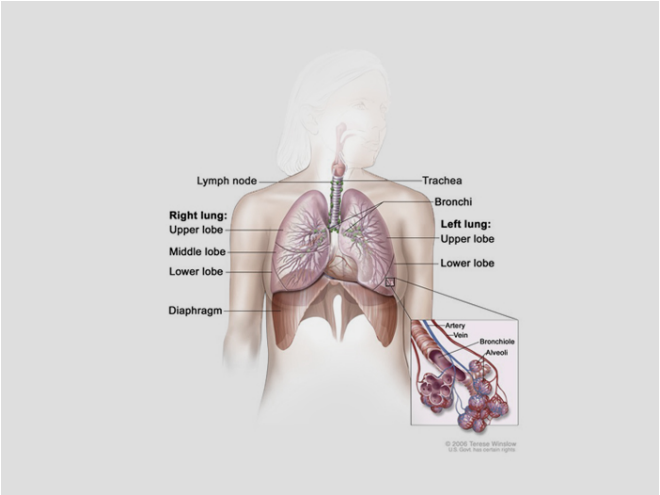

The activity level of a particular gene in lung tumors might identify lung-cancer patients who will likely be helped by a particular chemotherapy regimen given to prevent recurrence after surgery. The finding comes from a study led by researchers at The Ohio State University Comprehensive Cancer Center—Arthur G. James Cancer Hospital and Richard J. Solove Research Institute (OSUCCC—James).

The study, published in the journal *Clinical Cancer Research*, looked at the expression of a gene called SMARCA4/BRG1 in tumor cells from patients with earlier-stage non-small-cell lung cancer (NSCLC).

The researchers found that low SMARCA4 expression signals a poor prognosis, but also a significant sensitivity to the chemotherapy drug cisplatin. "Our study suggests that SMARCA4, a gene that is commonly mutated in NSCLC, might identify patients who will benefit from cisplatin and other platinum-based drugs," says first author and OSUCCC—James researcher Erica Hlavin Bell, PhD, assistant professor of radiation oncology.

An estimated 1.8 million new cases of lung cancer occurred worldwide in 2012, making it the most common cancer globally. It also killed an estimated 1.6 million people worldwide that year, making it the leading cause of cancer death. In the United States, 85 percent of lung cancers are NSCLC.

"Lung cancer is such a deadly disease because the majority of the cases are detected at advanced stages and because most patients harbor tumors that do not have targetable mutations," Bell says. "This leaves chemotherapy as the only therapeutic option after surgery, but there are few biomarkers to indicate which agents will benefit a particular patient.

"We found that patients with earlier-stage NSCLC whose tumors show low expression of SMARCA4 will likely see a large benefit from cisplatin-based chemotherapy compared to patients with high expression of the gene.

"Furthermore, we found that patients with tumors showing high SMARCA4 expression received no benefit from adjuvant chemotherapy compared to observation alone after surgery."

"If our findings are confirmed, it means that these patients should be treated with an alternative therapy, thereby sparing them from cisplatin's harsh side effects and allowing them to try an alternate therapy sooner," says study leader Arnab Chakravarti, MD, chair and professor of Radiation Oncology at the OSUCCC—James.

To learn whether SMARCA4/BRG1 expression was associated with cisplatin sensitivity, Bell, Chakravarti and their colleagues analyzed patient specimens from the JBR.10 phase III randomized trial (NCT00002583), which had an untreated control group.

Based on an overall survival advantage in the JBR.10 trial, the researchers concluded that even patients older than 65 with early-stage NSCLC and low SMARCA4 expression might benefit from platinum-based chemotherapy regimens.

Using data from the 440-patient Director's Challenge Lung Study, Bell and her colleagues also confirmed that low SMARCA4 expression also signals a poor prognosis.

"Overall, the findings from this study might help us individualize chemotherapy treatment options in lung cancer patients after surgery," Bell says.

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Other researchers involved in this study were Arup R. Chakraborty, PhD, Xiaokui Mo, PhD, Ziyan Liu, MS, Konstantin Shilo, MD, Maureen McNulty, BS, David P. Carbone, MD, PhD, and Arnab Chakravarti, MD, The Ohio State University; Simon Kirste, MD, Petra Stegmaier, MD, University Medical Center Freiburg, Freiburg, Germany; Niki Karachaliou, MD, Quirón Dexeus University Hospital and Catalan Institute of Oncology, Barcelona, Spain; Rafael Rosell, MD, PhD, Catalan Institute of Oncology, Barcelona, Spain; and Gerold Bepler, MD, PhD, Wayne State University.

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