New biomarker for common lung cancer predicts responses to chemotherapy

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Patients with the most common type of lung cancer are notoriously insensitive to chemotherapy drugs, including cisplatin. New findings related to the cellular pathways that regulate responses to cisplatin have now been published by Cell Press on July 26th in the journal *Cell Reports*. The findings reveal a potential biomarker that can be used to predict how these patients will respond to chemotherapy, as well as the patients' overall prognosis, paving the way for personalized treatment strategies.

Non-small cell lung cancer (NSCLC) is one of the leading causes of cancer-related death in men, and it is frequently treated with cisplatin. However, responses are often brief and ineffective because cancer cells become resistant to cisplatin-induced cell death. "We were interested in finding new genes, proteins, and pathways that would govern the response to cisplatin and might explain cisplatin resistance," says senior study author Guido Kroemer of INSERM—the French National Institute of Health and Medical Research.

To identify factors that affect whether cells die in response to cisplatin, Kroemer and his team performed a genome-wide screen in which they interfered with the expression of tens of thousands of genes in cells from patients with NSCLC. They identified 85 factors that modify drug responses, including pyridoxal kinase (PDXK), an enzyme that converts vitamin B6 precursors into their active form.

Treatment with a vitamin B6 precursor enhanced the anti-tumor effects

of cisplatin in mouse models of lung cancer and promoted cisplatin-induced death in a variety of cancer cell lines, but only when PDXK was present. Moreover, NSCLC patients with high expression levels of PDXK had higher survival rates than those with low levels of the enzyme, regardless of whether they were being treated with cisplatin.

Together, the findings point to PDXK as an easy-to-monitor potential biomarker for predicting both the responses of NSCLC patients to cisplatin and their general outcomes. "Patients who have high levels of PDXK might benefit from combination therapies of cisplatin and vitamin B6," Kroemer says. "However, for those patients whose tumors express low levels of PDXK, new strategies of cancer treatment have to be developed."

More information: Galluzzi et al.: "Prognostic Impact of Vitamin B6 Metabolism in Lung Cancer." dx.doi.org/10.1016/j.celrep.2012.06.017

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