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Genomic signatures identify targeted therapies for lung cancer

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Any number of things can go wrong in the cells of the body to cause cancer -- and clinicians can't tell by just looking at a tumor what exactly triggered the once normal cells to turn cancerous.

New tests developed by researchers at Duke University can determine the precise patterns among thousands of genes to identify the cascade of events, or pathways, that led to the cancer.

These "genomic signatures" will give clinicians the tools they need to pursue alternatives to the traditional blunt force of chemotherapy. Following this test, patients might be treated with drugs that specifically target the faulty pathway, the researchers said.

"Traditional chemotherapy is not always effective," said Anil Potti, M.D., the study's lead investigator and an assistant professor of medicine in the Duke Institute for Genome Sciences & Policy. "Even when we are able to match the right chemotherapy with the right patient, 70 percent of patients with lung cancer may not respond to therapy. We need to take a different approach to those patients, and that is where these targeted therapeutics come in."

Potti and colleagues presented their findings on Sunday, June 3, at the annual meeting of the American Society for Clinical Oncology, in Chicago. The work was funded by the Jimmy V Foundation and the National Institutes of Health.

Mutations in individual cancer-causing genes, called oncogenes, set off a cascade of changes in the activity of hundreds of other interacting genes -- either increasing or decreasing their activity.

Rather than looking at each of these oncogenes individually, this new method presents a more global view by identifying the pathway encompassing all of the gene mutations that could have caused that cancer, Potti said.

The genomic test can theoretically apply to any cancer, but the Duke team focused on lung cancer because the survival rate is just 15 percent. Lung cancer now kills more Americans each year than breast, prostate and colorectal cancers combined.

The tests work by scanning thousands of genes in cells taken from the tumors of cancer patients and kept alive in laboratory cultures to produce a genomic profile of the tumor's molecular makeup. These patterns led to the identification of defective pathway in patients with both early stage and advanced disease. In particular, tumors with defects in two specific pathways -- called Src and Myc -- had much worse prognosis than those with defects in another pathway, called Ras.

The researchers then treated the laboratory tumors with drugs that specifically blocked one of the three different pathways. In all cases, the cancer responded to treatment with the appropriate targeted therapy.

Targeted therapeutics such as this could be "smart bombs" in comparison to the standard chemotherapy that obliterates all the cells that are actively reproducing.

Hundreds of drugs are currently available to target specific pathways. But because these therapies are effective only in a small percentage of patients, the majority of these drugs go unused.

Potti said the genomic signature tests would give patients another option to traditional chemotherapy. The Duke team plans to begin a clinical trial of the genomic tests in lung cancer patients this year.

"We hope that using this research to selectively add targeted drugs to current chemotherapy regimens will increase the response rate dramatically for patients with lung cancer," Potti said.

Source: Duke University Medical Center