

New study helps predict which lung cancer drugs are most likely to work

January 10 2012

(Medical Xpress) -- Researchers at Johns Hopkins have shown that DNA changes in a gene that drives the growth of a form of lung cancer can make the cancer's cells resistant to cancer drugs. The findings show that some classes of drugs won't work, and certain types of so-called kinase inhibitors like erlotinib—may be the most effective at treating non-small cell lung cancers with those DNA changes. Some kinase inhibitors block a protein known as EGFR from directing cells to multiply.

In their paper published online November 20 in *Nature Structural & Molecular Biology*, the researchers describe the molecular details of how some [cancer drugs](#) work.

“Some anticancer pharmaceuticals that we showed to be ineffective made it to clinical trials because they appeared to prevent the EGFR protein from sending growth signals,” says Philip A. Cole, M.D., Ph.D., Director and E.K. Marshall and Thomas H. Maren Professor of Pharmacology and Molecular Sciences at the Johns Hopkins University School of Medicine. “But we found that different forms of EGFR protein reacted in unexpected ways; and by sorting out these forms in advance, we may be better able to determine which drugs will be better candidates for future clinical trials,” Cole says.”

The researchers found that not all EGFR proteins variations responded to the same drugs that normal EGFR protein did.

The scientists note that non-small cell [lung cancer](#), the most common

form of the disease, generally results from [DNA changes](#) in the EGFR gene, a gene that normally controls cell growth. The genetic changes cause uncontrolled cell growth, the hallmark of cancer.

“Many [clinical trials](#) that used cetuximab and lapatinib were unsuccessful,” says Cole, “and our findings suggest why they failed and why erlotinib succeeded.”

The new discoveries were prompted by an effort to learn which drugs would work best in non-small cell lung cancer linked to EGFR protein alterations. To start, the researchers first tested cetuximab, a monoclonal antibody that prevents growth factors from binding EGFR. Cetuximab is currently used to treat head and neck and colon cancers, but researchers believed it could be a treatment for lung cancer too.

They added the drug to purified EGFR protein—both normal and two altered versions that have been implicated in lung cancer—and measured the protein’s activity. Normal EGFR had a rate of growth-stimulating activity 100 times less when treated with cetuximab. Both altered EGFRs had much higher rates of growth-stimulating activity, 200 times more than normal EGFR when treated with cetuximab. The researchers concluded that while cetuximab does dampen the activity of normal EGFR protein, it does not significantly reduce the altered EGFR activity, which is not enough to stop cells from growing.

Because cetuximab was unsuccessful at blocking altered EGFR activity, the researchers tested kinase inhibitors. The researchers tested lapatinib, an FDA-approved breast cancer drug, and erlotinib, a drug currently used to treat non-small cell lung and pancreatic cancers. The researchers added different concentrations of lapatinib and erlotinib to the purified normal and altered EGFR proteins and measured the drugs’ effectiveness. Both erlotinib and lapatinib reduced normal EGFR activity, but lapatinib did not block altered EGFR activity. Erlotinib did

appear to prevent altered EGFR from working, similar to the way it reduced the normal EGFR protein activity. This led the Hopkins team to conclude that that erlotinib is a better drug treatment for non-small cell lung cancers that are associated with altered forms of EGFR [protein](#).

Provided by Johns Hopkins Medical Institutions

Citation: New study helps predict which lung cancer drugs are most likely to work (2012, January 10) retrieved 4 May 2024 from <https://medicalxpress.com/news/2012-01-lung-cancer-drugs.html>

<p>This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.</p>
--