

# Lung Cancer

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Molecular Genetic Testing

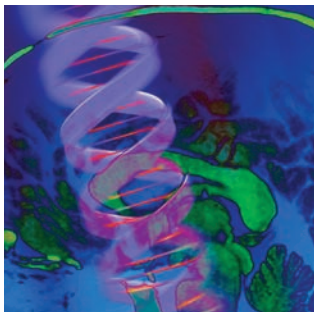


## What is non-small cell lung cancer?

Lung cancer cells that are small and round are classified as "small cell" lung cancer. Cancer cells of a larger size and of any other shape are classified as "non-small cell" lung cancer and account for approximately 85 percent of all lung cancers.<sup>1</sup> Lung cancer treatment generally consists of surgical resection, radiation therapy and/or chemotherapy. Recently, two new chemotherapy drugs, erlotinib (also known by the brand name Tarceva), and gefitinib (Iressa), have been used for treating patients with non-small cell lung cancer.

## What is EGFR?

Epidermal growth factors are proteins in the body that are important for normal cell growth and multiplication. One of these receptors is the epidermal growth factor receptor, or EGFR.



## What is KRAS?

KRAS is a proto-oncogene; it acts as a molecular on/off switch in the EGFR signaling pathway. Once KRAS is switched on, it stimulates cell growth.

## How do gefitinib and erlotinib work?

Gefitinib and erlotinib inhibit the growth of cancer cells by attaching to EGFRs. Tumors that have a mutation in the EGFR gene are much more likely to respond to gefitinib and/or erlotinib therapy.<sup>3-5</sup>

Unfortunately, not all patients benefit from gefitinib or erlotinib. Depending on ethnicity and other factors, the likelihood of detecting a responsive mutation is 10 to 25 percent.

Recent studies have found that patients with KRAS mutations are less likely to respond to anti-epidermal growth factor receptor (anti-EGFR) therapies such as erlotinib and gefitinib.<sup>6</sup>

Approximately 15 to 30 percent of lung adenocarcinomas have mutations in the KRAS gene.

As a result, treatment decisions regarding the use of erlotinib and gefitinib might be improved by determining the mutational status of both EGFR and KRAS.

**Note:** It is important to understand that a mutation in the EGFR gene of a tumor cell is only in the tumor cells and not in other cells in a person's body. This means that there is no risk of passing the mutation on to other family members.

## Who should be tested for EGFR and KRAS mutations?

Individuals with a clear diagnosis of non-small cell lung cancer should consider being tested for mutations in the EGFR and KRAS genes in their tumor cells.

## Who does the testing?

The City of Hope Molecular Diagnostic Laboratory (CMDL) performs these tests. CMDL was the first to offer testing for mutations in EGFR. For additional information and Test Request Forms, please visit our Web site at <http://mdl.cityofhope.org>



## How is the test performed?

Tissue samples are taken from the patient via biopsy or surgery and prepared by your physician's laboratory for EGFR and KRAS testing. Blood samples cannot be used for this test because the mutation of interest is at the site of the tumor.

Test results will be returned to your physician approximately two weeks following insurance approval (if applicable).



For more information about specimen requirements, visit our Web site at <http://mdl.cityofhope.org>.

## Will medical insurance cover this test?

Testing is often covered by insurance. **Pre-verification for services must be obtained by City of Hope before testing begins.** \*Patients can always contact their insurance company beforehand to determine coverage.

**If a patient prefers that testing begin immediately,** the patient or institution may offer a guarantee of payment which would be used only if insurance denies coverage for testing. Additional information regarding the insurance verification process is available at <http://mdl.cityofhope.org> or 888-826-4362, ext. 0.

\*All HMO's require the primary physician to obtain pre-authorization for the services to be rendered.

## Resources

### **Alliance for Lung Cancer Advocacy, Support and Education**

Phone: 202-463-2080

Web: [www.alcase.org](http://www.alcase.org)

### **The American Cancer Society**

Phone: 1-800-ACS-2345

Web: [www.cancer.org](http://www.cancer.org)

### **Cancer Information Network**

Web: [www.cancerlinksusa.com](http://www.cancerlinksusa.com)

## References

1. Diamandidis D, Huber M, Pisters K. 1997. Non-Small-Cell Lung Cancer. In: MEDICAL ONCOLOGY: A COMPREHENSIVE REVIEW 2nd ed. Pazdur R (ed.) www.cancernetwork.com.
2. Fukuoka, M., Yano, S., Giaccone, G., et al., Multiinstitutional randomized phase II trial of gefitinib for previously treated patients with advanced non-small-cell lung cancer., J. Clin. Oncol.; 21:2237-46, 2003.
3. Lynch et al., Activating mutations in the Epidermal Growth Factor Receptor underlying responsiveness of Non-Small-Cell Lung Cancer to Gefitinib. NEJM, 2004; 350(21):2129-2139.
4. Paez et al., EGFR mutations in lung cancer: correlation with clinical response to Gefitinib therapy. Science, 2004; 304: 1497-1500.
5. Pao et al., EGF receptor gene mutations are common in lung cancers from "never smokers" and are associated with sensitivity of tumors to gefitinib and erlotinib. PNAS, 2004; 101(36): 13306-13311.
6. Tsao et al., Role of KRAS and EGFR as biomarkers of response to erlotinib in National Cancer Institute of Canada Clinical Trials Group Study BR.21. J Clin Oncol. 2008; 26(26):4268-75.



## About us

The City of Hope Molecular Diagnostic Laboratory (CMDL) specializes in clinical genetic testing services for cancer, pharmacogenetics, muscular dystrophies, neuropsychiatric diseases, connective tissue disorders and coagulopathies. CMDL continues to establish new genetic tests for these diseases. For more up-to-date information about our tests, please visit our Web site at <http://mdl.cityofhope.org>.

## Contact Information for Patients

Patients should talk with their physicians about genetic testing. Genetic counseling is generally recommended when discussing the option of appropriate genetic testing, the implications of test results, residual risks and uncertainties, and reproductive or medical options. See our patient friendly Web site at <http://mdl.cityofhope.org>.

## Contact Information for Clinicians

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