

FACT SHEET

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Types of Lung Cancer

According to the American Cancer Society, lung cancer is the second most commonly diagnosed cancer in both men and women in the United States and the leading cause of cancer deaths. An estimated 222,520 Americans were diagnosed in 2010, and approximately 157,000 died from the disease. Each year, more people die from lung cancer than breast, colon and prostate cancers combined.¹

There are several different types of lung cancer. Classification has traditionally been based on histology, or the type of cell that became cancerous and what the tumor looks like under a microscope.^{2,3} This is important in lung cancer because histology is often used to guide treatment strategies.⁴

More recently, researchers have been investigating whether classifying lung cancers based on certain molecular characteristics, known as biomarkers, may also be clinically useful.⁵ These biomarkers may be changes in a particular gene, increases in the number of copies of a gene, or an increase in the amount of a certain protein. Strategies for specifically addressing tumors with certain biomarkers are currently being explored.⁵

Histology

Small Cell Lung Cancer (SCLC) and Non-Small Cell Lung Cancer (NSCLC)

SCLC accounts for approximately 10-15 percent of lung cancer cases. Its name comes from the small size of the cells found in the tumors. SCLC tends to spread quickly and widely. It is almost always caused by smoking. It is rare for SCLC to affect someone who has never smoked.⁶

NSCLC is the most common type of lung cancer, accounting for about 85-90 percent of all cases.⁷ Many cases of NSCLC can be linked to smoking, but other risk factors include secondhand smoke; exposure to radon, asbestos, certain chemicals or diesel exhaust; and genetic factors.⁸

NSCLC can be further divided into squamous and non-squamous NSCLC.⁷

NSCLC: Squamous Cell Carcinoma and Non-Squamous Cell Carcinoma

Squamous cell carcinoma accounts for approximately 25-30 percent of all lung cancers. This form of the disease is named for the squamous cells in which it starts, which are thin, flat and

fish scale-like. These tumors are usually associated with a history of smoking and tend to start in the middle of the lungs.^{2,7}

Non-squamous cell carcinoma encompasses all other types of NSCLC. There are several kinds of non-squamous cell carcinoma, but the two main types are:

- Adenocarcinomas – The most common type of NSCLC tumors are adenocarcinomas. These tumors tend to begin in the mucus-producing cells that line the tiny air sacs in the lungs (alveoli). Adenocarcinomas are the type of lung cancer most often found in people who have never smoked.^{2,7,9}
- Large-cell (undifferentiated) carcinoma – A smaller number of NSCLC tumors are large-cell carcinomas. These tumors can start anywhere in the lungs and tend to grow and spread quickly, making treatment difficult.⁷

Biomarkers

Research is ongoing to determine if the molecular characteristics (biomarkers) of a tumor can also be used to classify the disease and possibly inform future treatment decisions. Some biomarkers that are currently being investigated in lung cancer include:

EGFR

Epidermal Growth Factor Receptor (EGFR) activating mutations are found in approximately 10-30 percent of NSCLC tumors. These mutations keep the EGFR protein locked into an active state, which inappropriately sends growth and survival signals into the cell.^{5,10,11}

Some NSCLC tumors have been found to have an overabundance of the EGFR protein (overexpression). The extra EGFR proteins may amplify growth and survival signals to the tumor.¹²

KRAS

Mutations in the gene encoding KRAS, a cell-signaling protein located inside of cells, have been observed in approximately 20 percent of NSCLC tumors. Mutations in the KRAS gene may inappropriately activate growth and survival pathways within cells.¹³

EML4-ALK

It is estimated that the cells of five percent of NSCLC tumors carry a fusion between two genes, EML4 and ALK. This EML4-ALK fusion produces a protein that may lead to uncontrolled growth of the tumor.¹⁴

MET

The MET protein, like EGFR, is a cell surface receptor that sends growth and survival signals into cells when activated.¹⁵ The cells of approximately 50 percent of NSCLC tumors overproduce the MET protein, which may play a role in activating tumor growth.¹⁵⁻¹⁷

References

1. American Cancer Society. Cancer Facts and Figures 2010. <http://www.cancer.org/acs/groups/content/@epidemiologysurveillance/documents/document/acspc-026238.pdf>. Accessed October 18, 2010.
2. National Cancer Institute. General Information About Non-Small Cell Lung Cancer. <http://www.cancer.gov/cancertopics/pdq/treatment/non-small-cell-lung/patient>. Accessed on October 18, 2010.

3. National Cancer Institute. Definition of histology. http://www.cancer.gov/Templates/db_alpha.aspx?CdrID=44171. Accessed on October 18, 2010.
4. American Cancer Society. What is non-small cell lung cancer? <http://www.cancer.org/Cancer/LungCancer-Non-SmallCell/DetailedGuide/non-small-cell-lung-cancer-what-is-non-small-cell-lung-cancer>. Accessed on October 18, 2010.
5. John T, Liu G, Tsao M-S. Overview of molecular testing in non-small-cell lung cancer: mutational analysis, gene copy number, protein expression and other biomarkers of EGFR for the prediction of response to tyrosine kinase inhibitors. *Oncogene*. 2009;28:S14-S23.
6. American Cancer Society. What is small cell lung cancer? <http://www.cancer.org/Cancer/LungCancer-SmallCell/DetailedGuide/small-cell-lung-cancer-what-is-small-cell-lung-cancer>. Accessed October 18, 2010.
7. American Cancer Society. What is non-small cell lung cancer? <http://www.cancer.org/Cancer/LungCancer-Non-SmallCell/DetailedGuide/non-small-cell-lung-cancer-what-is-non-small-cell-lung-cancer>. Accessed October 18, 2010.
8. American Cancer Society. What are the risk factors for non-small cell lung cancer? <http://www.cancer.org/Cancer/LungCancer-Non-SmallCell/DetailedGuide/non-small-cell-lung-cancer-risk-factors>. Accessed October 18, 2010.
9. Subramanian J, Govindan R. Lung cancer in never smokers: a review. *J Clin Oncol*. 2007;25(5):561-70.
10. Shigematsu H and Gazdar AF. Somatic mutations of epidermal growth factor receptor signaling pathway in lung cancers. *Int J Cancer*. 2006;118: 257-262.
11. Shigematsu H, Lin L, Takahashi T, et al. Clinical and biological features associated with epidermal growth factor receptor gene mutations in lung cancers. *J Nat Cancer Inst*. 2005;97(5):339-346.
12. Dacic S, Flanagan, M, Cieply K, et al. Significance of EGFR protein expression and gene amplification in non-small cell lung carcinoma. *Am J Clin Pathol*. 2006;125:860-865.
13. Zhang X, Chang A. Molecular predictors of EGFR-TKI sensitivity in advanced non-small cell lung cancer. *Int J Med Sci*. 2008;5(4):209-217.
14. Shaw AT, Yeap BY, Mino-Kenudson M. et al. Clinical features and outcome of patients with non-small-cell lung cancer who harbor EML4-ALK. *J Clin Onc*. 2009;27(26):4247-4253.
15. Cipriani NA, Abidoye OO, Vokes EE, et al. MET as a target for treatment of chest tumours. *Lung Cancer*. 2009;63(2):169-179.
16. Tsao M, Liu N, Chen J, et al. Differential expression of Met/hepatocyte growth factor receptor in subtypes of non-small cell lung cancer. *Lung Cancer*. 1998;20:1-16.
17. Ichimura A, Maeshima A, Nakajima T, et al. Expression of *c-met*/HGF Receptor in human non-small cell lung carcinomas *in vitro* and *in vivo* and its prognostic significance. *Jpn J Cancer Res*. 1996; 87:1063-1069.

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