

Your Guide to Understanding Genetic Conditions

lung cancer

Lung cancer is a disease in which certain cells in the lungs become abnormal and multiply uncontrollably to form a tumor. Lung cancer may or may not cause signs or symptoms in its early stages. Some people with lung cancer have chest pain, frequent coughing, breathing problems, trouble swallowing or speaking, blood in the mucus, loss of appetite and weight loss, fatigue, or swelling in the face or neck. Lung cancer occurs most often in adults in their sixties or seventies. Most people who develop lung cancer have a history of long-term tobacco smoking; however, the condition can occur in people who have never smoked.

Lung cancer is generally divided into two types, small cell lung cancer and nonsmall cell lung cancer, based on the size of the affected cells when viewed under a microscope. Non-small cell lung cancer accounts for 85 percent of lung cancer, while small cell lung cancer accounts for the remaining 15 percent.

Small cell lung cancer grows quickly and often spreads to other tissues (metastasizes), most commonly to the adrenal glands (small hormone-producing glands located on top of each kidney), liver, brain, and bones. In more than half of cases, the small cell lung cancer has spread beyond the lung at the time of diagnosis. After diagnosis, most people with small cell lung cancer survive for about one year; less than seven percent survive 5 years.

Non-small cell lung cancer is divided into three main subtypes: adenocarcinoma, squamous cell carcinoma, and large cell lung carcinoma. Adenocarcinoma arises from the cells that line the small air sacs (alveoli) located throughout the lungs. Squamous cell carcinoma arises from the squamous cells that line the passages leading from the windpipe to the lungs (bronchi). Large cell carcinoma describes non-small cell lung cancers that do not appear to be adenocarcinomas or squamous cell carcinomas. As the name suggests, the tumor cells are large when viewed under a microscope. The 5-year survival rate for people with non-small cell lung cancer is usually between 11 and 17 percent; it can be lower or higher depending on the subtype and stage of the cancer.

Frequency

In the United States, it is estimated that more than 221,000 people develop lung cancer each year. An estimated 72 to 80 percent of lung cancer cases occur in tobacco smokers.

Approximately 6.6 percent of individuals will develop lung cancer during their lifetime. It is the leading cause of cancer deaths, accounting for an estimated 27 percent of all cancer deaths in the United States.

Genetic Changes

Cancers occur when genetic mutations build up in critical genes, specifically those that control cell growth and division or the repair of damaged DNA. These changes allow cells to grow and divide uncontrollably to form a tumor. In nearly all cases of lung cancer, these genetic changes are acquired during a person's lifetime and are present only in certain cells in the lung. These changes, which are called somatic mutations, are not inherited. Somatic mutations in many different genes have been found in lung cancer cells.

Mutations in the *EGFR* and *KRAS* genes are estimated to be present in up to half of all lung cancer cases. These genes each provide instructions for making a protein that is embedded within the cell membrane. When these proteins are turned on (activated) by binding to other molecules, signaling pathways are triggered within cells that promote cell growth and division (proliferation).

Mutations in either the *EGFR* or *KRAS* gene lead to the production of a protein that is constantly turned on (constitutively activated). As a result, cells are signaled to constantly proliferate, leading to tumor formation. When these gene changes occur in cells in the lungs, lung cancer develops.

Mutations in many other genes have each been found in a small proportion of cases.

In addition to genetic changes, researchers have identified many personal and environmental factors that expose individuals to cancer-causing compounds (carcinogens) and increase the rate at which somatic mutations occur, contributing to a person's risk of developing lung cancer. The greatest risk factor is long-term tobacco smoking, which increases a person's risk of developing lung cancer 20-fold. Other risk factors include exposure to air pollution, radon, asbestos, or secondhand smoke; longterm use of hormone replacement therapy for menopause; and a history of lung disease such as tuberculosis, emphysema, or chronic bronchitis. A history of lung cancer in closely related family members is also an important risk factor; however, because relatives with lung cancer were likely smokers, it is unclear whether the increased risk of lung cancer is the result of genetic factors or exposure to secondhand smoke.

Inheritance Pattern

Most cases of lung cancer are not related to inherited gene changes. These cancers are associated with somatic mutations that occur only in certain cells in the lung.

When lung cancer is related to inherited gene changes, the cancer risk is inherited in an autosomal dominant pattern, which means one copy of the altered gene in each cell is sufficient to increase a person's chance of developing cancer. It is important to note that people inherit an increased risk of cancer, not the disease itself. Not all people who inherit mutations in these genes will develop lung cancer.

Other Names for This Condition

- cancer of bronchus
- cancer of the lung
- lung malignancies
- lung malignant tumors
- lung neoplasms
- malignant lung tumor
- malignant neoplasm of lung
- malignant tumor of lung
- pulmonary cancer
- pulmonary carcinoma
- pulmonary neoplasms
- respiratory carcinoma

Diagnosis & Management

These resources address the diagnosis or management of lung cancer:

- Genetic Testing Registry: Lung cancer
 https://www.ncbi.nlm.nih.gov/gtr/conditions/C0684249/
- Genetic Testing Registry: Non-small cell lung cancer https://www.ncbi.nlm.nih.gov/gtr/conditions/C0007131/
- Lung Cancer Mutation Consortium: About Mutation Testing http://www.golcmc.com/about-mutation-testing.html
- MedlinePlus Encyclopedia: Lung Cancer--Non-Small Cell https://medlineplus.gov/ency/article/007194.htm
- MedlinePlus Encyclopedia: Lung Cancer--Small Cell https://medlineplus.gov/ency/article/000122.htm
- National Cancer Institute: Drugs Approved for Lung Cancer https://www.cancer.gov/about-cancer/treatment/drugs/lung
- National Cancer Institute: Non-Small Cell Lung Cancer Treatment https://www.cancer.gov/types/lung/patient/non-small-cell-lung-treatmentpdq#section/_164
- National Cancer Institute: Small Cell Lung Cancer Treatment https://www.cancer.gov/types/lung/patient/small-cell-lung-treatment-pdq#section/ _92

These resources from MedlinePlus offer information about the diagnosis and management of various health conditions:

- Diagnostic Tests
 https://medlineplus.gov/diagnostictests.html
- Drug Therapy https://medlineplus.gov/drugtherapy.html
- Surgery and Rehabilitation https://medlineplus.gov/surgeryandrehabilitation.html
- Genetic Counseling
 https://medlineplus.gov/geneticcounseling.html
- Palliative Care
 https://medlineplus.gov/palliativecare.html

Additional Information & Resources

<u>MedlinePlus</u>

- Encyclopedia: Lung Cancer--Non-Small Cell https://medlineplus.gov/ency/article/007194.htm
- Encyclopedia: Lung Cancer--Small Cell
 https://medlineplus.gov/ency/article/000122.htm
- Health Topic: Lung Cancer
 https://medlineplus.gov/lungcancer.html

Additional NIH Resources

- National Cancer Institute: Lung Cancer Overview https://www.cancer.gov/types/lung
- National Cancer Institute: Lung Cancer Prevention https://www.cancer.gov/types/lung/patient/lung-prevention-pdq#section/all
- National Institute of Environmental Health Sciences https://www.niehs.nih.gov/health/topics/conditions/lung-disease/index.cfm
- NIH Senior Health https://nihseniorhealth.gov/lungcancer/lungcancerdefined/01.html

Educational Resources

- Atlas of Genetics and Cytogenetics in Oncology and Haematology http://atlasgeneticsoncology.org//Tumors/LungTumOverviewID5030.html
- Cancer Research UK
 http://www.cancerresearchuk.org/about-cancer/type/lung-cancer/

- Centers for Disease Control and Prevention https://www.cdc.gov/cancer/lung/
- Cleveland Clinic
 http://my.clevelandclinic.org/health/articles/lung-cancer
- Disease InfoSearch: Lung Cancer http://www.diseaseinfosearch.org/Lung+Cancer/4334
- Johns Hopkins Medicine http://www.hopkinsmedicine.org/healthlibrary/conditions/adult/ respiratory_disorders/lung_cancer_85,p01316/
- MalaCards: lung cancer
 http://www.malacards.org/card/lung_cancer
- Massachusetts General Hospital http://www.massgeneral.org/conditions/condition.aspx?id=279
- MD Anderson Cancer Center https://www.mdanderson.org/cancer-types/lung-cancer/lung-cancer-symptoms.html
- Memorial Sloan Kettering Cancer Center https://www.mskcc.org/cancer-care/types/lung
- Merck Manual Consumer Version http://www.merckmanuals.com/home/lung-and-airway-disorders/tumors-of-thelungs/lung-cancer
- Orphanet: Small cell lung cancer http://www.orpha.net/consor/cgi-bin/OC_Exp.php?Lng=EN&Expert=70573

Patient Support and Advocacy Resources

- American Cancer Society
 http://www.cancer.org/cancer/lungcancer/
- American Lung Association
 http://www.lung.org/lung-health-and-diseases/lung-disease-lookup/lung-cancer/
- Bonnie J. Addario Lung Cancer Foundation http://www.lungcancerfoundation.org/
- Free to Breathe http://www.freetobreathe.org/
- Lung Cancer Alliance
 http://www.lungcanceralliance.org/
- Lung Cancer Foundation of America http://lcfamerica.org/

- Lung Cancer Research Foundation
 https://www.lungcancerresearchfoundation.org/
- lungcancer.org http://www.lungcancer.org/
- Lungevity https://www.lungevity.org/

Genetic Testing Registry

- Lung cancer https://www.ncbi.nlm.nih.gov/gtr/conditions/C0684249/
- Non-small cell lung cancer https://www.ncbi.nlm.nih.gov/gtr/conditions/C0007131/

ClinicalTrials.gov

 ClinicalTrials.gov https://clinicaltrials.gov/ct2/results?cond=%22lung+cancer%22+OR+%22Lun g+Neoplasms%22+OR+%22Thoracic+Neoplasms%22+OR+%22cancer+of+b ronchus%22+OR+%22pulmonary+cancer%22+OR+%22respiratory+carcinoma %22

Scientific articles on PubMed

PubMed

https://www.ncbi.nlm.nih.gov/pubmed?term=%28Lung+Neoplasms%5BMAJR%5D %29+AND+%28lung+cancer%5BTI%5D%29+AND+genetics%5Bmh%5D+AND+re view%5Bpt%5D+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22la st+1080+days%22%5Bdp%5D

<u>OMIM</u>

 LUNG CANCER http://omim.org/entry/211980

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Reprinted from Genetics Home Reference: https://ghr.nlm.nih.gov/condition/lung-cancer

Reviewed: October 2015 Published: January 17, 2017

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