Lung cancer

Description

Lung cancer is a disease in which certain cells in the lungs become abnormal and multiply uncontrollably to form a tumor. Lung cancer may not cause signs or symptoms in its early stages. Some people with lung cancer have chest pain, frequent coughing, blood in the mucus, breathing problems, trouble swallowing or speaking, loss of appetite and weight loss, fatigue, or swelling in the face or neck. Additional symptoms can develop if the cancer spreads (metastasizes) into other tissues. 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 non-small 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 in more than half of cases the cancer has spread beyond the lung by the time the condition is diagnosed. Small cell lung cancer often metastasizes, most commonly to the liver, brain, bones, and adrenal glands (small hormone-producing glands located on top of each kidney). After diagnosis, most people with small cell lung cancer survive for about 1 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 squamous cells that line the passages leading from the windpipe (trachea) to the lungs (bronchi). Large cell carcinoma arises from epithelial cells that line the lungs. Large cell carcinoma encompasses non-small cell lung cancers that do not appear to be adenocarcinomas or squamous cell carcinomas. 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, lung cancer is the second most commonly diagnosed cancer, after breast cancer, accounting for about one-quarter of all cancer diagnoses. It is estimated

that more than 222,500 people develop lung cancer each year. Approximately 6.6 percent of individuals will develop lung cancer during their lifetime. An estimated 72 to 80 percent of lung cancer cases occur in tobacco smokers. Lung cancer is the leading cause of cancer deaths, accounting for an estimated 27 percent of all cancer deaths in the United States.

Causes

Cancers occur when genetic mutations build up in critical genes, specifically those that control cell growth and division (proliferation) 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. In rare cases, the genetic change is inherited and is present in all the body's cells (germline mutations).

Somatic mutations in the *TP53*, *EGFR*, and *KRAS* genes are common in lung cancers. The *TP53* gene provides instructions for making a protein, called p53, that is located in the nucleus of cells throughout the body, where it attaches (binds) directly to DNA. The protein regulates cell growth and division by monitoring DNA damage. When DNA becomes damaged, p53 helps determine whether the DNA will be repaired or the cell will self-destruct (undergo apoptosis). The *EGFR* and *KRAS* 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 proliferation.

TP53 gene mutations result in the production of an altered p53 protein that cannot bind to DNA. The altered protein cannot regulate cell proliferation effectively and allows DNA damage to accumulate in cells. Such cells may continue to divide in an uncontrolled way, leading to tumor growth. Mutations in the *EGFR* or *KRAS* gene lead to the production of a protein that is constantly turned on (constitutively activated). As a result, cells constantly receive signals to proliferate, leading to tumor formation. When these genetic changes occur in cells in the lungs, lung cancer develops.

Mutations in many other genes have been found to recur in lung cancer cases. Most of these genes are involved in the regulation of gene activity (expression), cell proliferation, the process by which cells mature to carry out specific functions (differentiation), and apoptosis.

Researchers have identified many lifestyle 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 25-fold. Other risk factors include exposure to air pollution, radon, asbestos, certain metals and chemicals, or secondhand smoke; long-term use of hormone 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 are frequently smokers, it is unclear whether the increased risk is the result of genetic factors or exposure to secondhand smoke.

Learn more about the genes associated with Lung cancer

- ALK
- BRAF
- CDKN2A
- EGFR
- KRAS
- MAP2K1
- NF1
- NRAS
- PIK3CA
- PRKN
- PTEN
- RB1
- RET
- RIT1
- SMARCA4
- STK11
- TP53

Additional Information from NCBI Gene:

- DDR2
- DLEC1
- ERBB2
- IRF1
- KEAP1
- MAP3K8
- MET
- NRG1
- PPP2R1B
- RASSF1
- ROS1
- SLC67A1

Inheritance

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

When lung cancer is related to inherited genetic changes, the cancer risk follows 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 the disease. 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

Additional Information & Resources

Genetic Testing Information

- Genetic Testing Registry: Lung carcinoma (https://www.ncbi.nlm.nih.gov/gtr/conditions/C0684249/)

Genetic and Rare Diseases Information Center

- Small cell lung cancer (https://rarediseases.info.nih.gov/diseases/9344/index)

Patient Support and Advocacy Resources

- National Organization for Rare Disorders (NORD) (https://rarediseases.org/)

Clinical Trials

- ClinicalTrials.gov (https://clinicaltrials.gov/search?cond=%22Lung cancer%22)

Catalog of Genes and Diseases from OMIM

- LUNG CANCER (https://omim.org/entry/211980)

Scientific Articles on PubMed

- PubMed (https://pubmed.ncbi.nlm.nih.gov/?term=%28Lung+Neoplasms%5BMAJR%5D%29+AND+%28lung+cancer%5BTI%5D%29+AND+genetics%5Bmh%5D+AND+review%5Bpt%5D+AND+english%5Bla%5D+AND+human%5Bmh%5D+AND+%22last+1080+days%22%5Bdp%5D)

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