

LUNG CANCER



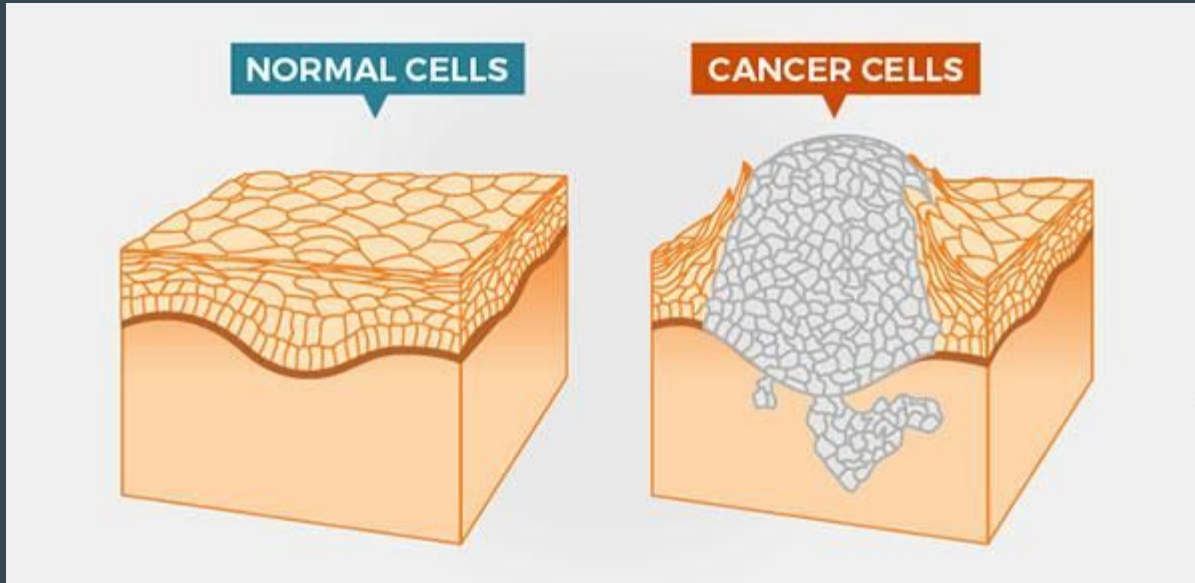
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MECHANISM

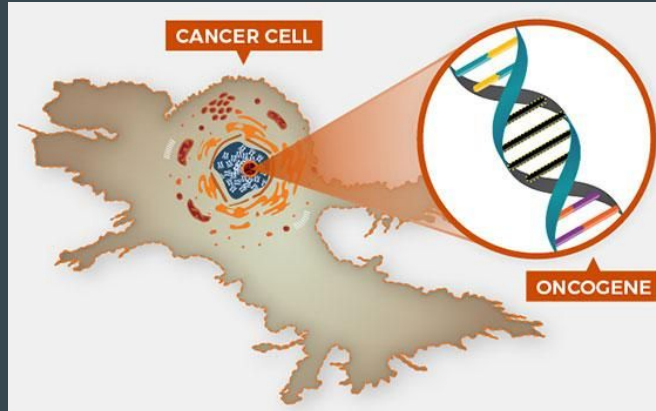
What is Cancer?

An abnormal growth of cells which tend to proliferate in an uncontrolled way and in some cases to metastasize(spread).



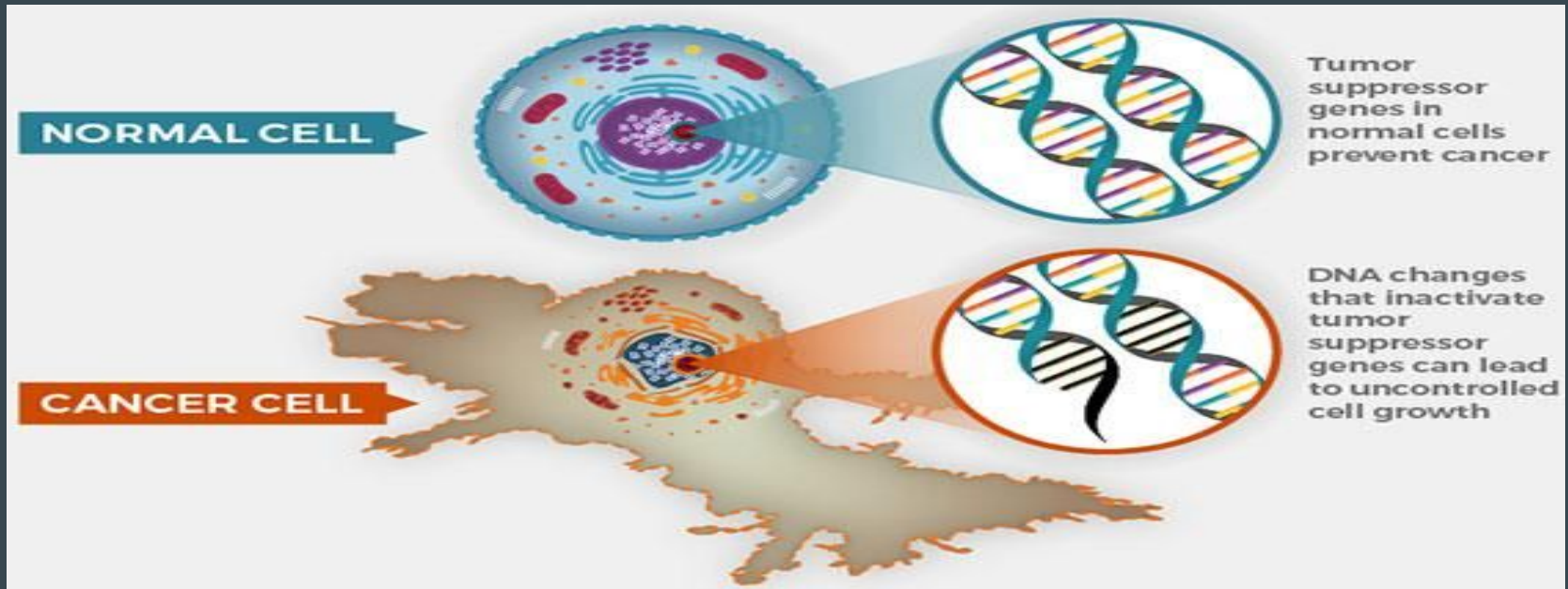
When and why do cells divide uncontrollably?

- Changes in the sections of DNA(genes) are called Genetic changes.
- There are three main types of genes involved in cell division.
 - Proto-oncogenes :
 - Involved in normal cell growth and division.
 - When altered becomes oncogenes which allow cells to grow and survive when they should not.



When and why do cells divide uncontrollably?

- Tumor Suppressor genes :
 - Involved in controlling cell growth and division.
 - Cells when altered in these genes divide uncontrollably.



When and why do cells divide uncontrollably?

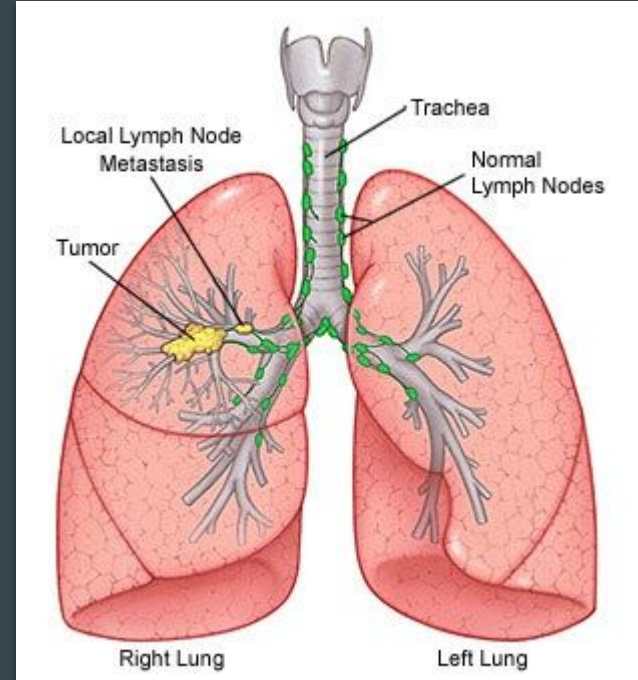
- DNA repair genes :
 - Involved in fixing Damaged DNA.
 - Mutations in these genes causes mutation in other genes
- The Genetic changes which when affect these three types of genes contribute to cancer. These changes are also called as drivers of cancer.
- These cells accumulate and form tumors which are classified into :
 - Benign Tumor : Tumors that do not spread or invade into nearby tissues.
 - Malignant Tumor : Tumors that spread and invade nearby tissues. They can travel to distant places in the body through the blood or the lymph system and form new tumors far from the original tumor(metastasis).

What is Lung Cancer?

Lung cancers typically start in the cells lining the bronchi and parts of the lung such as the bronchioles or alveoli. A variety of benign and malignant tumors may arise in the lung.

Cancers that start in other organs (such as the breast, pancreas, kidney, or skin) can sometimes spread (metastasize) to the lungs, but these are not lung cancers.

As the early symptoms mimic a cold or other common conditions, so most people don't seek medical attention right away. That's one reason why lung cancer isn't usually diagnosed in an early stage.



How do a person get Lung Cancer?

As Lungs are the two spongy organs involved in the respiration(Inhaling Oxygen exhaling Carbon dioxide), the Inhaled air if contains any carcinogens(cancer causing substances) will alters the genes in the cells(lining the lungs mostly).

At first our body may be able to repair this damage but on repeated exposure the damage causes cells to act abnormal which eventually may develop cancer.

Cigar, asbestos, nickel, chromium, arsenic are some of the carcinogenic substances.

Classification

Based on the histologic patterns the tumor is classified in several types.

- Adenocarcinoma :
 - It starts in the cells that would secrete mucus.
 - More common in women than in men.
- Squamous cell carcinoma :
 - Starts in squamous cells(flat cells lining the inside of airways).
- Large cell carcinoma :
 - Can appear in any part of the lung.
 - Tends to grow and spread quickly which makes it harder to treat.
- Small cell carcinoma :
 - It tends to grow and spread very fastly.
 - It tends to respond well to chemotherapy and radiation therapy.

As these treatment and prognosis for Adenocarcinoma, Squamous cell carcinoma and Large cell carcinoma are similar these are grouped as Non-small cell lung cancer(NSCLC).

Stages in Lung Cancer

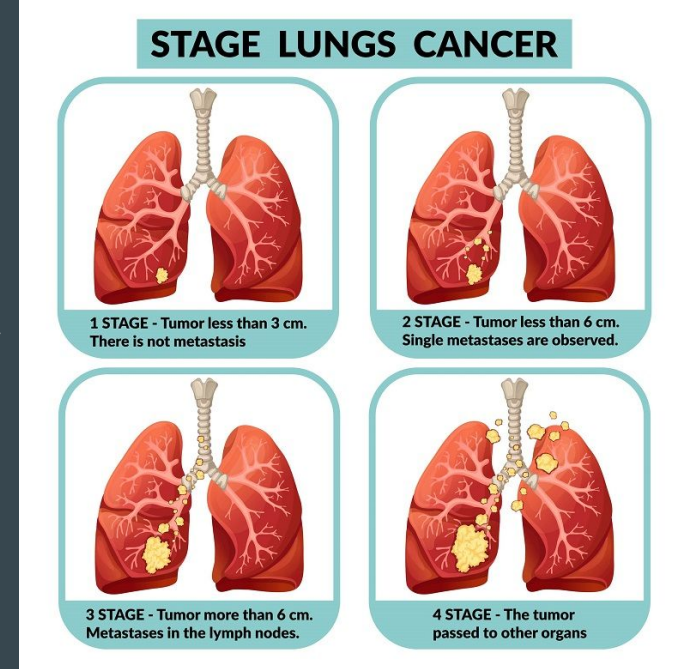
Small-cell lung cancer (SCLC) has two main stages.

- Limited stage : cancer is found in only one lung or nearby lymph nodes on the same side of the chest.
- Extensive stage : cancer has spread
 - throughout one lung
 - to the opposite lung
 - to lymph nodes on the opposite side
 - to fluid around the lung
 - to bone marrow
 - to distant organs

Stages in Lung Cancer

Based on the TNM staging system the Non-small cell lung cancer has four main stages :

- Stage 1: Cancer is found in the lung, but it has not spread outside the lung.
- Stage 2: Cancer is found in the lung and nearby lymph nodes.
- Stage 3: Cancer is in the lung and lymph nodes in the middle of the chest.
 - Stage 3A: Cancer is found in lymph nodes, but only on the same side of the chest where cancer first started growing.
 - Stage 3B: Cancer has spread to lymph nodes on the opposite side of the chest or to lymph nodes above the collarbone.
- Stage 4: Cancer has spread to both lungs, into the area around the lungs, or to distant organs



EPIDEMIOLOGY

What Is Epidemiology?

- Epidemiology is the branch of medical science that investigates all the factors that determine the presence or absence of diseases and disorders. Epidemiological research helps us to understand how many people have a disease or disorder, if those numbers are changing, and how the disorder affects our society and our economy.

How common is Lung Cancer?

The American Cancer Society estimates for lung cancer in the U.S for 2020 are:

- About 228,820 new cases of lung cancer (116,300 in men and 112,520 in women)
- About 135,720 deaths from lung cancer (72,500 in men and 63,220 in women)

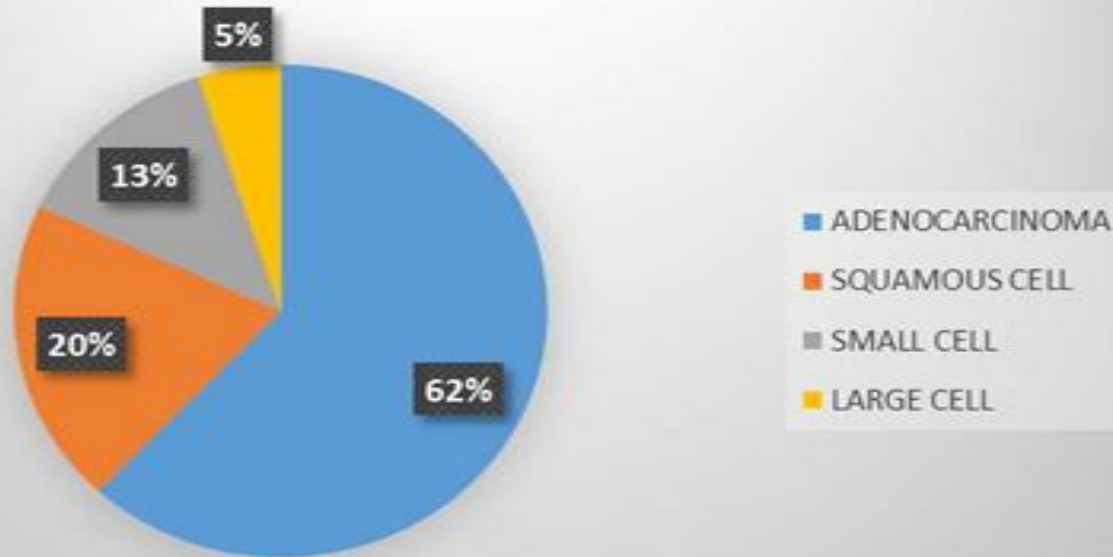
The chance that a man will develop lung cancer in his lifetime is about 1 in 15; for a woman, the risk is about 1 in 17.

- The leading cause of lung and bronchus cancer deaths in both men and women
 - 160,000 die each year, more than breast, colon, prostate and pancreatic cancer combined
 - 5 year survival at 16.8% essentially unchanged since 1975

DISTRIBUTION OF TYPES OF LUNG CANCER

87% Non-Small Cell Lung Cancer (NSCLC); 13% Small Cell Lung Cancer (SCLC) Histology

LUNG CANCER HISTOLOGY



There are 2 main types of lung cancer:

- Non-small cell lung cancer (NSCLC)
- Small cell lung cancer (SCLC)

NSCLC further characterized histologically into:

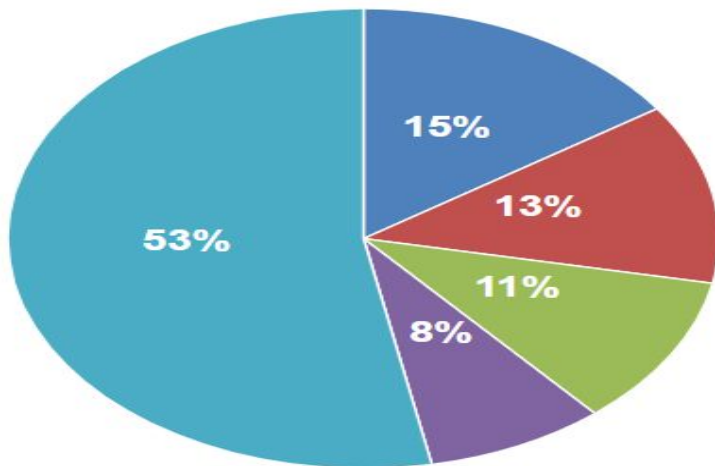
- Adenocarcinoma
- Squamous Cell
- Large Cell

Incidence and Mortality of Cancer as per 2020

At a Glance

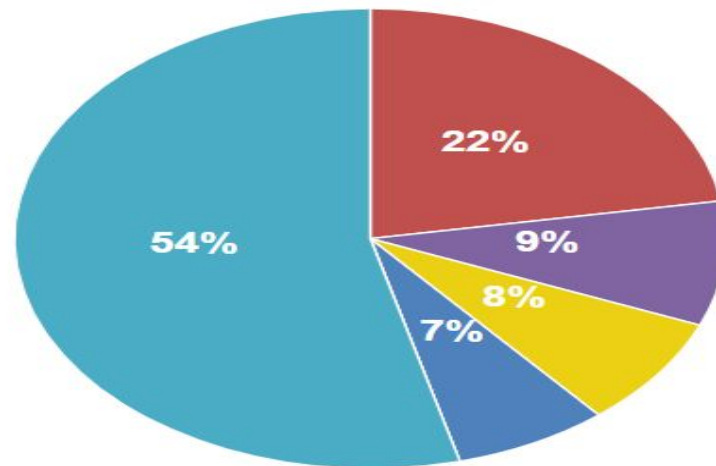
Breast, lung and bronchus, prostate, and colorectal cancers account for almost 50% of all new cancer cases in the United States. Lung and bronchus, colorectal, pancreatic, and breast cancers are responsible for nearly 50% of all deaths.

New Cancer Cases, 2020



- Breast: 279,100 (15%)
- Lung and bronchus: 228,820 (13%)
- Prostate: 191,930 (11%)
- Colon and rectum: 147,950 (8%)
- Other: 958,790 (53%)

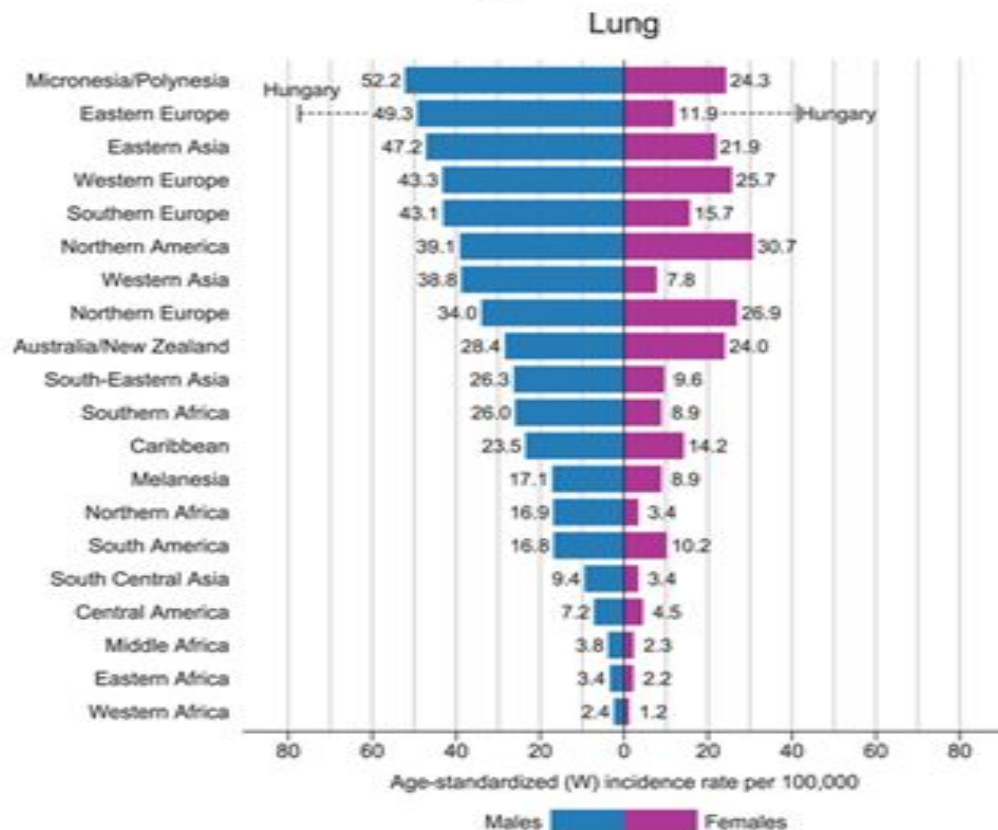
Cancer Deaths, 2020



- Lung and bronchus: 135,720 (22%)
- Colon and rectum: 53,200 (9%)
- Pancreas: 47,050 (8%)
- Breast: 42,690 (7%)
- Other: 327,860 (54%)

Incidence of Lung Cancer as per 2020

Global Lung Cancer Distribution



Most common cancer worldwide

- 1.6 million deaths in 2012

Fifty eight percent of new cases in underdeveloped regions

Highest incidence and mortality in men

- Central and Eastern Europe
- Eastern Asia

Women have lower incidence and mortality

- Highest in North America – cultural differences in smoking prevalence
- Lag in when women started smoking

The Environment Comprises Government Policies and Social Context

Warning Labels on Tobacco Products

- Many now advocating for “plain packaging”

Ban on Cigarette and Smokeless Tobacco Advertising on TV and Radio

Smoking Restrictions in Public Places

Increased Cigarette Taxes

- 10% increase reduces consumption 3 to 5%



Lung cancer incidence reduced from 42% in 1965 to 18% in 2012

Decline in teen smoking incidence leveling off.

5.6 million youths will die prematurely of tobacco related illness

New threat E-cigarettes

Summary

- Lung Cancer is a Non-Infectious Chronic Disease
 - More than 80% of cases caused by tobacco use
 - 90% of regular tobacco use starts by age 18
 - Smoking harder to quit than heroin
 - Cigarettes more addictive now than in 1960's
- Lung cancer is the most common cancer worldwide and the leading cause of cancer deaths in men and women in the US
 - Mortality rate high due late stage at diagnosis
- Tobacco control efforts, although resulting in some success, have failed to eliminate smoking
 - E-cigarettes threaten to erode smoking incidence reduction achieved to date
- Increased research funding needed for improved screening and treatment modalities

PREVENTION

Risk Factors VS Protective Factors

- To prevent new cancers from starting, scientists look at risk factors and protective factors.
- **Cancer Risk Factor** - Anything that increases your chance of developing cancer.
- **Cancer Protective Factor** - Anything that decreases your chance of developing cancer.
- **Avoiding risk factors and increasing protective factors may lower your risk but it does not mean that you will not get cancer.**
- Some risk factors for cancer can be avoided, but many cannot.

Risk Factors

The following are *risk* factors for lung cancer:

- Cigarette, cigar, and pipe smoking
 - Secondhand smoke
 - Family history
 - HIV infection
 - Environmental risk factors
 - Beta carotene supplements in heavy smokers
-

Protective Factors

The following are *protective* factors for lung cancer:

- Not smoking
- Quitting smoking
- Lower exposure to workplace risk factors
- Lower exposure to radon

QUIT SMOKING!!

- **Tobacco smoking** is the most important risk factor for lung cancer. Cigarette, cigar, and pipe smoking all increase the risk of lung cancer. Tobacco smoking causes about **9 out of 10 cases of lung cancer in men** and about **8 out of 10 cases of lung cancer in women**.
- **Secondhand Smoke**

People who inhale secondhand smoke are **exposed to the same cancer-causing agents as smokers, although in smaller amounts**.

Lower exposure

Being exposed to radiation is a risk factor for lung cancer.

- Workplace
 - Some of the substances that increase the risk of lung cancer include **arsenic, cadmium, chromium, diesel exhaust, and nickel**.
 - It's important to **follow recommended safety procedures**.
 - Contact your workplace safety officer if you feel you have been exposed to these.
- Radon
 - It is the number **one cause among non-smokers**, according to EPA policy-oriented estimates.
 - Radon gas in the air breaks down into tiny **radioactive elements (radon progeny)** that can lodge in the lining of the lungs, where they can give off radiation, eventually leading to lung cancer.
 - Check radon levels in your home.
 - Do-it-yourself radon detection kits.

Misconceptions and More Information ...

The following do not decrease the risk of lung cancer:

- **Beta carotene supplements in nonsmokers** - Studies of nonsmokers show that taking beta carotene supplements does not lower their risk of lung cancer.
- **Vitamin E supplements** - Studies show that taking vitamin E supplements does not affect the risk of lung cancer.

It is not clear if the following decrease the risk of lung cancer:

- **Diet**
- **Physical activity**

Since smokers tend to have less healthy diets than nonsmokers, it is hard to know whether the decreased risk is from having a healthy diet or from not smoking.

TREATMENT

There are typically three objectives applied to the treatment of lung cancer and can vary by patient or individual diagnosis:

- Curing lung cancer
- Controlling lung cancer
- Being comfortable.

The 3 most common ways of treatment in lung cancer (or any cancer) that are currently used in hospitals around are -

- Chemotherapy
- Radiation therapy
- Surgery

Chemotherapy

- Chemotherapy drugs target cells at different phases of the cell cycle.
- Cancer cells tend to form new cells more quickly than normal cells and this makes them a better target for chemotherapy drugs.
- However, chemo drugs can't tell the difference between healthy cells and cancer cells.
- This means normal cells are damaged along with the cancer cells, and this causes side effects.
- Each time chemo is given, it means trying to find a balance between killing the cancer cells (in order to cure or control the disease) and sparing the normal cells (to lessen side effects).
- Most normal cells will recover from the effects of chemo over time.
- But cancer cells are mutated (not normal) cells, and they usually do not recover from the effects of chemo.



When and Why Chemotherapy

- Adjuvant chemotherapy is often recommended for people with stage II and stage IIIA non-small cell lung cancer to reduce the risk of recurrence.
 - Neoadjuvant chemo - To shrink a tumor before surgery
 - To cure cancer
 - Maintenance chemotherapy
 - To help with symptoms of cancer
-

Common Lung Cancer Chemotherapy Regimen

- Cisplatin and Etoposide
- Carboplatin and Etoposide.

Etoposide is a **TOPOISOMERASE INHIBITOR**

They interfere with enzymes called topoisomerases, which help separate the strands of DNA so they can be copied.

Cisplatin & Carboplatin are **ALKYLATING AGENTS**

An alkylating agent used in cancer treatment attaches an alkyl group to DNA.

The alkyl group is attached to the guanine base of DNA.

Cancer cells are more sensitive to DNA damage.

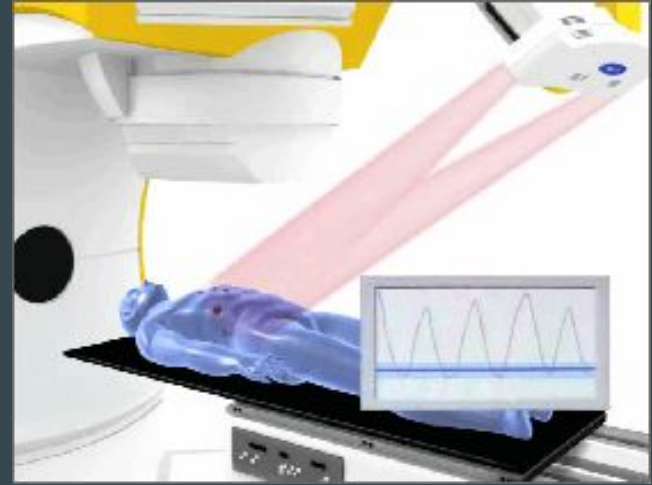
Surgery

- In most cases, the goal of lung cancer surgery is to remove the entire tumor, including a small amount of normal tissue (about 2 centimetres, 0.8 in) at the margin.
- The general name for surgery that enters the chest is thoracotomy, and specific named types of surgical interventions may be performed as part of the thoracotomy, such as wedge resection, segmentectomy, "sleeve resection", lobectomy, or pneumonectomy, depending on the tumor and patient characteristics.
- Surgery is very rarely used in cases of stage 3b or stage 4 non-small cell lung carcinoma.



Radiation

- Lung cancer radiation therapy uses powerful, high-energy X-rays to kill cancer cells or keep them from growing.
- Radiation may come from outside the body (external) or from radioactive materials placed directly inside the lung cancer tumor (internal/implant).
- The radiation is aimed at the lung cancer tumor and kills the cancer cells only in that area of the lungs.
- Radiation can be used before lung cancer surgery to shrink the tumor or after surgery to kill any cancer cells left in the lungs.

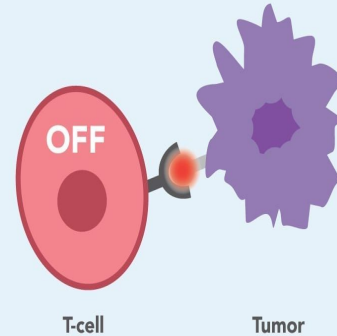


Immunotherapy

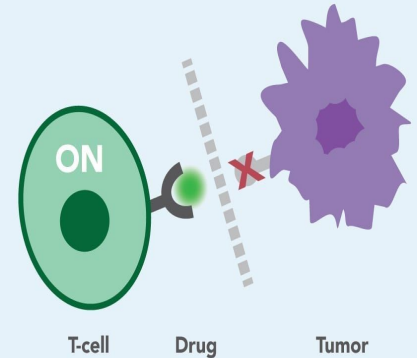
- Cancer immunotherapy (sometimes called immuno-oncology) is the artificial stimulation of the immune system to treat cancer, improving on the immune system's natural ability to fight the disease.
- Cancer immunotherapy exploits the fact that cancer cells often have tumor antigens.

How Does Immunotherapy Work?

Tumor cells bind to T-cells
to deactivate them



Immunotherapy drugs can block
tumor cells from deactivating T-cells

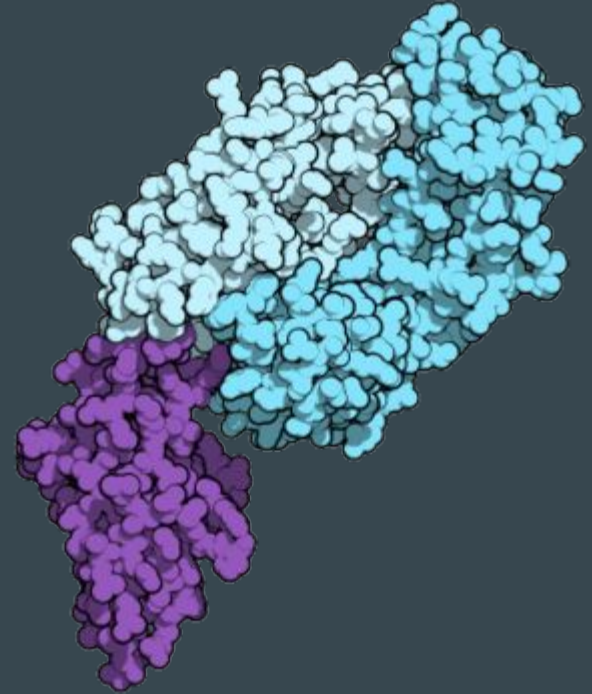


COLUMBIA UNIVERSITY
MEDICAL CENTER

Immunotherapy - New form of Cancer Treatment
Now available for patients in India



- T cells protect the body from cancer by killing certain cancer cells. But cancer cells evolve proteins to protect themselves from T cells.
- Nivolumab blocks those protective proteins. Thus, the T cells can kill the cancer cells. This is an example of immune checkpoint blockade.
- PD-1 is a protein on the surface of activated T cells. If another molecule, called programmed cell death 1 ligand 1 or programmed cell death 1 ligand 2 (PD-L1 or PD-L2), binds to PD-1, the T cell becomes inactive.
- Many cancer cells make PD-L1, which inhibits T cells from attacking the tumor. Nivolumab blocks PD-L1 from binding to PD-1, allowing the T cell to work.



CURRENT ONGOING RESEARCH

Early Detection of Lung Cancer

- Current ongoing research has been happening on early detection of lung cancer
- Early detection is very important because most lung cancers don't cause symptoms until the disease has advanced
- as the five-year survival rates are at least six times higher in patients whose tumors are detected before they spread to distant locations in the body.
- Long-term survival with lung cancer is sometimes possible, especially when the disease is caught in the early stages

CT Scan

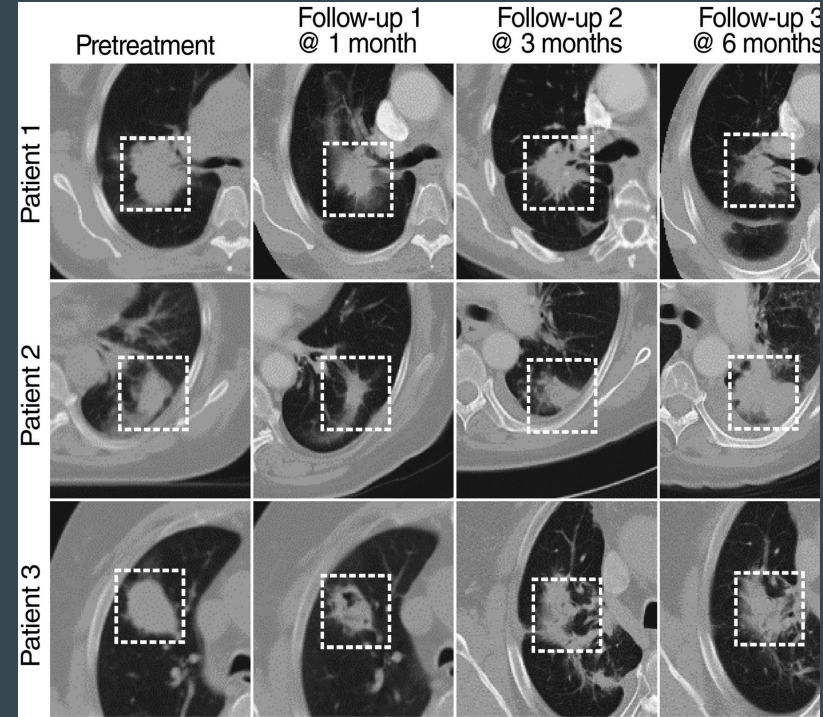
- The NCI has sponsored National Lung Screening Trial which showed that low-dose CT scans can be used to screen for lung cancer in people with a history of heavy smoking.
- low-dose CT is preferable,,it can decrease their risk of dying
- For better prediction whether cancer is present or not , researchers are looking for ways to refine CT screening.



MACHINE LEARNING

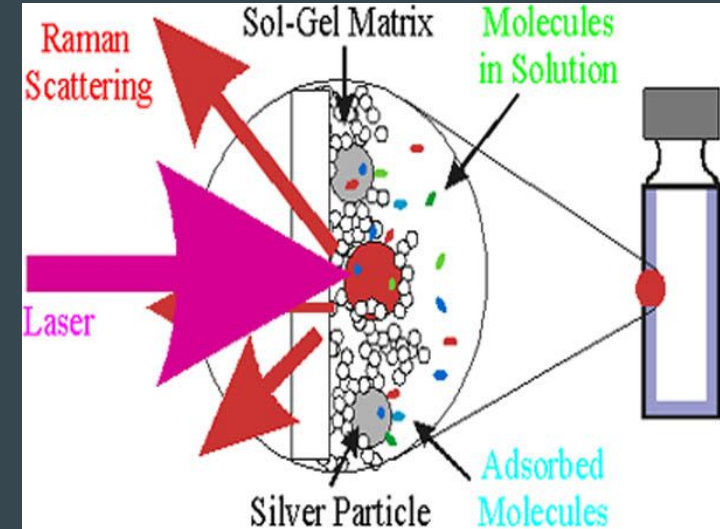
Machine learning is a method that allows computers to learn how to predict certain outcomes

- Identify cancer in CT scans
- 97% accuracy
- Detect cancer-related genetic mutations.
- A **biopsy** usually takes a Pathologist 10 days , where as A computer can do thousands of biopsies in a matter of seconds.



Surface-enhanced Raman scattering

- Early-stage lung cancer
- Platform that detects volatile organic compounds such as benzene, acetone, benzaldehyde and ethanol in a gas phase
- clinically established biomarkers in exhaled breath

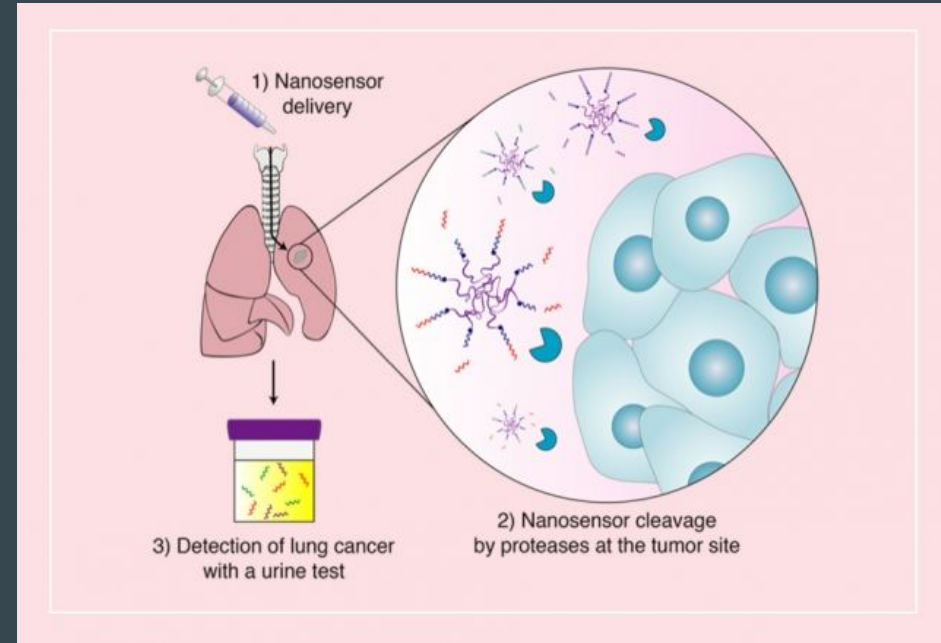


IIT Delhi research on lung cancer

The risk of lung cancer is higher among the people who live close to main roads in New Delhi. They may have more chances of lung cancer mortality. This is due to the inhalation of particulate matter that contains trace elements such as nickel and chromium.

Research at MIT

- Developed nanoparticles that can be delivered to the lungs, where tumor-associated proteases cut peptides on the surface of the particles.
- These enzymes make tumor cells to escape their original locations by cutting through proteins of the extracellular matrix. There by releasing biomarkers that can then be detected in a urine sample.
- They could accurately detect tumors as early as 7.5 weeks, when the tumors were only 2.8 cubic mm

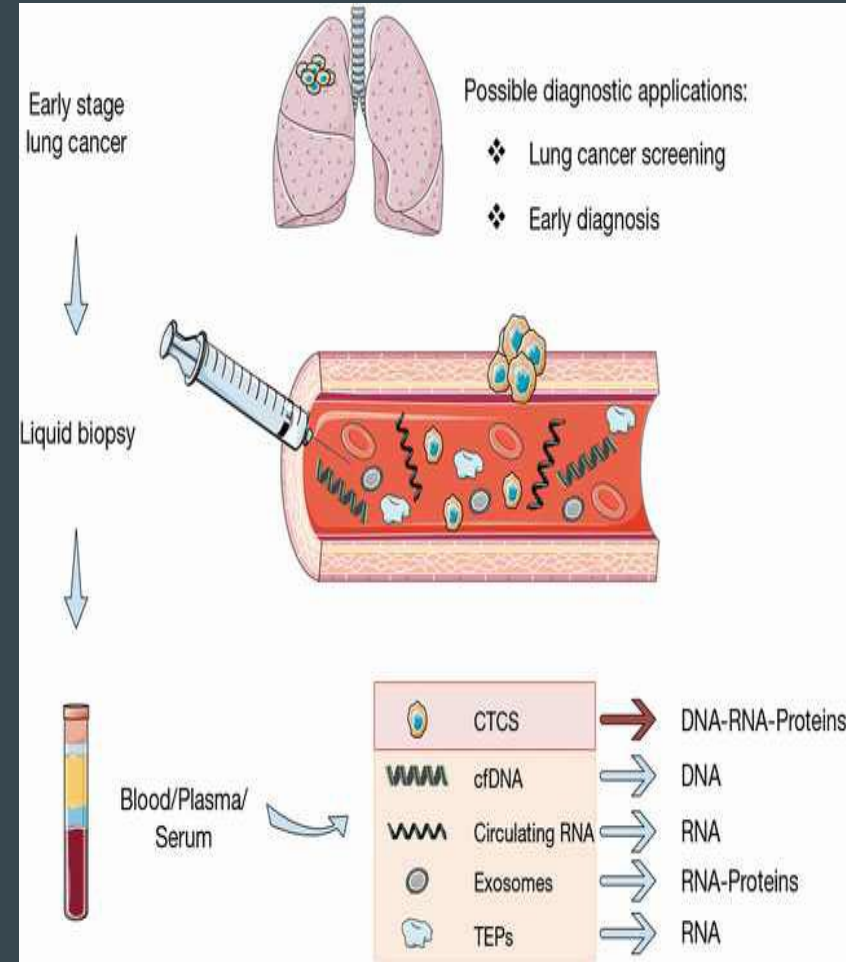


- They created a panel of 1-4 peptide-coated nanoparticles that could interact with these enzymes.
- To customize it, the researchers analyzed a database of cancer-related genes called the Cancer Genome Atlas and identified proteases that are abundant in lung cancer.

Markers in Blood and Sputum

Scientists are trying to develop or refine tests of sputum and blood that could be used to detect lung cancer early.

- Analyzing blood samples for finding tumor cells or molecular markers in the blood will help diagnose lung cancer early.*
- Examining sputum samples for the presence of abnormal cells or molecular markers that identify individuals who may need more follow-up.*



Targeted Therapies

→ EGFR Inhibitors

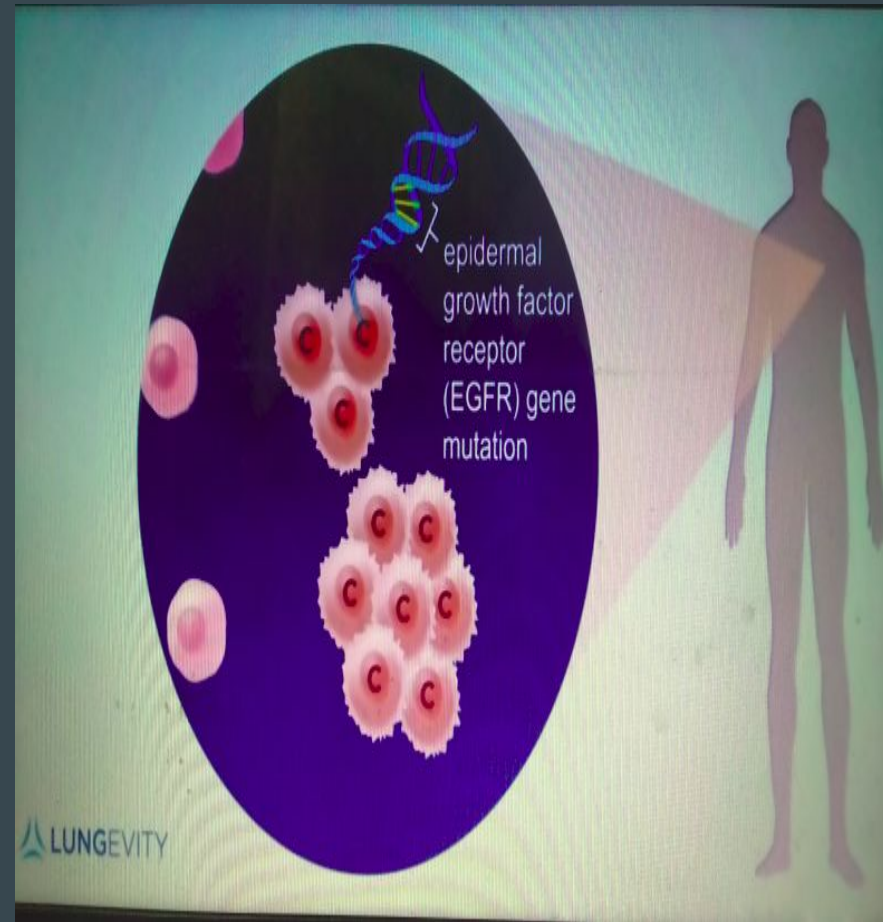
EGFR inhibitors block the activity of a protein called epidermal growth factor receptor (EGFR). EGFR may be found at higher levels than normal on cancer cells, causing them to grow and divide. Some drugs that target EGFR that are approved for treating lung cancer are:

- Afatinib (Non small cell lung cancer)
- Gefitinib (Metastatic lung cancer)
- Erlotinib (non small cell lung cancer)

Serious Side effects like kidney damage,liver damage.

→ ROS1 Inhibitors

which is involved in cell signaling and cell growth.of non small cell lung cancer



NCI-Supported Research Programs

NCI-funded researchers are seeking ways to address lung cancer more effectively.

The programs listed below are a small sampling of NCI's research efforts in lung cancer.

- ALCHEMIST is a multicenter NCI trial for patients with early stage non-small cell lung cancer. It tests to see whether adding a targeted therapy after surgery, based on the genetics of a patient's tumor, will improve survival.
- The Lung MAP trial is an ongoing multicenter trial for patients with advanced non-small cell lung cancer who have not responded to earlier treatment. Patients are assigned to specific targeted therapies based on their tumour's genetic makeup.

REFERENCES

- <https://www.cancer.org/content/dam/cancer-org/cancer-control/en>
- [**New sensors could offer early detection of lung tumors**](#)
- [Lung Cancer Treatment: Radiation Therapy, Treatment for Lung Cancer - UCLA Radiation Oncology](#)
- [Lung Cancer Resource Library | American Lung Association](#)
- [Lung Cancer Prevention \(PDQ®\)–Patient Version](#)

THANK YOU