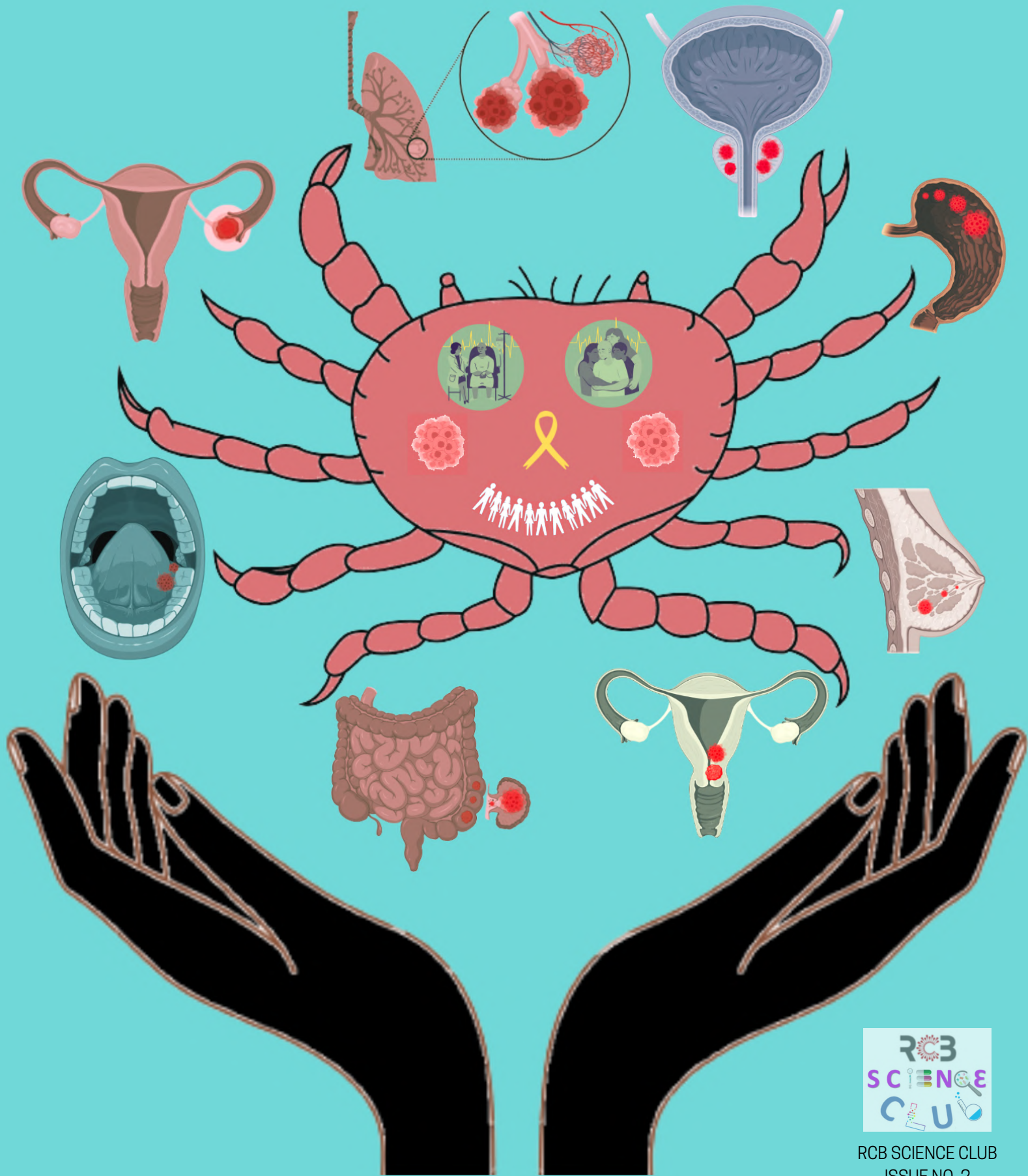
SciLogi



RCB SCIENCE CLUB
ISSUE NO. 2
NOVEMBER 2022

EDITORIAL

Cancer is one of the leading causes of deaths worldwide accounting for close to 10 million (1 crore) deaths annually. As per National Cancer Registry Programme, 1 in every 9 individuals in India is at a cumulative risk of encountering some sort of cancer during their lifetime. Considering India's population, this translates into huge patient load with a enormous economic burden on our healthcare system.

There are several reasons that contribute to poor survival of cancer patients such as late diagnosis; inadequate understanding of cancer pathobiology and limited treatment options. One of these i.e. at least late diagnosis is majorly associated with lack of awareness in general public about the common causes, symptoms and early health indications of cancer. Therefore, "RCB Science Club" has put together this cancer bulletin with an overarching goal of creating awareness regarding these topics among masses. In this magazine, we have provided information regarding common causes of prevalent cancers. Further, we have shared useful guidelines for regular self-examination so that cancer can be detected at early stage. In particular, it is useful for cancer types wherein painless lumps can be felt/observed externally such as breast cancer, oral cancers, skin cancers etc.

In the interest of general readers, we have also provided a brief historical perspective on cancer, discussed different types of cancers and deliberated on treatment and detection strategies. One of the reasons, because of which not all cancer patients respond to same therapy, is that multiple independent factors may contribute to same cancerous disease. Hence, we have discussed the futuristic personalized medicine concept wherein an individual specific treatment strategy may be adopted for better clinical outcome. Finally, our students have briefly shared their recently published cancer studies for highlighting the cancer research activities going on at RCB.

In summary, this magazine would serve as a useful resource for creating cancer associated awareness among general public. It has a right mix of topics starting from historical perspective to recent advancements in the clinical management of cancers. I would therefore like to congratulate "RCB Science Club" especially Integrated Ph.D. students for their sincere efforts in putting together this highly informative and useful resource.

Wishing best of health and happiness to all!

Dr. Rajender K Motiani
Cancer Biologist and Science Enthusiast
(Laboratory of Calciomics and Systemic Pathophysiology, Regional Centre for Biotechnology)

SNEAK PEEK

Contents — Page No.

CANCER COMPENDIUM

History of Cancer

Cancer has affected humanity from prehistoric times but the rapid increase, which we see now can be attributed to the increase in behavioral patterns that favour an unhealthy lifestyle along with the rise in the number of carcinogens in the environment and consumer products. The carcinogenicity of ionising, solar and UV radiation as well as of environmental agents (e.g., radon), industrial products (e.g., asbestos), and a growing list of consumer products (e.g. tobacco) is established.

Any significant scientific work in the field remained largely unknown and if known was based on crude understanding until Gabriele Fallopius described the clinical differences between benign and malignant tumours around 1500. This was followed by Henri François Le Dran who in 1775 postulated that cancer developed locally but spread through lymphatics becoming inoperable and fatal.

Percivall Pott pointed out the attention to scrotum cancer in chimney sweeps. Pott was well aware of the progressive nature of the disease, the benefits of early intervention, and of the fatal outcome of late surgical intervention.

During the early part of the 20th century, the introduction of innovative research tools enabled medical investigators to systematically explore old and new hypotheses on the origin and nature of cancer, leading to progress on many fronts.

The hypothesis of Percivall Pott's linking of a tar-cancer link in chimney sweeps was confirmed in 1915 by Katsusaburo Yamagiwa (1863–1930) and his colleague Koichi Ichikawa.They painted the pinna of rabbits ears with coal tar which than induced squamous cell carcinoma in rabbits' ears.

The viral association of cancer was first discovered by Peyton Rous (1879–1970) who confirmed the virus-cancer link by inducing cancer in healthy chickens injected with a cell- and bacteria-free filtrate of a tumour from a cancer-stricken fowl. Rous sarcoma virus, was acknowledged 50 years later as the causative agent for virus induced cancer and he won the 1966 Nobel Prize for Physiology or Medicine.

History of Treatment

Chemotherapy

Early in the 20th century, only cancers small and localised that had not metastasized, were amenable to be completely removed by surgery and were curable. Later, radiation was used after surgery to control small tumour growths that were difficult to be surgically removed. Chemotherapy was then used to destroy small tumour growths that had spread beyond the reach of the surgeon and radiotherapist. Chemotherapy used after surgery to destroy any remaining cancer cells in the body is called adjuvant therapy. This was tested for the first time for breast cancer and was found to be effective.

During the Second World War, the US Army was studying a number of chemicals related to mustard gas to develop more effective agents for war and also develop protective measures. In the course of that work, a compound called nitrogen mustard was studied and found to work against a cancer of the lymph nodes called lymphoma. This agent served as the model for a long series of similar but more effective agents that killed rapidly growing cancer cells by damaging their DNA.

Sidney Farber demonstrated that aminopterin, a compound related to the vitamin folic acid, produced remissions in children with acute leukaemia. Aminopterin was responsible for blocking the active site for folate binding in the dihydrofolate reductase enzyme resulting in the depletion of nucleotide precursors needed for

DNA replication. This was the predecessor of methotrexate, a cancer treatment drug used commonly today. Since then, other researchers have discovered drugs that block different regulators of cell growth and replication.

A major discovery was the advantage of using multiple chemotherapy drugs, which is now known as combination chemotherapy over single agents. The resistance of cancer as it proliferates leads to developing resistance to single or double agents of cancer therapy but the use of multi chemotherapeutic drugs circumvented this problem. Some types of very fast-growing leukaemia and lymphoma which are tumours involving the cells of the bone marrow and lymph nodes, respectively responded very well to combination of multiple chemotherapeutic drugs.

Immunotherapy

William B. Coley, the father of immunotherapy, was the first to attempt to harness the power of the immune system for treating cancer in the late 19th century. In 1891, Coley used a mixture of live and inactivated bacteria such as Streptococcus pyogenes and Serratia marcescens with the hope of inducing sepsis and thereby strong immune and antitumor responses. This dual combination of bacteria became widely known as "Coley's toxin" and represents the first documented active cancer immunotherapy intervention. The mechanism by which this worked remained elusive and it was only later after around 50 years that it was discovered that those mediators constitute a cytokine family including interleukins, interferons, and chemokines.

The recent discovery of T cell immune checkpoints, such as CTLA-4 and PD-1, ushered the field of immuno-oncology in the modern era. The 2018 Nobel prize in Physiology or Medicine to Dr James P. Allison and Dr. Tasuku Honjo. The T cell protein CTLA-4 along with PD-1 prevents T cell over activity and keeps it in check, they made an antibody against CTLA-4, which enabled the T cell to freely target tumour cells and now had antitumor activity. This has been tested in clinical trials that have been successful in treating certain cancers.

Mr. Abhigya Chhetri and Mr. Tenzin Ogyen Bhutia
MS–PhD students, Batch 2022

Sources/References:

https://onlinelibrary.wiley.com/doi/full/10.1002/ijc.29134#:~:text=This%20mini-review%20chronicles%20the%20history%20of%20cancer%20ranging,with%20the%20originators%20of%20radiation%20and%20medical%20oncology
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7194005/

Common Causes of Cancer and its Prevention

Chemical Carcinogens:
A prominent example is Tobacco Smoke (having Aromatic Amines as Carcinogens), which can cause cancer at multiple sites with the highest risk being Lung Cancer. However, most chemical carcinogens do not react directly to the intracellular components, they are activated via metabolic and biochemical processes. Other mutagens are:

A. Carcinogens In Food

Peanuts & Grains
A class of toxic, produced by certain Fungi (Aspergillus flavus). It initially affects Plants like Peanuts & Grains. Humans consuming infected foodstuffs will produce products containing Aflatoxin that will target the Liver. Women consuming infected foodstuffs can pass on Aflatoxin to infants through breast milk.

Salted Fishes
Consumers of Chinese-style Salted Fish are at high risk of Nasopharynx, Stomach, and Esophageal Carcinoma. The Nitroso-compounds are produced as by-products during the cooking of these Salted Fishes may act as the Carcinogen.

Alcohol
Heavy drinkers experience a higher rate of Oral, Pharyngeal, and Esophageal Cancer. One hypothesized mechanism behind this is that Ethanol will be converted into Acetaldehyde which may act as a Carcinogen.

Pickled Vegetables
Sometimes foods like Pickled Vegetables have Mutagens that will lead to the Mutation in Protooncogenes and Tumor Suppresser genes. This can lead to an increased risk of Esophageal cancer.

Meat
Cooking Meat at high temperatures results in the production of Heterocyclic Amines that are Mutagenic in Humans. The site of a Tumor depends on the route of exposure, including the Intestine, Prostate and Lymphomas.

B. Carcinogens in Industry

Denim
The blue dye that rubs off your new pair of jeans is likely azodye, the most common form of dye used in Textile production. Azodye can release Carcinogens called Amines that target the bladder.

Rain-coats
Waterproof & Stain Resistant clothes might seem like a bonus but these are found to contain some chemicals like Polyfluoroalkyl substances which are associated with Kidney and Testicular Cancers.

Heavy metals
Heavy metals including Cd, As, Cr, etc. are potential Carcinogens. Based on the data provided by IARC, Arsenic can cause Lung Cancer, Bladder Cancer, Skin Cancer, Kidney Cancer, Liver Cancer, and Prostate Cancer.

C. Carcinogens in Lab

Benzene
Benzene is a routinely used chemical as a solvent in the lab. According to IARC, Benzene is an efficient carcinogen that causes Acute Myeloid Leukemia (AML), Chronic Lymphocytic Leukemia (CLL).

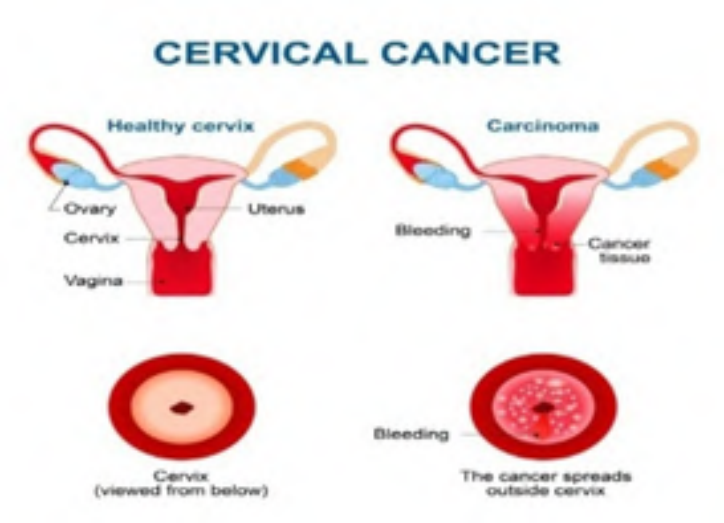
EtBr
EtBr is used for the staining purpose in the lab which can cause Cancer. It acts as a mutagen that will lead to Skin cancer.

D. Biological Carcinogens:

There are some biological agents like viruses and bacteria which interfere with tumor-suppressor genes and proto-oncogenes:

Papillomavirus
It is a dsDNA virus, which has E6 and E7 proteins, E6 has 158 Amino acids residues with two Zinc finger motifs. It forms a trimeric complex comprising E6, p53, and cellular ubiquitination

enzyme E6-AP these complexes degrade the tumor suppressor p53 gene. Finally, tumor cells will grow and form a tumor. E7- It binds the pocket domain of retinoblastoma protein(pRb) and disrupts its complex formation with the E2F transcription factor.

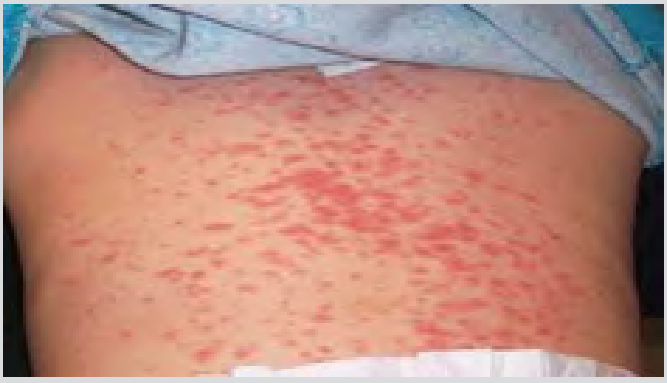


Hepatitis–B Virus

It contains a partially dsDNA genome. It causes liver cancer (hepatocellular carcinoma) its HBV-X gene has four orfs (S, C, P&X). Orf x is a small Orf that codes HBX protein, this protein (HBVX) targets on p53 proteasome and DNA-damaged binding protein so, tumor proliferation and DNA damage occurs which in turn initiates cancer.

Epstein-Barr Virus

This is the first human tumor virus. It consists of dsDNA. It causes Burkitt's lymphoma (B cell lymphocyte cancer). It is an aggressive non-Hodgkin B-cell lymphoma. Epstein-Barr Virus causes the overexpression of the C-myc gene.



Human T- Cell leukemia virus type 1

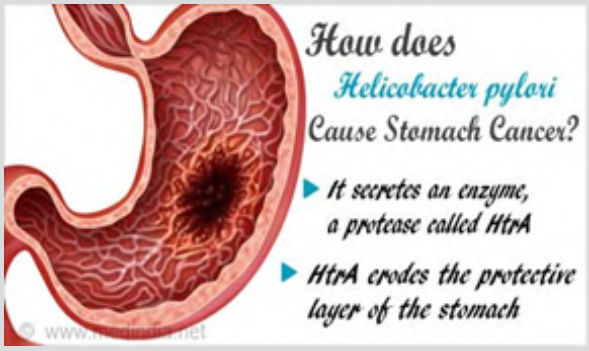
It is transmitted through breastfeeding, sexually and by blood transfusion and organ transplants and is known to cause lethal cancer, adult T-cell leukemia/lymphoma.

Human herpesvirus

It causes Kaposi's sarcoma. It can spread to the lungs, liver, stomach, intestines, and lymph nodes. The most visible signs of Kaposi's sarcoma are lesions on your skin, painless spots that are red or purple on light skin, and bluish, brownish, or black on dark skin, they don't change color when you press on them.

Helicobacter pylori

This is a gram-negative bacterial pathogen that selectively colonizes the gastric epithelium. Approximately half of the world's population is infected with H. pylori and the majority of individuals develop coexisting chronic inflammation.



E. Physical Carcinogens:

1. Physical Carcinogen includes Radon, Radioisotopes, and Rays like UV Rays, X-rays, and Gamma Rays. All of them have a similar mechanism to act as a mutagen and cause Cancer.
2. Certain medical procedures, such as chest X-rays, CT scans, PET scans, and Radiation Therapy cause cancer.
3. Radon is a radioactive gas given off by rocks and soils. It causes Lung Cancer.
4. UV rays cause Skin cancer by causing Thymine- Thymine dimer formation in DNA. People exposed to more sunlight are at higher risk of Skin Cancer due to UV rays. However, the Ozone layer acts as a protective layer.

F. Other Factors:

Age

Aging may lead to a predisposition to cancer by many different mechanisms: 1. Tissue accumulation of mutations 2. changes in homeostasis mechanisms like in immune response and endocrine biology.

Obesity

The latest research shows that many types of Cancers are common in humans, who are overweight. The most common Cancers are the breast, pancreas, liver and stomach.

Genetic Make-up

As per CRUK, only 5% of the total Cancer cases are linked to the inherited faulty gene. If you have inherited a faulty gene, it increases your risk of developing certain types of cancer.

Common steps for the Prevention

1. Don't use Tobacco

2. Eat a Healthy Diet

3. Maintain a healthy weight and be physically active

4. Protect yourself from the Sun

5. Get vaccinated

6. Avoid risky behaviors (don't share needles, practice safe sex)

7. Get regular medical care

8. Get enough Vitamin D (it will reduce the chances of prostate cancer)

Mr. Dharmendra Patel, Ms. Karishma Maddheshiya and Mr. Dhruvin Patel
MS–PhD students, Batch 2022

Sources/References:

- *Abnet C. C. (2007). Carcinogenic food contaminants. Cancer investigation, 25(3), 189–196. https://doi.org/10.1080/07357900701208733*
- *https://www.cancer.org/treatment/survivorship-during-and-after-treatment/long-term-health-concerns/second-cancers-in-adults.html*
- *https://www.businessinsider.in/7-toxic-chemicals-hiding-in-your-waterproof-stain-resistant-and-wrinkle-free-clothes/articleshow/70178950.cms*
- *https://www.allergystandards.com/news_events/chemicals-in-textiles-and-the-health-implications/*
- *https://www.preventcancer.org/education/seven-steps-to-prevent-cancer/*

Types Of Cancer

Serial no.	Type	Affected Organ / Tissue/ Gland	Most affected age group	Risk Factors	Occurrence	Fatality rate
1.	Breast cancer	Breast	Above 50	Oral contraceptive pills	12.5%	34%
2.	Lung cancer	Lung	45-60	Tobacco, Smoking	12.2%	44%
3.	Colorectal Cancer	Colon and rectum	Above 50	Inflammatory Bowel Disease, Cigarette	10.7%	29%
4.	Prostate cancer	Prostate gland	Above 65	Obesity, animal fat consumption, high Calcium intake	7.8%	2.5%
5.	Gastric Cancer	Stomach	Above 55	Helicobacter pylori infection, smoked and salted foods	6.0%	30%
6.	Liver cancer	Liver	Above 60	Medical conditions like hepatitis, liver cirrhosis, gallstones, diabetes	5.0%	65%
7.	Cervical cancer	Cervix	35-45	HPV infection, Smoking	3.3%	44%
8.	Esophageal cancer	Esophagus	45-70	Alcohol, High consumption of hot beverages	3.3%	35-60%
9.	Thyroid cancer	Thyroid gland	50-55	Gender(women), obesity, exposure to radiation, family history	3.2%	0.6-2%
10.	Bladder Cancer	Urothelial cells	Above 55	Exposure to chemicals like benzidine and beta-naphthylamine	3.2%	23%
11.	Non Hodgkin lymphoma	Cancer lymphocytes in lymph nodes	Above 60	Radiation exposure, immunosuppressed individuals and autoimmune diseases	3.0%	27%
12.	Pancreatic cancer	Pancreas	Above 45	Smoking, High caloric intake	2.7%	89%

Serial no.	Type	Affected Organ / Tissue/ Gland	Most affected age group	Risk Factors	Occurrence	Fatality rate
13.	Leukemia	Blood	Below 20 to above 65	Ionizing rays, Benzene exposure	2.6%	34.3%
14.	Kidney cancer	Kidney	60-64	Obesity, high blood pressure, exposure to trichloroethylene	2.4%	24%
15.	Lip and Oral cavity cancer	Mouth	55-65	Tobacco and alcohol consumption, HPV infection	2.1%	15%
16.	Skin melanoma	Skin		UV exposure especially in case of fair skinned people	1.8%	7%
17.	Ovarian cancer	Ovary		Increasing age, pregnancy and use of oral contraceptives	1.7%	50.3%
18.	Brain cancer	Brain tissue	20-69	Exposure to ionizing radiations, Epstein-Barr virus infection	1.7%	67.5%
19.	Uterine Cancer	Uterus		Obesity, use of Intrauterine devices, PCOS	1.1%	18.7%
20.	Larynx cancer	Larynx		Smoking, alcohol consumption, HPV infection	1.0%	39%
21.	Multiple Myeloma	Bone marrow		Increasing age, family history	1.0%	42.1%
22.	Nasopharynx cancer	Pharynx	55-65 yrs	HPV/EBV infection, diet containing salted fish	0.7%	7-15%
23.	Gallbladder and biliary tract cancer	Gall bladder and bile duct		Hepatitis B infection, liver cirrhosis, gallstones, obesity, diabetes	0.6%	44%

Serial no.	Type	Affected Organ / Tissue/ Gland	Most affected age group	Risk Factors	Occurrence	Fatality rate
24.	Hodgkin's Lymphoma	Lymphatic system		EBV infection, immunosuppressed individuals	0.5%	11.9%
25.	Penile cancer	Penis		HPV infection, not being circumcised, Smoking, HIV infection	0.2%	35%
26.	Kaposi Carcoma	Lining of blood and lymph vessels		HIV infection and immunosuppressed patients	0.1%	26%

Ms. Ragini, Ms. Sakshi and Mr. Adarsh Kumar
MS-PhD students, Batch 2022

Sources/References:

- *https://www.wcrf.org/cancer-trends/worldwide-cancer-data/*
- *https://seer.cancer.gov/statfacts/*
- *https://www.indiancancersociety.org/cancer-information/*
- *https://www.cancer.net/cancer-type-page-category/statistics*

Cancer detection strategies

The primary mortality in cancer is due to late detection; at this stage, most of the treatments fail to work due to the huge proliferation of cancerous cells. We have more than one detection strategy for cancer as a whole and then there are technologies specific to cancer types. Here, we will discuss some primary diagnostic features of the tumor that might be of serious concern; this process can be done at home and should be rushed for immediate physician care. The other technological advancements discussed here will be regarding technologies that might come to the market in a few years along with the ones that are already commercialized.

Self-checks

This type of check can be done at home and one must ensure they are paying attention to their body. If one feels a lump in any part of their body, immediately rush to a doctor to be on the safe side. There have been cases where tobacco-consuming individuals have faced problems in talking. We talked to an individual while writing this piece article and came to know that he had difficulty talking for 2 years, but left it undiagnosed. After having severe problems like lesions beside molars and extreme murkiness in speech, and then consulting a doctor, he was diagnosed with oral cancer, which had to be removed surgically; along with that, he lost 3 teeth in the process.

Humongous organizations like CDC support undergoing self-checks for the early detection of cancer. The most prominent success in self-checks has been seen with breast cancer, mammograms have been the most effective in the detection of breast cancer at an early stage.

Circulating tumor DNA

Also known as ctDNA, this has been an extremely useful tool in the field of diagnosis of cancer early. The best-known techniques can detect ctDNA in blood 4 years before it progresses to become cancer. The concept of ctDNA freely circulating the blood of the patient was developed by Dr. Dennins Lo after he found fetal DNA in the blood of the mother. In cell-free DNA of patients, freely floating DNA is found which can be tested against various kinds of the tumor to identify if the individual is having early signs of cancer. Popularly, this technique is known as liquid biopsy and has been popularized in the past few years due to its non-invasive nature. Examining a sample for ctDNA uses molecular tools and technologies to run it against a series of known genes causing cancer. While the most preferable sample is blood or plasma, saliva and spinal fluid have also been employed in the process.

Genetic and genomic testing

This is a relatively newer approach to dealing with cancer, and predicting if a person has a particular genetic predisposition for getting a certain kind of cancer i.e Changes in DNA under environmental and chemical influences, or genetic anomalies inherited from parents might a person more susceptible, or prone to acquire cancer. For instance, the mutation in BRCA1 and BRCA2 genes increase the risk of ovarian and breast cancers, and this mutation is inheritable. And not in cancer recurrence it has been seen that for certain cancers, certain genetic patterns or mutations make the cancer patient more prone to having a relapse of the disease. Genetic screening tests would collect samples (usually blood or mouthwash) from an individual analyze their genome and identify if there are any such anomalies (genetic anomalies which have been recorded to have a connection with cancer prognosis). In case, if there are such genetic abnormalities present the person undergoing the test can be warned so that they could take precautions, go through regular check-ups and consult a specialist, and try to prevent getting the absolute worst of the disease. So it is advisable to see a genetic counselor and to get genetic screenings done, especially if there is a family history of cancer.

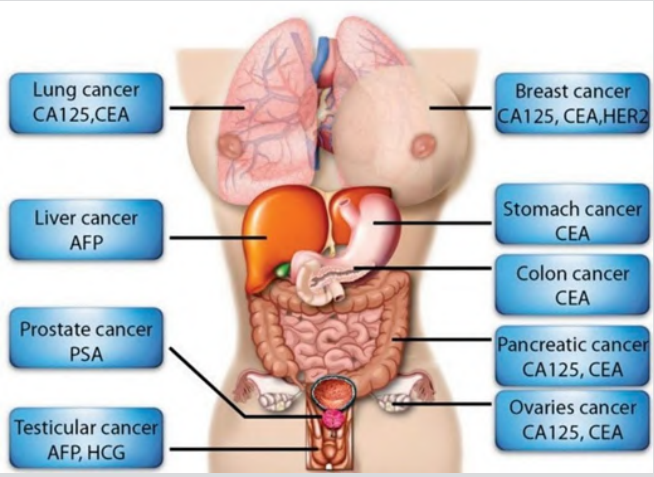
Mammogram

A mammogram is a specialized form of X-Ray procedure that is used for the diagnosis of breast cancer in patients, sometimes 3 years before the condition where it cannot be felt. Pictures are taken from all sides, by pressing against the breast on plastic plates to have a detailed analysis of the inside structures. This is important for the

visualization of any macroscopic cellular abnormalities. One of the common mistakes undergone by patients is asking for the technician's opinion, which should be avoided at all costs.

Cancer marker test

Predominantly, cancer marker tests are based on products called tumor markers present in tissues and blood. These substances, mostly proteins are made by normal as well as cancerous cells, but the quantity in which they are made differs significantly owing to the increase in cell number. Often, cancer marker tests are performed with other tests to make sure the diagnosis is accurate and it also helps in deciding the mode of the treatment plan. Some of the most common cancers and their markers are listed below.



Source: Positivebioscience.com

Pap test (Papanicolaou test)

A Pap test is a simple procedure, done generally to test for cervical cancer. A small brush is taken and gently swabbed on the cervical area to draw cells. This is then examined under a microscope to check for cell abnormality.

Imaging techniques

Cancer detection involves a variety of diagnosis and imaging techniques too, some of which are described in this section.

1. Barium enema – this is used for the detection of cancerous transformation in areas such as the throat and esophagus, the person under inspection is made to ingest a solution containing barium orally via a thin tube followed by taking X-rays. Barium is an X-ray absorber, which appears white on X-ray. So, the injected barium would coat the surface of the above-mentioned internal organs leading to visualization.

2. Bone Scan – Cancer that has spread into the bones can be detected by injecting a small quantity of radioactive dye intravenously followed by nuclear imaging of changes at the cellular level for cancerous changes.

3. Computed tomography (CT) scan – this uses a combination of X-rays and computer technologies which help produce images of internal organs. So, this technique would help visualize changes alterations, and disfigurations, such as tumor formation in the internal organs of people under inspection.

4. Magnetic Resonance Imaging – again another technique similar to CT, this utilizes radio frequencies to capture images of internal organs. It helps in finding a tumor in the body and estimating the size and location of the cancerous growth.

5. Ultrasounds – this method utilizes high-frequency sound waves for visualization of internal organs this provides the opportunity for doctors to visualize the inside of the teste's body in real-time and monitor the function and movement of internal organs, viewing their distortions and identifying tumor formations.

Diagnostic procedures

After visualization, when the doctor suspects the presence of a tumor or a cancerous growth, conventionally the next step would be to run some tests to confirm that the person under inspection has a cancerous transformation in a particular tissue/organ. This usually involves analyzing tissue samples or blood samples.

1. Biopsy - This procedure entails the removal of a piece of tissue, sample/fluid/or cells from the examinee's body, this sample would now be taken to a laboratory and tested for the presence of cancerous cells. This often becomes the only reliable test to know for sure whether the person being investigated has cancer or not.

2. Bronchoscopy - for the detection of oesophageal cancer, a thin instrument has a lighted camera that is inserted through the mouth or nose to have a better look at abnormal areas and to collect specimens for biopsy tests.

3. Colonoscopy – In this procedure, the doctor would insert a thin tube called a colposcope for the analysis and detection of cancerous growths in areas around the colon and rectum.

4. Lumbar puncture *– to detect cancers of the spinal cord and brain, this procedure is. This is commonly known as a spinal tap. It is done in the lower back/lumber region, a needle is inserted in the space between 2 lumbar vertebrae, and collect cerebrospinal fluid samples for testing.*

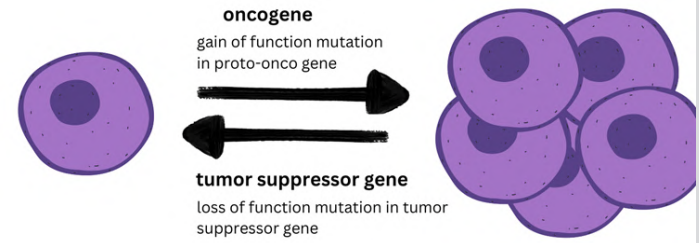
Ms. Oindrila Saha and Mr. Arka Dasgupta
MS-PhD students, Batch 2022

Sources/References:
http://cancer.gov
https://www.cdc.gov
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8700281/

Oncogenes

Molecular Mechanism of Cancer

A gene that has the potential to cause cancer is known as an oncogene. Proto-oncogenes normally control healthy cell division but mutations in proto-oncogenes can make them oncogenes. When a proto-oncogene mutates into an oncogene and causes the cell to divide and replicate uncontrolled, cancer can develop. Oncogenes are a broad category of genes that encode proteins that control cell motility, differentiation, death, and division.



J. Michael Bishop and Harold E. Varmus shared the 1989 Nobel Prize in Physiology or Medicine "for their discovery of the biological origin of retroviral oncogenes."

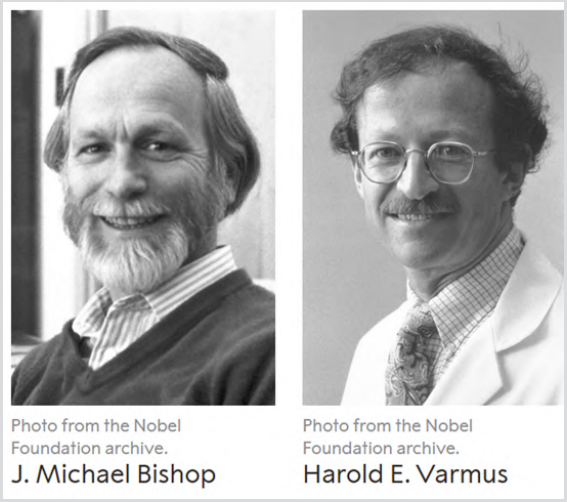
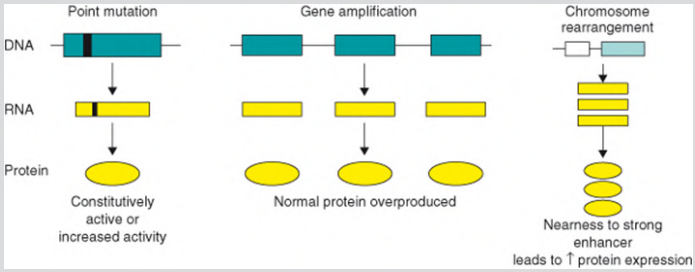


Photo from the Nobel Foundation archive.
J. Michael Bishop

Photo from the Nobel Foundation archive.
Harold E. Varmus

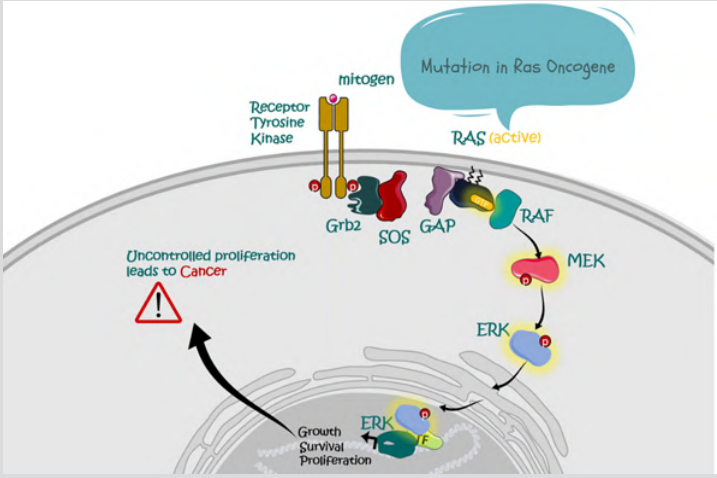
There are several methods by which a proto-oncogene might become an oncogene. Typically, these mutations either alter the gene's coding sequence, which causes the development of an aberrant oncoprotein with increased stability or activity, or they may affect regulatory elements, which causes the expression of the protein to be increased or dysregulated. Oncogene mutations cover a wide variety of genetic changes from specific point mutations that simply affect one amino acid in the protein product to significant chromosomal rearrangements that fundamentally change how genes are regulated. Oncogenes are activated mostly by structural changes, such as point mutations in a single gene or chromosomal translocations, or by gene amplification, which results in the oncogene's overexpression.



1. Ras

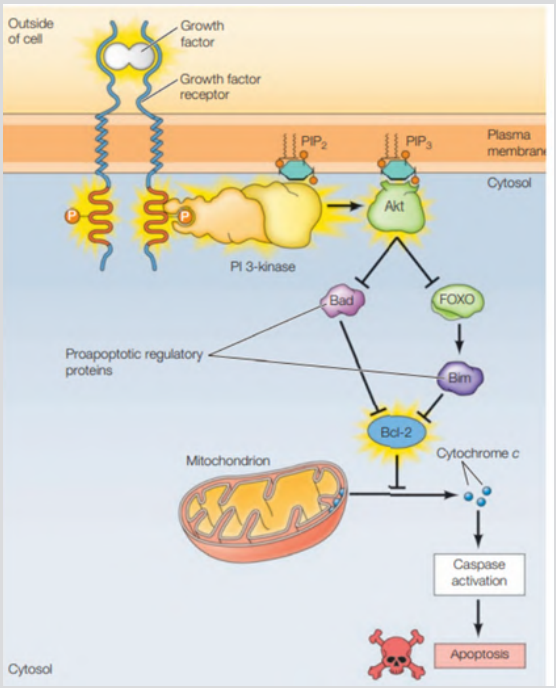
All animal cell lineages and organs express the Ras family of related proteins, which stands for "Rat Sarcoma Virus." All members of the Ras protein family are involved in signal transmission within cells and are members of the small GTPase protein class (cellular signal transduction). Ras is the representative member of the Ras superfamily of proteins, which all share a common three-dimensional structure and control a variety of cell behaviours. Incoming signals that activate Ras then activate other proteins, activating genes involved in cell growth, differentiation, and survival.

Ras gene mutations can result in the synthesis of chronically activated Ras proteins, which can result in unwanted and excessive cell signaling even in the absence of external inputs. Overactive Ras signaling can ultimately result in cancer because these signals cause cell growth and division. The most prevalent oncogenes in human cancer are the three Ras genes (HRAS, KRAS, and NRAS); mutations that irreversibly activate Ras are present in 20–25% of all human cancers and up to 90% in some cancer types (e.g., pancreatic cancer). Ras inhibitors are being investigated as a treatment for cancer and other conditions with Ras overexpression as a result.



2. PI 3-kinase/Akt signaling pathway

Many growth factor-activated cells are prevented from apoptosis by the PI 3-kinase/Akt signaling pathway. The genes encoding PI 3-kinase and Akt function as oncogenes in both retroviruses and human cancers. The proapoptotic Bcl-2 family member Bad, which Akt phosphorylates and inactivates, and the FOXO transcription factor, which controls the production of the proapoptotic Bcl-2 family member Bim, are examples of the downstream targets of PI 3-kinase/Akt signaling. It is also noteworthy that Bcl-2 was found to be a byproduct of an oncogene in human lymphomas. A chromosome translocation that leads to increased Bcl-2 expression, which prevents apoptosis and sustains cell survival under circumstances that would typically cause cell death, produces the BCL-2 oncogene.



3. p53

The gene that codes for the protein known as p53 sometimes referred to as TP53 or tumor protein53, controls cell cycle progression and hence acts as a tumor suppressor. The name refers to the molecular weight of the protein, which is in the 53 kilodalton range. Of its function in preserving stability by avoiding genome mutation, p53 has been referred to as "the custodian of the genome" (Strachan and Read, 1999). Its function as a tumor suppressor gene, which had previously been thought to be an oncogene, was discovered in 1989. In 1993, the Science magazine named the p53 protein its molecule of the year.

Located on the 17th chromosome, p53 makes up a phosphoprotein which is made up of 393 amino acids and consists of four domains, namely:

- A domain which activates the transcription factors
- Core domain recognizing specific DNA sequences
- Domain which has the role of tetramerization of the protein
- A region that could detect damaged DNA, such as single-stranded DNA or mismatched base pairs

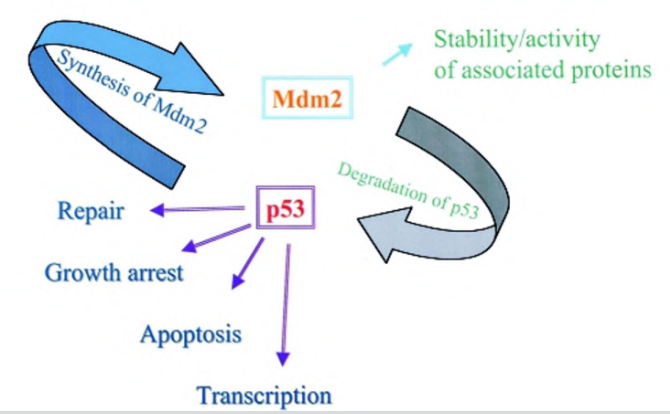
It is crucial for controlling the cell cycle and apoptosis. A faulty p53 gene could promote the growth of aberrant cells, leading to cancer. p53 mutations are present in up to 50% of all human malignancies. The p53 protein level is usually low in healthy cells. Growth arrest, DNA repair, and apoptosis are the three primary actions of the p53 proteins, which may be increased in response to DNA damage and other stress signals (cell death). The growth arrest halts the cell cycle's advancement, preventing damaged DNA from being replicated as p53 may stimulate the transcription of proteins involved in DNA repair during the growth halt. The last resort to prevent the multiplication of cells with faulty DNA is apoptosis. The main p53 regulator is Mdm2, which can cause the ubiquitin system to start degrading p53.

The target genes regulated by p53 are as follows:

- Growth arrest: 14-3-3s, Gadd45, and p21
- Repair of DNA: p53R2.
- Apoptosis: PUMA, Bax, NoxA, and Apaf-1

Regulation of p53:

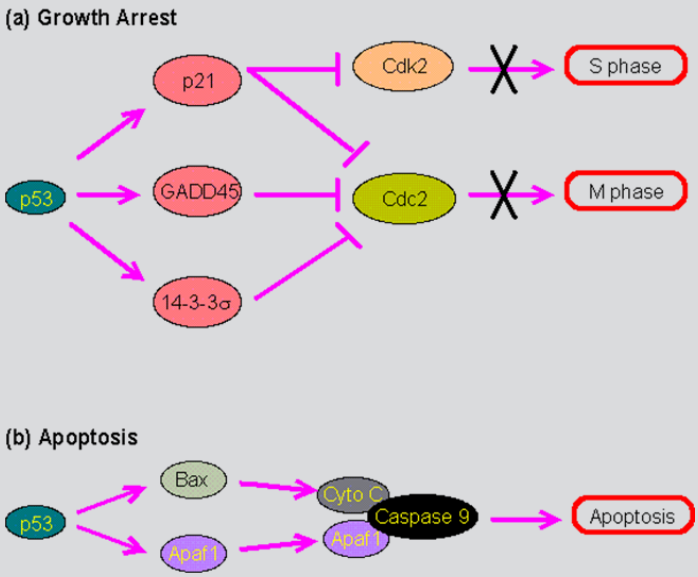
1. Mdm2 expression is induced by p53.
2. The ubiquitin system can cause p53 to degrade when Mdm2 binds to it.
3. When p53 is phosphorylated at Ser15, Thr18, or Ser20, it loses its ability to bind to Mdm2. These three residues are not phosphorylated in healthy cells, and hence Mdm2 keeps p53 at a low level.
4. Protein kinases (like ATM) may be activated by DNA damage to phosphorylate p53 at one of these three positions, boosting the level of p53. The ATM kinase is inactive after the DNA damage has been repaired and hence the accumulating Mdm2 will soon dephosphorylate and destroy p53.



(Source: D, A.-V. (2002, April 23). P53-mdm2--the affair that never ends. Carcinogenesis)

Role of p53 in growth arrest and cell apoptosis:

1. The enzyme Cdk2, which is required for the cell cycle progression to the S phase, can be blocked by p21. Cdc2 is necessary for the entry further into the M phase and it can be blocked by p21, GADD45, or 14-3-3s. To cause growth arrest, p53 controls the expression of these inhibitory proteins.
2. Caspase 9 can cause apoptosis by attaching to cytochrome c as well as Apaf1. Apaf1 expression and Bax expression may be induced by p53. The latter may then promote the mitochondria's release of cytochrome c.



(Source: Primary information of p53 gene. (n.d.), bioinformatics.org)

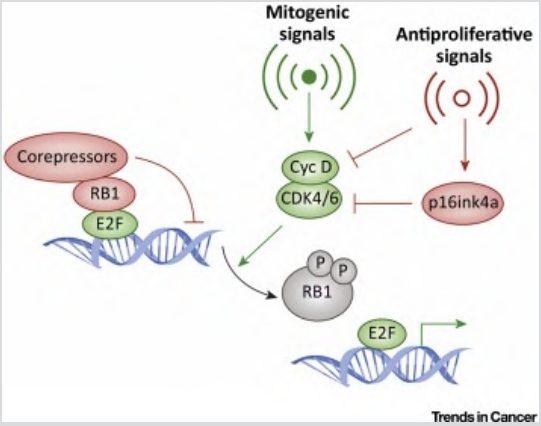
Thus, mutations in the p53 gene significantly lowers tumor suppression. People with Li-Fraumeni syndrome, a condition in which only one functional copy of p53 is inherited, are much more prone to develop cancers in their early adult years. Mutagens (chemicals, radiation, or viruses) can also harm p53 in cells, increasing the risk that the cell will start to divide uncontrollably. The p53 gene is mutated or deleted in more than 50% of human cancers.

4. RB1

RB1 gene coding for Retinoblastoma protein is the first tumor suppressor gene to be discovered. Rb protein is a nuclear protein present in different phosphorylated forms. It is involved in the regulation of many cellular activities including late G1 restriction point, the DNA damage response checkpoint, cell cycle exit, and differentiation.

Rb protein is phosphorylated at different sites. In normal conditions, hypo or unphosphorylated Rb binds with the E2F transcription factor and inhibits it. E2F is a Transcription factor of genes required in the S phase of the cell cycle. During the G1 phase, Rb protein is hypophosphorylated by the cyclin-CDK4/6 complex and in the late G1 phase it is hyperphosphorylated by the cyclin-CDK2 complex. In its hyperphosphorylated form, Rb dissociates from the E2F complex leading to the activation of E2F, which then leads to the

transcription of genes whose products are used in the S phase of the cell cycle. By this mechanism, the Rb protein regulates the entry of cells in the S phase. But in its mutated form, the Rb protein doesn't bind to the E2F transcription factor hence E2F always remains active so there is no regulation of G1/S transition as a result cells divide faster which then leads to cancer.



(Source:Knudsen et al, Tends in Cancer, 2019.)

Ms. Ojaswi Singh, Mr. Rohit Prajapati and Mr. Tajamul Islam
MS-PhD students, Batch 2022

Sources/References:

- *Bates, S., Phillips, A. C., Clark, P. A., Stott, F., Peters, G., Ludwig, R. L., & Vousden, K. H. (1998, September 10). p14ARF links the tumor suppressors RB and p53 - Nature*
- *Bell, S., Klein, C., Müller, L., Hansen, S., & Buchner, J. (2003, January 1). p53 contains large unstructured regions in its native state.*
- *Strachan, T., & Read, A. (2010, April 2). Human Molecular Genetics. Garland Science.*
- *Vogelstein, B., Lane, D., & Levine, A. J. (2000, November 16). Surfing the p53 network - Nature. Nature*
- *Narasimha, Kaulich, & Shapiro. (2014, June 4). Cyclin D activates the Rb tumor suppressor by mono-phosphorylation - PubMed*
- *Du, W., & Searle, J. S. (n.d.). The Rb Pathway and Cancer Therapeutics | Bentham Science*
- *Lee EY, Muller WJ. Oncogenes and tumor suppressor genes. Cold Spring Harb Perspect Biol. 2010 Oct;2(10):a003236. doi: 10.1101/cshperspect.a003236. Epub 2010 Aug 18. PMID: 20719876; PMCID: PMC2944361.*
- *Goodsell DS. The molecular perspective: the ras oncogene. Oncologist. 1999;4(3):263-4. PMID: 10394594.*
- *Ojeda L, Gao J, Hooten KG, Wang E, Thonhoff JR, Dunn TJ, Gao T, Wu P. Critical role of PI3K/Akt/GSK3β in motoneuron specification from human neural stem cells in response to FGF2 and EGF. PLoS One. 2011;6(8):e23414. doi: 10.1371/journal.pone.0023414. Epub 2011 Aug 24. PMID: 21887250; PMCID: PMC3160859.*

Personalized medicine for cancer

Concept of personalized medicine

We all are aware that the cases of cancer are increasing day by day but the progress in the field of treatment is very slow due to the pathological methods of treatment. In this scenario, a new form of medicine has become popular in recent years known as Personalized medicine. In this system, the information regarding the person's genetic, protein, and metabolic profile are taken into account for the prevention, diagnosis, and treatment of disease. Information regarding a person's tumor is based on the detection of specific markers which helps in the early diagnosis and treatment of cancer even before any pathological symptoms develop. Hence molecular diagnosis helps in the early detection of cancer.

Need for personalized medicine in the treatment of cancer

Mutations in the genetic setup of a person lead to cancer. These mutations may be hereditary or acquired by a person due to various factors such as environmental pollution, infections by certain pathogens, consumption of junk foods, smoking, alcohol consumption, etc. Like different cells may have the same DNA but varying genetic expression, in the same way, the expression of genes varies in different tumors among different individuals. In contrast to traditional medical care which is largely based on pathological symptoms and epidemiological studies, in personalized medicine, a person's genomic and pharmacogenomic profile as well as medical history is taken into account before the treatment process starts. This is because certain genes may respond during treatment by metabolizing various drugs. This may result in toxic by-products. Hence genetic information is very much needed to reduce the toxicity of drugs. Therefore in conclusion we can say that personalized medicine is a targeted therapy, in which information about the mutations and the metabolic pathway leading to cancer are needed. The main aim of personalized medicine is to cure cancer with minimal or no toxicity by using the right drug for the right person at right time.

Cancer is not a single disease. there are many molecularly distinct subtypes of various common cancers. So we need different therapeutic approaches for each subtype.Personalised medicine is an emerging approach in cancer treatments in which an individual's characteristics, genetic profile, deit etc guide theraputical decisions, aiming for the precise treatment for the right patient at the right time. personalized medicines are designed to provide "precision therapies," targete a specific molecular defect.

Breast cancer

In 20–25% of patients with breast cancer the oncogene HER2 is overexpresse. HER2 involved in cell proliferation.An well-known personalised medicine trastuzumab, a humanised IgG1 monoclonal antibody is used in breast cancer patients. HER2 overexpresse patients showed reduction in mortality rate when treated with trastuzuma.

Cetuximab in colorectal cancer (CRC)

The epidermal growth factor receptor (EGFR) is overexpressed in many epithelial cancers, causing in dysregulated cell proliferation and an malignant phenotype. So EGFR inhibition will be a promising therapeutic strategy in personalised medicine research. Cetuximab, a monoclonal antibody against EGFR, has used in patients with CRC expressing wild-type KRAS, a gene for downstream effector of EGFR involved in intracellular signalling.

Tyrosine kinase inhibitors in chronic myeloid leukaemia

In chronic myeloid leukaemia (CML),tumourigenes promotes deu to a reciprocal translocation between the long arms of chromosome 9 and 22, resulting an expression of a BCR-ABL fusion oncoprotein with constitutive tyrosine kinase (TK) activity.The TK inhibitor (TKI) imatinib is used in many patients. And it shows very promising results transforming CML into a manageable chronic disease requiring regular monitoring.

Malignant melanomas

66% of malignant melanomas have a BRAF oncogene mutations, Causing a single amino acid substitution, V600E, resulting in increased disease severity and decreased response to present cytotoxic chemotherapy. vemurafenib, a potent and selective Raf inhibitor is used. It shows reduction in the relative risk of mortality by sixty three percent and the risk of death or disease progression by 74%.

Poly(ADP-ribose) polymerase inhibitors

Many cancer patients carry the BRCA1 or BRCA2 mutations. BRCA mutant cells are unable to homologous recombination DNA repair mechanisms.However, base-excision DNA repair mechanisms rescue tumour cell from apoptotic death following DNA-damaging cancer treatments. poly(ADP-ribose) polymerase (PARP) inhibitors Olaparib,block base-excision repair, causing tumour cell death in BRCA deficient cells and normal cells cervive ,achieving selectivty cytotoxicity.

Ms. Samanwita Ghosh and Mr. Subhasis Roy
MS-PhD students, Batch 2022

Sources/References:

- *www.ncbi.nlm.nih.gov*
- *www.cancer.gov*

Peto's paradox

PETO'S PARADOX: The baffling realization that large animals have much less cancer than they should. Scientists think there are two main ways of explaining the paradox; evolution and hyper tumors.

Richard Peto (Peto's Paradox) epidemiologist studied how tumors form in mice and established the relationship between time and cancer. Cancer is a creepy and mysterious thing. Large animals seem to be immune to cancer!, which doesn't make any sense, the bigger a being, the more the cancer. Our cells are made out of hundreds of millions of protein robots. Guided by chemical reactions, they create, dismantle structures, sustain a metabolism to gain energy, or make almost perfect copies of the same. They are complex biochemical networks, intertwined and stacked on top of each other. Most of them are comprehended by the human mind and yet they function perfectly until they don't.

With billions of trillions of reactions happening in thousands of networks, the question is not if something will go wrong, but when?. Tiny mistakes add up until the grandiose machinery gets corrupted. To prevent this from getting out of hand, our cells have 'kill switches' that make them commit suicide. But these kill switches are not infallible. If they fail, a cell can turn into a cancer cell. Most of them are slain by the immune system very quickly. But this is a numbers game. Given enough time, a cell would accrue enough mistakes, slip by unnoticed and begin making more of itself. All animals have to deal with this problem. In general, the cells of different animals are the same size. The cells of a mouse aren't smaller than humans. It just has fewer cells in total and a shorter lifespan. Fewer cells and a short life means a lower chance of things going wrong or cells mutating.

Humans live about 50 times longer and have 3,000 times more cells than mice, yet the rate of cancer is basically the same in humans and in mice. Blue whales with about 3,000 times more cells than humans don't seem to get cancer!

Evolution

As multicellular beings developed 600 million years ago, animals became bigger and bigger. Which added more and more cells and hencemore and more chances that cells could be corrupted. So collectively cells had to invest in better and better cancer defenses.

The cells that donot have defense died out, however, cancer doesn't just happen. It's a process that involves many individual mistakes and mutations in several specific genes within the same cell. These genes are called proto-oncogenes and when they mutate it's bad news! For example with the right mutation, a cell will lose its ability to kill itself. Another mutation and it will develop the ability to hide. Another and it will send out calls for resources. Another one and it will multiply quickly. These oncogenes have an antagonist though; tumor suppressor genes. They prevent these critical mutations from happening or order the cell to kill itself if they decide it's beyond repair.

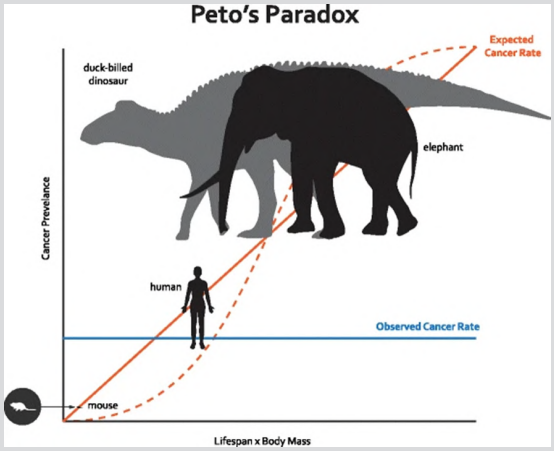
It turns out that large animals have an increased number of them. Because of this, elephant cells require more mutations than mice cells to develop a tumor. They are not immune but more resilient. This adaptation probably comes with a cost in some form but researchers still aren't sure what it is. Maybe tumor suppressors make elephants age quicker later in life or slow down how quickly injuries heal. We don't know yet.
But the solution to the paradox may actually be something different.

"Hyper Tumors"

Hypertumors are named after hyperparasites: the parasites of parasites. Hyper Tumors are tumors of tumors. Cancer can be thought of as a process of breakdown in cooperation. Normally, cells work together to form structures like organs, tissue or elements of the immune system. But cancer cells are selfish and only work for their own short-term benefit. When they're successful, they form tumors; huge cancer collectives can be very hard to kill. Though making a tumor is hard work. Millions or billions of cancer cells multiply rapidly,

which requires a lot of resources and energy. The amount of nutrients they can steal from the body becomes the limiting factor for growth. So the tumor cells trick the body to build new blood vessels directly to the tumor, to feed the thing killing it. And here, the nature of cancer cells may become their own undoing. Cancer cells are inherently unstable and so they can continue to mutate. Some of them are faster than their buddies. If they do this for a while, at some point one of the copies of the copies of the original cancer cell might suddenly think of itself as an individual again and stop cooperating. Which means just like the body, the original tumor suddenly becomes an enemy, fighting for the same scarce of nutrients and resources.

The newly mutated cells can create a hypertumor. Instead of helping, they cut off the blood supply to their former buddies, which will starve and kill the original cancer cells. Cancer is killing cancer! This process can repeat over and over, and this may prevent cancer from becoming a problem for a large organism. It is possible that large animals have more of these hyper tumors than we realize, they might just not become big enough to notice, which makes sense that, a two-gram tumor is 10% of a mouse's body weight, while It's less than 0.002% of a human and 0.000002% of a blue whale. In all three, tumors require the same number of cell divisions and have the same number of cells. An old blue whale might be filled with tiny cancers. There are other proposed solutions to Peto's paradox, such as different metabolic rates or different cellular architecture. But right now, we just don't know! Scientists are working on the problem. Figuring out how large animals are so resilient to one of the deadliest diseases we know, could open the path to new therapies and treatments. Cancer has always been a challenge. We are finally beginning to understand it and develop the therapy to prevent and to overcome.



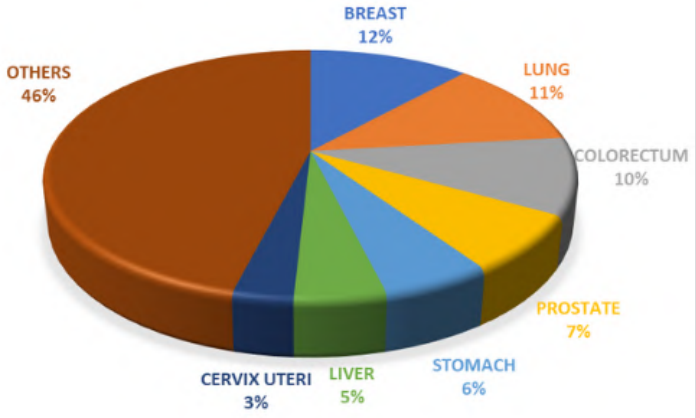
An illustration of Peto's Paradox. Cancer is a disease of uncontrolled cell growth and division. The risk of developing cancer increases with age. The solid red line indicates a linear relationship between cancer rate and (body mass) (lifespan) and the dashed red line represents an approximation of the expected cancer rate assuming a model describing the probability of an individual developing colorectal cancer after a given number of cell divisions.*

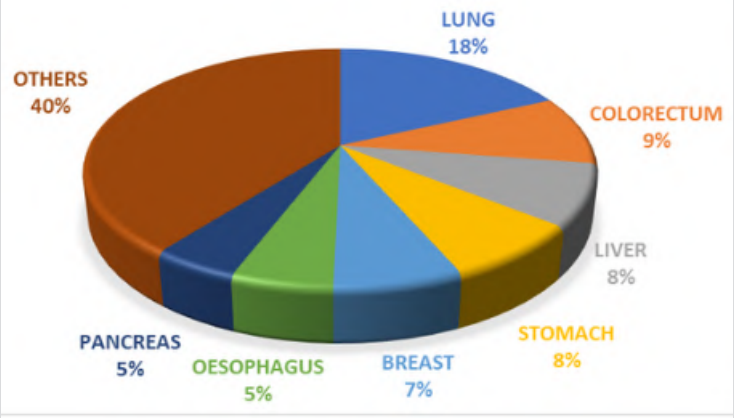
Mr. Rohit Prajapati
MS–PhD student, Batch 2022

Sources/References:

- *Tollis, M., Boddy, A.M. & Maley, C.C. Peto's Paradox: how has evolution solved the problem of cancer prevention?. BMC Biol 15, 60 (2017). https://doi.org/10.1186/s12915-017-0401-7*
- *Nagy JD, Victor EM, Cropper JH. Why don't all whales have cancer? A novel hypothesis resolving Peto's paradox. Integr Comp Biol. 2007 Aug;47(2):317-28. doi: 10.1093/icb/icm062. Epub 2007 Jun 28. PMID: 21672841.*

Cancer Statistics





Incidence

Estimated number of new cases in 2020, both sexes, all ages: 19,292,789 Worldwide, breast and lung cancer accounts for 2.26 million and 2.21 million cases, respectively. Other common cancers are the colorectum, prostate, and stomach. Each year, approximately 400,000 children develop cancer.

Mortality

Estimated number of deaths in 2020, both sexes, all ages: 9958133 Cancer is a leading cause of death in the world. It accounted for nearly one in six deaths in 2020. Lung cancer has the highest mortality rate, killing nearly 1.80 million people.

As per data published by GLOBOCAN 2020, India is placed third, after China and USA, accounting for nearly 7% of new cases of cancer.

Estimated number of people with Cancer: 2.7 million

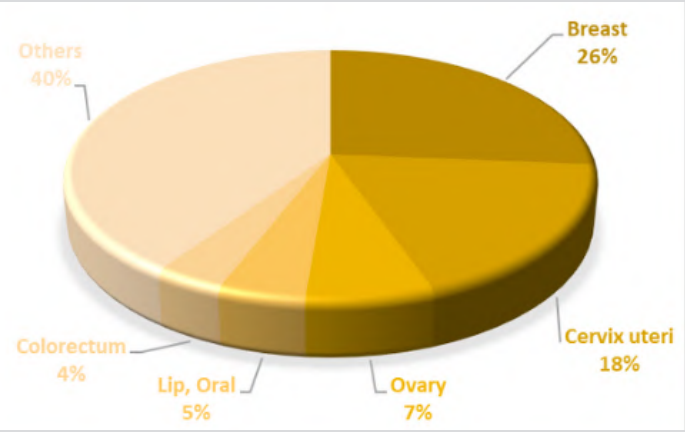
New cancer patients registered: 13.9 lakhs

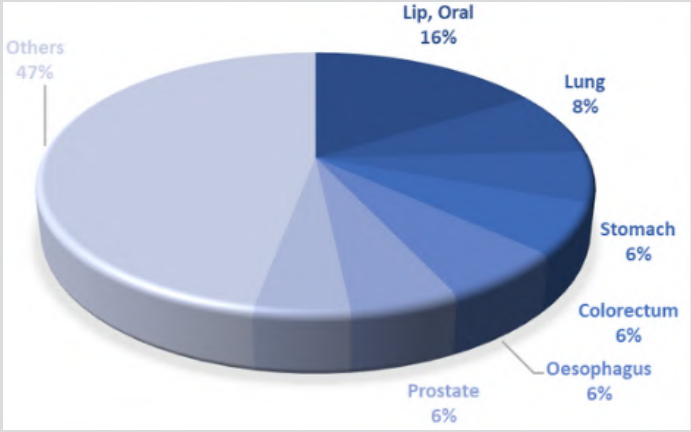
Total deaths: 851,678

Second highest after China

Total deaths Men: 438,297

Total deaths Women: 413,381





Breast Cancer is the most common cancer in women in India (26%).

New cases registered: 178,361 Total Deaths: 90,408

Cervical cancer is the second most common in women. One woman dies of cervical cancer every 8 minutes in India

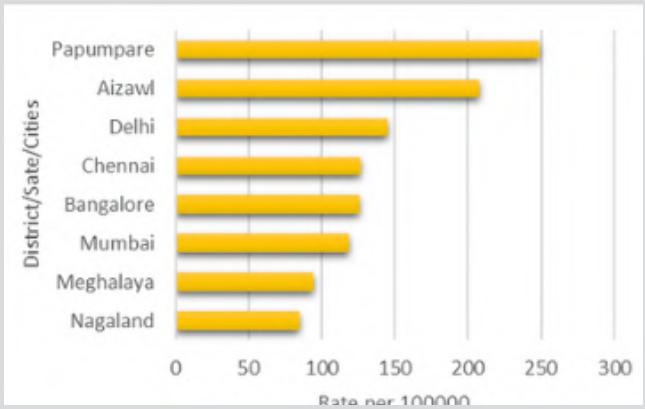
Lip and Oral cancer is the most frequent cancer in India amongst men (Around 16%) and fourth most common among Indian women.

New cases registered: 135,929 Total Deaths: 75,290

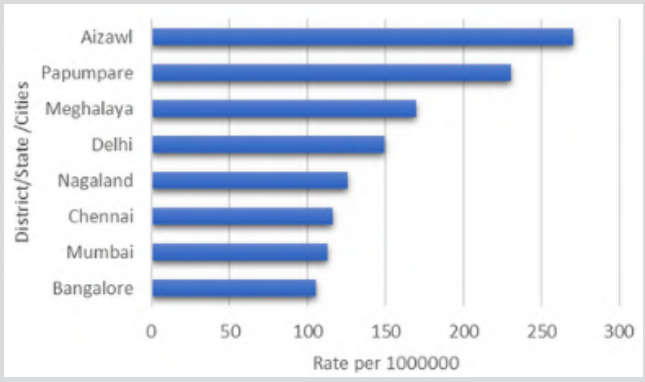
Approximately, 80-90% of oral cancers are directly attributable to tobacco use.

Cancer Statistics

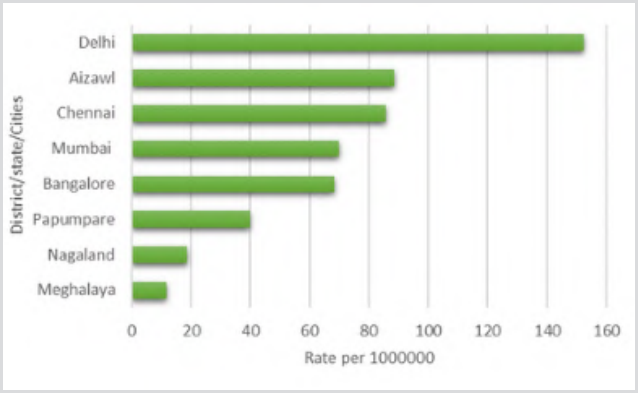
Comparison of Age Adjusted Incidence Rates (AARs) per million of all types of Cancers of several sites of India



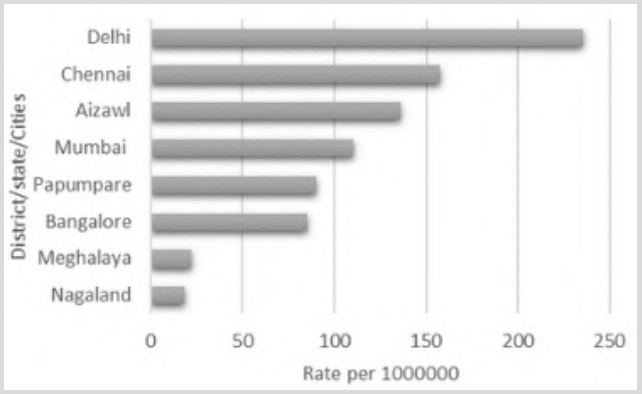
Females



Males



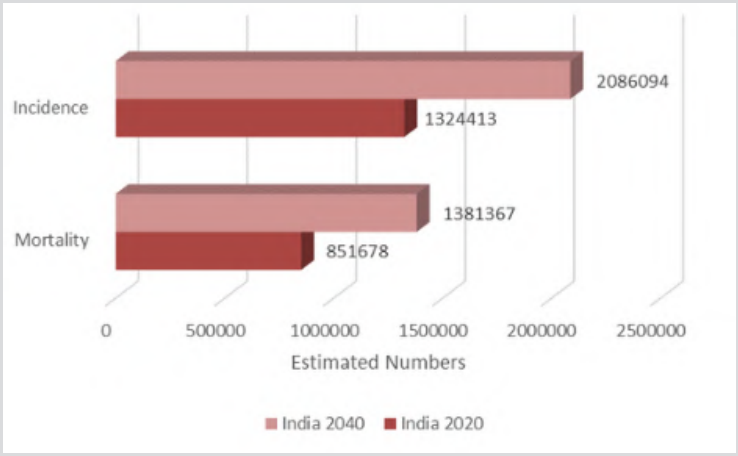
Girls (0-14)

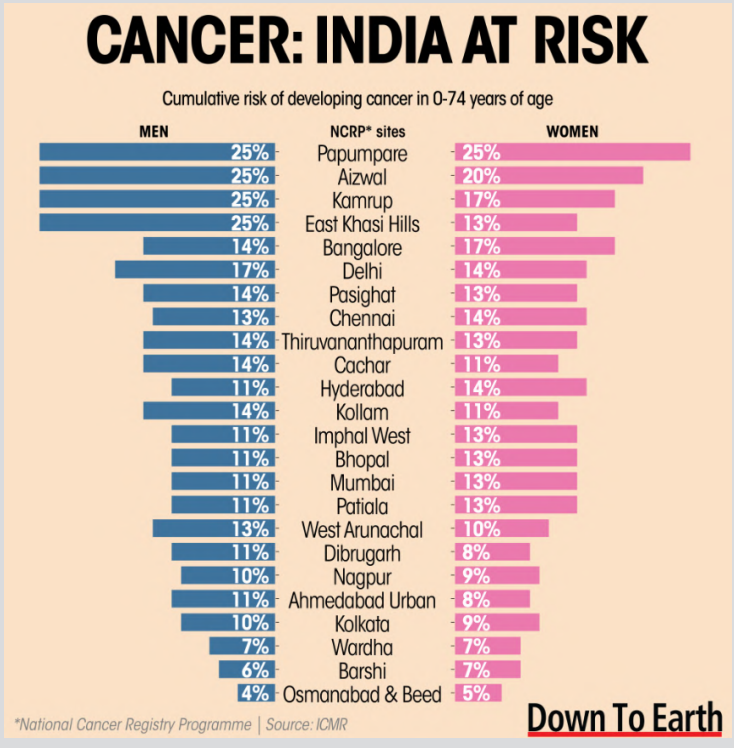


Boys (0-14)

CANCER TOMORROW

The projected cancer burden for 2021 in India was 26.7 million DALYs and is AMI expected to increase to 29.8 million in 2025



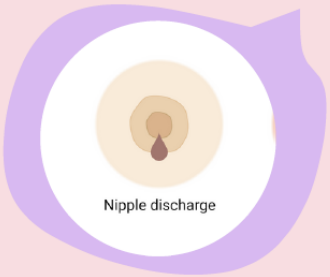


(Source:National Cancer Registry Programme, Indian Council For Medical Research)

Ms.Neha Guliya, Mr. Abhishek Raj, Mr. Aryan and Mr. Shirish Kumar Gangber
MS-PhD students, Batch 2022

Warning Signs of Breast Tumour

Considering the low level of awareness in men and women regarding the warning signs of Breast cancer, the focus of this article is to create BREAST AWARENESS. People should be sensitized to recognize any unusual changes in their breasts and report to health care providers at the earliest. According to the National Breast Cancer Foundation, when breast cancer is detected early and hasn't spread in the body, the 5-year relative survival rate is 99 percent.

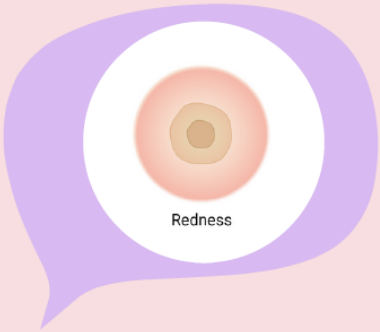


Nipple discharge

Nipple discharge can be an early sign of breast cancer. isolated discharge particularly if not blood stained are usually ignored by patients. Diffusely spreading intraductal carcinomas having no palpable breast mass usually manifest as pathological Nipple discharge.

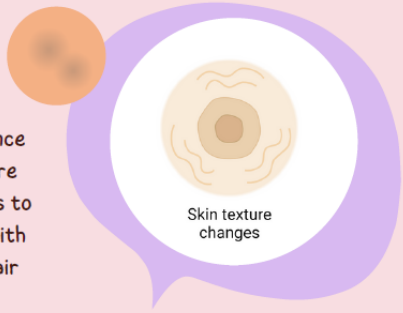
Redness

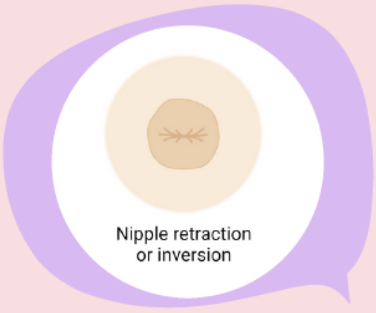
In inflammation breast cancer. when such cancer cells block the lymphatic vessels in skin covering the breast, thus causes characteristic red, swollen appearance. it is associated with unusual warmth of affected breast.



Skin texture changes

Presence of dimpling can indicate presence of tumor below the surface. skin texture called as "peau d'orange"- the skin begins to resemble uneven surface of an orange with swelling and indentation of pores and hair follicles. sometimes it comes with associated edemas.





Nipple retraction or inversion

It could be a natural variation of nipple type when one is born with it. the nipple that turns inward instead outward, except when stimulated.

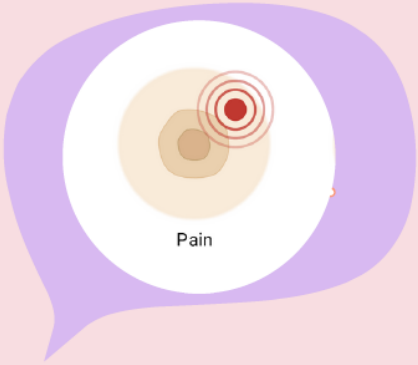
Most effective screening for breast cancer early detection includes SelfExams. people particularly women should be familiar with how their breasts should look and feel. Thus it is important that women of all ages regularly perform their own breast exams and follow up with health care provider as soon as possible.

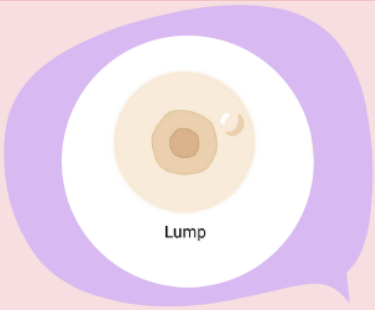
Swelling

Red marks that appear on our skin could be appeared by using inappropriate skincare products. It might be trivial, but the red spots usually occur because the ingredients are too hard for the skin, so it causes a sunburn effect.

Pain

There are a number of harmless causes for breast pain primarily related with hormone levels in women. Rarely does a breast tumor causes pain, but generally cancerous tumors are not reported as painful



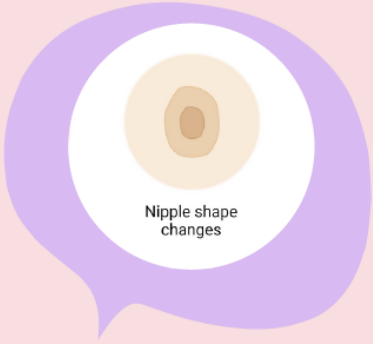


Lump

Lumps could be cysts, Fibrocystic breast changes, Fibroadenomas, Injuries and Infections or Breast cancer. Breast cancer is associated with a lump that is painless, hard, irregularly shaped and different from surrounding breast tissue.

Nipple shape changes

Normal hormonal shifts, pregnancy or breast feeding are associated with temporary changes in changes in nipple color, size and texture changes. Any change in nipple position, such as being pulled in or pointing differently are the changes to look out for.



Ms. Kusuma B
PhD (Integrated) student, Batch 2021

FRESH OUT OF THE LAB

Orai3 is a novel regulator of pancreatic cancer metastasis

Dr. Rajender K. Motiani & Ms. Samriddhi Arora
Laboratory of Calciomics and Systemic Pathophysiology, Regional Centre for Biotechnology

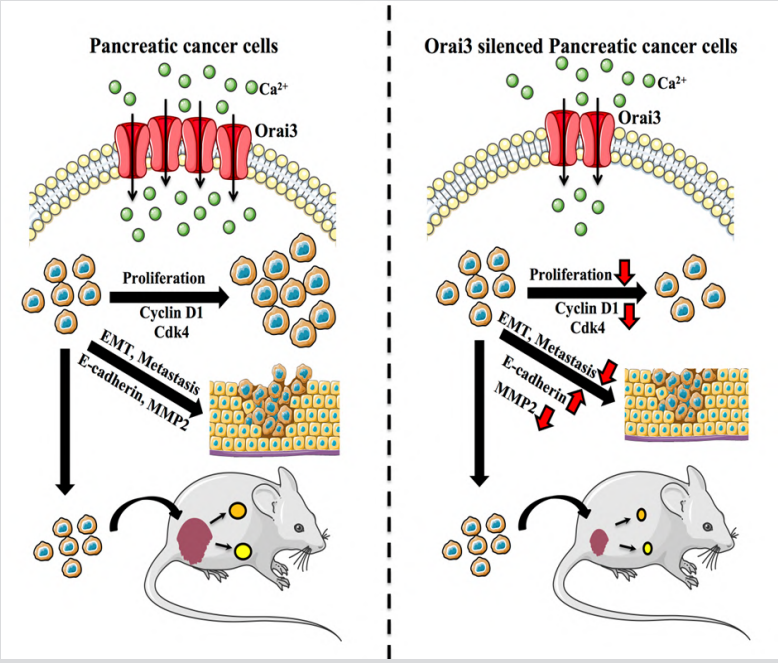


Figure 1: Diagrammatic illustration of the work (Adapted from Arora et al. Cancers, 2021)

Pancreatic cancer (PC) is one of the most lethal forms of cancers with 5-year mean survival rate of less than 10%. Most of the PC associated deaths are due to metastasis to secondary sites. Calcium (Ca2+) signaling plays a critical role in regulating hallmarks of cancer progression including cell proliferation, migration and apoptotic resistance. In our recently published study, we demonstrated that a highly Ca2+ selective plasma membrane channel "Orai3" is overexpressed in PC and is associated with poor prognosis in PC patients (Arora et al. Cancers 2021). We performed extensive bioinformatic analysis of publicly available datasets and observed that Orai3 expression is inversely associated with the mean survival time of PC patients. Orai3 expression analysis in a battery of PC cell lines corroborated its differential expression profile. We then carried out thorough Ca2+ imaging experiments in multiple PC cell lines and found that Orai3 forms a functional Ca2+ influx channel in PC cells. Our in vitro functional assays showed that Orai3 regulates PC cell cycle progression, apoptosis and migration. Most importantly, our in vivo mice xenograft studies demonstrated a critical role of Orai3 in PC tumor growth and secondary metastasis (please refer to Figure 1 for the diagrammatic summary). Mechanistically, we found that Orai3 controls G1 phase progression, matrix metalloproteinase expression and epithelial-mesenchymal transition in PC cells. Therefore, our study for the first time reported that Orai3 drives aggressive phenotypes of PC cells, i.e., migration in vitro and metastasis in vivo. Considering that Orai3 overexpression leads to poor prognosis in PC patients, it appears to be a highly attractive therapeutic target. Future studies aimed at understanding precise spatio-temporal role of Orai3 in pancreatic cancer progression would eventually establish Orai3 as a therapeutic target for managing PC metastasis, which may lead to better prognosis.

Reference: Arora S, Tanwar J, Sharma N, Saurav S and Motiani RK (2021). Orai3 regulates pancreatic cancer metastasis by encoding a functional store operated calcium entry channel. Cancers 2021 Nov 25;13(23):5937.

CREDITS

Editorial Page by Dr. Rajender K Motiani

Editing and Magazine design by Ms. Anushka Das & Ms. Sanjana Singh

Coverpage design by Ms. Neha Guliya & Mr. Abhishek Raj

Science Club Members : Prof. Prasenjit Guchhait, Dr. Ramu S Vemanna, Dr. Rajender K. Motiani, Dr. Prashant Pawar, Dr. Anil Thakur, Dr. Masum Saini, Dr. Nidhi Sharma, Mr. Ramesh Chandiramouli, Ms. Sanjana Singh, Mr. Abhay Deep Pandey, Ms. Anushka Das, Mr. Shivam Aggarwal

scienceclub@rcb.res.in