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Cancer Biology-Causes & Biomarkers of Cancer

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Abstract

Cancer is a disease of the cell **[1]**. This rather simple statement implies an enormous complexity when attempting to identify efficacious anticancer agents. One of the major issues associated with anticancer research is that traditional target-directed strategies are confronted with the essentiality of the function of the target in healthy cells. Inevitably, targeting proteins that have essential functions are likely to lead to chemical entities with narrow therapeutic windows and significant toxic effects. An additional challenge is the unstable epigenetic and genetic status of cancer cells, undergoing multiple mutations, gene copy alterations, and chromosomal abnormalities that have a direct impact on the efficacy of anticancer agents at different stages of the disease **[2].** All these aspects make cancer drug discovery extremely difficult and have led to poor clinical approval success rates compared to other therapeutic areas.

Therefore, individualized therapy is paramount for improving of cancer treatment. The development of rationalized and individualized therapy is reliant on the identification of the specific biomarkers, validation of the biomarkers to identify the therapeutic targets, and drug development against the identified.

A Cancer marker or tumor marker is a biomarker found in blood, pee, or body tissues that can be raised by the proximity of at least one sorts of development. There are different tumor markers, each illustrative of a particular alignment. In addition to their use in cancer medicine, biomarkers are often used throughout the cancer drug discovery process. For instance, in the 1960s, researchers discovered the majority of patients with chronic myelogenous leukemia possessed a particular genetic abnormality.

Biomarkers are molecules that indicate normal or abnormal process taking place in your body and may be a sign of an underlying condition or disease. Various types of molecules, such as DNA (genes), proteins or hormones, can serve as biomarkers, since they all indicate something about your health. A biomarker, or biological marker, generally refers to a measurable indicator of some biological state or condition. The term is also occasionally used to refer to a substance whose detection indicates the presence of a living organism. Biomarkers are often measured and evaluated to examine normal biological processes, Biomarkers are distinct biological indicators (cellular, biochemical or molecular) of a process, event or condition that can be measured reliably in tissues, cells or fluids, and can be used to detect early changes in a patient's health. Some examples of biomarker include blood cholesterol a well-known biomarker of risk for, Biomarker is short for biological marker, and is used as an indication that a biological process in the body has happened or is ongoing. While some biomarkers are used to show that the body has been exposed to a chemical toxin or other environmental impact - most associate biomarkers with medicine. A biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease. A biomarker may be used to see how well the body responds to a treatment for a disease or condition. NIH Biomarkers Definitions Working Group: "A characteristic that is objectively measured and evaluated as an indicator of normal biological processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention." World Health Organization: "Any substance, structure, or process that. Biomarkers are characteristics of the body that you can measure. So your blood pressure is actually a biomarker. Biomarkers are very important to medicine in general. We're all used to going to the doctor and getting all our test results, right, and even imaging x-ray results or CAT scans.

1. Keywords: Biomarkers; Cancer Cells; Cancer Therapy; Cancer Targets

2. Introduction

Cancer is a gathering of sicknesses including irregular cell development with the possibility to attack or spread to different parts of the body. These stand out from benevolent tumors, which don't spread to different parts of the body. Possible signs and side effects incorporate a bump, strange dying, delayed hack, unexplained weight reduction, and an adjustment in gut movements**.** Tobacco use is the cause of about 22% of cancer deaths. Another 10% are due to obesity, poor diet, lack of physical activity, and excessive drinking of alcohol. Other factors include certain infections, exposure to ionizing radiation and environmental pollutants. In the developing world, 15% of cancers are due to infections such as Helicobacter pylori, hepatitis B, hepatitis C, human papillomavirus infection, Epstein–Barr virus and human immunodeficiency virus. , Colorectal cancer, Non-Hodgkin lymphoma, Prostate cancer, Lung cancer, stomach cancer. Cancer starts when cells change abnormally. Cancer is when abnormal cells divide in an uncontrolled way. Some cancers may eventually spread into other tissues. There are more than 200 different types of cancer. 1 in 2 people in the UK will get cancer in their lifetime. Thanks to research many people are cured **(Figure 1).**

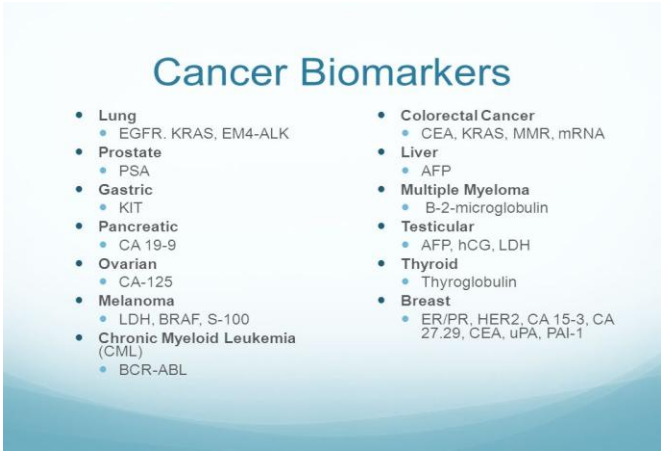

Figure 1: Cancer Biomarkers.

Cancer grows as cells multiply over and over. Cancer starts when gene changes make one cell or a few cells begin to grow and multiply too much. This may cause a growth called a tumor. Some cancers can spread to other parts of the body. A primary tumor is the name for where a cancer starts. Cancer can sometimes spread to other parts of the body – this is called a secondary tumor or a metastasis. Cancer and its treatments can affect body systems, such as the blood circulation, lymphatic and immune systems, and the hormone system. Most cancers start due to gene changes that happen over a person's lifetime. More rarely cancers start due to inherited faulty genes passed down in families. Genes, DNA and cancer Genes and inherited cancer risk. Cancer can sometimes come back. Many cancers are cured. But in some people cancer can return. Some cancers can't be cured but treatment is often able to control them for some years. Cancers are divided into groups according to the type of cell they start from. They include, Carcinomas, Lymphomas, Leukaemias, Brain tumors, Sarcomas. Stages and grading of cancer. Staging and grading give an idea of how quickly a cancer may grow and which treatments may work best. The stage of a cancer means how big it is and whether it has spread. Grading looks at how abnormal the cancer cells **[3].**

3. Material and Methods

Cancer biomarkers can be DNA, mRNA, proteins, metabolites, or processes such as apoptosis, angiogenesis or proliferation. The markers are produced either by the tumor itself or by other tissues, in response to the presence of cancer or other associated conditions, such as inflammation. Such biomarkers can be found in a variety of fluids, tissues and cell lines. "A biological molecule found in blood, other body fluids, or tissues that is a sign of a normal or abnormal process, or of a condition or disease. A biomarker may be used to see how well the body responds to a treatment for a disease or condition. Also called molecular marker and signature molecule. Diagnostic (screening) biomarker, Prognostic biomarker, Stratification (predictive) biomarker. Biomarkers play a key role in the diagnosis and management of patients with cancer, and are important for fulfilling the promise of precision medicine in oncology. However, although numerous biomarkers have been shown to have clinical validity, many have not undergone rigorous testing to demonstrate clinical utility so that they can be appropriately incorporated into clinical care. This review article highlights the characteristics of a good biomarker and the steps required to demonstrate clinical utility, and gives examples of both successful established biomarkers and promising new tissue-based and circulating biomarkers on the horizon**.** Circulating tumor cell, circulating tumor DNA, clinical utility **[4] (Figure 2).**

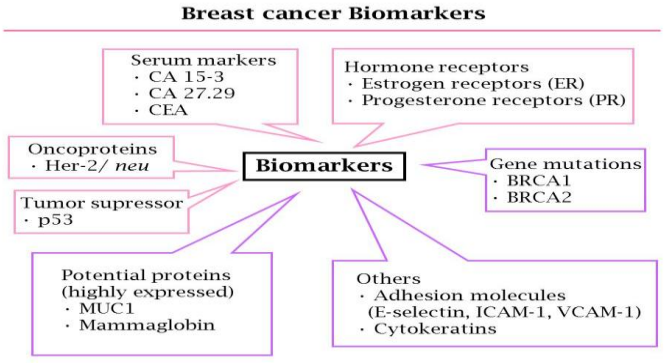

Figure 2: Breast cancer biomarkers.

A Biomarker is the organic particle found in blood, other body liquids, or tissues that is an indication of a typical or anomalous process, or of a condition or disease. A biomarker

might be utilized to perceive how well the body reacts to a treatment for a malady or condition. Likewise called molecular marker and mark particle. Cancer biomarkers are arranged by their diverse capacities: Biomarkers that Trigger Cells to Grow and Multiply Abnormally, Biomarkers That Support a Treatment's Cellular or Molecular Action, Biomarkers That Disrupt a Treatment's Cellular or Molecular Action, Detecting and Measuring Biomarkers to Develop a Personalized Anticancer Treatment Plan. Genomic biomarker, Transcriptomic biomarker, Metabolomics biomarker, Drug activity markers, Imaging biomarker, Surgical oncology is the branch of surgery applied to oncology; it focuses on the surgical management of tumors, especially cancerous tumors. Surgery is used to diagnose, stage and treat cancer, and certain cancer-related symptoms. Surgeons have performed thousands of procedures and will discuss appropriate surgical options that meet your individual needs. Childhood cancers are different from adult cancers. The Advanced Surgical Recovery Program (ASURE) is designed to help patients recover from surgery more quickly and with fewer complications. Lymphadenectomy. ASURE is intended to improve surgical outcomes and enhance the patient experience before, during and after surgery, while also reducing patients' overall hospital stay. Pancreaticoduodenectomy, Thyroidectomy, Appendix surgery.

Childhood growth (otherwise called pediatric malignancy) is disease in a kid. Pediatric oncology is the branch of medication worried about the determination and treatment of disease in kids. A pediatric oncologist spends significant time in research and treatment for growths that create in babies, little children, youngsters, youths and adolescents. This is one reason why there is a requirement for pediatric oncologists who are prepared in treating the two youngsters and growth. Numerous pediatric oncologists additionally represent considerable authority in hematology, which is the investigation and treatment of sicknesses identified with the blood. These specialists are in some cases alluded to as pediatric oncologists/hematologists, Neuroblastoma, Wilms tumour, Pediatric Neuro oncologist, Hepatoblastoma and hepatocellular carcinoma **[5].**

A haematologist-oncologist is a physician who specializes in the diagnosis, treatment and/or prevention of blood diseases and cancers such as iron-deficiency anemia, hemophilia, sickle-cell disease, leukemia and lymphoma. This physician is trained in haematology the study of blood and oncology the study of cancer. Hematologist-oncologists do not usually treat operable cancers such as prostate cancer, but specialize in treating blood cancers, such as Hodgkins and non-Hodgkins lymphomas, leukemias and multiple myelomas., Haemophilia, Bone marrow disease, Anticoagulation therapy, Blood transfusion.

Breast cancer begins in the cells of the breast. A harmful tumor is a gathering of growth cells that can develop into and annihilate close-by tissue. It can likewise metastasize to different parts of the body. Cells in the breast some of the time change and never again develop or act ordinarily. These progressions may prompt non-malignant bosom conditions, for example, atypical hyperplasia and sores. They can likewise prompt non-carcinogenic tumors, for example, intraductal papillomas. Breast cancer screening, Breast reconstruction, Lobular carcinoma, Abortion breast cancer hypothesis.

Atomic Cancer Therapeutics will concentrate on fundamental research that has suggestions for growth therapeutics in the accompanying zones: Experimental Cancer Therapeutics, Identification of Molecular Targets, Targets for Chemoprevention, New Models, Cancer Chemistry and Drug Discovery, Molecular and Cellular Pharmacology, Molecular Classification of Tumors, and Bioinformatics and Computational Molecular Biology. The diary gives a production discussion to these rising orders that is centered particularly on disease look into. Papers are stringently looked into and just those that report aftereffects of novel, opportune, and noteworthy research and meet exclusive expectations of logical legitimacy will be acknowledged for production. Molecular cancer Therapeutics, Neurotherapeutics, Pharmacology and clinical Toxicology, Therapeutics, Bimolecular and Therapeutics. Cancer epigenetics is the investigation of epigenetic alterations to the DNA of malignancy cells that don't include an adjustment in the nucleotide arrangement. Epigenetic changes might be similarly as vital, or much more critical, than hereditary changes in a cell's change to malignancy. A variety of compounds are considered as epigenetic carcinogens such as arsenite, diethylstilbestrol, hexachlorobenzene and nickel compounds. They result in an increased incidence of tumors, but they do not show mutagen activity. DNA binding proteins, Histone modification, Genetic mutations, Tumour suppressor gene tests, Bone marrow aspiration. There are several methods of diagnosing cancer. With advances in technologies that understand cancers better, there is a rise of number of diagnostic tools that can help detect cancers. Once suspected diagnosis is usually made by pathologists and oncopathologists and imaging radiologists. Diagnostic testing involves tests and procedures to confirm the presence of disease and identify the correct tumor type, location, extent and stage. Diagnostics plays an important role throughout your cancer treatment it includes before treatment, during your treatment, after you complete treatment. Biopsy, Sentinel node biopsy, Endoscopy, Blood the expulsion of cells or tissues for examination by a pathologist. The pathologist may ponder the tissue under a magnifying lens or perform different tests on the cells or tissue. There are a wide range of sorts of biopsy techniques. The most widely recognized sorts include: (1) incisional biopsy, in which just an example of tissue is evacuated; (2) excisional biopsy, in which a whole irregularity or suspicious zone is expelled; and (3) needle biopsy, in which a specimen of tissue or liquid is expelled with a needle. At the point when a wide needle is utilized, the strategy is known as a center biopsy. At the point when a thin needle is utilized, the methodology is known as a fine-needle goal biopsy. Bone

marrow aspiration and biopsy, Endoscopic biopsy, Needle biopsy, Tumor Marker Tests.

Magnetic resonance imaging (MRI) is a scanning procedure that uses strong magnets and radiofrequency pulses to generate signals from the body. These signals are detected by a radio antenna and processed by a computer to create images (or pictures) of the inside of your body. The MRI scanner is generally shaped like a large, covered box with a tunnel passing through it. A table, on which you lie, slides into the tunnel. Both ends of the scanner are open and will not close. The tunnel has lights in it and sometimes a mirror. Real time MRI, Interventional MRI, Medical imaging, NMR applications, diagnostic medicine.

4. Results

Cancer pharmacology **[6]** incorporate investigations of the fundamental mechanism of signal transduction related with cell multiplication and apoptosis, the mechanism of activity of anti-neoplastic specialists, the outline and revelation of new medications, essential components of DNA repair and DNA harm resilience and the advancement of novel techniques for quality treatment. Human cancer cell lines, Genetic manipulation of cancer, Malignant transformation, Cancer cell proliferation **[7] (Figure 3).**

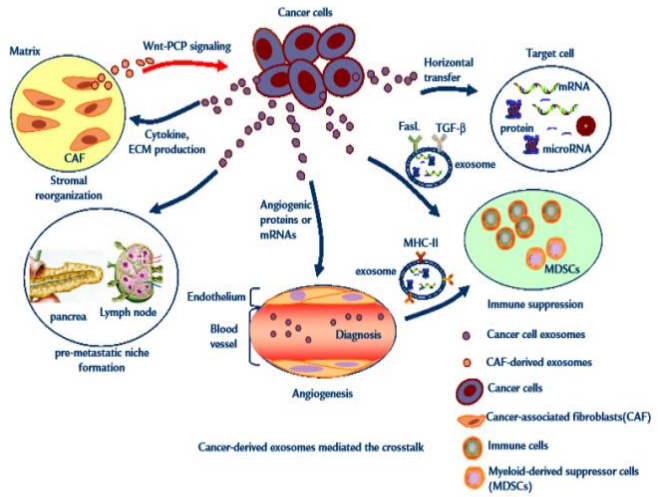

Figure 3: Cancer derived exosomes mediated the cross link.

Tumor is one of the best wellbeing challenges, and a main source of death in each edge of the world. The worldwide market for Cancer drugs is anticipated to develop twice as quickly as that of different pharmaceuticals throughout the following couple of years. Top organizations incorporate Janssen biotech, Takeda oncology, Boehringer ingelheim, Roche, Novartis, Celgene, Johnson and Johnson, and Amgen. The growth business is the most ordinarily profitable business in the USA. It has been seen that, there are 1,665,540 new malignancy cases analyzed and 585,720 growth passing in the US in the year 2014. $6 billion of citizen stores are spun through different government organizations for malignancy explore for the most part as the National Cancer Institute. The NCI states that the restorative expenses of disease mind are $125 billion, with the ascent of 39 percent to $173 billion by the up and coming year that is 2020. The most well-known maxim of the growth business is it utilizes an excessive number of individuals and delivers excessively pay to enable a cure to be found. Cancer drugs, Novartis, Johnson & Johnson, Cancer research, National Cancer Institute.

Cancer **[1]** is a disease caused by genetic changes leading to uncontrolled cell growth and tumour formation. The basic cause of sporadic (non-familial) cancers is DNA damage and genomic instability. A minority of cancers are due to inherited genetic mutations. Most cancers are related to environmental, lifestyle, or behavioural exposures. Cancer is generally not contagious in humans, though it can be caused by oncoviruses and cancer bacteria. The term "environmental", as used by cancer researchers, refers to everything outside the body that interacts with humans. The environment is not limited to the biophysical environment (e.g. exposure to factors such as air pollution or sunlight), but also includes lifestyle and behavioural factors. Over one third of cancer deaths worldwide (and about 75-80% in the United States) is potentially avoidable by reducing exposure to known factors. Common environmental factors that contribute to cancer death include exposure to different chemical and physical agents (tobacco use accounts for 25-30% of cancer deaths), environmental pollutants, diet and obesity (30-35%), infections (15-20%), and radiation (both ionizing and non-ionizing, up to 10%). These factors act, at least partly, by altering the function of genes within cells. Typically many such genetic changes are required before cancer develops. Aging has been repeatedly and consistently regarded as an important aspect to consider when evaluating the risk factors for the development of particular cancers. Many molecular and cellular changes involved in the development of cancer accumulate during the aging process and eventually manifest as cancer.

4.1. Heredity

Although there are over 50 identifiable hereditary forms of cancer, less than 0.3% of the population are carriers of a cancer-related genetic mutation and these make up less than 3-10% of all cancer cases. The vast majority of cancers are non-hereditary ("sporadic cancers"). Hereditary cancers are primarily caused by an inherited genetic defect. A cancer syndrome or family cancer syndrome is a genetic disorder in which inherited genetic mutations in one or more genes predisposes the affected individuals to the development of cancers and May also cause the early onset of these cancers. Although cancer syndromes exhibit an increased risk of cancer, the risk varies. For some of these diseases, cancer is not the primary feature and is a rare consequence **[8].**

Many of these syndromes are caused by mutations in tumour suppressor genes that regulate cell growth. Other common mutations alter the function of DNA repair

genes, oncogenes and genes involved in the production of blood vessels. Certain inherited mutations in the genes BRCA1 and BRCA2 with a more than 75% risk of breast cancer and ovarian cancer. Some of the inherited genetic disorders that can cause colorectal cancer include familial adenomatous polyposis and hereditary non-polyposis colon cancer; however, these represent less than 5% of colon cancer cases. In many cases, genetic testing can be used to identify mutated genes or chromosomes that are passed through generations. Multiple colon polyps within the colon of an individual with familial adenomatous polyposis.

4.2. Cancer Syndromes

Ataxia telangiectasia, Bloom syndrome, BRCA1 & BRCA2,Fanconi anemia, Familial adenomatous polyposis, Hereditary breast and ovarian cancer, Hereditary non-polyposis colon cancer, Li-Fraumeni syndrome, Nevoid basal cell carcinoma syndrome, Von Hippel-Lindau disease, Werner syndrome, Xeroderma pigmentosum.

4.3. Physical and Chemical Agents

Particular substances, known as carcinogens, have been linked to specific types of cancer. Common examples of non-radioactive carcinogens are inhaled asbestos, certain dioxins, and tobacco smoke. Although the public generally associates carcinogenicity with synthetic chemicals, it is equally likely to arise in both natural and synthetic substances. It is estimated that approximately 20,000 cancer deaths and 40,000 new cases of cancer each year in the U.S. are attributable to occupation. Every year, at least 200,000 people die worldwide from cancer related to their workplace. Millions of workers run the risk of developing cancers such as lung cancer and mesothelioma from inhaling asbestos fibers and tobacco smoke, or leukemia from exposure to benzene at their workplaces. Cancer related to one's occupation is believed to represent between 2-20% of all cases. Most cancer deaths caused by occupational risk factors occur in the developed world. Job stress does not appear to be a significant factor at least in lung, colorectal, breast and prostate cancers.

4.4. Smoking

Tobacco smoking is associated with many forms of cancer, and causes 80% of lung cancer. Decades of research has demonstrated the link between tobacco use and cancer in the lung, larynx, head, neck, stomach, bladder, kidney, esophagus and pancreas. There is some evidence suggesting a small increased risk of developing myeloid leukemia, squamous cell sinonasal cancer, liver cancer, colorectal cancer, cancers of the gallbladder, the adrenal gland, the small intestine, and various childhood cancers. Tobacco smoke contains over fifty known carcinogens, including nitrosamines and polycyclic aromatic hydrocarbons. Tobacco is responsible for about one in three of all cancer deaths in the developed world, and about one in five worldwide. Lung cancer death rates in the United States have mirrored smoking patterns, with increases in smoking followed by dramatic increases in lung cancer death rates and, more recently, decreases in smoking rates since the 1950s followed by decreases in lung cancer death rates in men since 1990. However, the numbers of smokers worldwide is still rising, leading to what some organizations have described as the tobacco epidemic [9].

Electronic cigarettes or e-cigarettes are handheld electronic devices that simulate the feeling of tobacco smoking. Daily long-term use of high voltage (5.0 V) electronic cigarettes may generate formaldehyde-forming chemicals at a greater level than smoking, which was determined to be a lifetime cancer risk of approximately 5 to 15 times greater than smoking. However, the overall safety and long-term health effects of electronic cigarettes is still uncertain **[10].**

5. Materials

Some substances cause cancer primarily through their physical, rather than chemical, effects on cells. A prominent example of this is prolonged exposure to asbestos, naturally occurring mineral fibres which are a major cause of mesothelioma, which is a cancer of the serous membrane, usually the serous membrane surrounding the lungs. Other substances in this category, including both naturally occurring and synthetic asbestos-like fibres such as wollastonite, attapulgite, glass wool, and rock wool, are believed to have similar effects. Non-fibrous particulate materials that cause cancer include powdered metallic cobalt and nickel, and crystalline silica (quartz, cristobalite, and tridymite). Usually, physical carcinogens must get inside the body (such as through inhaling tiny pieces) and require years of exposure to develop cancer. Common occupational carcinogens include: arsenic, asbestos, benzene, beryllium, cadmium, chromium, ethylene oxide, nickel, radon, vinyl chloride, radium, plutonium.

5.1. Lifestyle

Many different lifestyle factors contribute to increasing cancer risk. Together, diet and obesity are related to approximately 30-35% of cancer deaths. Dietary recommendations for cancer prevention typically include an emphasis on vegetables, fruit, whole grains, and fish, and avoidance of processed meat, red meat, animal fats, and refined carbohydrates. The evidence to support these dietary changes is not definitive **[6]**.

5.2. Alcohol

Chronic damage due to alcohol consumption can lead to liver cirrhosis (pictured above) and the development of hepatocellular carcinoma, a form of liver cancer **[11].** Alcohol is an example of a chemical carcinogen. The World Health Organization has classified alcohol as a Group 1 carcinogen. In Western Europe 10% of cancers in males and 3% of cancers in females are attributed to alcohol. Worldwide, 3.6% of all cancer cases and 3.5% of cancer deaths are attributable to alcohol. In particular, alcohol use has been shown to increase the risk of developing cancers of the mouth, esophagus, pharynx, larynx, stomach, liver, ovaries, and colon. The main mechanism of cancer development involves increased exposure to acetaldehyde, a carcinogen and breakdown product of ethanol. Other mechanisms have been proposed, including alcohol-related nutritional deficiencies, changes in DNA methylation, and induction of oxidative stress in tissues.

5.3. Diet

Some specific foods have been linked to specific cancers. Studies have shown that individuals that eat red or processed meat have a higher risk of developing breast cancer, prostate cancer, and pancreatic cancer. This may be partially explained by the presence of carcinogens in food cooked at high temperatures. Several risk factors for the development of colorectal cancer include high intake of fat, alcohol, red and processed meats, obesity, and lack of physical exercise. **[12]** A high-salt diet is linked to gastric cancer. Aflatoxin B1, a frequent food contaminate, is associated with liver cancer. Betel nut chewing has been shown to cause oral cancers.

The relationship between diet and the development of particular cancers may partly explain differences in cancer incidence in different countries. For example, gastric cancer is more common in Japan due to the frequency of high-salt diets and colon cancer is more common in the United States due to the increased intake of processed and red meats. Immigrant communities tend to develop the cancer risk profile of their new country, often within one to two generations, suggesting a substantial link between diet and cancer.

5.4. Obesity

In the United States, excess body weight is associated with the development of many types of cancer and is a factor in 14-20% of all cancer deaths. Every year, nearly 85,000 new cancer diagnoses in the United States are related to obesity. Individuals who underwent bariatric surgery for weight loss have reduced cancer incidence and mortality **[13]**.

There is an associated between obesity and colon cancer, post-menopausal breast cancer, endometrial cancer, kidney cancer, and esophageal cancer. Obesity has also been linked with the development of liver cancer. The current understanding regarding the mechanism of cancer development in obesity relates to abnormal levels of metabolic proteins (including insulin-like growth factors) and sex hormones (estrogens, androgens and progestogens). Adipose tissue also creates an inflammatory environment which may contribute to the development of cancers. Physical inactivity is believed to contribute to cancer risk not only through its effect on body weight but also through negative effects on immune system and endocrine system. More than half of the effect from diet is due to overnutritionrather than from eating too little healthy foods **(Table 1).**

Cancers Related to Obesity	
Men	Women
Colorectal cancer	Colorectal cancer
Esophageal adenocarcinoma	Endometrial cancer
Kidney cancer	Esophageal adenocarcinoma
Pancreatic cancer	Gallbladder cancer
Thyroid cancer	Kidney cancer
-	Pancreatic cancer
-	Post-menopausal breast cancer

Table 1: Cancers Related to Obesity.

5.5. Hormones

Macroscopic appearance of invasive ductal carcinoma of the breast. The tumour is the pale, crab-shaped mass at the center, surrounded by normal, yellow fatty tissue.Some hormones play a role in the development of cancer by promoting cell proliferation. Insulin-like growth factors and their binding proteins play a key role in cancer cell growth, differentiation and apoptosis, suggesting possible involvement in carcinogenesis. Hormones are important agents in sex-related cancers such as cancer of the breast, endometrium, prostate, ovary, and testis, and also of thyroid cancer and bone cancer For example, the daughters of women who have breast cancer have significantly higher levels of estrogen and progesterone than the daughters of women without breast cancer. These higher hormone levels may explain why these women have higher risk of breast cancer, even in the absence of a breast-cancer gene. Similarly, men of African ancestry have significantly higher levels of testosterone than men of European ancestry, and have a correspondingly much higher level of prostate cancer. Men of Asian ancestry, with the lowest levels of testosterone-activating androstanediol glucuronide, have the lowest levels of prostate cancer. Other factors are also relevant: obese people have higher levels of some hormones associated with cancer and a higher rate of those cancers. Women who take hormone replacement therapy have a higher risk of developing cancers associated with that hormones. On the other hand, people who exercise far more than average have lower levels of these hormones, and lower risk of cancer. Osteosarcoma may be promoted by growth hormones. Some treatments and prevention approaches leverage this

cause by artificially reducing hormone levels, and thus discouraging hormone-sensitive cancers. Because steroid hormones are powerful drivers of gene expression in certain cancer cells, changing the levels or activity of certain hormones can cause certain cancers to cease growing or even undergo cell death. Perhaps the most familiar example of hormonal therapy in oncology is the use of the selective estrogen-receptor modulator tamoxifen for the treatment of breast cancer. Another class of hormonal agents, aromatase inhibitors, now have an expanding role in the treatment of breast cancer.

5.6. Infection and Inflammation

Worldwide, approximately 18% of cancer cases are related to infectious diseases. This proportion varies in different regions of the world from a high of 25% in Africa to less than 10% in the developed world. Viruses are the usual infectious agents that cause cancer but bacteria and parasites also contribute. Infectious organisms that increase the risk of cancer are frequently a source of DNA damage or genomic instability.

5.7. Viruses

HPV is the most common virus that infects the reproductive tract. Infection can lead to the development of cervical cancer in women. Viral infection is a major risk factor for cervical and liver cancer. A virus that can cause cancer is called an oncovirus. These include human papillomavirus(cervical carcinoma), Epstein–Barr virus (B-cell lymphoproliferative disease and nasopharyngeal carcinoma), Kaposi's sarcoma herpesvirus (Kaposi's sarcomaand primary effusion lymphomas), hepatitis B and hepatitis C viruses (hepatocellular carcinoma), and Human T-cell leukemia virus-1 (T-cell leukemias). In Western developed countries, human papillomavirus (HPV), hepatitis B virus (HBV) and hepatitis C virus (HCV) are the most common oncoviruses. In the United States, HPV causes most cervical cancers, as well as some cancers of the vagina, vulva, penis, anus, rectum, throat, tongue and tonsils. Among high-risk HPV viruses, the HPV E6 and E7 oncoproteins inactivate tumor suppressor genes when infecting cells. In addition, the oncoproteins independently induce genomic instability in normal human cells, leading to an increased risk of cancer development. Individuals with chronic hepatitis B virus infection are more than 200 times more likely to develop liver cancer than uninfected individuals. Liver cirrhosis, whether from chronic viral hepatitis infection or alcohol abuse, is independently associated with the development of liver cancer, but the combination of cirrhosis and viral hepatitis presents the highest risk of liver cancer development [14].

5.8. Bacteria and Parasites

Certain bacterial infections also increase the risk of cancer, as seen in Helicobacter pylori-induced gastric carcinoma. The mechanism by which H. pylori causes cancer may involve chronic inflammation or the direct action of some of the bacteria's virulence factors. Parasitic infections strongly associated with cancer include Schistosoma haematobium (squamous cell carcinoma of the bladder) and the liver flukes, Opisthorchis viverrini and Clonorchis sinensis (cholangiocarcinoma). Inflammation triggered by the worm's eggs appears to be the cancer-causing mechanism. Certain parasitic infections can also increase the presence of carcinogenic compounds in the body, leading to the development of cancers. Tuberculosis infection, caused by the mycobacterium M. tuberculosis, has also been linked with the development of lung cancer.

5.6. Inflammation

There is evidence that inflammation itself plays an important role in the development and progression of cancer. Chronic inflammation can lead to DNA damage over time and the accumulation of random genetic alterations in cancer cells. Inflammation can contribute to proliferation, survival, angiogensis and migration of cancer cells by influencing tumor microenvironment. Individuals with inflammatory bowel disease are at increased risk of developing colorectal cancer **[15]**

5.9. Radiation

Up to 10% of invasive cancers are related to radiation exposure, including both non-ionizing radiation and ionizing radiation. Unlike chemical or physical triggers for cancer, ionizing radiation hits molecules within cells randomly. If it happens to strike a chromosome, it can break the chromosome, result in an abnormal number of chromosomes, inactivate one or more genes in the part of the chromosome that it hit, delete parts of the DNA sequence, cause chromosome translocations, or cause other types of chromosome abnormalities. Major damage normally results in the cell dying, but smaller damage may leave a stable, partly functional cell that may be capable of Three independent stages appear to be involved in the creation of cancer with ionizing radiation: morphological changes to the cell, acquiring cellular immortality (losing normal, life-limiting cell regulatory processes), and adaptations that favor formation of a tumor. Even if the radiation particle does not strike the DNA directly, it triggers responses from cells that indirectly increase the likelihood of mutations.

5.10. Non-Ionizing Radiation

Not all types of electromagnetic radiation are carcinogenic. Low-energy waves on the electromagnetic spectrum including radio waves, microwaves, infrared radiation and visible light are thought not to be because they have insufficient energy to break chemical bonds. Non-ionizing radio frequency radiation from mobile phones, electric power transmission, and other similar sources have been described as a possible carcinogen by the World

Health Organization's International Agency for Research on Cancer. However, studies have not found a consistent link between cell phone radiation and cancer risk.

Higher-energy radiation, including ultraviolet radiation (present in sunlight), x-rays, and gamma radiation, generally is carcinogenic, if received in sufficient doses. Prolonged exposure to ultraviolet radiation from the sun can lead to melanoma and other skin malignancies. The vast majority of non-invasive cancers are non-melanoma skin cancers caused by non-ionizing ultraviolet radiation. Clear evidence establishes ultraviolet radiation, especially the non-ionizing medium wave UVB, as the cause of most non-melanoma skin cancers, which are the most common forms of cancer in the world.

5.11. Ionizing Radiation

Sources of ionizing radiation include medical imaging, and radon gas. Ionizing radiation is not a particularly strong mutagen. Medical use of ionizing radiation is a growing source of radiation-induced cancers. Ionizing radiation may be used to treat other cancers, but this may, in some cases, induce a second form of cancer. Radiation can cause cancer in most parts of the body, in all animals, and at any age, although radiation-induced solid tumors usually take 10–15 years, and can take up to 40 years, to become clinically manifest, and radiation-induced leukemias typically require 2–10 years to appear. Radiation-induced meningiomas are an uncommon complication of cranial irradiation. Some people, such as those with nevoid basal cell carcinoma syndrome or retinoblastoma, are more susceptible than average to developing cancer from radiation exposure. Children and adolescents are twice as likely to develop radiation-induced leukemia as adults; radiation exposure before birth has ten times the effect.

Ionizing radiation is also used in some kinds of medical imaging. In industrialized countries, medical imaging contributes almost as much radiation dose to the public as natural background radiation. Nuclear medicine techniques involve the injection of radioactive pharmaceuticals directly into the bloodstream. Radiotherapy deliberately deliver high doses of radiation to tumours and surrounding tissues as a form of disease treatment. It is estimated that 0.4% of cancers in 2007 in the United States are due to CTs performed in the past and that this may increase to as high as 1.5–2% with rates of CT usage during this same time period.

Residential exposure to radon gas has similar cancer risks as passive smoking. Low-dose exposures, such as living near a nuclear power plant, are generally believed to have no or very little effect on cancer development. Radiation is a more potent source of cancer when it is combined with other cancer-causing agents, such as radon gas exposure plus smoking tobacco.

6. Rare Causes

6.1. Organ Transplantation

The development of donor-derived tumors from organ transplants is exceedingly rare. The main cause of organ transplant associated tumors seems to be malignant melanoma that was undetected at the time of organ harvest. There have also been reports of Kaposi's sarcoma occurring after transplantation due to tumorous outgrowth of virus-infected donor cells.

6.2. Trauma

Physical trauma resulting in cancer is relatively rare. Claims that breaking bones resulted in bone cancer, for example, have never been proven. Similarly, physical trauma is not accepted as a cause for cervical cancer, breast cancer, or brain cancer one accepted source is frequent, long-term application of hot objects to the body. It is possible that repeated burns on the same part of the body, such as those produced by kanger and kairo heaters (charcoal hand warmers), may produce skin cancer, especially if carcinogenic chemicals are also present. Frequently drinking scalding hot tea may produce esophageal cancer. Generally, it is believed that the cancer arises, or a pre-existing cancer is encouraged, during the process of repairing the trauma, rather than the cancer being caused directly by the trauma. However, repeated injuries to the same tissues might promote excessive cell proliferation, which could then increase the odds of a cancerous mutation.

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