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Gene- Environment Interaction

Adinath Pandurang Kakade, Kalyani Balasaheb Gorde, Swati Shivaji Sandan(faculty)

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ABSTRACT:
Evolution has shaped life on Earth through intricate interactions between genetics and environmental factors. This article delves into the profound influence of these forces on the development and progression of various cancers, focusing on skin, lung, breast, and ovarian cancers.
Temperature, as an extrinsic environmental factor, plays a pivotal role in determining eye coloration, showcasing the intricate relationship between genotype and environment. Furthermore, it elucidates how alterations in gene sequences due to harmful environmental factors like UV radiation can lead to the development of skin cancer, particularly in individuals with lighter skin tones.
Lung cancer, predominantly caused by tobacco smoke and asbestos exposure, exemplifies the multifaceted nature of cancer etiology, where genetic predisposition intertwines with environmental carcinogens. The classification and pathological identification of lung cancer subtypes underscore the importance of personalized treatment approaches.
Breast and ovarian cancers, often associated with hereditary mutations in BRCA1 and BRCA2 genes, highlight the critical need for genetic testing and early detection strategies. Additionally, the disparity in survival rates underscores the urgency of raising awareness and investing in research for improved diagnostic and therapeutic modalities.
Through an exhaustive examination of genetic predisposition, environmental carcinogens, and the interplay between these factors, this article aims to provide a comprehensive understanding of cancer etiology. By elucidating the intricate mechanisms underlying cancer development, it seeks to pave the way for innovative approaches in prevention, diagnosis, and treatment, ultimately offering hope for a future free from the burden of cancer.
Keywords: Evalution, Skin cancer, Oncogenes, Melamine, SCLC, NSCLC, Adenocarcinomas, Squamous cell carcinomas, Large cell carcinomas, Breast & Ovarian cancer.

I. INTRODUCTION:

The article discusses the intricate relationship between genetics, environmental factors, and various types of cancer, focusing on skin, lung, breast, and ovarian cancers. It highlights how both genetic predispositions and environmental influences contribute to the development of these cancers. For instance, skin cancer incidence is affected by temperature, with higher temperatures increasing the risk, especially for individuals with lighter skin tones. Lung cancer is predominantly linked to smoking but can also occur in non-smokers due to genetic factors and exposure to substances like asbestos. The article also delves into the different subtypes of lung cancer, such as small-cell and non-small-cell carcinomas.

Moreover, it explores inherited genetic changes, such as mutations in genes like BRCA1 and BRCA2, which significantly increase the risk of breast and ovarian cancers in women. It further lists other genes associated with mutations contributing to these cancers. Throughout the article, the interplay between genetics and the environment in cancer development is emphasized, with examples illustrating how both factors influence cell behavior and contribute to tumor formation. Additionally, it mentions ongoing research and clinical trials aimed at better understanding and treating these cancers. Overall, the article underscores the complex nature of cancer etiology, involving a combination of genetic predispositions and environmental exposures, and the importance of continued research efforts for effective prevention and treatment strategies.

Evolution:

An important phenomenon on earth is here through various forces that cause change-alteration or polymorphism. Genotype or genetics is one of the forces that have here the process of evolution. Simply we can say that, today we are here because of the continuous changes in our

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genes or genome through the process of evolution. But the question arises how do changes occur in the gene and DNA are there any other forces? The answer is yes, "environment"- one of the many factors that produce various phenotypes. The environment here is our surroundings-atmosphere temperature, pollution, humidity or everything around us is an environment for us.

Temperature:

The temperature has an important effect on eye coloration. A bunch of genes from our genome are responsible for developing eye color. More than 150 various genes play important roles in eye coloration. Not only those genes but temperature (extrinsic environmental factor) also decides eye color.[1]Oncogenes are mutated genes that grow cells out of control which leads to cancer. Proto-oncogenes controls the cell growth but if they become mutated they can turn into oncogenes.[2]The disturbance in the cell function pathways due to environmental factors leads to an unregulated growth of cells. When oncogenes are turned on, and the tumor suppressor genes are turned off, by shifting the control of cell division the cancer begins in a single cell.[3] Sometimes the environment also changes a gene in its DNA sequence or its activity level. Any one from these changes can change the proteins that are formed from a gene which in turn affects characteristics. Gene's nucleotide sequence also changes due to some harmful environmental factors. Such as UV radiation can break DNA strands.[4]

Fig 1: Affect of temperature for developing skin cancer.

Skin cancer:

The people, who are living at a higher temperature and have higher bright skin. People have a high rate of skin cancer The bright or white skin tone was originally evolved to live at a lower temperature.Genes to code for melanin, convey in a lower amount under low temperatures and skin tone becomes brighter. But, when they try to live in a higher temperature area, the activity of melamine disturbs and causes skin cancer, in most cases. Malignancy of skin cancer is most common in the U.S (United States) and represents 35 to 45% of all neoplasm in people of European origin,[5]4 to 5% Hispanics (Spanish), 2 to 4% in Asians and 1 to 2% in Blacks.[6]From harmful UV extra layer of melanin protects our skin hence having higher Melamine can protect our skin from harmful UV radiation easily in comparison with others.[7,8]The problems of melanomas develop in younger only after puberty. 1% to 4% of melanomas develop in younger people, and 0.3% to 0.4% develop in prepubertal people. There are many factors are developing melanomas as follows:[9]

Factors for the development of melanoma:

1. Freckles, actinic lentigines (sun spots)
2. Tendency to sunburn when exposed to UV light
3. Previous malignant disease
4. Impaired DNA repair, especially xeroderma pigmentosum
5. Congenital melanocytic nevus, especially giant nevus
6. Large number of common melanocytic nevi
7. Light skin, red or blond hair, light eyes
8. Immunosuppression
9. Melanoma in the family
10. Several atypical melanocytic nevi
11. Intermittent intensive exposure to UV light

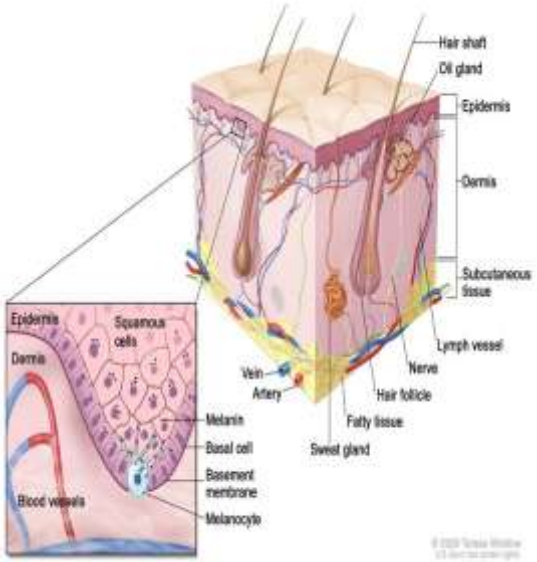

Fig 3: Normal skin layer

In Figure No.3, There is a schematic representation of normal human skin. In normal skin, melanocytes

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are also present and act as source cells of melanoma.[10]

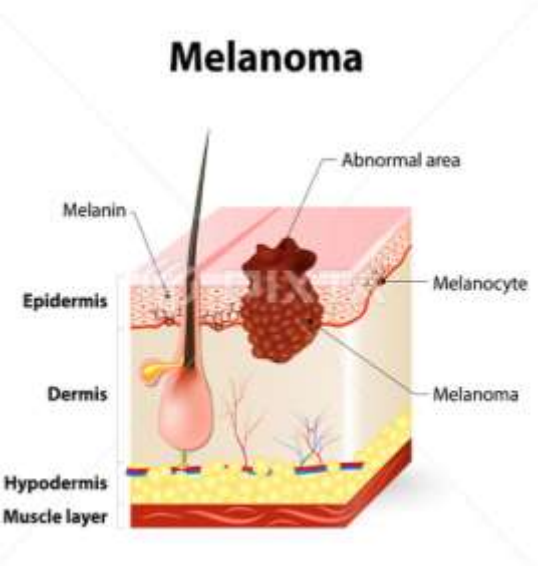

Fig 3: Melanoma

In most cases, however, skin cancer is a hereditary risk of developing adisease that can be passed from parent to child. As per data, it is estimated that roughly 5-10% of melanoma cases are hereditary and caused by pathogenic genes. It is also caused due to changes in gene sequence.[11]

CDKN2A (Cyclin Dependent Kinase Inhibitor 2A) is a gene that is a major germline tumor suppressor that is associated with increased melanoma risk. Pathogenic variants in CDKN2A may account for 35% to 40% of all familial melanomas.[12]

Lung cancer:

Lung cancer is a type of cancer that impacts on lungs. Our lungs are smooth & soft organs in our chest, which help to exchange carbon dioxide with oxygen. Too many environmental factors impact on lungs and cause lung cancer.[13] The smoke is the most dangerous factor in lung cancer. The people who smoke daily mostly suffer from lung cancer, but lung cancer although found in non-smoking people. Also in the smoking condition, vintage smokers cause lung cancer rapidly compared with new ones.[14] Cigarette smoking is the most risk factor for lung cancer. In the United States, there are 80-90% of deaths are caused by lung cancer. Cancer is also a genetic disease that is carried forward from the parents to our child. If you have any family history of lung cancer which is risky for a new generation. Immediately make a concern with your doctor to prevent lung cancer. There are 7000 plus chemicals mixed in tobacco which makes it more toxic and poisonous. Of 7000, only 70 are enough to cause lung cancer.[15]

Fig 4: Lung cancer

Asbestos is one of the most harmful substanceswhich cause lung cancerand is known as mesothelioma. Mesothelioma is the thin membrane that lines the abdomen andthe chest. Lung cancer is caused by inhaling the fibers of asbestos. Pleural thickening unrelated to asbestos frostbite is genetic and environmental both factors are responsible for the development of asbestos.[16]

There are main two types of asbestos lung cancer which are rarely found in the human body.[17,18]

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

Small cell lung cancer:

Small cell lung cancer is rarely diagnosed in the body. It is only about 15% SCLC found in 100%.Small cell carcinoma (SCLC) is a type of cancer made up of small, round, oval, or angulated cells. These cells have a small amount of cytoplasm and are roughly the size of a resting lymphocyte. They do not have any distinct nucleoli. SCLCs are often extensively necrotic. They typically test positive for chromogranin or synaptophysin. Previously, the WHO classified SCLC into three different cell subtypes: oat cell, intermediate cell, and combined cell.[19]

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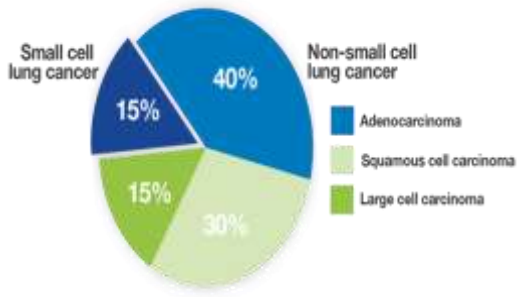

Fig 5: percent ratio of lung cancer

Non-small cell lung cancer:

NSCLC is the most common lung cancer. It is about 85% found in 100%. Most lung cancer happens because of non-small cell lung cancer. There are 4 stages of NSCLC which increase the risk of lung cancer.[15]

The first 3 stages are identified and cured easily. But stage 4 is very harmful compared to the first 3 stages. Most commonly cancer is spread to the lymph node in the mediastinum. Discover the mediastinum, the vital area situated in the chest between the lungs that plays an integral role in the proper functioning of the heart, great vessels, trachea, esophagus, and lymphatic system. Understanding the importance of this crucial area can help diagnose and treat various medical conditions that may arise.Stage 4 is the most advanced and harmful form of lung cancer. Stage 4 causes lining on the lungs in the body. After the stage 4 lung cancer diagnosis you might have a few days, months, or years to live.[20]

In this non-small cell lung cancer category, there are three subtypes-

- **Adenocarcinomas**
- **Squamous cell carcinomas**
- **Large cell carcinomas**

Adenocarcinomas: Adenocarcinoma is the most common form of lung cancer which is located inthe outer part of the lungs and begins in the cells in the gland. Adenocarcinoma is oftentimes found in nonsmokers, women, and people under the age of 45. Adenocarcinoma is a type of cancer that is characterized by the formation of neoplastic glands, expression of pneumocyte markers such as thyroid transcription factor 1 (TTF-1), and intracytoplasmic mucin. The cancer is further classified into mucinous and nonmucinous subtypes based on the extent and architecture of the neoplastic gland formation. The nonmucinous subtypes include acinar, papillary, micropapillary, lepidic, and solid, while mucinous adenocarcinomas can have papillary, micropapillary, solid, and cribriform architecture.[20]

Pathological identification of the subtypes is important for prognosis, with solid, micropapillary, and cribriform patterns indicating poor prognosis. However, the World Health Organization (WHO) does not provide any grading recommendations for mucinous carcinomas based on the growth patterns in a tumor.[21]

It's worth noting that adenocarcinoma can come in various forms, some of which are not as well-known. Colloid, enteric-like, lymphoepithelial, and fetal adenocarcinomas are all worth keeping in mind as potential diagnoses.Minimally invasive adenocarcinoma (MIA) is a type of adenocarcinoma that is small, solitary, and less than or equal to 3 cm in size with minimal invasion (less than 5 mm) and a predominant lepidic growth pattern. Did you know that if the cancer cells have invaded more than 5 mm, it is classified as lepidic-predominant adenocarcinoma? It's important to stay aware of the extent of invasion so that you can take the necessary steps for early detection and treatment. Remember, detecting cancer early can make all the difference.Invasive mucinous adenocarcinoma comprises mucinous lesions that cannot be classified as MIA, and if more than 10% of mucinous and nonmucinous growth patterns are present, the lesion is classified as mixed adenocarcinoma.[22]

Squamous cell carcinomas comprise 80 to 90% of all lung cancers. This is linked to a history of smoking. Squamous cell carcinoma is most common in men as well as women.[23] This squamous cell carcinoma majorly starts from the center of the lungs. The major symptom of the squamous cell carcinomais coughing up blood.Squamous Cell Carcinoma (SCC) lung disease is a grave concern that needs our immediate attention. The disease originates from the transformation of the squamous cells lining the airways, which are found in many organs of the human body. The tobacco smoke is primarily caused by cellular transformation, which contains over 40 potential carcinogens and 300 plus harmful agents. The transformed squamous cells exhibit a high degree of mutation frequency and are characterized by keratinization and/or intercellular bridges. The disease is preventable if we take necessary measures to quit tobacco use and avoid exposure to secondhand smoke. Let's raise

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awareness about the harmful effects of tobacco use and work towards a healthier future.[24]

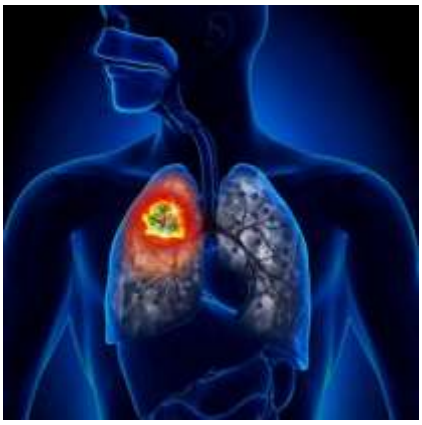

Fig 6: Squamous cell carcinoma (Lung cancer)

Large cell carcinomas: Large-cell carcinoma (LCC) of the lung represents around 7.5% of all lung cancers. Large cell carcinomas tend to grow quickly. These are usually undetected until they have percolated. This is one of the rarest lung cancers. This only appears 1 person in 10 cases.[25]

It has been observed that Asian women are at a greater risk of developing lung cancer. This is mainly due to their exposure to second-hand tobacco smoke and the combustion products that are released from indoor heating and cooking oil. It is important to note that the risk of lung cancer is also increased by ambient air pollution from both indoor and outdoor environments, which has been a long-standing pathogenic risk factor. Air pollutants from industries, waste sites, and incineration harm air quality.Many researchers are working on lung cancer to treat the cancer in a better way. There are many clinical trials done for the better treatment of the patient.[26]

Breast and ovarian cancer:

Breast and ovarian cancer is the most common type of cancer which is generally found in women. The genes are affected in hereditary breast and ovarian cancer. There are 2 types of genes included in breast and ovarian cancer. BRCA1 and BRCA2 genes. 3% of women are suffering from breast cancer which is nearly7500 women per year and 10% of women are suffering from ovarian cancer which is nearly 2000 women per year because of the inherited mutation in the BRCA1 and BRCA2.[27]

Did you know that epithelial ovarian cancer is the leading cause of death among gynecologic cancers and the fourth leading cause of cancer death in women in the United States? We must raise awareness about this debilitating disease and support ongoing efforts to find a cure. Together, we can make a difference in the lives of countless women and their families.[28]

Ovarian cancer is a deadly disease, and its high mortality rate is mainly due to its hidden development. Unfortunately, around 75% of women experience widespread disease at the time of diagnosis, leading to an overall 5-year survival rate of only 30%. However, there is hope for those whose disease is confined to the ovary (stage I), with a 5-year survival rate of over 90%. On the other hand, women with advanced disease face a survival rate of just 10 "Ensuring early detection and treatment is critical when it comes to improving survival rates. Don't wait until it's too late - act now to give yourself the best possible chance for a healthy and happy future."Please make sure to schedule regular check-ups to stay on top of your health.[29]

Key facts about breast cancer:

- Breast cancer causes 670,000 deaths globally in 2022.
- Roughly half of all breast cancers occur in women with no specific risk factors other than sex and age.
- Breast cancerwas found to be the most prevalent cancer in women in 157 out of 185 countries, in 2022.
- Breast cancer occurs in every country in the world.
- Approximately 0.5–1% of breast cancers occur in men.[30]

Fig 7: Factors affecting breast cancer

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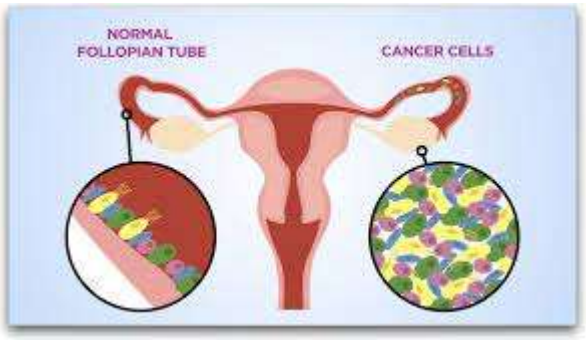

Fig 8: Ovarian cancer

There are several different genes included in the mutation which are as follows-

BARD1- BRCA1-Associated Ring Domain protein 1
BRIP1- BRCA1 Interacting Protein 1
CASP8- Caspase-8 (casp-8)
CTLA4- cytotoxic T lymphocyte-associated antigen 4
CYP19A1- Cytochrome P450 Family 19 Subfamily A Member 1
FGFR2- fibroblast growth factor receptor 2
H19- H19 Imprinted Maternally Expressed Transcript
LSP1- Leukocyte-specific protein 1
MAP3K1- Mitogen-Activated Protein Kinase 1
NBN- Nijmegen breakage syndrome.
RAD51- RAD51 Recombinase
TERT- Telomerase reverse transcriptase

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