# Risk Factors for Cancer

Yazhao Liu

Beijing University of Chemical Technology Beijing, China

2020090002@mail.buct.edu.cn

**Abstract.** Cancer accounts for almost one sixth of global deaths, which has become a major cause of death. There are various studies concerning the development of cancer. It has been found that genetic factors, low immunity and gene mutations are the main reasons for the body's cells losing their normal regulation and over proliferating. Those finally contributes to tumorigenesis. With the development of technology and a large number of investments in research, we know more about the causes of disease. Especially the mechanism of carcinogenesis on physical and chemical factors, which contributes to the future research on treatment. Although many treatments such as surgery, radiation, chemotherapy, and immunotherapy are available, not all types and stages of cancer can be cured. Currently 30-50% of cancers could be prevented by avoiding risk factors and implementing existing evidence-based prevention strategies. Therefore, research on cancer-causing factors is necessary. In this article, I will categorize the carcinogenesis factors in three categories: physical factors, chemical factors and biological factors. I will also discuss and summarize some specific cancer-causing mechanisms. This article will provide reference and new idea for future research on mechanism and treatment of cancer.

**Keywords:** cancer, radiation, tobacco smoking, inflammation.

## 1. Introduction

The World Health Organization (WHO) report shows that in 2020, nearly 10 million deaths were caused by cancer, which accounts for nearly one sixth of total global deaths. This figure shows that cancer has become a major cause of death worldwide. Among them, there were 1.80 million deaths from lung cancer, 0.92 million from colon and rectal cancer, 0.83 million from liver cancer, 0.77 million from stomach cancer and 0.69 million from breast cancer. Of the 19.3 million cancer cases that has been diagnosed, 2.26 million cases of breast cancer exceeded the 2.21 million cases of lung cancer[1]. Cancer has not only affected the daily life and health of people all over the world, but also caused a serious burden on the economy and society.

Considering the negative impact of cancer on individuals, society and the world, tumorigenesis has become one of the most important questions in modern medicine and basic biology. It attracted many scholars to devote themselves to related studies. Based on the existing research, we found that cancer is the result of cellular dysfunction[2]. It is manifested in the excessive proliferation and inability of cells to regulate their own functions, such as immune disorders, proliferation disorders, transport disorders. The development of cancer is a long process. Chemotherapy, surgery, radiation therapy, hormonal therapy, targeted therapy, immunotherapy and so on have been widely used in the treatment of various cancers and achieved good effects saving many lives[3]. But we can't ignore that there are still some cancers that are too complex or at an advanced stage. There is still no cure for them.

In addition to treatment, early prevention of tumors is also necessary. There are a lot of research on cancer. Abnormal changes in cell genes and functions caused by exposure to risk factors are an important cause of cancer. Research shows that by avoiding risk factors, 30%-50% of cancers could be effectively prevented. Then the number of people getting cancer or dying from cancer in the world would be greatly reduced. The identification of carcinogenic risk factors has become very important.

At present, research on carcinogenic factors is an important aspect of cancer prevention. In this article, I will categorize the risk factors in physical factors, chemical factors and biological factors. Through an extensive literature review and summary, I will discuss the carcinogenic mechanism of

the factors mentioned in the article. At present, the carcinogenic mechanism of most risk factors has been clarified. But we still don't understand a few mechanisms, which restricts the development of carcinogenic mechanism and treatment methods.

## 2. Methods

I searched PubMed databases, World Health Organization regional websites and International Agency for Research on Cancer websites for relevant articles and data. In this article I reviewed the published studies from 1987.. to 2022 and results were classified as physical factors, chemical factors and biological factors.

The overview analysis was based on the confidence interval method to give a summary estimate of ORs and 95% CIs. Twenty-six studies, based on 9,121 incident cancer cases, which assessed cancer risk factors were used in the analysis. Studies had to be excluded if no OR or 95% CI result was published or could be calculated from the information provided because this applied to only a few results.

## 3. Result and Discussion

### 3.1 Physical factors

3.1.1Exposure to electromagnetic fields

The electromagnetic field consists of electrical waves and magnetic energy that move together in space. Electromagnetic waves exist in different forms in the universe. According to the range of electromagnetic spectrum, electromagnetic fields can be classified from low to high frequencies as static electric fields, magnetic fields, radio frequency (RF), infrared radiation, visible light, X-rays, and gamma rays. The most common one we are exposed to is RF, the electromagnetic spectrum of which extends from 3 kHz to 300 GHz. Televisions, mobile phones, radar, Wi-Fi, tablets and other commonly used devices in daily life emit electromagnetic fields in the RF band.

As early as the late 1860s, reports indicated that workers in Russian substations may suffer from certain diseases due to their occupation. However, those sample data were not large enough and the commonality of the disease was not obvious, it did not attract researchers' attention at that time. Until 1979, numerous studies have shown that exposure to electromagnetic fields can have chronic effects on human health, which point to cancer and birth defects[4]. People began to study the carcinogenic mechanism of electromagnetic field. Stevens put forward the possibility of the association between electromagnetic fields and breast cancer[5]. Wilson et al. found that adult rats exposed to 60 Hz electromagnetic fields producing less melatonin in pineal through a comparative test. The amount of melatonin directly affects the estrogen levels, stimulating the mammary tissue proliferation which finally lead to the breast cancer[6]. In addition to breast cancer, there are also various statistics that link electromagnetic fields to the development of leukemia. Based on epidemiological studies, Wertheimer and Leeper demonstrated that American children living in high magnetic field strengths for long periods have a higher risk of developing leukemia [7]. International Agency for Research on Cancer(IARC) has also evaluated electromagnetic fields as possible human carcinogens(Group 2B)[8]. Although there are many studies finding a relationship between EMFs and cancer at the epidemiological level, there is still no clear study stating the mechanism. Electromagnetic filed began to be applied in therapy. Pulsed electromagnetic filed (PEMF) can treat various pathologies noninvasively by delivering electromagnetic fields to tissues through induction coils[9]. However, the mechanism of EMF carcinogenesis is still unclear, which can lead to concerns about the increased risk of cancer while performing treatment. So it's in urgent need of investigating the mechanism of EMF carcinogenesis.

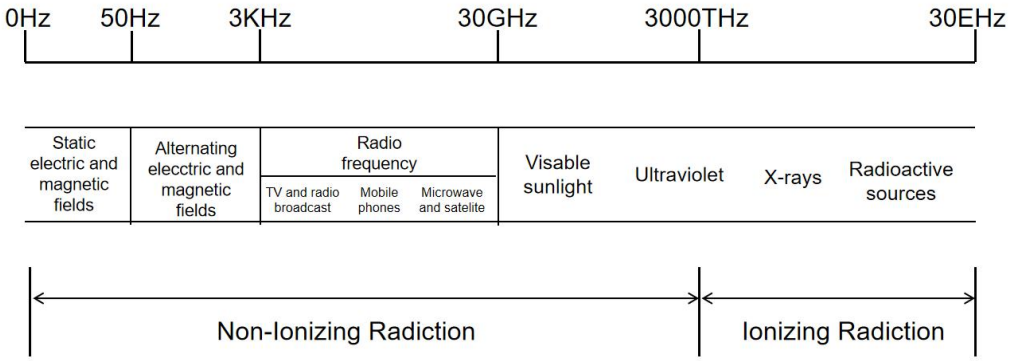


Fig 1 The Electromagnetic Spectrum

3.1.2Ionizing radiation

Radiation is the process by which energy travels through space in the form of particles or electromagnetic waves, in other words the process by which sunlight radiates light energy to the Earth is radiation. When the energy of a particle or photon is greater than 12 eV, it can cause ionization of atoms and it's known as ionizing radiation. Since the discovery of X-rays in 1895 and radioactivity in 1896, ionizing radiation has played an important role in advancing modern physics.

At the end of the nineteenth century, Marie Curie discovered uranium and radium. Under the long-term work with radioactive substances, she suffered from leukemia because of ionizing radiation. But people didn't pay attention to the injury to human body caused by ionizing radiation. It was not until many years later that the effects of radiation on the human body were really realized. The first report concerning ionizing radiation on human health was in the mid-twentieth century, it was reported that children who survived the atomic bombings in Hiroshima and Nagasaki were more likely to develop leukemia and thyroid cancer [7]. There are a great number of studies revealing the relationship between ionizing radiation and cancer. IR could directly or indirectly cause oxidative stresses to the biological systems, which is known as a strong inducer of reactive species[10]. It mainly induce the reactive oxygen(ROS) and reactive nitrogen(RNS)[11]. In the normal human body, there are low levels of oxidative stress and inflammatory effects contributing to maintaining the homeostasis of organisms[12]. However, ROS and RNS can attack DNA, resulting in base damage, DNA breaks, cross links, destruction of sugars and telomere dysfunction[13]. The body can repair DNA damage normally, but a large amount of damage will result in a series of biochemical and molecular signaling events. Finally, it may lead to cell death and tumor formation. Nowadays, radiation therapy for cancer has been widely used in cancer treatment. Now we need to think about how to minimize the damage caused by ionizing radiation while treating because even receiving radiation treatment for cancer could also increase the risk of cancer in other organs [14].

3.1.3Ultraviolet radiation

The outer layers of the Earth are surrounded by atmosphere that allows light energy photons to provide energy for biosynthesis on earth while absorbing harmful ultraviolet radiation, with the ozone layer at 10-50 km above sea level absorbing UVB (290 to 320 nm) and UVA (320 to 400 nm) waves[15]. In 2011, a hole in the ozone layer was observed in the Arctic, where UV radiation is already posing a threat to human health.

In 2009, the International Agency for Research on Cancer (IARC) listed UV radiation from fluorescent lamps as a carcinogenic factor associated with skin cancer[7]. Excessive UV radiation increases the risk of pigmented and non-pigmented skin cancers.

There are two main mechanisms of UV carcinogenesis, DNA damage and immunosuppression[16]. Proto-oncogenes can cause cancer and oncogenes can suppress cancer. Proto-oncogenes are activated and oncogenes are inactivated by prolonged exposure to UV radiation[17]. In a normal body, proto-oncogenes and oncogenes are mutually regulated and in a

balance. When this balance is disturbed, it can lead to the possible development of cancer. It has been shown that UV radiation can act as an inducer to induce mutations in the proto-oncogene ras and the suppressor genes p53, CDKN2A and PTCH, which in turn lead to the development of skin cancer. UV radiation exposure can also induce immunosuppression by altering skin cell-mediated immunity. After long term exposure to UV radiation, Langerhans cells in the epidermis undergo changes in number and morphology and decrease in function[18]. At the same time, the number of T-helper lymphocytes and T-cytotoxic lymphocytes decreases[19]. The weakening of the immune system directly increases the possibility of cancer development. Statistics show that the incidence of skin cancer in the United States has continued to rise in recent years. UV radiation, as a known carcinogenic factor, can be prevented by simple chemical or physical sun protection methods. However, some fashion-conscious young people are seeking a healthy wheatish complexion and are even addicted to sunbathing. But excessive UV radiation has greatly increased the probability of developing skin cancer[20]. People need to be aware that they should ensure their health while pursuing fashion.

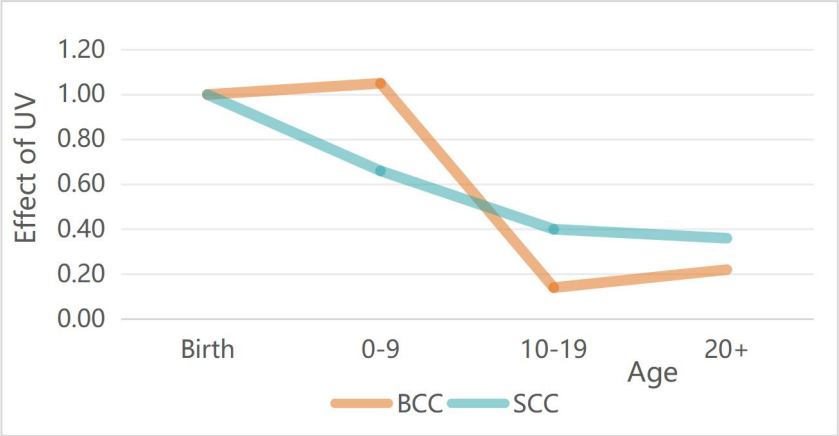


Fig 2 The Relationship of age at arrival in Australia and BCC, SCC under the effect of UV

### 3.2 Chemical factors

3.2.1Tobacco smoking

Globally, smoking is responsible for 6 million deaths each year. Smoking has been recognized as a major avoidable cause of death for a long time. Although smoking prevalence in high-income countries has been on a downward trend in recent years, it is still at a high level[7].

Tobacco smoking is a major risk factor for lung cancer, which includes adenocarcinoma, small cell carcinoma, squamous cell carcinoma and large cell carcinoma[21]. There are 7000 compounds in cigarette smoke (CS), which could be divided into three primary types: 1) mainstream CS (MCS); 2) sidestream CS (SCS); 3) environment tobacco smoke (ETS)[22]. Among 7000 compounds in CS, polycyclic aromatic hydrocarbons and nicotine-derived nitrosamines have been identified as potent carcinogens[23]. Nicotinic acetylcholine receptors (nAChRs) are the central regulatory factors of stimulatory and inhibitory neurotransmitters that control the cancer cells and the cancer microenvironment[24]. The neurotransmitter acetylcholine is the physiological agonist for all nAChRs in normal conditions[25]. The nicotine in CS could substitute acetylcholine binding to the α subunits of nAChRs[26]. Then the conformation of nAChRs will change, resulting in the flow of ions from the extracellular space to the cell[27]. Excess cations in the membrane eventually lead to the membrane depolarization. Nicotine has higher affinity with α4β2nAChR, than with the α7nAChR. When exposed to the environment full of nicotine, it directly led to the long-term inactivation (or desensitization) of the α4β2nAChR. By contrast, the sensitivity of α7nAChR remained stable[28]. When α4β2nAChR and α7nAChR combine with physiological agonist, they could jointly stimulate the release of dopamine. In addition to its ability of regulating cognition and memory in the brain, dopamine can also stimulate the proliferation of cancer cells in the prostate and mammary gland[29]. What's more, α4β2nAChR could stimulate the release of neurotransmitter

γ-aminobutyric acid (GABA), which is the tumor suppressor for adenocarcinoma of the lung, pancreas, breast and colon[24]. As explained above, upregulation of the stimulatory α7nAChR and inactivation of the inhibitory α4β2nAChR serve as central driving forces for the development of the most common human cancers. Tobacco smoking sever as central driving forces for the change of α7nAChR and α4β2nAChR. It indirectly promote the development of lung cancer.

| Class | | Name and CAS number | IARC Group |
|---|---|---|---|
| Hydrocarbons | Alkenes | 1,3-Butadiene (106-99-0) | 1 |
| | | Isoprene (78-79-5) | 2B |
| | | Styrene (100-42-5) | 2A |
| | Monocyclic Aromatic Hydrocarbons (MAH) | Benzene (71-43-2) | 1 |
| | | Ethylbenzene (100-41-4) | 2B |
| | | Cumene (98-82-8) | 2B |
| | Polycyclic Aromatic Hydrocarbons (PAH) | Naphthalene (NAP, 91-20-3) | 2B |
| | | Benz[a]anthracene (B[a]A, 56-55-3) | 2B |
| | | Benzo[c]phenanthrene (B[c]P, 195-19-7) | 2B |
| | | Chrysene (CHR, 218-01-9) | 2B |
| | | 5-Methylchrysene (3697-24-3) | 2B |
| | | Benz[j]aceanthrylene (B[j]A, 202-33-5) | 2B |
| | | Benzo[b]fluoranthene (B[b]F, 205-99-2) | 2B |
| | | Benzo[j]fluoranthene (B[j]F, 205-82-3) | 2B |
| | | Benzo[k]fluoranthene (B[k]F, 207-08-9) | 2B |
| | | Cyclopenta[cd]pyrene (CP[cd]P, 27208-37-3) | 2A |
| Amines | Aliphatic Amine | Hydrazine (302-01-2) | 2A |
| | Aromatic Amines | Aniline (62-53-3) | 2A |
| | | ortho-Toluidine (95-53-4) | 1 |
| | | 2,6-Dimethylaniline (87-62-7) | 2B |
| | | ortho-Anisidine (90-04-0) | 2A |
| | | 4-Aminobiphenyl (4-ABP, 92-67-1) | 1 |
| | | 2-Naphthylamine (2-NA, 91-59-8) | 1 |
| | Heterocyclic Aromatic Amines (HAA) | 2-Methylimidazole (693-98-1) | 2B |
| | | 4-Methylimidazole (822-36-6) | 2B |
| | | Pyridine (110-86-1) | 2B |
| | | 2-Amino-1-methyl-6- phenylimidazo[4,5- b]pyridine (PhIP, 105650-23-5) | 2B |
| | | Quinoline (91-22-5) | 2B |
| | | 2-Amino-9H-pyrido[2,3- b]indole (A-α-C, 26148-68-5) | 2B |
| | | 2-Amino-3-methyl-9H- pyrido[2,3-b]indole (MeA- α-C, 68006-83-7) | 2B |
| | | 3-Amino-1,4-dimethyl-5H- pyrido[4,3-b]indole (Trp-P-1, 62450-06-0) | 2B |
| | | 3-Amino-1-methyl-5H- pyrido[4,3-b]indole (Trp-P-2, 62450-07-1) | 2B |
| N-Nitrosamines | Acylic N-Nitrosamines | N-Nitrosodimethylamine (NDMA) (62-75-9) | 2A |
| | | N-Nitrosoethylmethylamine (NEMA, 10595-95-6) | 2B |
| | | N-Nitrosodiethylamine (NDEA, 55-18-5) | 2A |
| | | N-Nitrosodi-n-butylamine (NDBA, 924-16-3) | 2B |
| | | N-Nitrososarcosine (NSAR, 13256-22-9) | 2B |
| | | N-Nitrosodiethanolamine (NDELA, 1116-54-7) | 2B |
| | Cyclic N- | N-Nitrosopyrrolidine (NPYR, 930-55-2) | 2B |

| | | | |
|---|---|---|---|
| | Nitrosamines | N′-Nitrosonornicotine (NNN, 16543-55-8) | 1 |
| | | N-Nitrosopiperidine (NPIP, 100-75-4) | 2B |
| | | N-Nitrosomorpholine (NMOR, 59-89-2) | 2B |
| Ethers | | Ethylene oxide (75-21-8) | 1 |
| | | Methyleugenol (93-15-2) | 2B |
| | | Furan (110-00-9) | 2B |
| | | Benzofuran (271-89-6) | 2B |
| Aldehydes | | Formaldehyde (50-00-0) | 1 |
| | | Acetaldehyde (75-07-0) | 2B |
| | | Acrolein (107-02-8) | 2A |
| | | Crotonaldehyde ((E/Z), 4170-30-3) | 2B |
| Halogenated compounds | | Vinyl chloride (75-01-4) | 1 |
| | | 2,3,4,7,8- Pentachlorodibenzofuran (2,3,4,7,8-PeCDF, 57117-31-4) | 1 |
| Nitro compounds | | Nitromethane (75-52-5) | 2B |
| | | 2-Nitropropane (79-46-9) | 2B |
| | | Nitrobenzene (98-95-3) | 2B |
| Phenolic compounds | | Catechol (120-80-9) | 2B |
| | | Caffeic acid (331-39-5) | 2B |
| Miscellaneous compounds | | Acetamide (60-35-5) | 2B |
| | | Acrylamide (79-06-1) | 2A |
| | | Ethyl carbamate (51-79-6) | 2A |
| | | Vinyl acetate (108-05-4) | 2B |
| | | Acrylonitrile (107-13-1) | 2B |
| Inorganic compounds | | Arsenic | 1 |
| | | Beryllium | 1 |
| | | Cadmium | 1 |
| | | Chromium(VI) | 1 |
| | | Cobalt | 2B |
| | | Lead (inorganic) | 2A |
| | | Nickel | 1 |
| | | Polonium-210 | 1 |

Table1 The carcinogenic component in cigarette smoke

### 3.2.2Alcohol

Alcohol consumption is closely related to human health, in addition to cancer there are vast diseases caused by alcohol, including alcoholic polyneuropathy, alcoholic cardiomyopathy, alcoholic gastritis, depression, other psychiatric disorders, hypertension, liver cirrhosis, fibrosis, chronic pancreatitis and so on [30]. As early as 1988, the International Agency for Research on Cancer (IARC) classified alcoholic beverages as Group I carcinogens, which is the most potent category of carcinogens. Worldwide, about 4% of cancers are caused by alcohol consumption, which equates to 740,000 cases of cancer caused by alcohol intake in 2020. Alcohol consumption increases the risk of developing many types of cancer, such as upper gastrointestinal tract, liver, colorectal and breast cancers [31].

There are several mechanisms by which alcohol can cause cancer. Firstly, alcohol acts as a solvent in which carcinogenic compounds can dissolve, thereby increasing the contact time of carcinogens with mucous membranes, with the cell membranes being altered or even destroyed as a result[32]. Alcohol also enhances cancer indirectly by impairing the detoxification function of the liver by acting directly on the mucosa and eliminating the lipid component of the barrier surrounding the granularity of the epithelium [7]. Furthermore, the mechanism of ethanol-induced carcinogenesis is closely linked to the metabolism of ethanol, in which ethanol is metabolized to produce acetaldehyde [33]. Acetaldehyde is highly toxic and mutagenic. It promotes tumourigenesis by interfering with DNA synthesis and repair. Numerous in vitro and in vivo experiments have

demonstrated the direct carcinogenic effects of acetaldehyde, including experiments in rats and hamsters in which acetaldehyde inhalation was shown to cause nasal and squamous cell carcinomas when inhaled in large quantities over a long period of time [34]. At present, several mechanisms of alcohol carcinogenesis have been shown, but further understanding of the pathways that alcohol leads to cancer development will inform future research directions and prevention of alcohol carcinogenesis.

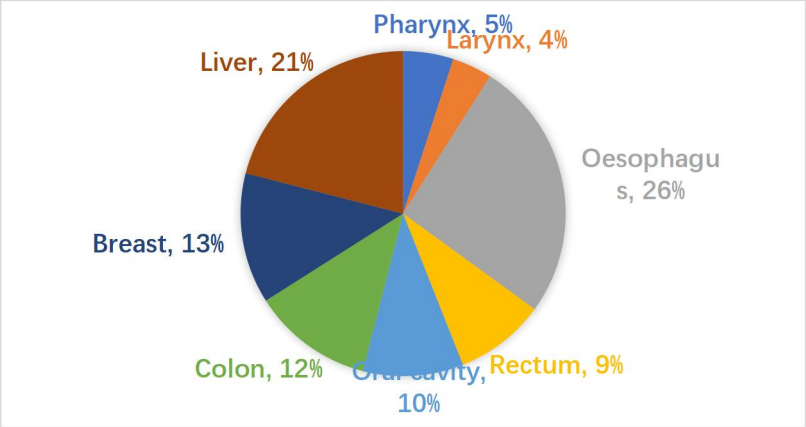

Fig 3 Alcohol drinking caused more than 74000 cases of cancer globally.

3.2.3Nitrosamine

Nitrosamines are found in many foods, mainly in cured meats and smoked fish, but also in foods such as beer and soy sauce [7]. N-nitrosodiethylamine (NDEA) and N-nitrosodimethylamine (NDMA) have been identified by the International Agency for Research on Cancer (IARC) as potentially carcinogenic to humans [35]. It has been shown that nitrosamine intake is associated with the development of gastric cancer. Long-term excessive intake of these foods can pose a health risk[36].

### 3.3 Biological factors

3.3.1Bacteria

The link between microorganisms and cancer was discovered more than 4,000 years ago. This idea began to be studied after the bacterial theory of infectious disease was established. Long-term studies have found that few bacteria directly cause cancer, but many have been linked to the development of cancer acting through the host's immune system or promoting abnormal cell proliferation[37]. There are common cancer-causing bacteria: clostridium pneumoniae is associated with lung cancer, chlamydia trachomatis is a susceptibility factor for cervical carcinogenesis and Helicobacter pylori closely related to gastric cancer[7].

At present, nearly half of the world's people are infected with Helicobacter pylori (H. pylori)[38]. H. pylori, a gram-negative bacterium, has been described by the World Health Organization as a class I carcinogen for the development of gastric cancer since 1994[39]. There are two mechanisms stating the effect of H. pylori on the tumorigenic process: the effects of virulence factors on cell proliferation and inflammatory response of the gastric mucosa to H. pylori infection[40]. Cytotoxin-associated gene A (Cag A) and vacuolating cytotoxin A (Vac A) are typical virulence factors. They promote mitosis and cell proliferation through a series of phosphorylation reactions in host cells, combining with specific proteins and activating specific enzymes[41]. In other words, it's a process of activating specific cell proliferation pathway. The second mechanism is concerned with the helicobacter outer membrane proteins: HomB, HopQ and HopH[42]. They could bind to interferon γ- activated sequence (GAS) and induce the expression of inflammatory genes[43]. The attack on DNA caused by inflammation finally leads to cancer. Now we usually use the combination of a proton pump inhibitor (e.g.,omeprazole), a macrolide (e.g., clarithromycin), and a beta-lactam (e.g., amoxicillin) is prescribed to treat the infection caused by H. pylori. By identifying the existing oncogenic mechanism, we get some new ideas for the treatment. HomB, HopQ and

HopH could be used for the development vaccine. The pathway CagA and VacA activated need some further research.

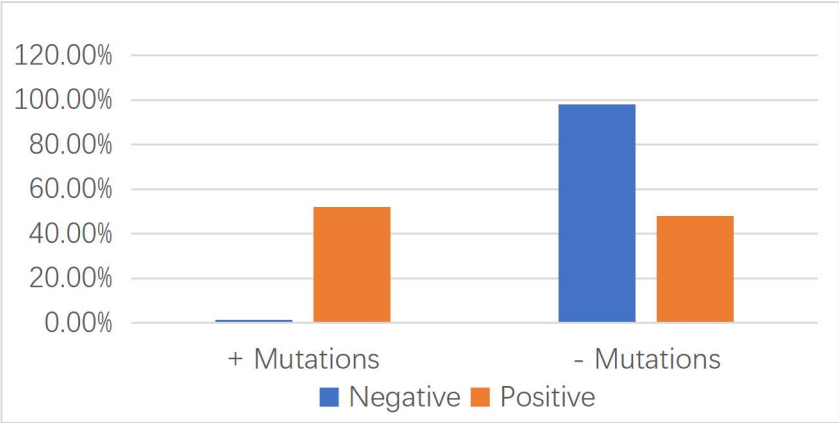

Fig 4 Helicobacter pylori status and p53 mutations in human

3.3.2Virus

There are studies stating that between 20-25% of all cancers are associated with microbial infections. Of these cancer-related pathogens, HPV accounts for approximately 30% of all of them. The HPV vaccine, which has become a big hit in recent years, is a vaccine against Human papillomavirus infection, which is closely related to the development of many diseases[44].

Mucous membranes and skin are the most common sites of infection, and HPV infection occurs through histopathology as a means of allowing the virus to enter the basal keratin. Epidemiological studies have shown that HPV is present in 99% of cervical cancers and therefore HPV infection is considered to be the main cause of cervical cancer. Cervical cancer is the third most common malignancy worldwide and the fourth leading cause of death in women. According to Torre et al, 527,600 new cases and 265,700 deaths from the disease were confirmed worldwide in 2012. The disease is highly prevalent in sub-Saharan Africa, Eastern Europe and Latin America [45].

3.3.3Obesity

Obesity is usually determined by the body mass index (BMI). If adult's BMI is greater than or equal to 30, then he or she is considered to be obese. Worldwide, obesity has become a growing health problem and a serious threat to human life and health. When the BMI is greater than 25 kg/m2, for every 5 unit increase in BMI there is a 29% increase in total mortality, a 41% increase in vascular mortality and a 210% increase in diabetes-related mortality [46]. The world health reports that 13% of adults over the age of 18 suffer from clinical obesity, totaling over 600 million people [47]. This health problem is particularly acute in Western countries, with recent reports indicating that obesity prevalence in young people is 40% in the US and 23% in the UK. There is no doubt that obesity in youth increases the risk of premature death [48]. Studies have shown that obesity is also associated with the development of cancers such as breast, colorectal, liver, pancreatic, endometrial, ovarian and esophageal cancers [47].

Chronic inflammation has been recognized as the bridge between obesity and cancer. The possible link between inflammation and cancer was first proposed in the 19th century when Rudolf Virchow observed the presence of white blood cells in tumors[49]. Obese people develop inflammation in specific metabolic tissues made up of fat cells due to excessive nutrient intake. Specifically, excess nutrients induce low levels of inflammatory cytokines by activating metabolic signaling pathways. Excess nutrients also induce changes in adipokine production and a low level of inflammatory response by promoting adipocyte proliferation. Excess nutrients also lead to an increase in endoplasmic reticulum stress, which activates unfolded protein responses, finally leading to inflammation[47]. Tumor-prone areas are at risk of developing cancer if there is persistent inflammation[50].

## 4. Conclusion

Regardless of physical, chemical and biological risk factors, most of them indirectly affect the occurrence of various cancers through the influence of genes and immune response. They can activate or inhibit genes. The change of gene activity affects a certain pathway, thus disturbing the normal proliferation and differentiation of cells. With the development of science technology and the investment of research, the carcinogenic mechanism of various factors has been studied to different degrees. However, we still do not know the specific mechanism of carcinogenic factors such as electromagnetic fields. Other risk factors that have been extensively studied also need further research. After studying the carcinogenic mechanism, we can promote the development of treatment by inhibiting the formation of certain pathways or promoting the development of some specific protein vaccines.

## Reference

[1] 3 February 2022; Available from: https://www.who.int/news-room/fact-sheets/detail/cancer.

[2] Weiderpass, E., Lifestyle and cancer risk. J Prev Med Public Health, 2010. 43(6): p. 459-71.

[3] Wang, J.J., K.F. Lei, and F. Han, Tumor microenvironment: recent advances in various cancer treatments. Eur Rev Med Pharmacol Sci, 2018. 22(12): p. 3855-3864.

[4] Aldrich, T.E. and C.E. Easterly, Electromagnetic fields and public health. Environ Health Perspect, 1987. 75: p. 159-71.

[5] Caplan, L.S., et al., Breast cancer and electromagnetic fields--a review. Ann Epidemiol, 2000. 10(1): p. 31-44.

[6] Tynes, T., Electromagnetic fields and male breast cancer. Biomed Pharmacother, 1993. 47(10): p. 425-7.

[7] Lewandowska, A.M., et al., Environmental risk factors for cancer - review paper. Ann Agric Environ Med, 2019. 26(1): p. 1-7.

[8] Moon, J.H., Health effects of electromagnetic fields on children. Clin Exp Pediatr, 2020. 63(11): p. 422-428.

[9] Gaynor, J.S., S. Hagberg, and B.T. Gurfein, Veterinary applications of pulsed electromagnetic field therapy. Res Vet Sci, 2018. 119: p. 1-8.

[10] Islam, M.T., Radiation interactions with biological systems. Int J Radiat Biol, 2017. 93(5): p. 487-493.

[11] O'Neill, P. and P. Wardman, Radiation chemistry comes before radiation biology. Int J Radiat Biol, 2009. 85(1): p. 9-25.

[12] Spitz, D.R., et al., Metabolic oxidation/reduction reactions and cellular responses to ionizing radiation: a unifying concept in stress response biology. Cancer Metastasis Rev, 2004. 23(3-4): p. 311-22.

[13] Sahin, E., et al., Telomere dysfunction induces metabolic and mitochondrial compromise. Nature, 2011. 470(7334): p. 359-65.

[14] Abalo, K.D., et al., Early life ionizing radiation exposure and cancer risks: systematic review and meta-analysis. Pediatr Radiol, 2021. 51(1): p. 45-56.

[15] Dugo, M.A., F. Han, and P.B. Tchounwou, Persistent polar depletion of stratospheric ozone and emergent mechanisms of ultraviolet radiation-mediated health dysregulation. Rev Environ Health, 2012. 27(2-3): p. 103-16.

[16] Mancebo, S.E. and S.Q. Wang, Skin cancer: role of ultraviolet radiation in carcinogenesis. Rev Environ Health, 2014. 29(3): p. 265-73.

[17] Matsumura, Y. and H.N. Ananthaswamy, Toxic effects of ultraviolet radiation on the skin. Toxicol Appl Pharmacol, 2004. 195(3): p. 298-308.

[18] Taguchi, K., et al., The role of epidermal Langerhans cells in NB-UVB-induced immunosuppression. Kobe J Med Sci, 2013. 59(1): p. E1-9.

[19] Calzavara-Pinton, P., et al., Photobiology, photodermatology and sunscreens: a comprehensive overview. Part 1: damage from acute and chronic solar exposure. G Ital Dermatol Venereol, 2013. 148(1): p. 89-106.

[20] Watson, M., D.M. Holman, and M. Maguire-Eisen, Ultraviolet Radiation Exposure and Its Impact on Skin Cancer Risk. Semin Oncol Nurs, 2016. 32(3): p. 241-54.

[21] Brambilla, E., et al., The new World Health Organization classification of lung tumours. Eur Respir J, 2001. 18(6): p. 1059-68.

[22] De Flora, S., et al., Modulation of cigarette smoke-related end-points in mutagenesis and carcinogenesis. Mutat Res, 2003. 523-524: p. 237-52.

[23] Hecht, S.S., Tobacco smoke carcinogens and lung cancer. J Natl Cancer Inst, 1999. 91(14): p. 1194-210.

[24] Schuller, H.M., Is cancer triggered by altered signalling of nicotinic acetylcholine receptors? Nat Rev Cancer, 2009. 9(3): p. 195-205.

[25] Wessler, I. and C.J. Kirkpatrick, Acetylcholine beyond neurons: the non-neuronal cholinergic system in humans. Br J Pharmacol, 2008. 154(8): p. 1558-71.

[26] Lindstrom, J., et al., Structure and function of neuronal nicotinic acetylcholine receptors. Prog Brain Res, 1996. 109: p. 125-37.

[27] Le Novère, N. and J.P. Changeux, Molecular evolution of the nicotinic acetylcholine receptor: an example of multigene family in excitable cells. J Mol Evol, 1995. 40(2): p. 155-72.

[28] Xiao, Y., et al., Rat neuronal nicotinic acetylcholine receptors containing alpha7 subunit: pharmacological properties of ligand binding and function. Acta Pharmacol Sin, 2009. 30(6): p. 842-50.

[29] Lang, K., et al., Induction of a metastatogenic tumor cell type by neurotransmitters and its pharmacological inhibition by established drugs. Int J Cancer, 2004. 112(2): p. 231-8.

[30] Boffetta, P. and M. Hashibe, Alcohol and cancer. Lancet Oncol, 2006. 7(2): p. 149-56.

[31] Rumgay, H., et al., Alcohol and Cancer: Epidemiology and Biological Mechanisms. Nutrients, 2021. 13(9).

[32] Personal habits and indoor combustions. IARC Monogr Eval Carcinog Risks Hum, 2012. 100(Pt E): p. 1-538.

[33] Seitz, H.K. and F. Stickel, Molecular mechanisms of alcohol-mediated carcinogenesis. Nat Rev Cancer, 2007. 7(8): p. 599-612.

[34] Pöschl, G. and H.K. Seitz, Alcohol and cancer. Alcohol Alcohol, 2004. 39(3): p. 155-65.

[35] Jakszyn, P. and C.A. Gonzalez, Nitrosamine and related food intake and gastric and oesophageal cancer risk: a systematic review of the epidemiological evidence. World J Gastroenterol, 2006. 12(27): p. 4296-303.

[36] González, C.A. and A. Agudo, Carcinogenesis, prevention and early detection of gastric cancer: where we are and where we should go. Int J Cancer, 2012. 130(4): p. 745-53.

[37] Sepich-Poore, G.D., et al., The microbiome and human cancer. Science, 2021. 371(6536).

[38] Alipour, M., Molecular Mechanism of Helicobacter pylori-Induced Gastric Cancer. J Gastrointest Cancer, 2021. 52(1): p. 23-30.

[39] Khatoon, J., R.P. Rai, and K.N. Prasad, Role of Helicobacter pylori in gastric cancer: Updates. World J Gastrointest Oncol, 2016. 8(2): p. 147-58.

[40] Machlowska, J., et al., Gastric Cancer: Epidemiology, Risk Factors, Classification, Genomic Characteristics and Treatment Strategies. Int J Mol Sci, 2020. 21(11).

[41] Hatakeyama, M., Helicobacter pylori CagA and gastric cancer: a paradigm for hit-and-run carcinogenesis. Cell Host Microbe, 2014. 15(3): p. 306-16.

[42] Cover, T.L., Helicobacter pylori Diversity and Gastric Cancer Risk. mBio, 2016. 7(1): p. e01869-15.

[43] Ismael, A.B., et al., Interferon-γ receptor-1 gene promoter polymorphisms and susceptibility for brucellosis in Makkah region. Afr Health Sci, 2018. 18(4): p. 1157-1165.

[44] Yang, A., et al., Perspectives for therapeutic HPV vaccine development. J Biomed Sci, 2016. 23(1): p. 75.

[45] Araldi, R.P., et al., The human papillomavirus (HPV)-related cancer biology: An overview. Biomed Pharmacother, 2018. 106: p. 1537-1556.

[46] Apovian, C.M., Obesity: definition, comorbidities, causes, and burden. Am J Manag Care, 2016. 22(7 Suppl): p. s176-85.

[47] Kolb, R., F.S. Sutterwala, and W. Zhang, Obesity and cancer: inflammation bridges the two. Curr Opin Pharmacol, 2016. 29: p. 77-89.

[48] Kang, S.Y. and H.S. Park, Gender Differences in Comorbidities and Attitudes Regarding Weight Control among Young Adults with Obesity in Korea. Obes Facts, 2022. 15(4): p. 581-589.

[49] Colotta, F., et al., Cancer-related inflammation, the seventh hallmark of cancer: links to genetic instability. Carcinogenesis, 2009. 30(7): p. 1073-81.

[50] Singh, N., et al., Inflammation and cancer. Ann Afr Med, 2019. 18(3): p. 121-126.