Open Access Library Journal
2024, Volume 11, e12607
ISSN Online: 2333-9721
ISSN Print: 2333-9705

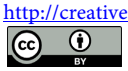
Exploring the Role of Chemicals and Environmental Factors for Cancer Proliferation

Asad Ullah[1], Muhammad Arif[2], Muhammad Waqas[3], Muhammad Hasnain[4], Anam Saira[5], Roha Tariq[6], Faiza Shahzad[7], Hamza Khaliq[7*]

[1]School of Chemical Engineering, Tianjin University, Tianjin
[2]Department of Safety Health and Environmental Engineering, Ming Chi University of Technology, New Taipei
[3]School of Biochemistry, Agriculture University, Faisalabad
[4]Institute of Molecular Aggregation, School of Science, Tianjin University, Tianjin
[5]College of Life Science, Northwest Agriculture and Forestry University, Xianyang
[6]Department of Biotechnology, Lahore College for Women University, Lahore
[7]College of Environment, Hohai University, Nanjing
Email: asadullahdgk9@gmail.com, m13168031@o365.muct.edu.wt, biochemistjamali@outlook.com, hasnain_chem@tju.edu.cn, anamsaira51@gmail.com, rohatariq248@gmail.com, D20200505@hhu.edu.cn, *hamzakhosa01@hhu.edu.cn

How to cite this paper: Ullah, A., Arif, M., Waqas, M., Hasnain, M., Saira, A., Tariq, R., Shahzad, F. and Khaliq, H. (2024) Exploring the Role of Chemicals and Environmental Factors for Cancer Proliferation. *Open Access Library Journal*, **11**: e12607.
https://doi.org/10.4236/oalib.1112607

Received: November 10, 2024
Accepted: December 17, 2024
Published: December 20, 2024



Abstract

Cancer is a multifaceted process influenced by a complex relationship of genetic, environmental, and lifestyle factors and remains a major global health concern. This review explores the intricate connections between environmental pollutants, industrial chemicals such as polycyclic aromatic hydrocarbons, benzene, asbestos, dioxins, and cancer, focusing on both their role in the initiation and progression of carcinogenesis and the potential for interventions to mitigate their effects. To understand the underlying mechanisms, the current review article summarized how these environmental factors interact with cellular pathways, including those involved in DNA damage repair, cell cycle regulation, and apoptosis. Key environmental risk factors such as air, radiation, and water pollution, exposure to hazardous industrial chemicals, and lifestyle-related toxins like tobacco are discussed in detail. A holistic strategy that involves reducing exposure to environmental carcinogens and advancing safer chemical therapies may hold the key to breaking the cancer cycle.

Subject Areas

Environmental Sciences and Chemical Engineering

Keywords

Cancer, Environmental Carcinogens, Chemical Intervention, Pollution Control

1. Introduction

Cancer is a multifaceted disease characterized by uncontrolled cell growth and proliferation. While genetic mutations play a significant role, environmental factors and chemicals are increasingly recognized as critical contributors to cancer development. Cancer has become a leading global health challenge, with an estimated 19.3 million new cases and 10 million cancer-related deaths reported in 2020. The prevalence of cancer continues to rise, not only due to the aging population but also because of increasing exposure to environmental carcinogens. The burden of cancer is felt worldwide, but the impact is particularly heavy in low- and middle-income countries, where healthcare infrastructure is less developed, and environmental regulations may be more lax [1]. The economic costs of cancer are staggering. In 2020 alone, the global economic burden of cancer was estimated at $1.16 trillion, factoring in healthcare costs, lost productivity, and the long-term care of patients. The social toll is equally severe, as cancer affects the quality of life, mental health, and life expectancy of individuals and communities. Beyond the direct impact on patients, families and societies bear a heavy burden, with many experiencing financial hardship due to treatment costs [2].

Global disparities in cancer incidence and mortality reflect differences in healthcare systems, access to early detection, and the prevalence of risk factors, including several environmental and lifestyle factors (Figure 1). In high-income

Figure 1. This figure exhibits the number of leading of risk factors leading to the development and progression of various human cancers globally.

countries, cancer survival rates tend to be higher due to better access to treatment, whereas in lower-income regions, preventable cancers often go undiagnosed or untreated [3]. Epidemiological studies have provided some evidence of an association between exposure to environmental contaminants such as organochlorines and increased cancer risk. However, many epidemiological studies have been inconclusive. Similar reviews concerning environmental influences in cancer aetiology concluded that exposures to carcinogenic or endocrine-disrupting chemicals exist at concentrations too low or have carcinogenic potential too weak to be considered a major factor in cancer aetiology [4]. In addition, studies show that low oestrogenic potency cannot be used as a marker of the capability of a chemical to cause oestrogenic responses and endocrine disruption. Genetic polymorphisms, which can predispose people to cancer, may interact with environmental contaminants such as organochlorines and endocrine disrupters, thus providing a modifying effect. Prevention measures have hitherto predominately centered on tobacco smoking cessation and diet education [5]. Anecdotal evidence from practicing physicians in pre-industrial and traditional living societies, such as Canadian Inuits and Brazilian Indians suggests malignant disease was rare. A relatively new theory other than the somatic mutation theory has been proposed, the main premise being that carcinogenesis is a problem of tissue organization, comparable with organogenesis. It is feasible that chemical environmental contaminants, in particular synthetic pesticides and organochlorines with endocrine-disrupting properties, could be major factors in cancer aetiology, particularly for hormone-dependent malignancies, such as breast, testicular and prostate cancers [6] [7]. Animal and in vitro studies provide good evidence of a feasible mechanism whereby environmentally relevant levels of organochlorines and substances of low oestrogenic potency can cause endocrine disruption and consequently malignant disease. In addition, low oestrogenic potency should not be used as a marker of the capability of a chemical to cause oestrogenic responses and endocrine disruption. Preventative measures other than education about tobacco, diet and the promotion of physical activity should be considered [8]. Moreover, it seems to be the most vulnerable members of society: the developing foetus, the developing child and adolescent and the genetically predisposed, who are at risk of developing cancer following involuntary exposure to environmental contaminants. This may be an appropriate time for governments to adopt the precautionary principle until substances to which members of society are involuntarily exposed are proven safe from long-term, low-level effects on human health. The World Health Organization estimates that between 1% and 5% of malignant diseases in developed countries are attributable to environmental factors, this figure may be underestimated. Some Studies suggest that cancer could be caused by several risk factors from industrialization [9].

This review article investigates the relative contribution of different environmental factors and chemicals to the proliferation of specific cancer types. By integrating insights from recent studies, we aim to provide a comprehensive un-

derstanding of how these factors influence cancer development and progression. Our research question is: How do specific environmental chemicals and factors contribute to the proliferation of different types of cancer, and what are the underlying mechanisms? We aim to explore how specific environmental chemicals and factors contribute to the proliferation of different types of cancer and what the underlying mechanisms are.

2. Research Strategy

We conducted a systematic review of the literature, focusing on studies published from 2020 to 2024. We used databases such as PubMed, Scopus, and Web of Science, and employed keywords such as "environmental chemicals", "cancer proliferation", "breast cancer", and "lung cancer". Studies were selected based on their relevance to the research question and the quality of their methodology.

3. Breast Cancer

Breast cancer is the most prevalent form of cancer among women globally. Recent studies have investigated the role of environmental chemicals, such as endocrine-disrupting chemicals (EDCs), in breast cancer proliferation. EDCs, including bisphenol A (BPA) and polychlorinated biphenyls (PCBs), have been shown to alter the expression of microRNAs (miRNAs) involved in cell proliferation and apoptosis. For instance, BPA exposure has been linked to the upregulation of miR-21, which promotes cell survival and proliferation. Additionally, exposure to pesticides and other agricultural chemicals has been associated with an increased risk of breast cancer. Epidemiological studies have found that women with higher levels of pesticide residues in their blood have a higher incidence of breast cancer 26. The mechanisms underlying these effects include the activation of estrogen receptors and the disruption of hormonal balance, which can lead to uncontrolled cell growth.

4. Lung Cancer

Lung cancer is another major health concern, with environmental pollutants and chemicals playing a significant role in its development. Air pollution, particularly fine particulate matter (PM 2.5), has been linked to an increased risk of lung cancer. PM 2.5 can induce oxidative stress and inflammation, leading to DNA damage and mutations in lung cells. Furthermore, exposure to asbestos and radon gas, common in occupational settings, has been strongly associated with lung cancer. Recent studies have also highlighted the role of tobacco smoke in lung cancer proliferation. Tobacco smoke contains numerous carcinogenic chemicals, including polycyclic aromatic hydrocarbons (PAHs) and nitrosamines, which can cause DNA adducts and mutations. These changes can lead to the activation of oncogenes and the inactivation of tumor suppressor genes, promoting uncontrolled cell growth.

5. Colorectal Cancer

Colorectal cancer is influenced by a combination of genetic and environmental

factors. Dietary habits, such as high consumption of red and processed meats, have been linked to an increased risk of colorectal cancer. These foods contain heterocyclic amines (HCAs) and polycyclic aromatic hydrocarbons (PAHs), which can cause DNA damage and mutations in colon cells. Exposure to certain chemicals, such as organochlorine pesticides and polychlorinated biphenyls (PCBs), has also been associated with an increased risk of colorectal cancer. These chemicals can disrupt cellular signaling pathways and promote inflammation, leading to the proliferation of cancer cells. Additionally, chronic inflammation, often caused by environmental factors such as poor diet and lack of physical activity, can create a microenvironment that supports cancer growth.

6. Role of Genetics and Environmental Factors in Cancer Development

Cancer is a multifactorial disease that arises from the interplay of genetic, chemical, and environmental factors (Table 1). While hereditary genetic mutations account for approximately 5% - 10% of all cancers, the majority are influenced significantly by environmental exposures, lifestyle choices, and interactions between the two. Understanding this balance is critical in developing effective prevention and treatment strategies [10]. Certain inherited genetic mutations, such as those in the BRCA1 and BRCA2 genes, significantly increase the risk of breast and ovarian cancers. Families with a history of hereditary cancer syndromes often exhibit a higher incidence of specific cancers due to these genetic predispositions. Genetic testing and counseling are vital for individuals with a family history of such cancers, enabling early detection and preventive measures. However, not all individuals with genetic mutations will develop cancer; this variability is often influenced by environmental factors [11].

Table 1. Key chemicals and their mechanisms in cancer proliferation.

Chemical agent	Mechanism of action	Cancer types affected	References
Polycyclic aromatic hydrocarbons (PAHs)	Bind to the aryl hydrocarbon receptor (AhR), leading to DNA damage and mutations	Lung, skin, bladder	[12]
Benzene	Induces oxidative stress and DNA adducts, causing chromosomal aberrations	Leukemia, lymphoma	[13]
Asbestos	Causes chronic inflammation and DNA damage, leading to mutations	Lung, mesothelioma	[14]
Dioxins	Disrupt endocrine and immune systems, leading to cell proliferation and tumor formation	Liver, soft tissue sarcoma	[15]
Formaldehyde	Causes DNA-protein cross-links and mutations	Nasopharyngeal, leukemia	[16]

The cancerous patients with a BRCA mutation may reduce their cancer risk through lifestyle changes, such as maintaining a healthy weight and avoiding smoking. Carcinogenesis is a multistep process, and tumors frequently harbor multiple mutations regulating genome integrity, cell division and death. The integrity of the cellular genome is closely controlled by the mechanisms of DNA damage signaling and DNA repair. The association of breast cancer susceptibility genes BRCA1 and BRCA2 with breast and ovarian cancer development was first demonstrated over 20 years ago [17] [18]. Since then, the germline mutations within these genes were linked to genomic instability and increased risk of many other cancer types. Genomic instability is an engine of the oncogenic transformation of non-tumorigenic cells into tumor-initiating cells and further tumor evolution. In this review, we discuss the biological functions of BRCA1 and BRCA2 genes and the role of BRCA mutations in tumor initiation, regulation of cancer stemness, therapy resistance and tumor progression. Environmental factors encompass a broad range of influences, including chemical exposures, radiation, infectious agents, and lifestyle behaviors [19]. The relationship between the domain functions of BRCA1/2 proteins and tumor development has been intensively investigated in animal models, as reviewed elsewhere, although the results of these studies are still awaiting confirmation by clinical data. About 70% - 80% of the mutations in BRCA genes result in protein dysfunction or the absence of protein products [20]. These mutations were confirmed as clinically relevant and are associated with an increased risk for the development of hereditary malignancies. Many studies have also reported an association of BRCA1/2 mutations with tumor aggressiveness and poor clinical outcomes in cancer patients. A large number of studies demonstrated the association of BRCA1/2 mutations in prostate cancer patients with an increased rate of intermediate- and high-risk disease [21]. On the other hand, clinical studies of the potential correlation between BRCA1 and BRCA2 mutations and outcomes in breast cancer patients provide conflicting results. Cancer stem cells (CSCs) are hypothesized to be the driving force behind tumor formation and recurrence. Genetic alterations that deregulate signaling pathways controlling stem cell proliferation, self-renewal, and metabolism are crucial in the formation and maintenance of CSCs [18]. Epigenetic modifications, such as DNA methylation and histone modification, can also play a significant role in cancer proliferation. (See **Table 2**) These changes can alter gene expression without changing the DNA sequence, leading to uncontrolled cell growth and tumor development [22].

7. Gene-Environment Interactions

The interaction between genetic predispositions and environmental factors is complex (**Figure 2**). Certain individuals may be more susceptible to environmental carcinogens due to their genetic makeup. This concept is known as gene-environment interaction, where specific genetic variants may modify an individual's response to environmental exposures. For instance, individuals with specific

Table 2. Environmental factors and their impact on cancer proliferation.

Environmental factor	Mechanism of action	Cancer types affected	References
Air pollution	Releases particulate matter and toxic gases, causing oxidative stress and DNA damage	Lung, bladder, breast	[23]
Radiation	Induces DNA double-strand breaks and chromosomal aberrations	Thyroid, leukemia, breast	[24]
Occupational exposure	Exposure to carcinogenic chemicals in the workplace	Lung, bladder, liver	[25] [26]
Diet	High intake of processed foods and red meat, low intake of fruits and vegetables	Colorectal, breast, prostate	[27]
Lifestyle factors	Smoking, alcohol consumption, sedentary lifestyle	Lung, liver, colorectal, breast	[28] [29]

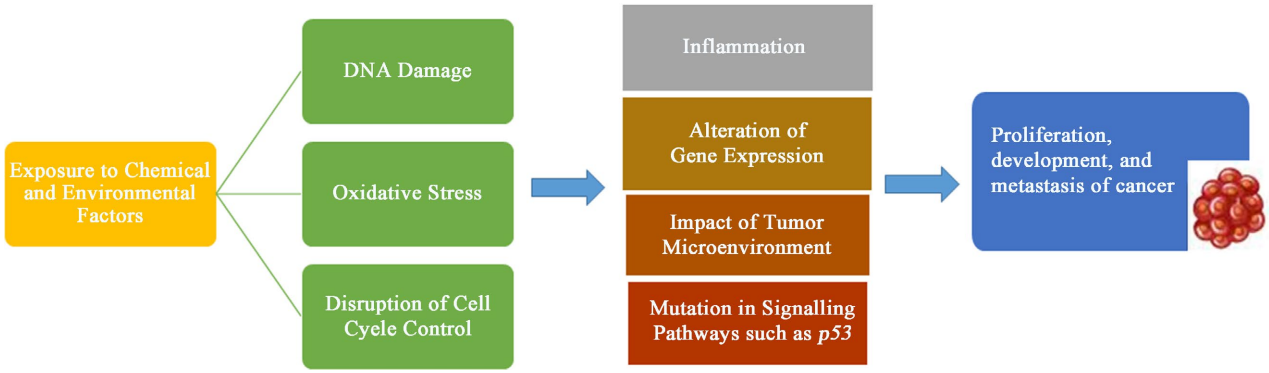


Figure 2. This diagrammatic figure illustrates the key alterations upon exposure to chemical and environmental factors, leading to several changes, including inflammation, alteration of gene expression, the impact of tumor microenvironments, and mutation in signaling pathways ultimately resulting in the development and metastasis of cancer cell.

metabolic enzyme variants may metabolize carcinogens more efficiently, thereby increasing their risk of developing cancer when exposed to environmental toxins [30]. Understanding the interplay between genetic and environmental factors is crucial for developing personalized prevention strategies and targeted therapies. Advances in genomics and epigenetics provide promising avenues for identifying high-risk individuals and tailoring interventions to mitigate their cancer risk. Environmental factors play a significant role in cancer development, contributing to the majority of cancer cases worldwide. This section explores the major environmental risk factors, including pollution, industrial chemicals, radiation, and lifestyle choices, and their association with various types of cancers [31].

8. Pollution

Pollution is a well-documented risk factor for cancer, particularly lung cancer. Studies have shown that exposure to particulate matter (PM 2.5 and PM 10), nitrogen oxides, and volatile organic compounds increases the risk of developing respiratory and other cancers. Furthermore, urban areas with high traffic density

often experience elevated levels of pollution, exacerbating health risks for residents. Water pollution is another critical concern, as contaminants such as arsenic, lead, and nitrates have been linked to various cancers, including bladder and skin cancer. Long-term exposure to arsenic through drinking water has been associated with skin lesions, internal cancers, and developmental effects [32]. Long-term exposure to ambient air pollution, particularly fine particulate matter (PM 2.5) and nitrogen dioxide (NO_2), can cause DNA damage and mutations. For example, a study found that a 5 $\mu g/m^3$ increase in PM 2.5 exposure is associated with a 6% increased risk of overall urological cancer, and a 10 $\mu g/m^3$ increase in NO_2 is linked to a 3% higher risk. Indoor pollutants such as cooking fumes and secondhand smoke can also cause DNA damage. A study analyzing pleural fluid for common air pollutants found biological evidence of these pollutants in the lungs, suggesting their role in lung cancer [33]. Environmental pollutants can induce epigenetic changes, including DNA methylation, histone modifications, and non-coding RNAs, which alter gene expression without changing the DNA sequence. These changes can contribute to the development and progression of lung cancer. Pollutants can trigger chronic inflammation, which is a known risk factor for cancer. Inflammation can lead to the production of reactive oxygen species (ROS), causing oxidative stress and further DNA damage [34]. Particulate matter and other pollutants can generate ROS, leading to oxidative stress and cellular damage, which can initiate and promote cancer development. PAHs, found in vehicle exhaust and industrial emissions, are potent carcinogens. They can bind to DNA and form adducts, leading to mutations and cancer. Arsenic and other heavy metals in drinking water and air can also cause cancer. Arsenic is particularly linked to skin, lung, and bladder cancer [35].

9. Industrial Chemicals

Occupational exposure to hazardous chemicals has been implicated in the development of many cancers. Carcinogens such as asbestos, benzene, formaldehyde, and polycyclic aromatic hydrocarbons (PAHs) are commonly found in industrial settings and have well-established links to specific cancers. Regulatory measures to limit exposure to these chemicals in the workplace have proven effective in reducing cancer incidence among exposed populations [36]. Pollution from chemical facilities will likely affect the health of any exposed population; however, the majority of scientific evidence available has focused on occupational exposure rather than environmental [37]. Consequently, this study assessed whether there could have been an excess of cancer-related mortality associated with environmental exposure to pollution from chemical installations for populations residing in municipalities in the vicinity of chemical industries [38].

Many industrial chemicals are genotoxic, meaning they can directly damage DNA. This damage can lead to mutations that initiate or promote cancer. For example, benzene, a common industrial solvent, has been shown to cause genetic damage and is linked to leukemia [18]. Polycyclic aromatic hydrocarbons (PAHs),

which are produced in the petrochemical industry, are known to cause DNA damage and are associated with lung cancer. Some chemicals can alter gene expression without changing the DNA sequence, leading to epigenetic changes. These changes can activate oncogenes or deactivate tumor suppressor genes, promoting cancer development [39]. For instance, bisphenol A (BPA) has been shown to affect epigenetic markers and is linked to colon cancer. Industrial chemicals can induce oxidative stress by generating reactive oxygen species (ROS). ROS can damage DNA, proteins, and lipids, leading to cellular dysfunction and cancer. For example, exposure to hexavalent chromium (Cr (VI)) causes oxidative stress and is linked to lung cancer. Chronic inflammation can create a microenvironment that supports cancer growth. Chemicals that cause inflammation can indirectly contribute to cancer. For instance, exposure to certain solvents has been associated with an increased risk of breast cancer [40].

10. Radiation

Radiation exposure, both ionizing and non-ionizing, is a well-known risk factor for several cancers. Ionizing radiation, such as that from X-rays and nuclear fallout, has been linked to cancers including leukemia, thyroid cancer, and breast cancer [41]. The risk is particularly heightened in children, who are more sensitive to radiation effects. Non-ionizing radiation, including ultraviolet (UV) radiation from the sun, is a significant cause of skin cancer, particularly melanoma [42]. Prolonged UV exposure leads to DNA damage in skin cells, increasing the likelihood of mutations that result in cancer. Diagnostic medical radiation has been the most rapidly increasing component of population background radiation exposure in Western countries over the past decade. This trend is set to increase as CT scanning is readily available with burgeoning use in everyday clinical practice. Consequently, the issue of cancer induction from the doses received during diagnostic medical exposures is highly relevant. The current understanding of potential cancer induction at low doses of sparsely ionizing radiation [41] [43]. For cancers that may be induced at low doses, a mechanistic description of radiation-induced cancer is discussed, which, in combination with extrapolation of data based on population cohort studies, provides the basis of the currently accepted linear no-threshold model. The assumptions made in deriving risk estimates, the controversies surrounding the linear no-threshold model and the potential future challenges facing clinicians and policy-makers about diagnostic medical radiation and cancer risk, most notably the uncertainties regarding deriving risk estimates from epidemiological data at low doses [44].

11. Lifestyle Factors

Lifestyle choices, including diet, physical activity, smoking, and alcohol consumption, significantly influence cancer risk [45]. Smoking is the leading preventable cause of cancer, linked to various malignancies, including lung, mouth, throat, and bladder cancers [46]. Lung cancer was a rare disease until the beginning of

the twentieth century, but since then it has become the most common nonskin malignancy worldwide, in terms of both incidence and mortality [47]. It accounts for an estimated 772,000 new cases each year in men (18% of all nonskin cancers) and 265,000 new cases amongst women (7%), less than half (42%) of which occur in developing countries. The main histological types of lung cancer are squamous cell carcinoma, small cell carcinoma, adenocarcinoma and large cell carcinoma [48] [49]. The geographical and temporal patterns of lung cancer incidence are largely determined by tobacco consumption patterns that took place two or more decades earlier. Populations with a high incidence of lung cancer are, therefore, those where tobacco consumption has been high during the last decades such as the USA, Canada and the UK and lung cancer incidence is low in countries where tobacco consumption has recently declined, including Sweden or consumption has only increased lately (e.g. China, India, Africa) [50]. As men took up tobacco use earlier than women, the increase in lung cancer incidence in men generally precedes that in women by several decades. There is a vast body of evidence supporting a causal association between tobacco smoking and the risk of lung cancer, but few data show an effect of smokeless tobacco [51]. Relative risks (RR) in the region of 10 - 15 are frequently quoted for the effect of smoking on lung cancer risk, although this reflects the contribution of different aspects of tobacco smoking. They concluded that the excess lung cancer risk rises in proportion to the square of the number of cigarettes smoked per day but to the fourth or fifth power of the duration of smoking. Other studies, however, suggest a comparable effect of the amount and duration of smoking. Furthermore, the results of a recent large case-control study conducted in several Western European countries suggest a plateau in the excess risk above 15 - 20 cigarettes per day, although others have not found evidence for this [52]. An important aspect of tobacco-related lung carcinogenesis is the effect of cessation of smoking. As compared with continuous smokers, the excess risk sharply decreases in ex-smokers after approximately 5 years after quitting. Although in some studies the risk after 20 years since cessation approaches that of never smokers, an excess risk probably persists throughout life. Age at the start of regular tobacco smoking is also important; smokers who started before age 15 had a four- to fivefold higher risk of lung cancer than smokers who started at age 25 or later. However, as periods of temporary quitting tend to be short, there is a strong relationship between age, age at start, duration of smoking and time since quitting, which makes it difficult to assess the independent effect of each temporal variable on lung cancer risk [53].

The risk of lung cancer is lower amongst smokers of low-tar and low-nicotine rather than high-tar/nicotine cigarettes, smokers of filtered rather than unfiltered cigarettes, and smokers of blond rather than black tobacco. It is difficult to separate these effects as tar content, presence of filter and type of tobacco are not independent, as cigarettes are often high tar because they are unfiltered and/or made of black tobacco. Other tobacco products, including cigars, cigarillos, pipes, hooka or bidis and Chinese water pipes also increase lung cancer incidence, probably at

a similar order of magnitude to cigarettes for comparable levels of consumption [54]. Although tobacco smoking induces all major histological types of lung cancer, the strongest associations are with squamous cell and small cell carcinoma: the RR for adenocarcinoma is four- to fivefold lower than for other histological types. The frequency of different histological types of lung cancer has changed over the last two decades in the USA and Europe, so squamous cell carcinoma has become less common and adenocarcinoma more frequent. This potentially reflects changes in patterns of tobacco consumption, such as deeper inhalation of low nicotine and tar tobacco smoke [55].

12. Diet and Obesity

A diet high in processed foods, red meats, and sugars, coupled with sedentary behaviour, contributes to obesity, which is a risk factor for several cancers, including breast, colorectal, and endometrial cancers. Most of the molecular mechanisms that induce obesity are also involved in the twelve Hallmarks of Cancer, with the fundamental process being the consumption of a highly processed, energy-dense diet and the deposition of fat in white adipose tissue and the liver. The generation of crown-like structures, with macrophages surrounding senescent or necrotic adipocytes or hepatocytes, leads to a perpetual state of chronic inflammation, oxidative stress, hyperinsulinemia, aromatase activity, activation of oncogenic pathways and loss of normal homeostasis [56]. Metabolic reprogramming, epithelial-mesenchymal transition, HIF-1α signalling, angiogenesis and loss of normal host immune surveillance are particularly important. Obesity-associated carcinogenesis is closely related to metabolic syndrome, hypoxia, visceral adipose tissue dysfunction, oestrogen synthesis and detrimental cytokine, adipokine and exosomal miRNA release [42]. This is particularly important in the pathogenesis of oestrogen-sensitive cancers, including breast, endometrial, ovarian and thyroid cancer, but also 'non-hormonal' obesity-associated cancers such as cardio-oesophageal, colorectal, renal, pancreatic, gallbladder and hepatocellular adenocarcinoma. Effective weight loss interventions may improve the future incidence of overall and obesity-associated cancer [57].

13. Alcohol Consumption

Regular consumption of alcohol has been associated with an increased risk of cancers such as breast, liver, and colorectal cancer. Among the risk factors for cancer that can be modified, tobacco and alcohol use are noteworthy. Alcohol is one of the few psychoactive drugs that are encouraged and accepted by society. Its consumption is increasing worldwide, especially in developing countries. According to Cancer Research UK (2012), there is evidence that, when compared to individuals who do not consume alcohol and do not use tobacco, those who drink and smoke have 50 times more chance of developing some form of cancer. In the UK, alcohol is responsible, every year, for 4% of cancers [58]. Deaths that are related to the consumption of alcoholic beverages amount to 1,804,000 per year or 3.2%

of all deaths in the world. In addition, when ingested in excess, alcohol may also be responsible for the development of heart disease, hypertension, stroke, pancreatitis and gastric ulcer [59] [60]. According to the World Health Organization, the number of deaths and limitations caused by alcohol exceeds those caused by tobacco use. There is convincing evidence linking the consumption of alcoholic beverages to cancers of the mouth, pharynx, larynx, oesophagus, breast and bowel, the latter being only in men. In addition, there is a likely relationship between the consumption of alcoholic beverages and an increased risk of colon cancer and liver cancer in women [61].

Addressing these environmental risk factors through public health interventions, regulations, and education can significantly reduce cancer incidence and improve overall health outcomes. (See **Table 3**)

Table 3. Summarizes the data for multiple risk factors responsible for skin cancer.

Risk factor	Description	Associated cancers	References
Pollution	Air pollution (PM 2.5, NOx) and water pollutants (arsenic, lead)	Lung cancer, bladder cancer, skin cancer	[25] [62]
Industrial chemicals	Carcinogenic substances like asbestos, benzene, formaldehyde, and PAHs	Mesothelioma, leukemia, nasopharyngeal cancer	[63] [64]
Radiation	Ionizing (X-rays, nuclear fallout) and non-ionizing (UV radiation)	Leukemia, thyroid cancer, skin cancer (melanoma)	[65] [66]
Lifestyle factors	Tobacco use, unhealthy diet, physical inactivity, and high alcohol consumption	Lung cancer, breast cancer, liver cancer, colorectal cancer	[28]

14. Comparative Perspectives and Controversies and Gaps in the Literature

Several studies have explored the role of chemical exposure in cancer risk, often with varying conclusions. For instance, while some studies have found a strong correlation between exposure to specific chemicals and increased cancer risk, others have reported mixed or inconclusive results. For example, the review assesses the risk of cancer-related to occupational exposure to pesticides, comparing regulatory toxicity results with epidemiological observations [67]. The authors highlight discrepancies between regulatory findings and epidemiological data, suggesting that current regulatory frameworks might not fully capture the true risk posed by pesticide exposure. Similarly, comparing different regression-based approaches for estimating interactions between chemical mixture components in a case-control study on non-Hodgkin's lymphoma, finding that different statistical methods can yield varying results, emphasizing the need for robust and consistent methodologies [68]. The impact of environmental factors on cancer proliferation is another area of active research. One of the studies emphasizes the importance of considering both genetic and environmental factors in cancer etiology, highlighting

that carcinogenic chemicals can initiate and promote tumorigenesis [69]. In contrast, several challenges in attributing cancer cases to specific environmental exposures have been observed, noting the lack of consensus within the scientific community on how to resolve controversies when both positive and negative studies exist [70]. This highlights the complexity and multifactorial nature of cancer etiology, where environmental factors interact with genetic predispositions in ways that are not yet fully understood.

One of the major controversies in the field is the mechanisms by which chemicals induce cancer. Organochlorine compounds, such as DDT and PCBs, are known animal carcinogens and tumor promoters. However, the extent to which these chemicals contribute to human breast cancer remains debated. Some studies, like, argue that exposure to environmental "estrogenic" chemicals can stimulate the proliferation of estrogen-sensitive breast cancer cells, while others, such as, report conflicting findings on the relationship between food intake and breast cancer risk [71]. These discrepancies underscore the need for more comprehensive and standardized research methodologies. Another significant controversy is the impact of chemical mixtures on human health. Most studies evaluate the risk of individual chemicals, but humans are typically exposed to a cocktail of chemicals in real life. The recent progress and tools for characterizing the health effects of chemical mixtures, highlighting the significance of the area to be explored [72]. We emphasize the need for a more holistic approach to assessing the combined effects of multiple chemicals, as traditional risk assessment methods may underestimate the true health impacts. There are also ongoing debates about the adequacy of current regulatory frameworks and risk assessment methods. This debate reflects broader concerns about the accuracy and reliability of current risk assessment practices. Additionally, highlights the challenges in comparing different statistical methods for estimating interactions between chemical mixtures, suggesting that more rigorous and standardized approaches are needed to ensure consistency and reliability in risk assessment [73].

15. Conclusion

The review highlights the complex interplay between environmental and genetic factors in the cancer cycle. For instance, exposure to environmental carcinogens, such as pollutants and dietary toxins, can interact with genetic predispositions, thereby increasing cancer susceptibility. However, their effectiveness can be influenced by individual genetic makeup and environmental exposures. For example, targeted therapies have revolutionized the treatment of specific cancers, but their success relies on accurate biomarker identification. This underscores the importance of integrating genetic testing into clinical practice to enhance treatment efficacy. Firstly, environmental chemicals, such as bisphenol A and perfluoro nonanoic acid, have been shown to contribute to sustained cell proliferation by interfering with basic cell control mechanisms. These chemicals can alter the immune microenvironment and the broader molecular landscape of cancers, such as he-

patocellular carcinoma and breast cancer, thereby promoting tumor growth and progression. Secondly, the role of cell proliferation in chemical carcinogenesis is a central theme. Induction of cell proliferation by environmental chemicals is a critical factor in both human cancer and rodent models. This underscores the importance of considering cell proliferation data in risk assessments for chemicals that are believed to cause cancer. Thirdly, the impact of environmental factors on cancer risk is not uniform across tissues. Some tissues are more susceptible to cancer induction due to specific susceptibility factors and cell proliferation patterns. For instance, gut microbiota dynamics and climate change have been implicated in the increased incidence of early-onset colorectal cancer. Moreover, the integration of clear endpoints that anchor key characteristics of cancer to the acquisition of a complete malignant phenotype is essential in chemical testing. This comprehensive approach helps in understanding the diverse manifestations and underlying mechanisms of cancer, including the role of the microenvironment. Additionally, the concept of green chemoprevention, which utilizes whole plant foods and extracts to prevent cancer, offers a promising avenue for reducing cancer risk. Phytochemicals, such as those found in broccoli sprouts and black raspberries, have demonstrated dose-responsive effects in both animal and human studies, highlighting their potential as natural anticancer agents. However, despite these advancements, significant challenges remain. The lack of standardized methodologies and the complexity of cancer biology necessitate further research to elucidate the precise mechanisms by which environmental chemicals induce cancer proliferation. Moreover, the development of personalized supplements and targeted therapies based on specific phytochemicals holds great promise but requires a deeper understanding of individual cellular responses. By addressing the challenges, we can move closer to reducing the global burden of cancer and improving patient outcomes.

Conflicts of Interest

The authors declare no conflicts of interest.

References

[1] Ghufran, M.S., Soni, P. and Duddukuri, G.R. (2023) The Global Concern for Cancer Emergence and Its Prevention: A Systematic Unveiling of the Present Scenario. In: Arunachalam, K., Yang, X. and Puthanpura Sasidharan, S., Eds., *Bioprospecting of Tropical Medicinal Plants*, Springer Nature, 1429-1455. https://doi.org/10.1007/978-3-031-28780-0_60

[2] Abrams, H.R., Durbin, S., Huang, C.X., Johnson, S.F., Nayak, R.K., Zahner, G.J., *et al.* (2021) Financial Toxicity in Cancer Care: Origins, Impact, and Solutions. *Translational Behavioral Medicine*, **11**, 2043-2054. https://doi.org/10.1093/tbm/ibab091

[3] Sawicki, T., Ruszkowska, M., Danielewicz, A., Niedźwiedzka, E., Arłukowicz, T. and Przybyłowicz, K.E. (2021) A Review of Colorectal Cancer in Terms of Epidemiology, Risk Factors, Development, Symptoms and Diagnosis. *Cancers*, **13**, Article 2025. https://doi.org/10.3390/cancers13092025

[4] Wan, M.L.Y., Co, V.A. and El-Nezami, H. (2021) Endocrine Disrupting Chemicals and Breast Cancer: A Systematic Review of Epidemiological Studies. *Critical Reviews in Food Science and Nutrition*, **62**, 6549-6576. https://doi.org/10.1080/10408398.2021.1903382

[5] Lacouture, A., Lafront, C., Peillex, C., Pelletier, M. and Audet-Walsh, É. (2022) Impacts of Endocrine-Disrupting Chemicals on Prostate Function and Cancer. *Environmental Research*, **204**, Article 112085. https://doi.org/10.1016/j.envres.2021.112085

[6] Soto, A.M. and Sonnenschein, C. (2021) The Cancer Puzzle: Welcome to Organicism. *Progress in Biophysics and Molecular Biology*, **165**, 114-119. https://doi.org/10.1016/j.pbiomolbio.2021.07.001

[7] Ahmed, U., Abubakar, M., Ayyoub, R. and Rehman, B. (2024) Stem Cells and Exosomes-Associated Therapeutic Applications. *Journal of Clinical and Nursing Research*, **8**, 232-246. https://doi.org/10.26689/jcnr.v8i6.7012

[8] Caserta, D., De Marco, M.P., Besharat, A.R. and Costanzi, F. (2022) Endocrine Disruptors and Endometrial Cancer: Molecular Mechanisms of Action and Clinical Implications, a Systematic Review. *International Journal of Molecular Sciences*, **23**, Article 2956. https://doi.org/10.3390/ijms23062956

[9] Ilic, M. and Ilic, I. (2022) Epidemiology of Stomach Cancer. *World Journal of Gastroenterology*, **28**, 1187-1203. https://doi.org/10.3748/wjg.v28.i12.1187

[10] Kachuri, L., Chatterjee, N., Hirbo, J., Schaid, D.J., Martin, I., Kullo, I.J., *et al.* (2023) Principles and Methods for Transferring Polygenic Risk Scores across Global Populations. *Nature Reviews Genetics*, **25**, 8-25. https://doi.org/10.1038/s41576-023-00637-2

[11] Pourmasoumi, P., Moradi, A. and Bayat, M. (2024) BRCA1/2 Mutations and Breast/Ovarian Cancer Risk: A New Insights Review. *Reproductive Sciences*, **31**, 3624-3634. https://doi.org/10.1007/s43032-024-01666-w

[12] Mallah, M.A., Changxing, L., Mallah, M.A., Noreen, S., Liu, Y., Saeed, M., *et al.* (2022) Polycyclic Aromatic Hydrocarbon and Its Effects on Human Health: An Overeview. *Chemosphere*, **296**, Article 133948. https://doi.org/10.1016/j.chemosphere.2022.133948

[13] Dewi, R., Hamid, Z.A., Rajab, N., Shuib, S. and Razak, S.A. (2019) Genetic, Epigenetic, and Lineage-Directed Mechanisms in Benzene-Induced Malignancies and Hematotoxicity Targeting Hematopoietic Stem Cells Niche. *Human & Experimental Toxicology*, **39**, 577-595. https://doi.org/10.1177/0960327119895570

[14] Mossman, B.T. and Gualtieri, A.F. (2020) Lung Cancer: Mechanisms of Carcinogenesis by Asbestos. In: Anttila, S. and Boffetta, P. Eds., *Occupational Cancers*, Springer International Publishing, 239-256. https://doi.org/10.1007/978-3-030-30766-0_12

[15] Jeno, J.G.A., Rathna, R. and Nakkeeran, E. (2021) Biological Implications of Dioxins/Furans Bioaccumulation in Ecosystems. In: Prasad, R., Ed., *Environmental and Microbial Biotechnology*, Springer, 395-420. https://doi.org/10.1007/978-981-15-5499-5_14

[16] Vijayraghavan, S. and Saini, N. (2023) Aldehyde-Associated Mutagenesis—Current State of Knowledge. *Chemical Research in Toxicology*, **36**, 983-1001. https://doi.org/10.1021/acs.chemrestox.3c00045

[17] Diez de los Rios de la Serna, C., Fernández-Ortega, P. and Lluch-Canut, T. (2022) Lifestyle Behavior Interventions for Preventing Cancer in Adults with Inherited Cancer Syndromes: Systematic Review. *International Journal of Environmental Research and Public Health*, **19**, Article 14098. https://doi.org/10.3390/ijerph192114098

[18] Abubakar, M., Ayyoub, R., Rehman, B., Zubair, M. and Ahmed, U. (2024) Advancing Cancer Stem Cell-Targeted Therapeutic Applications. *Proceedings of Anticancer Research*, **8**, 32-45. https://doi.org/10.26689/par.v8i5.7043

[19] Salmaninejad, A., Ilkhani, K., Marzban, H., Navashenaq, J.G., Rahimirad, S., Radnia, F., *et al.* (2021) Genomic Instability in Cancer: Molecular Mechanisms and Therapeutic Potentials. *Current Pharmaceutical Design*, **27**, 3161-3169. https://doi.org/10.2174/1381612827666210426100206

[20] Ahmed, U., Abubakar, M., Khan, S.S. and ur Rehman, B. (2024) Long Non-Coding RNA and Progression of Breast Cancer. *Oncology Treatment Discovery*, **2**, 38-64. https://doi.org/10.26689/otd.v2i3.7352

[21] Li, Q., Qian, W., Zhang, Y., Hu, L., Chen, S. and Xia, Y. (2023) A New Wave of Innovations within the DNA Damage Response. *Signal Transduction and Targeted Therapy*, **8**, Article No. 338. https://doi.org/10.1038/s41392-023-01548-8

[22] Verona, F., Pantina, V.D., Modica, C., Lo Iacono, M., D'Accardo, C., Porcelli, G., *et al.* (2022) Targeting Epigenetic Alterations in Cancer Stem Cells. *Frontiers in Molecular Medicine*, **2**, Article 1011882. https://doi.org/10.3389/fmmed.2022.1011882

[23] Lee, C., Vo, T.T.T., Wu, C., Chi, M., Lin, C., Fang, M., *et al.* (2020) The Inducible Role of Ambient Particulate Matter in Cancer Progression via Oxidative Stress-Mediated Reactive Oxygen Species Pathways: A Recent Perception. *Cancers*, **12**, Article 2505. https://doi.org/10.3390/cancers12092505

[24] Cheng, Z., Wang, Y., Guo, L., Li, J., Zhang, W., Zhang, C., *et al.* (2022) Ku70 Affects the Frequency of Chromosome Translocation in Human Lymphocytes after Radiation and T-Cell Acute Lymphoblastic Leukemia. *Radiation Oncology*, **17**, Article No. 144. https://doi.org/10.1186/s13014-022-02113-3

[25] Cani, M., Turco, F., Butticè, S., Vogl, U.M., Buttigliero, C., Novello, S., *et al.* (2023) How Does Environmental and Occupational Exposure Contribute to Carcinogenesis in Genitourinary and Lung Cancers? *Cancers*, **15**, Article 2836. https://doi.org/10.3390/cancers15102836

[26] Barsouk, A., Thandra, K.C., Saginala, K., Rawla, P. and Barsouk, A. (2021) Chemical Risk Factors of Primary Liver Cancer: An Update. *Hepatic Medicine: Evidence and Research*, **12**, 179-188. https://doi.org/10.2147/hmer.s278070

[27] Romaguera, D., Fernández-Barrés, S., Gracia-Lavedán, E., Vendrell, E., Azpiri, M., Ruiz-Moreno, E., *et al.* (2021) Consumption of Ultra-Processed Foods and Drinks and Colorectal, Breast, and Prostate Cancer. *Clinical Nutrition*, **40**, 1537-1545. https://doi.org/10.1016/j.clnu.2021.02.033

[28] Marino, P., Mininni, M., Deiana, G., Marino, G., Divella, R., Bochicchio, I., *et al.* (2024) Healthy Lifestyle and Cancer Risk: Modifiable Risk Factors to Prevent Cancer. *Nutrients*, **16**, Article 800. https://doi.org/10.3390/nu16060800

[29] Zelber-Sagi, S., Noureddin, M. and Shibolet, O. (2021) Lifestyle and Hepatocellular Carcinoma What Is the Evidence and Prevention Recommendations. *Cancers*, **14**, Article 103. https://doi.org/10.3390/cancers14010103

[30] Virolainen, S.J., VonHandorf, A., Viel, K.C.M.F., Weirauch, M.T. and Kottyan, L.C. (2022) Gene-Environment Interactions and Their Impact on Human Health. *Genes & Immunity*, **24**, 1-11. https://doi.org/10.1038/s41435-022-00192-6

[31] Li, Q., Lei, Y., Zhang, P., Liu, Y., Lu, Q. and Chang, C. (2024) Future Challenges and Prospects for Personalized Epigenetics. In: Tollefsbol, T., Ed., *Personalized Epigenetics*, Academic Press, 721-744. https://doi.org/10.1016/b978-0-443-23802-4.00019-3

[32] Shehata, S.A., Toraih, E.A., Ismail, E.A., Hagras, A.M., Elmorsy, E. and Fawzy, M.S.

(2023) Vaping, Environmental Toxicants Exposure, and Lung Cancer Risk. *Cancers*, **15**, Article 4525. https://doi.org/10.3390/cancers15184525

[33] Gavito-Covarrubias, D., Ramírez-Díaz, I., Guzmán-Linares, J., Limón, I.D., Manuel-Sánchez, D.M., Molina-Herrera, A., *et al.* (2024) Epigenetic Mechanisms of Particulate Matter Exposure: Air Pollution and Hazards on Human Health. *Frontiers in Genetics*, **14**, Article 1306600. https://doi.org/10.3389/fgene.2023.1306600

[34] Miguel, V., Lamas, S. and Espinosa-Diez, C. (2020) Role of Non-Coding-RNAs in Response to Environmental Stressors and Consequences on Human Health. *Redox Biology*, **37**, Article 101580. https://doi.org/10.1016/j.redox.2020.101580

[35] Santibáñez-Andrade, M., Quezada-Maldonado, E.M., Rivera-Pineda, A., Chirino, Y.I., García-Cuellar, C.M. and Sánchez-Pérez, Y. (2023) The Road to Malignant Cell Transformation after Particulate Matter Exposure: From Oxidative Stress to Genotoxicity. *International Journal of Molecular Sciences*, **24**, Article 1782. https://doi.org/10.3390/ijms24021782

[36] Riaz, S., Rasul, A., Khalil, M.A., Ameen, L., Riaz, K., Khan, S.G., *et al.* (2023) Cancer and Carcinogens. In: Ali, M.Y., Ed., *Cancer Targeting Therapies*, CRC Press, 20-40.

[37] Ahmad, M., Bangash, S.A., Shah, S.S., Chemingui, H. and Abubakar, M. (2024) Revolutionizing Healthcare in the Metaverse: The Power of Blockchain. In: Nijalingappa, P., Gururaj, T., Goyal, S.B., Shukla, V. and Bruno, A., Eds., *Examining the Metaverse in Healthcare*: *Opportunities*, *Challenges*, *and Future Directions*, IGI Global, 51-76. https://doi.org/10.4018/979-8-3693-1515-6.ch003

[38] Marquès, M., Domingo, J.L., Nadal, M. and Schuhmacher, M. (2020) Health Risks for the Population Living near Petrochemical Industrial Complexes. 2. Adverse Health Outcomes Other than Cancer. *Science of The Total Environment*, **730**, Article 139122. https://doi.org/10.1016/j.scitotenv.2020.139122

[39] Rehman, B., Abubakar, M., Kiani, M.N. and Ayyoub, R. (2024) Analysis of Genetic Alterations in TP53 Gene in Breast Cancer—A Secondary Publication. *Proceedings of Anticancer Research*, **8**, 25-35. https://doi.org/10.26689/par.v8i3.6720

[40] Denk, D. and Greten, F.R. (2022) Inflammation: The Incubator of the Tumor Microenvironment. *Trends in Cancer*, **8**, 901-914. https://doi.org/10.1016/j.trecan.2022.07.002

[41] Ali, Y.F., Cucinotta, F.A., Ning-Ang, L. and Zhou, G. (2020) Cancer Risk of Low Dose Ionizing Radiation. *Frontiers in Physics*, **8**, Article 234. https://doi.org/10.3389/fphy.2020.00234

[42] Abubakar, M., Ayyoub, R., Rehman, B., Kiani, M.N., Ahmed, U., Farooq, J., *et al.* (2024) Exploring Novel Therapeutic Breakthroughs for Cancers: Potential Roles of miRNAs. *Proceedings of Anticancer Research*, **8**, 11-24. https://doi.org/10.26689/par.v8i5.6924

[43] Khaliq, H., Shahzad, F., Ullah, A., Abid, M.A. and Gul, H. (2024) A Review on Emerging Contaminants: Effects on Human Health and Cancer Risks. *Journal of Clinical and Nursing Research*, **8**, 57-73. https://doi.org/10.26689/jcnr.v8i10.5724

[44] Wakeford, R. and Hauptmann, M. (2022) The Risk of Cancer Following High, and Very High, Doses of Ionising Radiation. *Journal of Radiological Protection*, **42**, Article 020518. https://doi.org/10.1088/1361-6498/ac767b

[45] Hussein, H.A., Thabet, A.A., Wardany, A.A. *et al.* (2024) SARS-CoV-2 Outbreak: Role of Viral Proteins and Genomic Diversity in Virus Infection and COVID-19 Progression. *Virology Journal*, **21**, 75.

[46] Lange, K.W. and Nakamura, Y. (2020) Lifestyle Factors in the Prevention of COVID-

19. *Global Health Journal*, **4**, 146-152. https://doi.org/10.1016/j.glohj.2020.11.002

[47] Abubakar, M. (2024) Overview of Skin Cancer and Risk Factors. *International Journal of General Practice Nursing*, **2**, 42-56. https://doi.org/10.26689/ijgpn.v2i3.8114

[48] Abubakar, M., Khatoon, N. and Saddique, A. (2024) Skin Cancer and Human Papillomavirus. *Journal of Population Therapeutics and Clinical Pharmacology*, **31**, 790-816.

[49] Yousaf, A., Tasneem, N., Mustafa, A., Fatima, R., Nabia, N., Khan, R.A., *et al.* (2021) Gastric Cancer Associated Risk Factors and Prevalence in Pakistan. *ASEAN Journal of Science and Engineering*, **1**, 73-78. https://doi.org/10.17509/ajse.v1i2.41124

[50] Islami, F., Torre, L.A. and Jemal, A. (2015) Global Trends of Lung Cancer Mortality and Smoking Prevalence. *Translational Lung Cancer Research*, **4**, 327-338. https://doi.org/10.3978/j.issn.2218-6751.2015.08.04

[51] Näsman, A., Du, J. and Dalianis, T. (2019) A Global Epidemic Increase of an HPV-Induced Tonsil and Tongue Base Cancer—Potential Benefit from a Pan-Gender Use of HPV Vaccine. *Journal of Internal Medicine*, **287**, 134-152. https://doi.org/10.1111/joim.13010

[52] Wang, X., Qian, Z., Zhang, Z., Cai, M., Chen, L., Wu, Y., *et al.* (2022) Population Attributable Fraction of Lung Cancer Due to Genetic Variants, Modifiable Risk Factors, and Their Interactions: A Nationwide Prospective Cohort Study. *Chemosphere*, **301**, Article 134773. https://doi.org/10.1016/j.chemosphere.2022.134773

[53] Cho, M. and Cho, Y.H. (2024) Factors Influencing the Intention for Lung Cancer Screening in High-Risk Populations for Lung Cancer. *Asia-Pacific Journal of Oncology Nursing*, **11**, Article 100332. https://doi.org/10.1016/j.apjon.2023.100332

[54] Hecht, S.S. and Hatsukami, D.K. (2022) Smokeless Tobacco and Cigarette Smoking: Chemical Mechanisms and Cancer Prevention. *Nature Reviews Cancer*, **22**, 143-155. https://doi.org/10.1038/s41568-021-00423-4

[55] Neuberger, M. (2021) Tobacco and Alternative Nicotine Products and Their Regulation. In: Reichl, F.X. and Schwenk, M., Eds., *Regulatory Toxicology*, Springer International Publishing, 1127-1151. https://doi.org/10.1007/978-3-030-57499-4_124

[56] Liang, Y., Kaushal, D. and Wilson, R.B. (2024) Cellular Senescence and Extracellular Vesicles in the Pathogenesis and Treatment of Obesity—A Narrative Review. *International Journal of Molecular Sciences*, **25**, Article 7943. https://doi.org/10.3390/ijms25147943

[57] Lathigara, D., Kaushal, D. and Wilson, R. (2023) Molecular Mechanisms of Western Diet-Induced Obesity and Obesity-Related Carcinogenesis—A Narrative Review. *Metabolites*, **13**, Article 675. https://doi.org/10.3390/metabo13050675

[58] Rumgay, H., Murphy, N., Ferrari, P. and Soerjomataram, I. (2021) Alcohol and Cancer: Epidemiology and Biological Mechanisms. *Nutrients*, **13**, Article 3173. https://doi.org/10.3390/nu13093173

[59] Barsouk, A., Aluru, J.S., Rawla, P., Saginala, K. and Barsouk, A. (2023) Epidemiology, Risk Factors, and Prevention of Head and Neck Squamous Cell Carcinoma. *Medical Sciences*, **11**, Article 42. https://doi.org/10.3390/medsci11020042

[60] Han, J., Ye, J., Shi, J., Fan, Y., Yuan, X., Li, R., *et al.* (2024) A Programmable Oral Nanomotor Microcapsule for the Treatment of Inflammatory Bowel Disease. *Advanced Functional Materials*. https://doi.org/10.1002/adfm.202413261

[61] Larsson, S.C., Carter, P., Kar, S., Vithayathil, M., Mason, A.M., Michaëlsson, K., *et al.* (2020) Smoking, Alcohol Consumption, and Cancer: A Mendelian Randomisation Study in UK Biobank and International Genetic Consortia Participants. *PLOS*

Medicine, **17**, e1003178. https://doi.org/10.1371/journal.pmed.1003178

[62] Abubakar, M. (2024) Exploring the Pivotal Association of AI in Cancer Stem Cells Detection and Treatment. *Proceedings of Anticancer Research*, **8**, 52-63. https://doi.org/10.26689/par.v8i5.7082

[63] Das, S., Kundu, M., Jena, B.C. and Mandal, M. (2020) Causes of Cancer: Physical, Chemical, Biological Carcinogens, and Viruses. In: Kundu, S.C. and Reis, R.L., Eds., *Biomaterials for 3D Tumor Modeling*, Elsevier, 607-641. https://doi.org/10.1016/b978-0-12-818128-7.00025-3

[64] Riaz, M.A., Abubakar, M., Ayyoub, R., Khan, A.N. and Hameed, Y. (2024) Expression Analysis of Caspase-3 (CASP3) Gene in Leukemia Patients Using Quantitative Polymerase Chain Reaction (qPCR) and Western Blot Techniques. *Journal of Cancer Biomoleculars and Therapeutics*, **1**, 10-16. https://doi.org/10.62382/jcbt.v1i2.17

[65] Ricci, A.M., Emeny, R.T., Bagley, P.J., Blunt, H.B., Butow, M.E., Morgan, A., *et al.* (2024) Causes of Childhood Cancer: A Review of the Recent Literature: Part I—Childhood Factors. *Cancers*, **16**, Article 1297. https://doi.org/10.3390/cancers16071297

[66] Abubakar, M. and Rehman, B. (2024) Roles of Mutant TP53 Gene in Cancer Development and Progression. *Proceedings of Anticancer Research*, **8**, 165-181. https://doi.org/10.26689/par.v8i5.7826

[67] Asefa, E.M., Damtew, Y.T. and Ober, J. (2024) Pesticide Water Pollution, Human Health Risks, and Regulatory Evaluation: A Nationwide Analysis in Ethiopia. *Journal of Hazardous Materials*, **478**, Article 135326. https://doi.org/10.1016/j.jhazmat.2024.135326

[68] Rakhshaninejad, M., Fathian, M., Shirkoohi, R., Barzinpour, F. and Gandomi, A.H. (2024) Refining Breast Cancer Biomarker Discovery and Drug Targeting through an Advanced Data-Driven Approach. *BMC Bioinformatics*, **25**, Article No. 33. https://doi.org/10.1186/s12859-024-05657-1

[69] Li, Q., Geng, S., Luo, H., Wang, W., Mo, Y., Luo, Q., *et al.* (2024) Signaling Pathways Involved in Colorectal Cancer: Pathogenesis and Targeted Therapy. *Signal Transduction and Targeted Therapy*, **9**, Article No. 266. https://doi.org/10.1038/s41392-024-01953-7

[70] Jansen, S.N.G., Kamphorst, B.A., Mulder, B.C., van Kamp, I., Boekhold, S., van den Hazel, P., *et al.* (2024) Ethics of Early Detection of Disease Risk Factors: A Scoping Review. *BMC Medical Ethics*, **25**, Article No. 25. https://doi.org/10.1186/s12910-024-01012-4

[71] Sharma, N., Kumar, V., S., V., Umesh, M., Sharma, P., Thazeem, B., *et al.* (2024) Hazard Identification of Endocrine-Disrupting Carcinogens (EDCs) in Relation to Cancers in Humans. *Environmental Toxicology and Pharmacology*, **109**, Article 104480. https://doi.org/10.1016/j.etap.2024.104480

[72] Bellingham, M., Evans, N.P., Lea, R.G., Padmanabhan, V. and Sinclair, K.D. (2024) Reproductive and Metabolic Health Following Exposure to Environmental Chemicals: Mechanistic Insights from Mammalian Models. *Annual Review of Animal Biosciences*, **13**. https://doi.org/10.1146/annurev-animal-111523-102259

[73] Woodruff, T.J., Rayasam, S.D.G., Axelrad, D.A., Koman, P.D., Chartres, N., Bennett, D.H., *et al.* (2023) A Science-Based Agenda for Health-Protective Chemical Assessments and Decisions: Overview and Consensus Statement. *Environmental Health*, **21**, Article No. 132. https://doi.org/10.1186/s12940-022-00930-3