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Review Article

Impact of Global Warming on Cancer Development: A Review of Environmental Carcinogens and Human Immunogenetics

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Abstract

This paper examines the impact of global warming on cancer development, specifically focusing on the intensified effects of environmental carcinogens such as ultraviolet (UV) radiation and air pollutants. Our review elucidates the intricate interplay between global warming, ecological carcinogens, human immunogenetics, and cancer susceptibility. The analysis highlights the exacerbating effects of rising temperatures and changes in atmospheric conditions on exposure to UV radiation and air pollutants, including particulate matter (PM), polycyclic aromatic hydrocarbons (PAHs), nitrogen dioxide (NO_2), nitrogen oxides (NOx), and ground-level ozone (O_3). Furthermore, the study explores the pivotal role of human immunogenetics in modulating individual responses to carcinogen exposure and shaping cancer susceptibility and progression. Genetic variations in key immune-related genes and their influence on the interplay between environmental carcinogens and cancer development are discussed. The paper underscores the importance of longitudinal cohort studies, integrative approaches, and interdisciplinary collaborations to advance our understanding of the complex interactions between global warming, environmental carcinogens, human immunogenetics, and cancer biology. Additionally, evidence-based public health interventions targeting environmental carcinogens and personalized prevention strategies based on genetic susceptibility profiles and environmental exposure assessments are proposed to address the growing challenges of environmentally induced cancers.

Keywords: global warming, environmental carcinogens, cancer immunogenetics, ultraviolet radiation, air pollutants, genetic susceptibility

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1. Introduction

The relationship between global warming and human health has garnered significant attention across interdisciplinary fields such as environmental science, public health, and genetics [1]. Global warming, primarily driven by human activities such as greenhouse gas emissions (e.g., carbon dioxide and methane), manifests in a range of environmental shifts, including alterations in temperature, precipitation patterns, and atmospheric conditions. These changes affect meteorological phenomena and have profound implications for human biology and susceptibility to diseases [2].

Environmental alterations induced by global warming significantly impact human health through various pathways, including increased exposure to carcinogens like ultraviolet (UV) radiation and air pollution [3, 4]. UV radiation exposure, exacerbated by global warming-induced ozone depletion, is associated with an elevated risk of skin cancer [3]. Similarly, exposure to air pollution has been linked to various types of cancer, including lung and breast cancer [5].

Understanding the connection between global warming and cancer is crucial due to the substantial health implications associated with cancer, a leading cause of morbidity and mortality worldwide [6]. Factors such as environmental exposures and genetic predisposition influence cancer incidence [7]. As awareness grows regarding the effects of global warming on cancer risk through increased exposure to UV radiation and air pollution, exploring how these factors interact with human immunogenetics to influence cancer susceptibility emerges as a novel area of research [8–10].

Immunogenetics, the branch of genetics concerned with the genetic basis of the immune response, plays a pivotal role in comprehending the complex interactions between environmental exposures and cancer susceptibility [11]. By elucidating how global warming contributes to cancer risk through environmental exposures and their interaction with human immunogenetics, targeted interventions and public health strategies can be developed to mitigate these risks and alleviate the burden of cancer on society.

In this review, we aim to bridge the gap in synthesizing the intricate mechanisms linking the impact of global warming, specifically the increase in UV radiation exposure and air pollution, to human immunogenetics and cancer susceptibility. We will examine current cancer trends and their relationship with global warming, focusing on exposure to UV radiation and air pollution. Furthermore, we will investigate the influence of genetic factors on cancer susceptibility and progression, particularly in the context of global warming's impact on immunogenetics. Finally, we will discuss the implications of these findings for future research directions and public health interventions aimed at mitigating the adverse effects of environmental changes on human health.

By integrating findings from molecular genetics, epidemiology, and environmental science, this review seeks to provide a perspective on the complex interplay between global warming, environmental exposures, human immunogenetics, and cancer biology. It aims to address critical knowledge gaps

regarding the mechanisms linking global warming to cancer outcomes and guide the development of targeted public health interventions.

2. Materials and Methods

This study employed a literature review approach to investigate the impact of global warming on cancer development, focusing on the interplay between environmental carcinogens and human immunogenetics. A systematic search was conducted in electronic databases including PubMed, Google Scholar, and Web of Science using relevant keywords such as “global warming,” “environmental carcinogens,” “cancer immunogenetics,” and related terms. The search was limited to articles published in English from inception to 1995, encompassing peer-reviewed research articles, review papers, and meta-analyses.

Inclusion criteria for articles consisted of studies that examined the association between global warming-induced environmental changes and cancer incidence, prevalence, or susceptibility. Additionally, articles investigating the role of environmental carcinogens, such as UV radiation, air pollutants, and other carcinogens, in cancer development were included. Studies exploring the impact of genetic variations in immune-related genes on individual responses to carcinogen exposure and cancer susceptibility were also considered.

Exclusion criteria comprised studies not relevant to the topic, including those focusing solely on non-human models, non-cancer outcomes, or lacking relevance to global warming or environmental carcinogens. Duplicate studies and articles lacking full-text availability were also excluded.

Data extraction was performed independently by two reviewers, and any discrepancies were resolved through discussion and consensus. Extracted data included study characteristics (e.g., author, year of publication, study design), participant demographics, exposure assessment methods, genetic analyses, cancer outcomes, and key findings related to the impact of global warming on cancer development and human immunogenetics.

Quality assessment of included studies was conducted using established criteria tailored to study design (e.g., Newcastle-Ottawa Scale for cohort and case-control studies, PRISMA guidelines for systematic reviews and meta-analyses). Studies were evaluated for methodological rigor, sample size adequacy, exposure assessment validity, genetic analysis reliability, and appropriateness of statistical analyses.

Data synthesis involved a narrative synthesis approach, whereby findings from included studies were qualitatively summarized and synthesized to elucidate the complex interplay between global warming, environmental carcinogens, and human immunogenetics in cancer development. Emphasis was placed on identifying common themes, patterns, and associations across studies, as well as gaps in the literature and areas warranting further investigation.

Overall, this methodology facilitated an exploration of the impact of global warming on cancer development through an integration of environmental, genetic, and epidemiological evidence, shedding light on the intricate mechanisms underlying carcinogen-induced alterations in cancer immunogenetics and informing future research directions and evidence-based interventions.

2.1. Cancer trends, global warming, and carcinogens

Global warming exacerbates exposure to various carcinogens, including increased UV radiation and elevated levels of air pollutants such as particulate matter (PMs), polycyclic aromatic hydrocarbons (PAHs), nitrogen dioxide (NO_2), nitrogen oxides (NOx), and ground-level ozone (O_3) [12–15]. Rising temperatures and changes in atmospheric conditions contribute to the depletion of the ozone layer, intensifying UV radiation reaching the Earth's surface. Concurrently, climate change influences weather patterns and atmospheric chemistry, accumulating air pollutants from sources like wildfires, transportation, and industrial activities.

Evidence shows that specific carcinogens, including air pollution and UV exposure, are associated with an increase in cancer incidence. Skin cancer, including melanoma and non-melanoma skin cancers, has become increasingly prevalent, particularly in regions experiencing higher levels of UV radiation due to climate change-induced alterations in atmospheric conditions [16,17]. The depletion of the stratospheric ozone layer due to human activities, such as the release of chlorofluorocarbons (CFCs), has increased UVR exposure on Earth's surface, heightening the risk of skin cancer [18]. According to the UK climate model, temperatures are expected to increase significantly due to climate change, potentially rising by 2 to 3.5°C by the 2080s. These higher temperatures might enhance the cancer-causing effects of UV radiation, possibly resulting in a 7.5% increase in cancer risk with a 3.5°C rise. This interaction could lead to an additional 5000–6000 cases of skin cancer each year in the UK by 2050 [18]. Certain populations, including outdoor workers and individuals with fair skin, are more vulnerable to the combined effects of UVR exposure and climate change, necessitating targeted public health strategies [18].

PM refers to tiny particles of solid or liquid suspended in the air, varying in size and composition. PM10 specifically refers to particles with a diameter of 10 μm or smaller. These particles can originate from various sources such as vehicle emissions, industrial activities, construction, and natural sources like wildfires and dust storms [19]. A recent cohort study by Lee et al. in Seoul Metropolitan revealed an association between long-term exposure to PM10 and increased lung cancer risks [20]. Similarly, a study by Liu et al. found a correlation between short-term exposure to PM10 and a higher risk of lung cancer death in Wuhai City, China [21].

PAHs are a group of chemicals naturally occurring in coal, crude oil, and gasoline and are produced during combustion processes involving coal, oil, gas, wood, garbage, and tobacco. These chemicals persist in the environment, accumulating in human tissues and increasing the risk of various cancers

[22–24]. For example, Moubarz et al. monitored PAH levels in secondary aluminum plant workers' air and serum, revealing significantly elevated levels of PAH biomarkers among exposed workers, especially those with specific genetic variants, suggesting a potential risk of lung cancer development [25]. Additionally, a systematic review and meta-analysis by Cebrián et al. analyzed epidemiological evidence on the association between PAH exposure and breast cancer, demonstrating a significant positive association between occupational and/or environmental PAH exposure and BC risk [26].

NO_2 and NOx are air pollutants composed of nitrogen and oxygen molecules, primarily released into the atmosphere through combustion processes such as vehicle emissions, industrial activities, and power generation, with contributions from natural sources like lightning and soil bacteria. Hamra et al. conducted a meta-analysis investigating the link between NOx exposure, including NO_2, and lung cancer risk. They found a consistent association between NO_2 exposure and lung cancer risk, with a 4% increase per 10-$\mu g/m^3$ rise in NO_2 levels, with similar results observed for NOx exposure [27]. Another meta-analysis by Praud et al., of 13 studies on NO_2 and NOx exposure, showed a significant positive association between NO_2exposure and breast cancer risk [28]. Raaschou-Nielsen et al. investigated the association between NOx concentrations and the risk of cancers in a Danish cohort, discovering that higher levels of NOx at residential addresses were significantly associated with increased risks of cervical cancer and brain cancer, suggesting a potential link between NOx and these cancers [29].

O_3, often referred to as "bad ozone," is a harmful air pollutant composed of oxygen molecules combined with volatile organic compounds and NOx. It forms near the Earth's surface through a complex chemical reaction involving sunlight and emissions from vehicles, industrial facilities, and other sources. O_3 can irritate the respiratory system, leading to shortness of breath, chest pain, coughing, and throat irritation [14, 30]. Kazemiparkouhi et al. examined the association between long-term, daily 1-hour maximum O_3 exposures and cause-specific mortality among 22.2 million US Medicare beneficiaries from 2000 to 2008. They found that long-term O_3 exposures were consistently associated with increased risks of mortality from lung cancer [31].

Epidemiological evidence supports the association between global warming and changes in cancer patterns, highlighting the complex interplay between environmental conditions and public health outcomes.

Understanding the impact of carcinogens such as UV radiation and air pollution, exacerbated by global warming, on immunogenetic associations with cancer risk requires a foundational understanding of human immunogenetics and its intricate role in cancer. This understanding sets the stage for examining how the changing environmental landscape, influenced by global warming, interacts with human immunogenetics to shape cancer trends and outcomes.

2.2. Human immunogenetics and cancer

Human immunogenetics, pivotal for understanding individual responses to cancer development and progression, explores genetic variation in the immune system. The immune system serves as a surveillance mechanism against malignant cells by recognizing and eliminating abnormal cells. As shown in Table 2, this process involves various components such as major histocompatibility complex (MHC) molecules, immune checkpoint proteins, cytokines, and diverse immune cell populations.

2.2.1. Major histocompatibility complex molecules

Major histocompatibility complex (MHC) molecules, also known as Human Leukocyte Antigen (HLA) molecules in humans, are vital components of the immune system responsible for presenting antigens to T cells and initiating immune responses against pathogens and cancer cells. MHC Class I (MHC-I) molecules, expressed on the surface of almost all nucleated cells in the body, including cancer cells, present endogenous antigens, including tumor-specific antigens, to cytotoxic T cells (CD8+ T cells). This presentation enables cytotoxic T cells to recognize and eliminate cells displaying abnormal or foreign proteins derived from tumor antigens, playing a critical role in immune surveillance and the eradication of cancer cells. Genetic variations in MHC-I genes, particularly the highly polymorphic HLA genes such as *HLA-A*, *HLA-B*, and *HLA-C*, can influence the efficiency of antigen presentation, impacting an individual's susceptibility to cancer and the effectiveness of immune responses against cancer cells [32, 33].

In contrast, MHC Class II (MHC-II) molecules, primarily expressed on antigen-presenting cells (APCs) such as dendritic cells, macrophages, and B cells, are crucial in coordinating immune responses against cancer. Although not present on cancer cells themselves, MHC-II molecules present exogenous antigens, including antigens derived from pathogens or cancer cells to helper T cells (CD4+ T cells). This interaction activates helper T cells, enhancing immune responses against cancer cells by activating cytotoxic T cells and other immune cells. Although MHC-II molecules are not directly involved in presenting tumor antigens on cancer cells, they are essential for initiating and coordinating immune responses against cancer by presenting antigens derived from cancer cells to helper T cells [34, 35].

Genetic variations in MHC genes can influence the efficiency of antigen presentation, impacting an individual's susceptibility to cancer. Specific HLA alleles, different variants of HLA genes, have been associated with either increased or decreased risk of developing certain types of cancer. The binding affinities and antigen presentation capabilities of different HLA molecules toward various tumor-associated antigens significantly impact their affinity and effectiveness in immune responses against cancer cells [36, 37].

2.2.2. Immune checkpoint proteins

Immune checkpoint proteins, including T-lymphocyte-associated protein 4 (CTLA-4), programmed cell death protein 1 (PD-1), and Programmed Death Ligand 1 (PD-L1), are essential for modulating immune responses and maintaining self-tolerance. In cancer, tumor cells exploit these checkpoints to evade immune surveillance by upregulating the expression of checkpoint proteins, particularly PD-L1, which engages with PD-1 receptors on T cells, serving as brakes to inhibit T cell activity, leading to T cell exhaustion and immune suppression. This immune evasion mechanism enables tumor growth and progression. Immune checkpoint inhibitors such as ipilimumab, pembrolizumab, and nivolumab have emerged as groundbreaking therapies by disrupting these interactions and reinvigorating anti-tumor immune responses [38]. Polymorphisms in immune checkpoint genes such as CTLA-4, PD-1, and PD-L1 can impact cancer susceptibility and progression by altering the expression or function of these proteins. For example, a single nucleotide polymorphism (SNP) in the PD-L1 gene, known as rs4143815, has been associated with increased susceptibility to various cancers, including gastric, bladder, and liver cancer [39].

2.2.3. Cytokines

Cytokines are a diverse group of signaling molecules that regulate immune responses and inflammation. In the immunogenetics of cancer, cytokines play crucial roles in modulating tumor development, progression, and the host immune response against cancer cells. For instance, Interleukin-6 (IL-6), a pro-inflammatory cytokine encoded by the IL6 gene, has been extensively studied in various cancers due to its pleiotropic effects on tumor growth, angiogenesis, and metastasis. Genetic variations in the IL6 gene, such as the –174G/C polymorphism, have been associated with increased susceptibility to skin, liver, and gastric cancer [40–42]. Similarly, Interleukin-10 (IL-10), an anti-inflammatory cytokine encoded by the IL10 gene, plays a crucial role in regulating immune responses and has been implicated in cancer immune evasion. Pan et al. conducted a meta-analysis studying the association between the A allele of IL-10-1082 promoter polymorphism and the risk of gastric cancer in both Asian and Caucasian populations. They found a significant association between the A allele and a decreased risk of gastric cancer in both ethnic groups, suggesting that the IL-10-1082 polymorphism may serve as a genetic marker for gastric cancer susceptibility [43]. Additionally, Tumor Necrosis Factor-alpha (TNF-α), a pro-inflammatory cytokine encoded by the TNF gene, has been implicated in cancer development and progression. Variations in the TNF gene, such as the –308G/A polymorphism, have been associated with upper aerodigestive tract cancer [44].

2.2.4. Genetic diversity within immune cell populations

Genetic diversity within immune cell populations, including T cells, B cells, natural killer (NK) cells, and macrophages, significantly influences their effector functions in tumor immunity. For example, NK cells are pivotal in immune surveillance against cancer cells. The interaction between Killer-cell Immunoglobulin-like Receptors (KIRs), located on NK cells, and HLA molecules plays a critical role in cancer immunogenetics. This interaction regulates NK cell activity, with KIRs capable of either activating or inhibiting NK cell responses upon binding to HLA molecules on target cells [45]. Ghaderi et al. conducted a study in southern Iran, revealing specific KIR genotypes, such as KIR2DL2 and 2DS2, and their interactions with HLA-C1 ligands, which were associated with an increased risk of lung cancer. Additionally, genotype ID19, a specific KIR genotype pattern, was implicated in lung cancer susceptibility [46]. In another example, Wang et al. developed a unique mouse model of head and neck squamous cell carcinoma to investigate the underlying mechanisms of heterogeneous antitumor immunity. They found that genetically identical mice responded differently to the same tumors, with some mice reproducibly eradicating tumors without intervention. This heterogeneous response depended on CD8 T cells, and T cell receptor (TCR) sequences analysis revealed distinct TCR repertoires and activation states between regressing and growing tumors, suggesting individualized antitumor immune responses with implications for personalized cancer immunotherapy [47].

2.2.5. Immunodeficiency

Individuals with immunodeficiencies, whether congenital or acquired, face an increased risk of developing certain cancers due to impaired immune system function, leading to a higher frequency of tumor development. For example, individuals with HIV/AIDS have an elevated risk of developing cancers such as Kaposi's sarcoma, non-Hodgkin lymphoma, and cervical cancer due to the weakened immune response caused by the virus, which allows oncogenic viruses like human papillomavirus to proliferate unchecked and contribute to tumor formation [48, 49]. In another example, patients with Crohn's disease have been reported to have a higher risk of small bowel cancer [50].

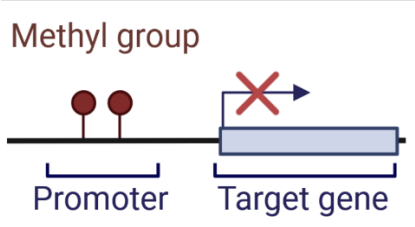
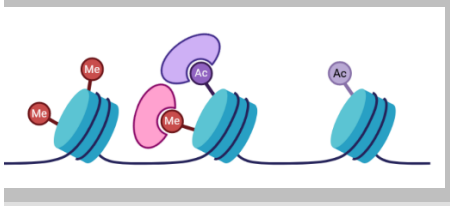
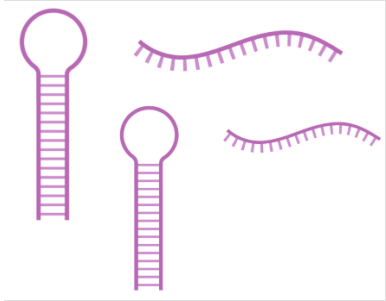
2.2.6. Epigenetic modifications

Epigenetic modifications, encompassing DNA methylation, histone modifications, and non-coding RNA regulation, are pivotal in regulating gene expression patterns and consequently influencing cancer susceptibility and progression (Table 1). DNA methylation alterations, such as hypermethylation of tumor suppressor genes and hypomethylation of oncogenes, disrupt normal cellular functions by modulating gene accessibility to transcription factors. Similarly, histone modifications, including acetylation and methylation, dictate chromatin structure and gene expression profiles, with aberrations contributing to

cancer initiation and metastasis. Moreover, non-coding RNAs, such as microRNAs (miRNAs), long non-coding RNAs (lncRNAs), and circular RNAs (circRNAs), intricately regulate gene expression by targeting mRNAs for degradation or modifying chromatin structure, and their dysregulation is associated with various cancer hallmarks [51].

The dysregulation of epigenetic mechanisms in cancer arises from diverse factors, including genetic mutations in epigenetic regulator genes, alterations in cofactor availability, and changes in non-coding RNA expression levels. These disruptions lead to abnormal gene expression patterns characteristic of cancer cells, promoting uncontrolled proliferation, evasion of cell death, and metastatic spread. For instance, Kim et al. demonstrated how overexpression of miR-619-5p induces lung cancer cell growth and metastasis by suppressing RCAN1.4, which functions as a tumor suppressor [52].

Table 1: Epigenetic mechanisms in cancer.

Epigenetic Mechanism	Contribution to Cancer
DNA Methylation 	Hypermethylation of tumor suppressor gene promoters leads to transcriptional silencing, promoting tumorigenesis. Hypomethylation of oncogene promoters results in their overexpression, contributing to cancer progression.
Histone Modification 	Alterations in histone acetylation and methylation patterns dysregulate gene expression associated with oncogenes and tumor suppressors. These modifications often result in aberrant gene activation or silencing, fueling cancer development and progression. Aberrant histone modifications also promote chromosomal instability and genomic instability in cancer cells, further exacerbating tumorigenesis.
Non-coding RNAs 	Dysregulated miRNAs disrupt the expression of oncogenes and tumor suppressors by post-transcriptionally targeting their mRNAs, facilitating cancer progression. Abnormal lncRNAs expression modulates the gene expression involved in oncogenic and tumor suppressive pathways. These lncRNAs serve as key regulators of gene expression and chromatin dynamics, contributing to the dysregulated cellular processes observed in cancer.

The epigenetic mechanisms summarized in this table represent key contributors to the complex landscape of cancer biology. While this table provides a concise overview, it is important to note that the interplay between these mechanisms and other genetic and environmental factors is dynamic and

multifaceted. Further research is warranted to elucidate the specific molecular pathways involved and to explore the potential therapeutic implications of targeting epigenetic dysregulation in cancer treatment.

2.2.7. Gene-environment interactions

Gene-environment interactions significantly modulate cancer risk. Environmental factors such as exposure to carcinogens, dietary habits, lifestyle choices, and infectious agents interact with genetic predispositions, influencing cancer susceptibility. For instance, Palli et al. investigated interactions between BRCA1/2 mutations and occupation in male breast cancer (MBC) patients, finding a significant association between truck-driving occupation and carrier status for BRCA1/2 mutations, suggesting a potential modifying effect of occupational exposure to chemicals like PAH on MBC risk in mutation carriers [53].

Table 2: Key players in cancer immunogenetics: roles and mechanisms.

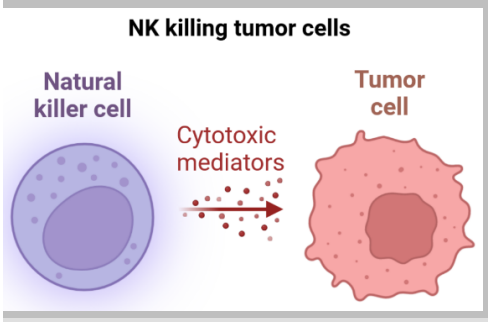
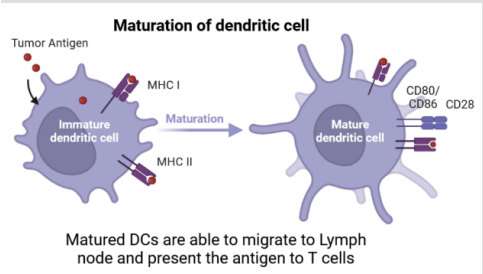
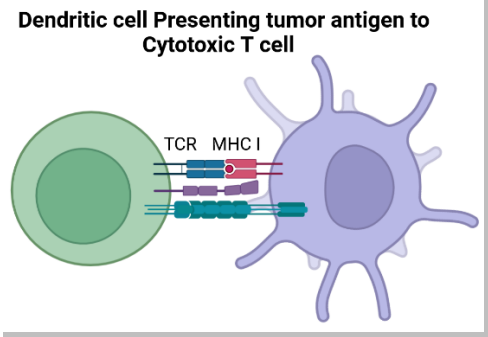
Player	Function/Role	Contribution to Cancer
Innate Immune Cells 	Recognize and respond to pathogens and cancer cells.	Initiate immune responses against tumor cells. For example, NK cells directly lyse tumor cells and produce immunomodulatory cytokines to regulate immune responses.
Dendritic Cells 	Antigen-presenting cells; Initiate and regulate T cell responses to tumor antigens.	Prime adaptive immune responses; Enhance tumor-specific immune surveillance.
Major Histocompatibility Complex (MHC) Class I 	Presents endogenous antigens to cytotoxic T cells; Facilitates immune recognition of cancer cells.	Enables cytotoxic T cell-mediated killing of cancerous cells; Immune surveillance against tumor antigens.

Table 2: Continued.

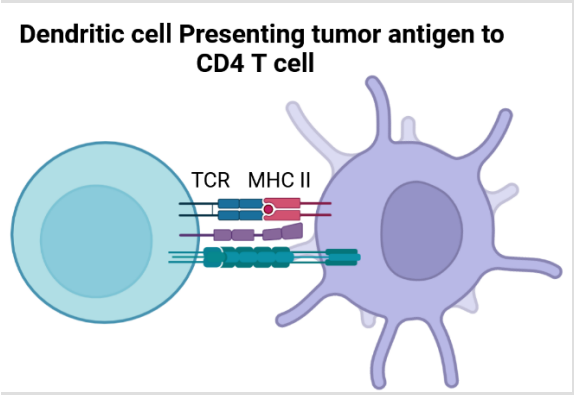
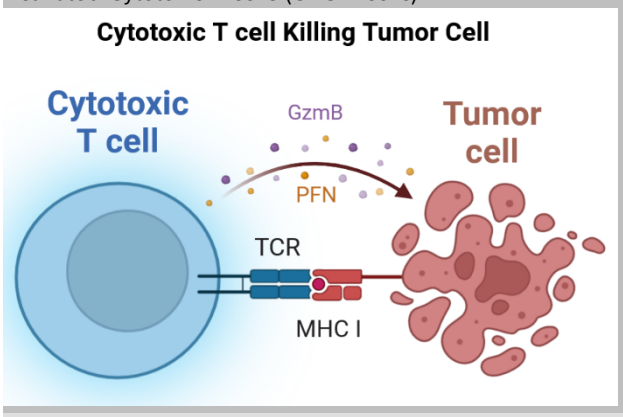
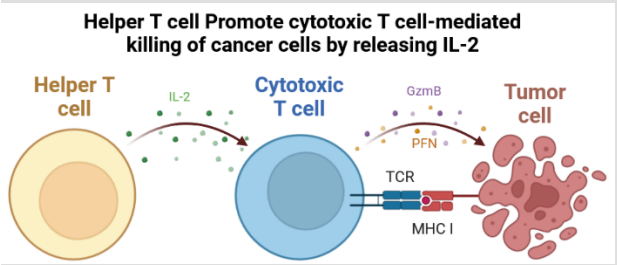
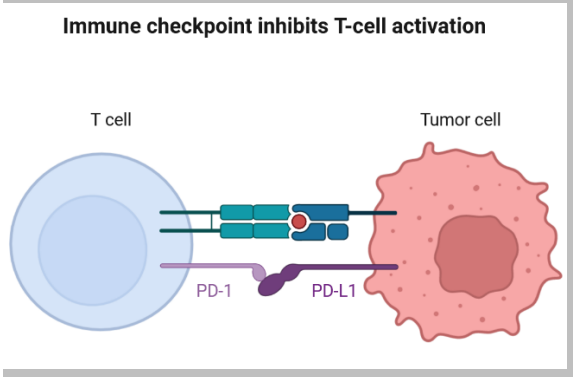
Player	Function/Role	Contribution to Cancer
Major Histocompatibility Complex (MHC) Class II 	Presents exogenous antigens to helper T cells; Initiates adaptive immune responses against tumor cells.	Activates helper T cells to orchestrate immune responses; Enhances antigen presentation to immune effectors.
Activated Cytotoxic T cells (CD8 T cells) 	Induce apoptosis in infected or cancerous cells; Eliminate abnormal cells.	Recognize and destroy tumor cells; Release cytotoxic molecules such as perforin and granzyme.
Activated Helper T cells (CD4 T cells) 	Produce pro-inflammatory cytokines; Enhance cell-mediated immune responses.	Activate macrophages; Promote cytotoxic T cell-mediated killing of cancer cells.
Immune Checkpoints 	Regulate immune responses, ensuring a delicate balance between immune activation and tolerance.	Immune checkpoints (e.g., PD-1, CTLA-4) are exploited by tumors to evade immune surveillance, facilitating tumor growth and metastasis. For example, when PD-1 binds to PD-L1, it inhibits the activation of T cells, leading to immune evasion by cancer cells.

Table 2: Continued.

Player	Function/Role	Contribution to Cancer
Cytokines	Regulate immune cell communication and activity; Influence tumor microenvironment.	Modulate inflammation; Enhance or suppress immune responses against tumors.
Environment	Modifies gene–environment interactions; Influences cancer susceptibility and progression.	Alters immune cell function; Induces epigenetic changes in cancer-related genes.
Epigenetics	Modulate gene expression and cellular functions; Influence cancer development.	Regulate DNA methylation and chromatin structure; Impact tumor suppressor gene activity.
Immunodeficiency	Compromises immune surveillance; Increases cancer susceptibility.	Impairs immune response to tumors; Raises risk of tumor development.
Single Nucleotide Polymorphism (SNP)	Modifies gene expression patterns; Affects susceptibility to cancer.	Contributes to variations in cancer risk; Influences individual predisposition to specific types of cancer.

This table summarizes the roles and mechanisms of various players involved in cancer immunogenetics, including major histocompatibility complex (MHC) molecules, immune checkpoints, innate and adaptive immune cells, environmental factors, cytokines, epigenetics, immunodeficiency, and SNPs. Understanding the functions of these players is crucial for elucidating the complex interplay between genetic factors, environmental exposures, and cancer susceptibility.

2.3. Impact of carcinogens intensified by global warming on cancer development

2.3.1. UV

This review exclusively focuses on two distinct types of cancer: basal cell carcinoma (BCC), recognized as the most prevalent form of cancer, and malignant melanoma (MM), acknowledged as the deadliest.

BCC, the most common type of skin cancer, is closely linked to UV radiation exposure, typically developing in sun-exposed areas such as the face, neck, and ears, often appearing as a flesh-colored, pearl-like bump, or a pinkish patch of skin. The process of BCC formation following UV exposure involves intricate interactions between environmental factors and genetic predisposition [54].

UV radiation has been identified as a significant factor in inducing BCC through various mechanisms, including DNA damage, impairment of DNA repair mechanisms, suppression of immune function, and initiation of genetic mutations, all of which ultimately promote tumorigenesis. Recent genetic studies have shed light on key genes and pathways involved in BCC development following exposure to UV radiation [55].

The Sonic Hedgehog (*SHH*) signaling pathway holds a central role in BCC tumorigenesis. Under normal conditions, this pathway regulates embryonic development and tissue homeostasis. However, dysregulation, often due to mutations in genes like *PTCH1* and *SMO*, leads to tumorigenesis. *PTCH1* acts as a tumor suppressor by inhibiting *SMO*, a G-protein-coupled receptor. Mutations in *PTCH1* relieve this inhibition, resulting in constitutive activation of *SMO* and downstream *SHH* pathway components, thereby promoting cell proliferation and tumor growth [55].

Additionally, the tumor suppressor protein p53, encoded by the *TP53* gene, plays a crucial role in BCC immunogenetics. p53 functions as a guardian of the genome, orchestrating cellular responses to DNA damage induced by UV radiation. In response to UV-induced DNA damage, particularly thymine dimers, p53 triggers cell cycle arrest, DNA repair, or apoptosis to prevent the propagation of damaged cells. However, mutations in *TP53*, often induced by UV exposure, disrupt its tumor-suppressive functions, allowing damaged cells to evade apoptosis and proliferate, thereby contributing to BCC development [55].

UV exposure directly stimulates the *SHH* signaling pathway by upregulating the expression of key pathway components, including *SMO* and *GLI* transcription factors, independently of DNA damage. Moreover, UV-induced DNA damage triggers the nucleotide excision repair (NER) pathway, which repairs UV-induced DNA lesions like thymine dimers. However, chronic UV exposure overwhelms the repair capacity of NER, leading to the accumulation of mutations in critical genes like *PTCH1* and *TP53*, further driving BCC pathogenesis [56].

Activating mutations in RAS oncogenes disrupt the MAPK/ERK signaling pathway, promoting cellular proliferation and survival. Moreover, genetic variations in genes involved in DNA repair pathways, cell cycle regulation, and immune response further enhance susceptibility to BCC following UV exposure. For instance, variants in genes such as *XPC*, *XPD*, and *XRCC1*, which play crucial roles in the NER pathway, have been implicated in this process [56].

UV radiation-induced immunosuppression plays a crucial role in the development of BCC by impairing the antigen-presenting capacity of skin dendritic cells, suppressing local immune responses, and facilitating the evasion of tumor immune surveillance by BCC cells. Furthermore, UV radiation promotes an imbalance in T cell populations, favoring regulatory T cells over effector and memory T cells, which contributes to immune evasion and tumor growth. Additionally, UV radiation stimulates the production of immunosuppressive molecules, such as prostaglandins, platelet-activating factors, IL-10, and reactive oxygen species (ROS), creating a microenvironment conducive to BCC progression [55].

UV radiation also contributes BCC by altering cells' epigenetic landscape. For instance, UV-induced DNA damage can cause hypermethylation of CpG islands within the promoter regions of tumor suppressor genes, such as *PTCH1* and p53. This hypermethylation silences these genes, allowing unchecked cell proliferation and tumorigenesis. Moreover, UV exposure alters histone modifications, such as histone acetylation and methylation, affecting chromatin structure and gene expression. Specifically, UV-induced

changes in histone acetylation can lead to the activation of oncogenes like MYC and the repression of tumor suppressor genes like *CDKN2A*. Additionally, UV radiation influences the expression of non-coding RNAs, including miRNAs, lncRNAs, and circRNAs, which play pivotal roles in BCC development. For example, UV exposure upregulates oncogenic miRNAs like miR-21, which promotes BCC progression by targeting tumor suppressor genes involved in the regulation of thyroid hormone and keratinocyte differentiation. Similarly, UV radiation induces the dysregulation of lncRNAs, such as H19, which acts as a competitive endogenous RNA to sequester tumor suppressor miRNAs and promote BCC growth and metastasis [57].

UV radiation represents a significant risk factor for MM development, attributed to its genotoxic, inflammatory, and immunosuppressive effects [58].

Inflammasomes, multiprotein cytoplasmic complexes involved in inflammation and immune responses, have emerged as pivotal contributors to MM pathogenesis. UV radiation induces DNA damage and cellular stress in skin cells, consequently activating inflammasomes as part of the immune response. This activation prompts the release of pro-inflammatory cytokines such as interleukin-1β (IL-1β) and interleukin-18 (IL-18), fostering an inflammatory milieu within the skin microenvironment that supports MM initiation and progression [59].

Moreover, inflammasome activation triggered by UV exposure may result in the release of factors that suppress the activity of immune cells, including T cells and NK cells, along with reduced production of immune-regulatory cytokines like IFN-γ. These events facilitate immune evasion by MM cells and unchecked proliferation [60]. Mast cells, integral to the innate immune system, have been implicated in UV-induced immunosuppression and subsequent melanoma development, with heightened mast cell density correlating with increased melanoma susceptibility [61].

Additionally, Toll-like receptors (TLRs), crucial components of innate immunity involved in pathogen and cancer cell detection, have been implicated in UV-induced immunosuppression. Studies in mice have demonstrated the involvement of *TLR4* in UV-induced immunosuppression, suggesting a potential mechanism by which UV exposure modulates innate immune responses in the skin. Furthermore, UV exposure may influence the expression of TLRs in melanoma cells, affecting their interaction with the immune system and potentially influencing melanoma prognosis [62].

UV radiation also promotes DNA methylation changes, leading to the silencing of tumor suppressor genes like *CDKN2A*, crucial in melanoma pathogenesis. Additionally, UV exposure triggers histone modifications, including increased H3K27 trimethylation mediated by EZH2, promoting a repressive chromatin state. This epigenetic alteration affects the expression of genes involved in cell cycle regulation and proliferation, facilitating melanoma progression. Furthermore, UV-induced oxidative stress modulates the expression of non-coding RNAs, such as SAMMSON, promoting melanoma cell survival and metastasis [63].

2.3.2. PM10

Exposure to PM10 initiates a complex cascade of molecular changes within immune cells, resulting in significant alterations in gene expression profiles and molecular pathways crucial for immune responses. This intricate interplay ultimately creates a pro-inflammatory environment conducive to various facets of lung cancer development and progression [64].

One of the primary effects of PM10 exposure is the activation of inflammatory pathways within immune cells, leading to the upregulation of crucial pro-inflammatory cytokines and chemokines such as IL-1β, IL-6, IL-8, TNF-α, CXCL1, CXCL5, and CCL7. These molecules play pivotal roles in orchestrating inflammation and recruiting immune cells to the site of exposure, thereby contributing to the chronic inflammatory milieu implicated in cancer pathogenesis [65].

PM10 exposure dysregulates the expression of transcription factors involved in inflammatory pathways. Upregulation of transcription factors such as *ATF3*, NFKB2, JUN, FOS, and RELB in response to PM10 exposure contributes to the regulation of genes involved in inflammation, cell proliferation, and apoptosis, all of which are processes implicated in cancer development [65].

Exposure to PM10 leads to the overexpression of specific genes, including *CYP1A1*, *CYP1B1*, *LINC01816*, and *BPIFA2*, within lung epithelial cells. These genes are known to be involved in responding to environmental pollutants such as PAHs, which are constituents of PM10. *CYP1A1* and *CYP1B1*, classified as cytochrome P450 enzymes, are responsible for metabolizing PAHs into potentially carcinogenic compounds, thereby initiating the process of carcinogenesis in lung cells. *LINC01816*, identified as an lncRNA, has been linked to cancer progression and is considered a promising candidate for both biomarker development and therapeutic targeting in lung cancer. Moreover, *BPIFA2*, a member of the PLUNC protein family, contributes to localized antibacterial responses in the respiratory tract. The observed upregulation of these genes suggests a direct link between exposure to PM10 and the activation of pathways associated with the development of lung cancer, potentially mediated through PAH metabolism, inflammatory responses, and cancer progression [66].

Furthermore, PM10 exposure instigates the generation of reactive oxygen species within immune cells, leading to oxidative stress. ROS-induced oxidative damage can result in DNA damage, genomic instability, and alterations in gene expression patterns, thereby promoting the initiation and progression of cancer by fostering mutations and genomic aberrations in key oncogenes and tumor suppressor genes. For instance, ROS activates transcription factors such as NF-kappaB and AP-1. NF-kappaB regulates the transcription of genes involved in immune and inflammatory responses, including cytokines, chemokines, and adhesion molecules, thereby promoting an inflammatory microenvironment conducive to tumorigenesis. AP-1, on the other hand, regulates the expression of genes implicated in cell proliferation and survival, such as cyclin D1 and c-fos, contributing to uncontrolled cell growth and tumor progression. Collectively, the activation of these redox-sensitive transcription factors by ROS generated from PM10 exposure orchestrates a

pro-inflammatory and pro-tumorigenic gene expression profile within lung epithelial cells, fostering an environment conducive to lung cancer initiation and progression [67].

In addition to inflammation, PM10 exposure induces immunosuppressive effects by downregulating genes associated with host defense against pathogens. Notably, genes encoding antimicrobial peptides (AMPs) and antiviral factors like CAMP, DEFA3, LYZ, and APOBEC3A are among those suppressed by PM10 exposure. This compromised immune response diminishes the immune system's capacity to effectively recognize and eliminate cancerous cells, thereby fostering tumor survival and progression [65].

Moreover, upon prolonged exposure to PM10, epithelial cells experience DNA damage, leading to the activation of signaling pathways involving STAT3, Src, and PKCζ kinases. These pathways induce phosphorylation of STAT3 at tyrosine 705 (Y705) and serine 727 (S727), promoting the expression of p21Waf1/Cip1, a key regulator of cell cycle arrest and apoptosis evasion. Consequently, PM10 exposure induces G0-G1 cell cycle arrest, preventing damaged cells from undergoing apoptosis and facilitating their survival. This prolonged survival of damaged cells increases the likelihood of oncogenic mutations and contributes to the progression of lung cancer, highlighting the intricate molecular mechanisms through which PM10 exposure promotes lung carcinogenesis [68]

PM10 exposure triggers intricate epigenetic alterations implicated in lung cancer pathogenesis. Specifically, PM10 exposure has been linked to diminished DNA methylation of long interspersed nucleotide element (LINE)-1 sequences, indicative of genomic instability. Furthermore, PM10 exposure disrupts histone modification dynamics, leading to increased histone acetylation, particularly histone H4, which is associated with heightened expression of pro-inflammatory cytokines in lung epithelial cells. Moreover, PM10 exposure alters miRNA expression profiles, with specific miRNAs involved in regulating pathways associated with inflammation and tumorigenesis showing dysregulation [69].

2.3.3. PAH

The involvement of PAHs in immunogenetic alterations contributing to lung cancer development and progression is well-documented. PAH exposure has been shown to modulate the expression of immune response genes, compromising immune surveillance against cancer cells. This modulation is partly mediated by epigenetic changes induced by PAHs, such as hypermethylation of tumor suppressor genes like *CDH13* and p16. These epigenetic alterations create an immunosuppressive microenvironment conducive to tumor growth. Additionally, PAH exposure disrupts the balance between histone acetyltransferases (HATs) and histone deacetylases (HDACs), promoting DNA damage and inflammation, further contributing to immune dysregulation and tumor development [70].

Furthermore, PAHs impact immune responses through alterations in non-coding RNA levels. miRNAs like miR-622 and miR-506, found in PAH-treated human bronchial epithelial cells, suppress malignant

transformation by targeting oncogenic proteins such as KRAS and NRAS. These miRNAs regulate immune-related pathways, affecting the immune response to PAH exposure. Moreover, PAHs upregulate LINE-1, leading to genetic instability that may affect immune-related gene expression and contribute to immune evasion by cancer cells [70].

The interplay between PAH metabolism and immune gene regulation exacerbates immunogenetic alterations. PAH-activated cytochrome P450 (CYP) enzymes generate reactive metabolites that form DNA adducts on immune-related genes, disrupting their function and impairing immune surveillance against cancer cells. However, hepatic *CYP1A2* enzymes may mitigate this effect by downregulating *CYP1A1* expression, thus preserving immune function [70].

PAH exposure also dysregulates immune cells, including macrophages, dendritic cells, and T cells, through alterations in cell signaling pathways and calcium homeostasis [71–73]. For instance, PAHs inhibit the differentiation and maturation of dendritic cells, impairing their antigen-presenting capabilities and leading to suboptimal activation of T cells and impaired anti-tumor immune responses [73]. The aryl hydrocarbon receptor (AHR) is implicated as a key mediator of these effects, driving proinflammatory responses in T cells and dendritic cells upon PAH exposure [74].

Furthermore, PAH exposure has been linked to alterations in the expression and function of Tregs, a subset of CD4+ T cells that play a key role in maintaining immune homeostasis and suppressing excessive immune responses. PAH-induced changes in Treg function may disrupt immune tolerance mechanisms, leading to unchecked inflammation and immune-mediated tissue damage that can promote tumorigenesis [75–77].

In breast cancer development, PAHs form DNA adducts and induce altered DNA methylation patterns in breast epithelial tissues. PAH-induced hypermethylation of gene promoter regions, such as the *TWIST* gene involved in epithelial-mesenchymal transition (EMT), contributes to tumor metastasis and invasion. Additionally, PAH exposure dysregulates genes like *DAPK1* and *LONP1*, involved in apoptosis, cell proliferation, and DNA repair, further contributing to breast cancer pathogenesis [78].

2.3.4. NO_2 and NOx

NO_2 and NOx are environmental pollutants known to exert immunogenetic effects and potentially contribute to cancer development through various mechanisms. These pollutants directly impact the immune system by inducing oxidative stress and inflammation, disrupting immune homeostasis, and promoting tumor growth.

Firstly, $NO_2$and NOx have been shown to modulate the expression and activity of inducible nitric oxide synthase (iNOS) in various cellular contexts. iNOS is an enzyme responsible for the production of nitric oxide (NO), a key signaling molecule with diverse roles in immune regulation and cancer biology. Studies have demonstrated that exposure to $NO_2$and NOx can upregulate iNOS expression, leading to increased

NO production in cells [79, 80]. This excess NO can cause DNA damage, mutations, and epigenetic modifications in immune cells, leading to dysregulated immune responses and potentially promoting tumorigenesis [81, 82].

NO_2 and NOx have been implicated in altering the epigenetic landscape of cells through their interactions with histone-modifying enzymes. Specifically, NO has been shown to inhibit JmjC domain-containing histone demethylases, leading to alterations in global histone methylation patterns. These changes in histone methylation can dysregulate gene expression programs, potentially promoting the development of cancerous phenotypes [83].

In addition to their direct effects on cellular pathways, NO_2 and NOx have been shown to influence angiogenesis, which is the process of forming new blood vessels from pre-existing ones and is crucial for tumor growth and metastasis. Studies have demonstrated that NO, generated from NOx, can enhance angiogenesis by stabilizing hypoxia-inducible factor 1-alpha (HIF-1α), leading to increased expression of vascular endothelial growth factor (VEGF). This promotes the formation of new blood vessels, providing nutrients and oxygen to tumor cells and facilitating their proliferation and dissemination [84–86]. However, contradictory findings exist, with some studies reporting that NO can also inhibit angiogenesis by suppressing the production of pro-angiogenic factors and inducing apoptosis in endothelial cells [87]. These contradictory findings highlight the dual nature of NO's impact on tumor angiogenesis and growth, indicating that its effects may be influenced by the concentration of NO within the tumor microenvironment and the specific context in which it operates.

Moreover, NO_2 and NOx have been reported to modulate EMT, a critical step in the acquisition of invasive and metastatic properties by cancer cells. EMT is a biological process wherein epithelial cells lose their characteristics and acquire mesenchymal traits, enabling enhanced motility and invasiveness. NO has been shown to suppress EMT by inhibiting NF-κB signaling and downregulating the expression of transcription factors such as Snail, which are involved in promoting EMT [88]. However, contradictory findings exist, as NO has been reported to induce EMT in certain cancer cell types, leading to reduced adhesiveness and altered expression of E-cadherin and vimentin [89]. Furthermore, NO-driven increases in matrix metalloproteinase (MMP) levels have been associated with promigratory responses in cells, potentially influencing tumor progression and metastasis [90]. The dual role of NO in EMT and metastasis further highlights the complex and context-dependent nature of its effects on tumor behavior, emphasizing the need for further research to elucidate its precise mechanisms and potential therapeutic implications.

In the context of breast cancer, $NO_2$and NOx have been implicated in increasing breast cancer risk through epigenetic mechanisms, particularly by influencing DNA methylation patterns. For example, studies have shown that NO_2 exposure was associated with lower methylation levels of specific CpG sites in genes such as Ephrin type-B receptor 2 (*EPHB2*), which is known to be overexpressed in breast cancer and implicated in its development and progression [91].

Additionally, prenatal exposure to NO_2 has been associated with lower DNA methylation levels in cord blood genes related to mitochondria in offspring, suggesting a potential link between NO_2 exposure during critical developmental periods and epigenetic alterations predisposing individuals to breast cancer later in life. The exact mechanisms by which NO_2 and NOx influence DNA methylation patterns are not fully understood. However, it is hypothesized that these pollutants may induce oxidative stress and inflammation, affecting the activity of enzymes involved in DNA methylation, such as DNA methyltransferases (DNMTs). Additionally, NO_2 and NOx may directly or indirectly interact with transcription factors and chromatin-modifying enzymes, leading to changes in gene expression profiles that contribute to breast cancer development [91].

2.3.5. Ground-level ozone

Ground-level ozone (O_3) exposure can significantly impact cancer immunogenetics through diverse molecular pathways. One significant aspect of O_3 exposure is its ability to induce epigenetic modifications, particularly DNA methylation alterations. Research has shown that exposure to elevated levels of O_3 leads to global DNA hypomethylation, particularly in repetitive elements such as LINE-1 and ALU. This epigenetic dysregulation can disrupt gene expression patterns, including those involved in immune responses and cancer pathways. Notably, hypomethylation of repetitive elements has been linked to genomic instability and inappropriate activation of oncogenes, contributing to the initiation and progression of cancer [92].

Furthermore, O_3 exposure has been associated with the generation of bulky DNA adducts, which are reliable biomarkers of carcinogen exposure and cancer risk. The formation of bulky DNA adducts can lead to mutations in critical genes involved in immune regulation and tumor suppression, ultimately predisposing individuals to cancer development. For instance, these adducts can disrupt the function of tumor suppressor genes such as *TP53*, which plays a crucial role in regulating cell growth and preventing tumor formation. When *TP53* function is compromised due to DNA damage caused by bulky adducts, cells may lose their ability to control proliferation and repair damaged DNA, ultimately leading to the development of cancer [92, 93].

O_3 exposure can cause DNA strand breaks and inflammation in the lungs, which manifests as a notable increase in IL-6 expression. IL-6 is a versatile cytokine involved in immune signaling and inflammation. Its heightened expression fosters a pro-inflammatory environment conducive to tumor growth and metastasis, suggesting a plausible connection between O_3 exposure and lung cancer development [94].

3. Discussion

Our review highlights the exacerbating effects of global warming on exposure to various environmental carcinogens, such as UV radiation and air pollutants like PM, PAHs, NO_2, NOx, and O_3. Rising temperatures

and changes in atmospheric conditions contribute to the intensification of UV radiation reaching the Earth's surface and the accumulation of air pollutants from anthropogenic sources. These environmental shifts have significant implications for cancer incidence and prevalence, as evidenced by the association between global warming-induced changes in carcinogen exposure and rising trends in skin cancer, lung cancer, breast cancer, and other malignancies.

Our analysis underscores the pivotal role of human immunogenetics in modulating individual responses to carcinogen exposure and shaping cancer susceptibility and progression. Genetic variations in key immune-related genes involved in immune surveillance, inflammation, DNA repair, and immune checkpoint regulation influence the interplay between environmental carcinogens and cancer development. Polymorphisms in genes encoding MHC molecules, immune checkpoint proteins (e.g., PD-1), cytokines (e.g., IL-6), and DNA repair enzymes (e.g., XPC) have been implicated in modifying cancer risk following exposure to UV radiation, air pollutants, and other carcinogens.

Our findings elucidate diverse molecular mechanisms underlying the impact of environmental carcinogens amplified by global warming on cancer immunogenetics (Table 3). These mechanisms encompass alterations in DNA methylation patterns, modulation of gene expression profiles, activation of inflammatory pathways, induction of oxidative stress, and dysregulation of immune cell function. For example, exposure to UV radiation and air pollutants can lead to epigenetic modifications, such as DNA hypomethylation and hypermethylation, which affect the expression of immune-related genes and contribute to chronic inflammation, genomic instability, and immune evasion in cancer cells. Additionally, environmental carcinogens can induce oxidative stress by generating ROS within cells, leading to DNA damage and genomic instability. These changes in DNA methylation, gene expression, and immune cell function collectively contribute to the intricate interplay between environmental exposures, genetic susceptibility, and cancer immunogenetics, ultimately influencing cancer susceptibility, progression, and outcomes.

This table provides a comparison of different carcinogens, including UV radiation, PM10, PAHs, NO_2/NOx, and ground-level O_3, detailing their associated cancer types, contributions to cancer development, and molecular mechanisms involved. It offers insights into the diverse ways in which these environmental factors contribute to cancer progression and underscores the importance of understanding their specific effects on human health.

One limitation of our review stems from the inherent heterogeneity in the data sources and methodologies of the studies included. The diverse range of study designs, populations, and cancer types covered in the literature contributes to variability in data presentation and interpretation. Differences in sample sizes, exposure assessment methods, and genetic analyses across studies may hinder the generalizability of our findings to broader populations and cancer types.

Understanding the complex interplay between genetic factors and environmental exposures in cancer development presents a challenge. While our review underscores the role of human immunogenetics

Table 3: Comparative analysis of carcinogens and their contributions to cancer development.

Carcinogen	Most Associated Cancer Type	Contribution to Cancer	Molecular Mechanisms
UV Radiation	Skin Cancer	DNA damage, Immune suppression, Genetic mutations, Impaired DNA repair	Disruption/mutation in Sonic Hedgehog (*SHH*) pathway Disruption/mutation in MAPK/ERK signaling pathway Mutation of *TP53* gene DNA methylation alterations
PM10	Lung Cancer	Oxidative stress, Inflammation, DNA damage	Upregulation of pro-inflammatory cytokines Dysregulation of transcription factors Epigenetic changes (DNA methylation, histone modifications)
PAHs	Lung Cancer	Oxidative stress, Immune suppression, DNA adducts	Hypermethylation of tumor suppressor genes *CDH13*, p16 Dysregulation of non-coding RNA levels Formation of DNA adducts on immune-related genes
NO_2/NOx	Lung Cancer	Oxidative stress, inflammation, DNA damage, Angiogenesis	Upregulation of NO production, DNA damage Inhibition of histone demethylases, altered histone methylation patterns
Ground-level O_3	Lung Cancer	Oxidative stress, DNA damage, Inflammation, DNA adducts	Global DNA hypomethylation, hypermethylation of repetitive elements Formation of bulky DNA adducts, disruption of tumor suppressor gene function

in modulating cancer susceptibility, elucidating the specific gene-environment interactions underlying carcinogen-induced alterations in cancer immunogenetics remains a daunting task. The intricate nature of these interactions requires more comprehensive studies to disentangle their contributions to cancer risk.

Another limitation arises from the observational nature of many studies included in our review. Establishing causality and temporality between global warming-induced environmental changes, alterations in cancer immunogenetics, and cancer outcomes is inherently challenging. Longitudinal studies and experimental research are warranted to delineate the causal relationships and temporal sequences underlying environmentally induced carcinogenesis.

The multifaceted nature of environmental exposures poses challenges in isolating the specific contributions of individual carcinogens to cancer susceptibility. Environmental carcinogens often exert synergistic effects, complicating the interpretation of their roles in cancer development. Integrative approaches combining epidemiological, molecular, and environmental data are imperative to unravel the complex environmental influences on cancer immunogenetics.

Our review highlights the importance of considering ethnic and geographical variability in genetic susceptibility to environmental carcinogens and cancer outcomes. However, the majority of studies included in our review focus on specific geographic regions, limiting the generalizability of findings to other ethnic and geographical contexts. Future research should strive to incorporate diverse ethnicities and geographical locations to enhance the robustness and applicability of findings.

Future research in the realms of global warming, environmental carcinogens, human immunogenetics, and cancer susceptibility should concentrate on several pivotal areas to enhance our comprehension and guide evidence-based interventions.

Firstly, there is a pressing need for longitudinal cohort studies encompassing diverse populations and geographic regions to unravel the causal relationships and temporal sequences underlying environmentally induced carcinogenesis. These studies, integrating comprehensive environmental exposure assessments, genetic analyses, and cancer outcomes data, will offer invaluable insights into the intricate interplay between global warming-induced environmental changes, alterations in cancer immunogenetics, and cancer development over time.

Secondly, integrative approaches that meld epidemiological, molecular, and environmental data are indispensable for untangling the complex environmental influences on cancer immunogenetics. Multi-omics studies integrating genomics, epigenomics, transcriptomics, metabolomics, and environmental exposomics will enable the identification of biomarkers, molecular pathways, and gene-environment interactions driving carcinogen-induced alterations in cancer immunogenetics.

Thirdly, research endeavors should prioritize the development and validation of predictive models and risk assessment tools incorporating genetic susceptibility, environmental exposures, and cancer outcomes data. Leveraging machine learning algorithms and artificial intelligence techniques on large-scale multi-ethnic cohorts can identify novel genetic variants, environmental factors, and their interactions contributing to cancer susceptibility, thereby facilitating personalized risk stratification and targeted interventions.

Moreover, interdisciplinary collaborations among researchers from environmental science, genetics, oncology, epidemiology, and public health are essential for advancing our understanding of the intricate interplay between global warming, environmental carcinogens, human immunogenetics, and cancer biology. Collaborative research consortia and international networks can foster data sharing, methodological harmonization, and replication of findings across diverse populations and geographical contexts.

Additionally, research efforts should prioritize the development and implementation of evidence-based public health interventions aimed at mitigating the adverse effects of environmental carcinogens on cancer incidence and prevalence in a changing climate. These interventions, including targeted environmental policies, community-based interventions, lifestyle modifications, and personalized prevention strategies informed by genetic susceptibility profiles and environmental exposure assessments, are crucial for addressing the growing challenges posed by environmentally induced cancers.

4. Conclusion

In conclusion, this review highlights the significant impact of global warming-induced changes on exposure to environmental carcinogens and their intricate interplay with human immunogenetics in shaping cancer

susceptibility and progression. By synthesizing evidence from studies focusing on various environmental carcinogens, including UV radiation, air pollutants, PAHs, NO_2, NOx, and O_3, the review underscores the complexity of the mechanisms underlying environmentally induced carcinogenesis. Despite inherent limitations in study methodologies and the challenges in establishing causality, the review emphasizes the importance of longitudinal cohort studies, integrative approaches, and interdisciplinary collaborations to unravel the causal relationships and temporal sequences involved in cancer development. Moving forward, prioritizing evidence-based public health interventions informed by genetic susceptibility profiles and environmental exposure assessments will be crucial in mitigating the adverse effects of environmental carcinogens on cancer incidence and prevalence in a changing climate.

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Ethical Considerations

For this review paper, no human or animal research was conducted, and therefore, no consent to participate or have their information published was required. Approval from the Ethical Committee was not applicable.

Conflicts of Interest

The authors declare no conflict of interest regarding the publication of this paper.

Availability of Data and Material

The data and materials supporting the findings of this study are available upon request from the corresponding author.

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