

## PERSPECTIVE

# Current status and perspectives in environmental oncology

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## Abstract

Cancer stands as a leading global cause of death, with its etiology characterized by complexity and multifaceted factors. Growing research indicates a strong correlation between environmental factors and cancer incidence, underscoring the critical importance of intervening in environmental risk factors to mitigate cancer occurrence. Despite this, specialized research institutions focusing on the intersection of environment and cancer remain scarce, with global investment in cancer prevention significantly trailing behind efforts in diagnosis and treatment. Against the backdrop of rapid global climate change, industrialization, urbanization, aging populations, and the globalization of lifestyles, we proposed the concept of *Environmental Oncology* (EO) to address these challenges. We discussed the rationale and necessity of developing EO and presented a comprehensive research framework focusing on cancer prevention and treatment. Future EO research will aim to identify cancer causes and implement early prevention strategies using advanced scientific technologies and methods. By emphasizing multidisciplinary collaboration and integrating molecular biology at the micro level, EO will explore the relationship between external and internal environments and cancer. EO will identify potential therapeutic targets by studying the pathways through which environmental exposures lead to carcinogenesis. EO will develop early warning systems and disseminate research findings by collecting big data, employing robust statistical models, and establishing research centers.

## KEYWORDS

cancer, climate, disparities, environment, environmental oncology, prevention

## Highlights

**Significant findings of the study:** There is an urgent need to establish the emerging discipline of Environmental Oncology.  
**What this study adds:** The study introduces the concept and framework of Environmental Oncology, highlighting the importance of multidisciplinary approaches and advanced technologies.

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## 1 | INTRODUCTION

Modern research shows cancer stems from genetic susceptibility, environmental factors, gene–environment interactions (GEIs), or spontaneous events. Environmental factors contribute to 70%–90% of cancer cases,<sup>1,2</sup> outweighing intrinsic (genetic) factors (<30%).<sup>2–4</sup> In 2020, there were 19,292,789 global cancer cases and 9,958,133 deaths. It is estimated that by 2050, there will be over 35 million new cancer cases, marking a 77% increase from the estimated 20 million cases in 2022. The escalating global cancer burden mirrors population aging and growth, along with shifts in environmental risk factors, some linked to socioeconomic development.<sup>5–7</sup> Reportedly, 42% of cancer cases and 45% of cancer deaths are attributable to modifiable risk factors.<sup>8</sup> The findings from the global burden of disease study indicated that lifestyle factors such as smoking, alcohol consumption, and unhealthy dietary habits accounted for 44.4% of global cancer-related mortality and 42% of disability-adjusted life-years in 2019.<sup>7</sup> The World Health Organization (WHO) identified tobacco, alcohol, and obesity as key drivers of rising cancer rates, with air pollution remaining as a major environmental risk factor.<sup>9</sup>

The United Nations has announced that the Earth has entered a new era of “global boiling,” characterized by intensified heat waves, climate-related disasters, and extreme weather patterns. These changes impact cancer occurrence and control, resulting from shifts in human behavior, exposure to environmental carcinogens, changes in food structures, and modifications in medical environments.<sup>5,10,11</sup> Consequently, addressing climate change has been dubbed “the greatest global health opportunity of the 21st century.”<sup>12</sup>

Reports indicated that 30%–50% of cancers could be prevented by avoiding environmental risk factors and implementing evidence-based prevention strategies.<sup>2,13,14</sup> Therefore, highlighting the importance of environmental oncology research is crucial and meaningful in combating cancer. In 1997, Russian scholars mentioned environmental oncology as studying the multifaceted relationship between the environment and organisms exposed to the modification of carcinogens.<sup>15</sup> Owing to the severity of the cancer issue and the confirmed role of environmental factors in causing most cancerous genetic mutations, coupled with the lag in cancer prevention efforts, the University of Pittsburgh proposed establishing an interdisciplinary center for environmental oncology by 2007.<sup>16</sup> In recent decades, research institutions and scholars have been interested in the intersection of the environment and cancer. However, this interest has predominantly focused on epidemiological research. Many epidemiological studies need more in-depth exploration of underlying etiology, while basic medical research often fails to delve into environmental influences within epidemiology and clinical medicine. Furthermore, clinical medicine usually

overlooks the study and awareness of environmental factors in cancer diagnosis and treatment processes.

Hence, an urgent need is to establish a burgeoning discipline—*Environmental Oncology* (EO)—that effectively integrates epidemiology, clinical medicine, and basic research. Looking ahead, such a discipline can contribute to cancer prevention in public health by leveraging epidemiological insights. By combining epidemiological discoveries with fundamental research, it can advance cancer diagnosis, treatment, and rehabilitation. Nevertheless, environmental oncology is still in its early stages and not formally defined and faces numerous challenges.

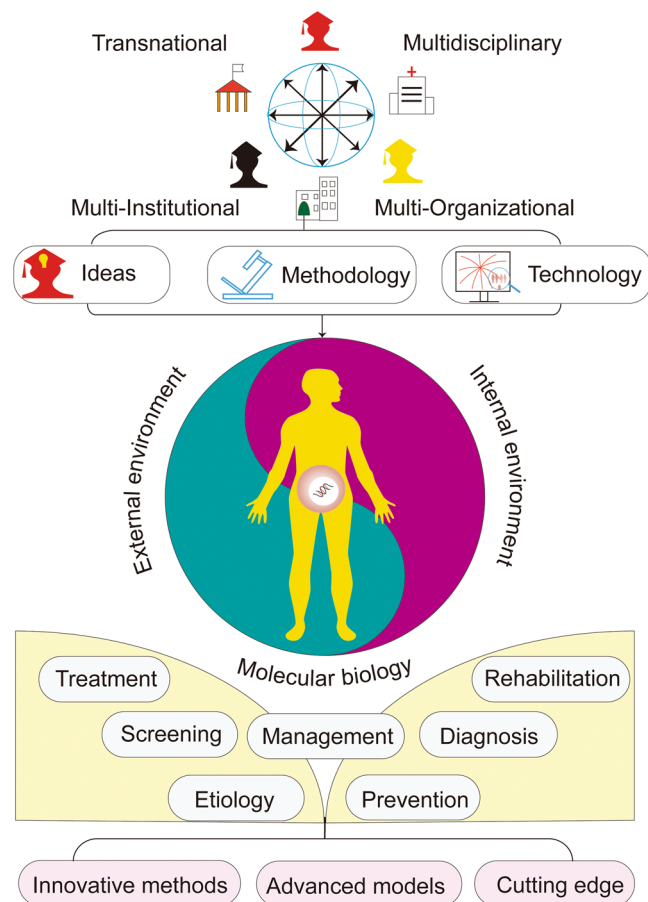
## 2 | THE DEFINITION OF EO AND ITS SCOPES

EO is a systematic, interdisciplinary emerging discipline that identifies cancer causes and early prevention, utilizing advanced scientific technologies and methods. Multidisciplinary collaboration and integration with molecular biology at the micro level emphasize the relationship between external and internal environments and cancer. This discipline spans various stages of cancer prevention, screening, diagnosis, treatment, rehabilitation, and management, providing scientific evidence for comprehensive cancer control predominantly influenced by environmental risk factors (Figure 1).

## 3 | ENVIRONMENT RISK FACTORS AND CANCER

Global warming induces various climate transformations, encompassing glacial melting, rising sea levels, intensified storms, floods, heat waves, and wildfires. These alterations may impact, alter, or exacerbate environmental factors such as air and water pollution, ultra-violet ray radiation, food availability, extreme weather, physical activity, exposure to toxins, infectious agents, healthcare systems, and socioeconomic conditions, thereby impacting cancer etiology, prevention, detection, treatment, and survival (Figure 2).<sup>5,10,11</sup> The intricate relationship between climate change and modifiable environmental factors creates barriers to intervening in cancer prevention, thus widening disparities in cancer risk.<sup>5,10,11</sup> Additionally, pandemics such as COVID-19 have had adverse effects on cancer healthcare systems and outcomes.<sup>17</sup>

Environmental risk factors of cancer are modifiable non-intrinsic risk factors encompassing external and internal environments (Figure 2).<sup>1</sup> External factors can be categorized into specific external (i.e., radiation, air pollution, etc.) and general external factors (i.e., social environment, psychological state, etc.).<sup>18</sup> The WHO lists 116 Group 1 carcinogens, 357 Group 2, and 499 Group 3.



**FIGURE 1** The research scopes of environmental oncology.

Notable Group 1 carcinogens include tobacco, alcohol, aflatoxins, salted fish, *Helicobacter pylori*, aristolochic acid, and betel quid. Wu et al.<sup>2</sup> revealed that diet linked to 75% of colorectal cancer risk, sun exposure to 65%–86% of melanoma risk, ultra-violet ray radiation to about 90% of nonmelanoma skin cancers, smoking, and alcohol consumption to at least 75% of esophageal and head and neck cancers, and *Helicobacter pylori* to 65%–80% of gastric cancers. The widespread use of industrial technologies has been associated with the current cancer epidemic. Emerging carcinogenic chemicals, air pollution, radiation, lack of green spaces, traffic noise, poverty, and light pollution are all contributing to increased cancer incidence and mortality. Supporting Information: Table S1 summarizes the associations between various environmental factors and cancer.

#### 4 | POTENTIAL MECHANISMS OF ENVIRONMENTAL CARCINOGENESIS

Cancer development is multifaceted, involving GEIs in about 95% of cases.<sup>2,19</sup> Genetic mutations, accounting for only 5%–10% (germline mutations), can substantially raise cancer risk when combined with environmental factors,

whether voluntary or involuntary.<sup>20</sup> About 90%–95% of cancer results from acquired mutations (somatic mutations). External and internal environmental factors typically induce somatic mutations through DNA damage,<sup>18,21</sup> with external factors interacting synergistically with internal ones to influence cancer initiation, promotion, and progression (Figure 2).<sup>22</sup> Somatic mutations chiefly implicate oncogenes, tumor suppressor genes, and DNA repair genes, impacting various stages of cancer development. In the dimension of time, the Darwinian theory of cancer evolution posits that the mismatch between the human ancestral environment and the modern environment leads to the accumulation of cellular genetic mutations, ultimately driving genetic alterations. Notably, significant gaps exist in understanding the complex etiological mechanisms linking the environment to cancer, requiring further in-depth research.

#### 5 | PAST AND CURRENT RESEARCH STATUS ON ENVIRONMENTAL FACTORS AND CANCER

The wide variation in the definition of “environment” from a broad to a narrow perspective presents a significant challenge in assessing the relative influence of endogenous (spontaneous) mutations and environmental factors on distinct cancer patients.<sup>23</sup> The early epidemiological association between environmental exposure and cancer dates back to 1761 (Supporting Information: Table S2). Milestones in environmental carcinogenesis include Johannes Fibiger's discovery of “Spiroptera carcinoma” in 1913 and Japanese scholars' identification of coal tar-induced skin cancer in 1915. In 1994, Davis and Muir highlighted challenges in investigating the impact of environmental pollution due to diverse carcinogenic sources and complex exposure assessments. Recent advances in cancer genomics have been significant. However, methodological limitations,<sup>7</sup> the complexity and dynamics of the environment, long latency periods,<sup>24</sup> and the broad scope of the issue contribute to the ongoing uncertainty regarding the scientific evidence linking environmental exposure and cancer.<sup>25–27</sup> Theories such as cancer evolution, developmental origins of health and disease, and GEI stand in contrast to the “bad luck” hypothesis. Furthermore, EO research is characterized by its long-term nature, posing challenges in funding and workforce. We have reviewed relevant studies in the field of environmental oncology using PubMed, Web of Science, and Google Scholar, and provided a brief summary of some typical environmental factors (Supporting Information: Table S2).

Despite significant human efforts in the long-term battle against cancer, global cancer incidence continues to rise. This is attributed to a disproportionate focus on cancer prevention compared to basic research,

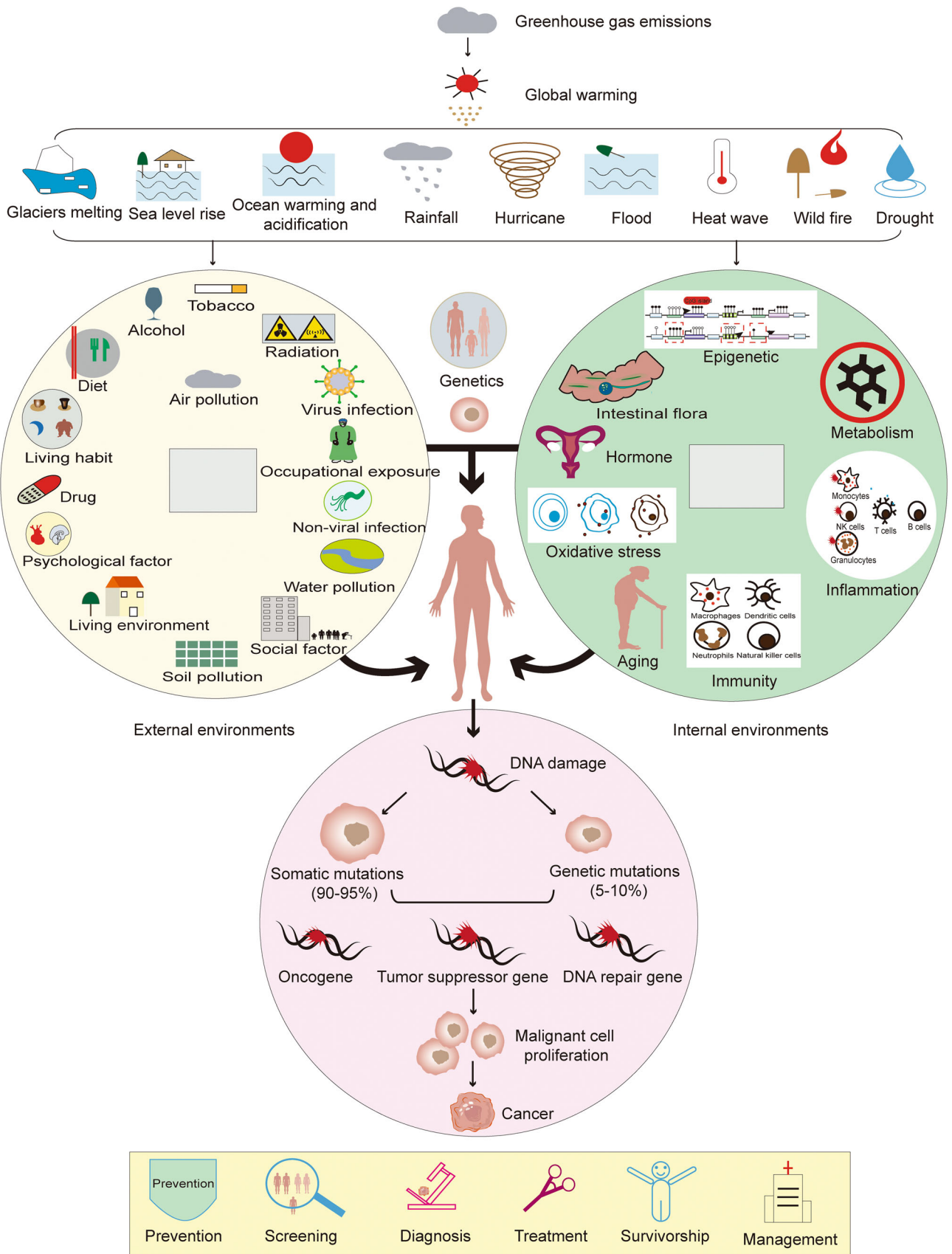


FIGURE 2 Environmental risk factors and potential etiological mechanisms of cancer.

diagnosis, and treatment worldwide. In the new era, health priorities have shifted to emphasize cancer prevention as the ultimate goal, advocating for safe and green measures to mitigate environmental health risks. The unequal allocation of funds, policies, and prevention awareness poses barriers to cancer prevention. Limited financial resources for international cancer prevention collaboration, disparities between global cancer risk factors and local prevention policies (e.g., tobacco and alcohol regulations),<sup>28</sup> and gaps in understanding human behavior and prevention awareness all contribute to these challenges. Global health disparities in cancer control and implementation<sup>29</sup> highlight significant challenges in survival rates, healthcare infrastructure, and environmental exposure. Unequal distribution of environmental hazards across countries, regions, and communities poses a pressing issue in cancer prevention.

EO can make significant strides but needs more systematic research, with relatively few institutions and centers dedicated to the field. Interdisciplinary collaboration needs to be improved, with a scarcity of multidisciplinary teams, fragmented research institutions, limited data sharing, and ineffective interdepartmental coordination. Environmental pollution and cancer incidence pose global challenges, yet international collaboration is constrained by restricted scope, inadequate resource sharing, and limited information exchange. These factors impede the advancement of EO to a certain extent.

## 6 | FUTURE RESEARCH DIRECTIONS OF EO

### 6.1 | Multidisciplinary collaboration

Multidisciplinary collaboration promotes knowledge exchange and integration, fosters innovation and cross-disciplinary cooperation, and deepens our understanding of the complex relationship between environmental factors and cancer. It also provides more effective approaches for prevention and treatment. EO involves various fields, including environmental science, epidemiology, biology, medicine, and public health. Environmental science offers insights into environmental factors; epidemiology helps identify associations with cancer; biology elucidates cancer mechanisms; medicine focuses on diagnosis and treatment; and public health addresses prevention and control. Additionally, disciplines such as chemical engineering, geography, sociology, psychology, and the fields above form a multidisciplinary research paradigm in EO. Simultaneously, interdisciplinary cross-pollination can foster the emergence of new disciplines in the future. Besides interdisciplinary collaboration, environmental cancer research encounters challenges related to the global nature of human health issues, leading to

geographic variations and difficulties in data sharing. International and domestic cooperation in public health to reform policies, systems, and environments will likely become the prevailing trend in environmental cancer research.<sup>30</sup> On November 17, 2023, leveraging the cross-integration of multidisciplinary talents and cutting-edge technologies, the Environmental Oncology Committee of the China Anti-Cancer Association was established (<http://www.caca.org.cn>). Establishing the Environmental Oncology Committee signifies a pivotal moment in the environmental and tumor research landscape, offering a new frontier and expansive platform for both domestic and international scholars in EO.

### 6.2 | Development of innovative research designs and advanced statistical methodologies

The main study types of EO research include epidemiology, experiments, meta-analyses, modeling, and clinical trials (Supporting Information: Table S2). Standard designs are cohort, case-control, ecological, cross-sectional, and longitudinal studies. Methods involve interventions, observations, biostatistics, genetics, molecular biology, cell biology, and toxicology. Techniques include genomics, bioinformatics, molecular biology tools, oncogenomics, metabolomics, microbiome analysis, spatial analysis, and modeling. Emerging areas include new technologies, epigenetics, health impact assessments, tumor-immune interactions, and microbiome-cancer relationships.

Molecular epidemiology investigates environmental factors' impact on cancer and identifies genetic biomarkers for detection. It is a crucial method in cancer research.<sup>25</sup> Environmental epidemiology examines the correlation between specific environmental factors and health outcomes through descriptive, analytical, and experimental research. Clinical environmental epidemiology merges clinical medicine and environmental epidemiology, examining how specific environmental factors affect individual health, focusing on diagnosis, treatment, and prognosis. Animal models, cell experiments, and high-throughput methods elucidate mechanisms behind increased cancer risk from environmental carcinogens. Medical big data and artificial intelligence help assess environmental cancer risks, enabling real-time monitoring, early warnings, and effective risk management. Cancer genomics provides evidence-based prevention and treatment strategies.<sup>31</sup> Recent advancements in EO, driven by the environmental-wide association study,<sup>32</sup> exosomes, metabolomics, environmental cancer epigenetics, metagenomics, and toxicogenomics, have shifted research focus from macro-environmental factors to micro-molecular biology mechanisms. Dynamic environmental exposure monitoring, next-generation sequencing, liquid biopsy, models, ecological research,

geographic information systems, and other technologies have introduced new methodologies in this field. Several studies have utilized databases such as the Comparative Toxicogenomics Database, Adverse Outcome Pathway Wiki, TOXNET, ECOTOX, and ACToR to identify gene expression, regulatory pathways, and potential targets related to environmental carcinogenesis. The UK Biobank provides excellent exposure and whole-genome data for analyzing environmental factors and cancer. Gene databases like the Cancer Genome Project and The Cancer Genome Atlas are crucial for exploring tumor biomarkers, oncogene mechanisms, and targeted therapies. The National Cancer Data Base and the Surveillance, Epidemiology, and End Results database offer clinical epidemiology data on environmental factors. In summary, existing databases hold significant potential for establishing a comprehensive EO database that integrates toxicology, epidemiology, environmental science, clinical medicine, and molecular biology. Future research should focus on data integration and sharing, technological innovation, and interdisciplinary collaboration to advance cancer prevention and treatment.

### 6.3 | Reduce environmental risks and intervention for cancer

Risk assessment evaluates potential cancer risks associated with environmental factors, requiring comprehensive, data-driven, interdisciplinary approaches involving the collection, compilation, and interpretation of diverse health-related data, encompassing toxicological mechanisms, epidemiology, and environmental and exposure factors, to inform policymakers in developing effective environmental and health strategies aimed at protecting public health and reducing cancer risks. Standard methods include epidemiology, biomonitoring, environmental monitoring, toxicology, and health risk assessments (Supporting Information: Table S2). Environmental cancer risk assessment includes hazard identification, dose–response relationship, exposure, and overall risk assessments. Among these components, the evaluation of the dose–response relationship represents a pivotal core element in assessing environmental carcinogens as it aims to establish a quantitative correlation between environmental carcinogens and specific cancer risks. The future assessment of environmental cancer risk will increasingly depend on mechanistic data and predictive tools for informed decision-making.<sup>33</sup>

After risk factor assessment, the WHO, International Agency for Research on Cancer (IARC), and scholars recommended lifestyle improvements (i.e., quitting smoking, moderating alcohol intake, maintaining a healthy weight, balanced diet, and regular exercise, etc.) and reducing carcinogen exposure (i.e., minimizing radiation and air pollution, etc.) to lower cancer

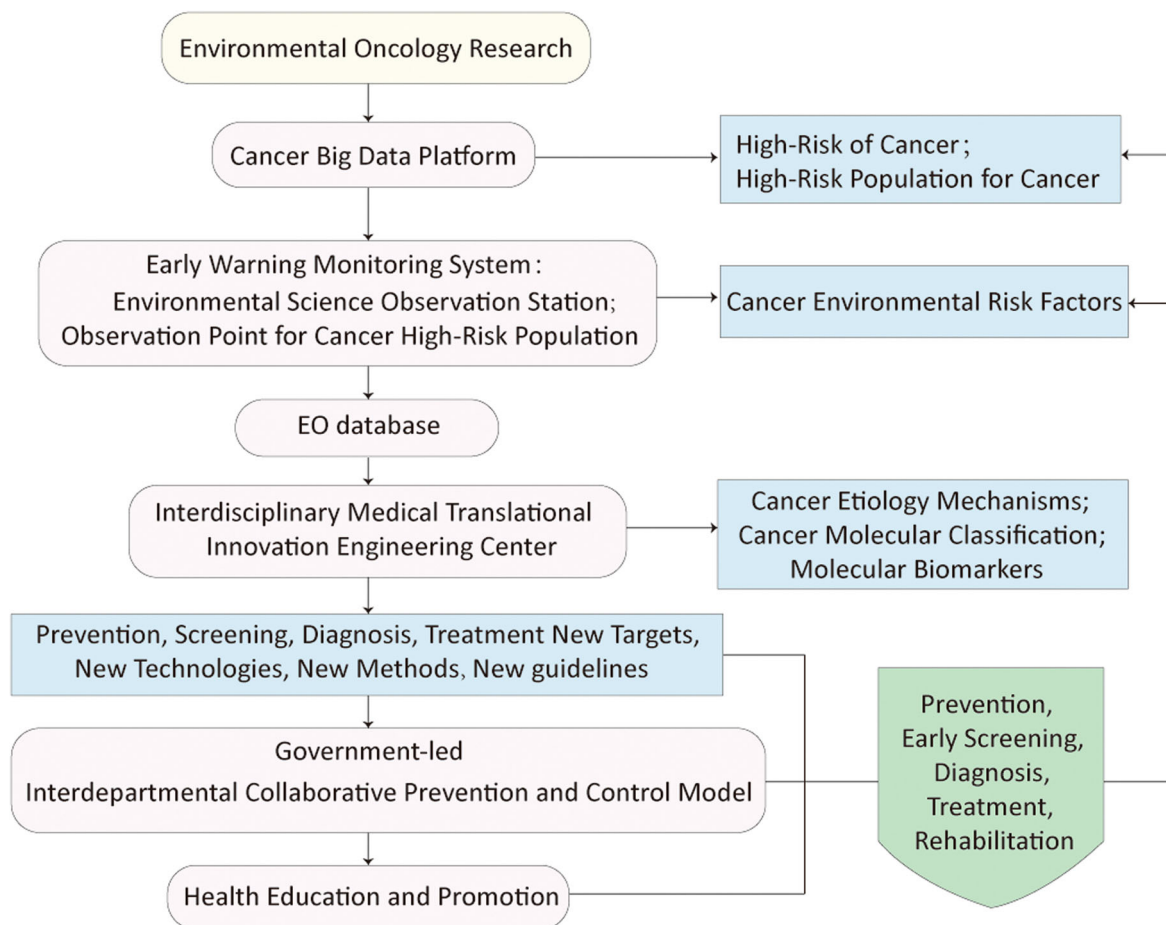
rates.<sup>9,34,35</sup> To counteract potential climate-induced cancer risks, scholars advocated for policy interventions across various sectors to reduce carbon emissions, control air pollution, establish sustainable agriculture, promote physical activity, ensure food security and healthcare access, and provide health education.<sup>5,6</sup> Meeting the air pollution reduction targets of the Paris Agreement could save one million lives annually by 2050. The WHO and IARC also emphasize more substantial political commitments and enhanced cancer research, monitoring, and treatment to bolster cancer prevention and control efforts.<sup>9</sup>

## 7 | THE STRATEGIES AND RESEARCH RECOMMENDATIONS FOR ADVANCING EO

The future of EO encompasses advocating for early intervention and fostering interdisciplinary and international collaboration. This strategy involves prioritizing cancers based on incidence rates, treatment potential, and socioeconomic impact. Such prioritization ensures more effective resource allocation, accelerates scientific advancements, reduces economic burdens, and enhances public health strategies. Key initiatives include establishing research bases in high-risk areas to investigate cancer causes and environmental factors, implementing monitoring and interventions for susceptible individuals, advancing molecular biology and big data-based diagnostic and therapeutic techniques, promoting the use of molecular biomarkers, and forming efficient teams and international cooperation networks to elevate cancer prevention, treatment, and healthcare standards.

Outlined in Figure 3 are the following key strategies:

1. Establish a big data platform involves collaborating with government agencies to create a networked cancer information system and monitoring center. This initiative aims to develop cancer risk maps and establish clinical databases at hospitals. Utilizing clinical data as a foundation enables the analysis, screening, and assessment of environmental cancer risk factors.
2. Implement a cancer environmental risk factor monitoring and warning system involves setting up environmental cancer observation stations and high-risk population observation points. This system includes establishing cohorts to proactively collect environmental and sample data and monitor the correlation between high-risk cancer populations and environmental risk factors.
3. Based on the data from EO research bases, researchers can integrate existing global databases in toxicology, epidemiology, environmental science, clinical medicine, and molecular biology to establish



**FIGURE 3** Strategies and recommendations for advancing environmental oncology.

a comprehensive, globally shared, and interdisciplinary EO database. This database will support research on EO mechanisms, prevention, and treatment.

4. Research on environmental oncology mechanisms and precision prevention and treatment technologies entails interdisciplinary collaboration based on extensive clinical and environmental databases. Advanced molecular biology techniques are used to study GEI, explore cancer etiology mechanisms, identify new cancer biomarkers, develop new technologies for early screening, diagnosis, and treatment, and establish innovative interdisciplinary research platforms.<sup>1,25</sup>
5. Collaboration mechanisms between EO centers, government departments, local medical institutions, and centers for disease control and prevention are established to create precision environmental cancer monitoring points and prevention and control systems. EO centers provide cancer prevention and treatment strategies and recommendations, while government leadership and societal participation are encouraged to form a new cancer prevention

and control model. These efforts are then promoted nationwide. Furthermore, incorporating modern e-health systems and social media platforms into the research and practice of EO contributes to process simplification, strengthened collaboration, and broader dissemination of health information and intervention measures.<sup>36</sup>

#### AUTHOR CONTRIBUTIONS

**Jie Liu:** Conceptualization; investigation; methodology; visualization; writing-original draft. **Ting Gan:** Conceptualization; investigation; methodology; visualization; writing-review & editing. **Wenbiao Hu:** Conceptualization; methodology; project administration; resources; supervision; writing-review & editing. **Yumin Li:** Conceptualization; funding acquisition; methodology; project administration; resources; supervision; writing-review & editing.

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## CONFLICT OF INTEREST STATEMENT

The authors declare no conflict of interest.

## DATA AVAILABILITY STATEMENT

None.

## ETHICS STATEMENT

None.

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## SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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