

## Cancer: A review

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Received: 03 Apr 2024; Received in revised form: 05 May 2024; Accepted: 15 May 2024; Available online: 21 May 2024

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**Abstract** – Cancer remains one of the most formidable challenges in modern medicine, posing significant health burdens globally. In recent years, extensive research efforts have aimed at understanding the intricate mechanisms underlying cancer development, progression, and treatment. This review provides a comprehensive overview of the latest advancements in cancer research across various domains. The elucidation of genetic and molecular alterations driving oncogenesis has revolutionized our understanding of cancer biology. Key discoveries in genomics, transcriptomics, and proteomics have unveiled the heterogeneous nature of tumors, paving the way for personalized treatment approaches. Moreover, advancements in high-throughput sequencing technologies have facilitated the identification of novel cancer biomarkers with diagnostic, prognostic, and therapeutic implications. The tumor microenvironment (TME) has emerged as a critical determinant of cancer progression and therapy response. Research focusing on the dynamic interactions between cancer cells, immune cells, and stromal components within the TME has led to the development of immunotherapeutic strategies, including immune checkpoint inhibitors and adoptive cell therapies, which have demonstrated remarkable efficacy in various cancer types. In addition to targeted therapies and immunotherapies, the advent of precision medicine has transformed cancer treatment paradigms. Molecular profiling of tumors enables clinicians to match patients with specific targeted therapies, optimizing therapeutic outcomes while minimizing adverse effects. Furthermore, the integration of artificial intelligence and machine learning algorithms in cancer research has facilitated the prediction of treatment responses and identification of novel therapeutic targets.

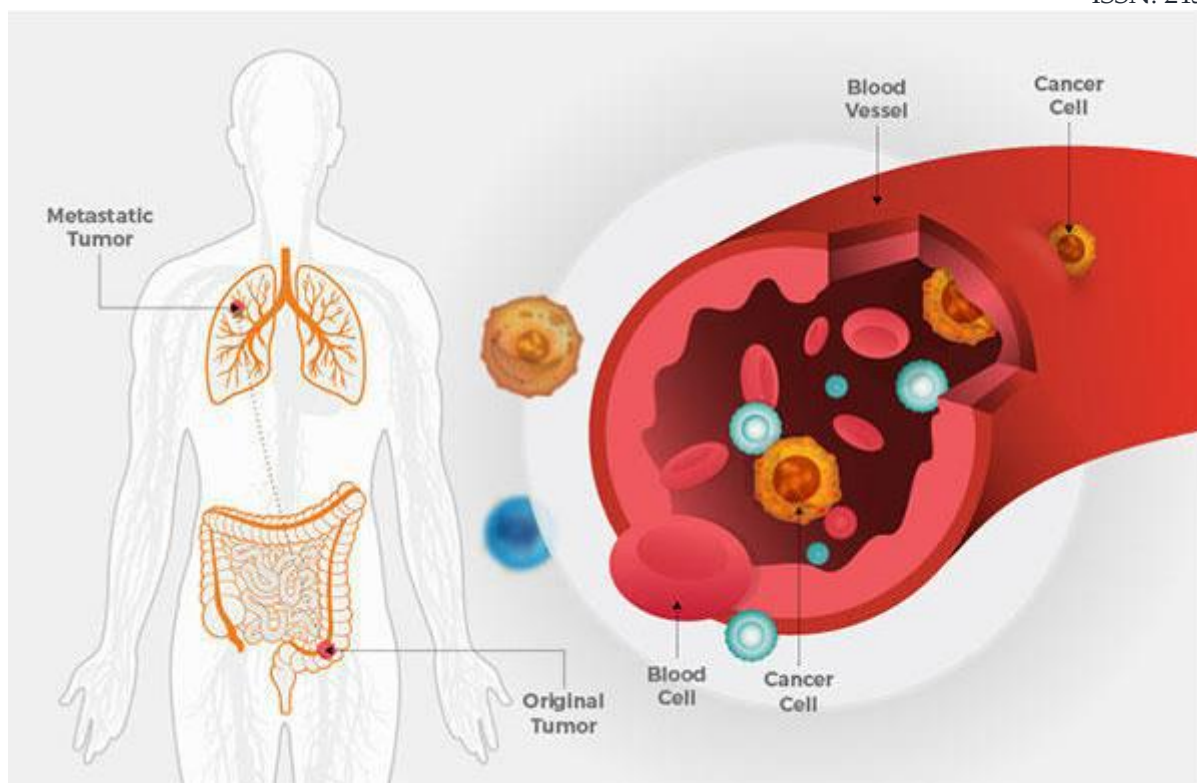


**Keywords** – Oncogenesis, Immunotherapy, Precision Medicine, Tumor Microenvironment (TME), Artificial Intelligence in Cancer Research

### I. INTRODUCTION

Cancer, characterized by uncontrolled cell growth and proliferation, stands as one of the most daunting health challenges of our time, exacting a heavy toll on individuals and societies worldwide. Its multifaceted nature, encompassing a diverse array of diseases with distinct etiologies, manifestations, and treatment responses, underscores the complexity inherent in combating this pervasive malady. Throughout

history, cancer has been documented in ancient texts, with descriptions dating back to ancient Egypt and Greece. However, it wasn't until the advent of modern science that significant strides were made in unraveling the intricacies of cancer biology. The seminal work of pioneers such as Rudolf Virchow, who proposed the concept of cellular pathology in the 19th century, laid the foundation for understanding cancer as a disease of aberrant cellular behavior[1].



Today, our comprehension of cancer extends far beyond Virchow's initial insights, thanks to the relentless efforts of generations of researchers and clinicians. The elucidation of cancer's genetic underpinnings, beginning with the discovery of oncogenes and tumor suppressor genes, has transformed our understanding of its molecular basis. Landmark achievements such as the Human Genome Project and subsequent large-scale sequencing initiatives have unraveled the genomic landscape of various cancer types, revealing the staggering heterogeneity that underlies their development and progression. Moreover, advances in imaging modalities, such as computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET), have revolutionized cancer diagnosis and staging, enabling clinicians to detect tumors with unprecedented precision. These technologies, coupled with innovations in molecular profiling techniques, have paved the way for personalized medicine approaches tailored to the unique genetic makeup of individual tumors[2].

Historical Perspective on Cancer Research and Treatment:

The history of cancer research and treatment spans millennia, with evidence of cancer documented in ancient texts dating back to antiquity. Early civilizations recognized the existence of tumors but attributed them to mystical or supernatural causes. It wasn't until the dawn of modern medicine that systematic efforts were made to understand cancer's etiology and develop effective treatments.

In the late 19th century, the German pathologist Rudolf Virchow proposed the theory that cancer arises from the proliferation of aberrant cells.

This laid the foundation for the field of cellular pathology, shifting the focus from mystical explanations to scientific inquiry. Virchow's insights paved the way for subsequent discoveries, including the identification of specific types of cancer and their histological characteristics. The 20th century witnessed significant advancements in cancer research, fueled by breakthroughs in genetics, biochemistry, and immunology.

In 1911, Peyton Rous demonstrated that a virus could induce tumors in chickens, providing early evidence of viral oncogenesis. Subsequent decades saw the

identification of oncogenes, tumor suppressor genes, and the elucidation of signal transduction pathways involved in cancer development[3].

In recent decades, the emergence of molecular biology and genomics has transformed cancer research and treatment paradigms. The completion of the Human Genome Project in 2003 provided a comprehensive map of the human genome, facilitating the identification of genetic mutations associated with cancer susceptibility and progression.

This genomic revolution has led to the development of targeted therapies tailored to the specific molecular alterations driving individual tumors. Immunotherapy, which harnesses the body's immune system to fight cancer, has emerged as a promising frontier in cancer treatment. The discovery of immune checkpoint inhibitors, such as pembrolizumab and nivolumab, has revolutionized the treatment of advanced malignancies, leading to durable responses in a subset of patients[4].

#### Epidemiology Of Cancer:

Cancer epidemiology is the study of the distribution, determinants, and frequency of cancer occurrences in populations. Understanding cancer epidemiology is crucial for developing effective prevention and control strategies. One key aspect of cancer epidemiology is incidence, which refers to the number of new cancer cases diagnosed within a specific population over a given period. Another important metric is prevalence, which indicates the total number of people living with cancer at a particular time. Additionally, cancer epidemiology examines mortality rates, survival rates, and trends over time to identify patterns and risk factors associated with different types of cancer[5]. Several factors contribute to cancer development, including genetic predisposition, environmental exposures, lifestyle choices, and socio-economic status. Tobacco use, excessive alcohol consumption, poor diet, physical inactivity, and exposure to carcinogens such as ultraviolet radiation, asbestos, and certain chemicals are well-established risk factors for various cancers. Cancer epidemiology also reveals disparities in cancer incidence, mortality, and survival among different population groups. These disparities may be influenced by factors such as race, ethnicity, gender,

age, geographic location, and access to healthcare services. For example, studies have shown higher rates of lung cancer among smokers and individuals from lower socio-economic backgrounds[6].

#### Etiology And Risk Factors:

The etiology of cancer is multifactorial, involving a complex interplay of genetic, environmental, lifestyle, and socio-economic factors. Understanding the various risk factors associated with cancer is crucial for prevention, early detection, and effective management strategies.

- (a) Genetic factors play a significant role in cancer susceptibility, with certain inherited mutations predisposing individuals to specific types of cancer. For example, mutations in the BRCA1 and BRCA2 genes are associated with an increased risk of breast and ovarian cancers, while mutations in the APC gene are linked to familial adenomatous polyposis and colorectal cancer.
- (b) Environmental exposures to carcinogens also contribute to cancer development. Carcinogens can be found in air, water, food, and workplace environments. Examples include tobacco smoke, asbestos fibers, ultraviolet radiation, ionizing radiation, and certain chemicals used in industries such as manufacturing, mining, and agriculture[7].
- (c) Lifestyle choices and behaviors can significantly influence cancer risk. Tobacco use is the leading cause of preventable cancer deaths worldwide, accounting for a substantial proportion of lung, throat, mouth, and bladder cancers. Excessive alcohol consumption is another modifiable risk factor associated with increased risks of liver, breast, colorectal, and other cancers.
- (d) Dietary factors play a role in cancer development, with diets high in processed foods, red meat, and saturated fats linked to an elevated risk of certain cancers, such as colorectal cancer. Conversely, diets rich in fruits, vegetables, whole grains, and lean proteins are associated with a lower risk of cancer.
- (e) Socio-economic factors, including income, education, access to healthcare, and environmental conditions, also influence

cancer risk. Disparities in cancer incidence, mortality, and survival exist among different population groups, with individuals from disadvantaged backgrounds often experiencing higher cancer burden and poorer outcomes[8].

#### Molecular Basis Of Cancer:

The molecular basis of cancer involves a complex interplay of genetic and epigenetic alterations that drive abnormal cell growth, proliferation, and survival. These alterations disrupt the intricate regulatory mechanisms that govern cell cycle progression, apoptosis, DNA repair, and cellular differentiation. One hallmark of cancer is the activation of oncogenes, which are genes that promote cell proliferation when mutated or overexpressed. Oncogenes encode proteins involved in signaling pathways that regulate cell growth and survival, such as the Ras, Myc, and EGFR (epidermal growth factor receptor) pathways. Mutations in these pathways can lead to uncontrolled cell proliferation and tumor formation[9]. Conversely, tumor suppressor genes act as guardians of the genome, inhibiting cell growth and promoting apoptosis. Loss-of-function mutations or epigenetic silencing of tumor suppressor genes, such as TP53 (encoding p53) and PTEN, can abolish their regulatory functions, allowing unchecked cell proliferation and tumor progression.

Another key aspect of cancer biology is genomic instability, characterized by increased rates of DNA mutations, chromosomal rearrangements, and copy number alterations. Genomic instability can arise from defects in DNA repair mechanisms, telomere dysfunction, or exposure to genotoxic agents such as radiation and chemicals. Epigenetic alterations, including DNA methylation, histone modifications, and non-coding RNA dysregulation, also contribute to cancer development by altering gene expression patterns without changing the underlying DNA sequence. Aberrant epigenetic changes can silence tumor suppressor genes or activate oncogenes, promoting tumor growth and metastasis[10].

#### Hallmarks of Cancer:

The "hallmarks of cancer" represent fundamental capabilities acquired by cancer cells during tumorigenesis, as proposed by Hanahan and

Weinberg in 2000 and updated in 2011. These hallmarks describe the key biological traits that distinguish cancer cells from normal cells and contribute to tumor growth, invasion, and metastasis.

1. Sustaining proliferative signaling: Cancer cells exhibit dysregulated signaling pathways that drive uncontrolled cell proliferation, often through mutations or amplifications of oncogenes such as Ras and Myc.
2. Evading growth suppressors: Cancer cells evade growth-inhibitory signals and apoptotic mechanisms mediated by tumor suppressor genes like TP53 (p53) and RB1 (retinoblastoma protein).
3. Resisting cell death: Cancer cells acquire resistance to apoptosis, allowing them to survive despite genomic instability and other stressors.
4. Enabling replicative immortality: Cancer cells activate mechanisms to bypass senescence and maintain telomere length, enabling indefinite proliferation.
5. Inducing angiogenesis: Tumors promote the formation of new blood vessels (angiogenesis) to ensure a sufficient nutrient and oxygen supply for sustained growth.
6. Activating invasion and metastasis: Cancer cells acquire the ability to invade surrounding tissues and metastasize to distant organs, facilitated by alterations in cell adhesion, motility, and extracellular matrix remodeling[11].
7. Deregulating cellular energetics: Cancer cells reprogram their metabolism to meet the increased energy demands of rapid proliferation, favoring glycolysis even in the presence of oxygen (the Warburg effect).
8. Avoiding immune destruction: Tumors evade immune surveillance by suppressing immune responses or expressing immune checkpoint molecules that inhibit T cell activation.
9. Tumor-promoting inflammation: Chronic inflammation contributes to tumorigenesis by creating a pro-tumorigenic microenvironment and promoting genetic instability.
10. Genome instability and mutation: Cancer cells exhibit increased genomic instability and

accumulate mutations, enabling adaptive evolution and tumor heterogeneity[10].

#### Tumor Microenvironment:

The tumor microenvironment (TME) is a complex ecosystem consisting of cancer cells, stromal cells, immune cells, blood vessels, extracellular matrix (ECM), and signaling molecules. Interactions within the TME play a crucial role in tumor development, progression, and response to therapy. One key component of the TME is stromal cells, including cancer-associated fibroblasts (CAFs), endothelial cells, and pericytes[12]. CAFs produce growth factors, cytokines, and ECM components that promote tumor growth, angiogenesis, and metastasis. Endothelial cells form blood vessels that supply oxygen and nutrients to the tumor, while pericytes stabilize the vessels and regulate blood flow. Immune cells within the TME have dual roles in tumor suppression and promotion. Tumor-infiltrating lymphocytes (TILs), such as cytotoxic T cells and natural killer cells, can recognize and eliminate cancer cells. However, tumors can evade immune surveillance by recruiting immunosuppressive cells like regulatory T cells (Tregs), myeloid-derived suppressor cells (MDSCs), and M2-polarized macrophages. These cells inhibit anti-tumor immune responses and promote tumor progression. The ECM provides structural support for the TME and regulates cell behavior through physical and biochemical cues. Tumors often exhibit abnormal ECM remodeling, leading to increased stiffness, altered signaling pathways, and enhanced invasive potential[13].

#### Diagnostic Approaches For Cancer:

Diagnostic approaches for cancer encompass a range of techniques aimed at detecting tumors, characterizing their molecular features, and assessing disease progression. These approaches play a crucial role in early detection, treatment planning, and monitoring of therapeutic response. Imaging modalities such as X-ray, computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET) are commonly used for cancer diagnosis. These techniques provide detailed anatomical information and help localize tumors within the body. Biopsy procedures involve the extraction of tissue or fluid samples from suspicious lesions for histological examination[13].

Histopathological analysis allows pathologists to assess cellular morphology, architecture, and molecular markers to determine the presence of cancer and its histological subtype. Molecular diagnostics, including genomic, transcriptomic, and proteomic analyses, provide insights into the molecular alterations driving cancer development and progression. Techniques such as next-generation sequencing (NGS), polymerase chain reaction (PCR), and immunohistochemistry (IHC) allow for the detection of specific genetic mutations, gene expression profiles, and protein biomarkers associated with cancer. Liquid biopsies, which analyze circulating tumor cells (CTCs), cell-free DNA (cfDNA), and extracellular vesicles (EVs) in blood or other bodily fluids, offer a minimally invasive alternative to traditional tissue biopsies. Liquid biopsies can provide real-time information on tumor dynamics, treatment response, and the emergence of drug resistance[14].

#### Therapeutic Modalities:

Therapeutic modalities for cancer encompass a diverse array of treatment options aimed at eradicating or controlling tumor growth, minimizing disease-related symptoms, and improving overall patient outcomes. These modalities can be broadly categorized into primary treatments, including surgery, radiation therapy, and chemotherapy, as well as emerging approaches such as immunotherapy, targeted therapy, and precision medicine.

- (a) Surgery remains a cornerstone of cancer treatment and is often used to remove localized tumors and adjacent lymph nodes. Advances in surgical techniques, such as minimally invasive and robotic-assisted procedures, have improved surgical outcomes and reduced postoperative morbidity.
- (b) Radiation therapy utilizes high-energy beams to target and destroy cancer cells while sparing surrounding healthy tissue. Modern radiation techniques, such as intensity-modulated radiation therapy (IMRT) and stereotactic body radiation therapy (SBRT), allow for precise delivery of radiation doses, resulting in improved tumor control and reduced side effects.
- (c) Chemotherapy employs cytotoxic drugs to kill rapidly dividing cancer cells or inhibit their

growth. While traditional chemotherapy is associated with systemic toxicity and adverse effects, the development of targeted chemotherapy agents and combination regimens has improved treatment efficacy and tolerability[15].

- (d) Immunotherapy harnesses the body's immune system to recognize and eliminate cancer cells. Immune checkpoint inhibitors, chimeric antigen receptor (CAR) T cell therapy, and cancer vaccines are among the immunotherapeutic approaches that have demonstrated remarkable efficacy in treating various cancers.
- (e) Targeted therapy exploits specific molecular targets or pathways that drive tumor growth and survival. These therapies, including tyrosine kinase inhibitors and monoclonal antibodies, block signaling pathways or inhibit proteins essential for cancer cell proliferation, leading to tumor regression and improved patient outcomes.
- (f) Precision medicine involves tailoring cancer treatment based on individual patient characteristics, including genetic mutations, biomarker expression, and tumor molecular profiling. By identifying actionable alterations and selecting targeted therapies accordingly, precision medicine aims to optimize treatment efficacy while minimizing adverse effects[16].

#### Challenges in Cancer Treatment:

Cancer treatment faces numerous challenges that impact patient outcomes, treatment efficacy, and healthcare systems. These challenges arise from the complexity of cancer biology, tumor heterogeneity, treatment resistance, and systemic barriers to care.

- (a) One major challenge is tumor heterogeneity, which refers to the presence of diverse cell populations within a tumor, each with distinct genetic, epigenetic, and phenotypic characteristics. Tumor heterogeneity contributes to treatment resistance, as certain cancer cells may evade therapy while others remain susceptible. Additionally, intra-tumoral heterogeneity poses challenges for accurate diagnosis, treatment selection, and monitoring of treatment response.
- (b) Another significant challenge is treatment resistance, whereby cancer cells develop

mechanisms to evade the effects of chemotherapy, radiation therapy, or targeted therapies. Resistance mechanisms may involve genetic mutations, activation of alternative signaling pathways, or adaptation to the tumor microenvironment. Overcoming treatment resistance requires the development of novel therapeutic strategies, combination therapies, and predictive biomarkers to guide treatment selection[17].

- (c) Access to cancer care is a major challenge, particularly in low- and middle-income countries (LMICs) where healthcare resources may be limited. Barriers to care include financial constraints, lack of infrastructure, shortages of trained healthcare professionals, and geographical disparities. Addressing these barriers requires investment in healthcare infrastructure, implementation of screening and early detection programs, and strategies to improve access to affordable cancer treatments.
- (d) Furthermore, disparities in cancer outcomes exist among different population groups, including racial and ethnic minorities, socioeconomically disadvantaged individuals, and rural communities. These disparities may arise from differences in access to care, quality of care, health literacy, and social determinants of health. Eliminating disparities in cancer care requires comprehensive approaches that address systemic inequalities and promote health equity[18].

#### Future Directions And Emerging Trends:

Future directions in cancer research and emerging trends are poised to revolutionize the diagnosis, treatment, and management of cancer, leading to improved patient outcomes and quality of life. Several key areas hold promise for shaping the future of cancer care:

- (a) Precision medicine: Advances in genomic sequencing technologies and molecular profiling have paved the way for precision medicine approaches tailored to individual patients' genetic makeup and tumor biology. By identifying actionable genetic alterations and selecting targeted therapies accordingly, precision medicine aims to optimize

treatment efficacy while minimizing adverse effects.

- (b) Immunotherapy: Immunotherapy has emerged as a transformative approach in cancer treatment, harnessing the body's immune system to recognize and eliminate cancer cells. Future developments in immunotherapy include combination therapies, personalized vaccines, and strategies to overcome resistance mechanisms, enhancing the effectiveness of immune-based treatments across various cancer types[19].
- (c) Liquid biopsies: Liquid biopsies, which analyze circulating tumor cells (CTCs), cell-free DNA (cfDNA), and other biomarkers in blood or other bodily fluids, offer a non-invasive and real-time approach to monitor tumor dynamics, treatment response, and the emergence of drug resistance. Future advancements in liquid biopsy technologies hold promise for early detection, minimal residual disease monitoring, and guiding treatment decisions in cancer patients.
- (d) Artificial intelligence (AI) and big data analytics: AI-driven approaches, including machine learning algorithms and deep learning models, have the potential to revolutionize cancer research and clinical practice. By analyzing large datasets of imaging, genomic, and clinical data, AI can identify patterns, predict treatment responses, and guide precision oncology approaches, leading to more personalized and effective cancer care.
- (e) Novel therapeutic modalities: Emerging therapeutic modalities, such as gene editing technologies (e.g., CRISPR-Cas9), oncolytic viruses, and cancer metabolism-targeting agents, hold promise for expanding the therapeutic arsenal against cancer and overcoming treatment resistance[20].

Trends in cancer incidence and mortality across different regions and demographics:

Trends in cancer incidence and mortality vary across different regions and demographics due to differences in risk factors, access to healthcare, screening practices, and socio-economic factors. While some

regions have experienced declines in cancer incidence and mortality rates due to advancements in early detection and treatment, others face rising cancer burden, particularly in low- and middle-income countries (LMICs) with limited healthcare resources. For example, developed countries often exhibit higher overall cancer incidence rates but lower mortality rates compared to developing countries. This discrepancy can be attributed to differences in lifestyle factors, such as smoking prevalence, obesity rates, and dietary habits, as well as variations in healthcare infrastructure and cancer screening programs. Furthermore, disparities in cancer outcomes exist among different demographic groups, including racial and ethnic minorities, socioeconomically disadvantaged individuals, and rural populations. These disparities may stem from inequalities in access to care, quality of care, health literacy, and cultural factors. Understanding these trends and disparities is essential for developing targeted interventions and public health policies aimed at reducing the global burden of cancer and promoting health equity across diverse populations[21].

## II. CONCLUSION

In conclusion, this review has provided a comprehensive overview of the multifaceted landscape of cancer, highlighting its complexities, challenges, and advancements in research and treatment. Cancer remains a formidable global health challenge, with its incidence steadily rising and its impact extending across demographics and geographies. Understanding the intricate interplay of genetic, environmental, and lifestyle factors is paramount for elucidating the mechanisms underlying cancer development and progression. Recent decades have witnessed remarkable progress in cancer research, with significant strides made in deciphering the molecular basis of cancer, identifying novel therapeutic targets, and developing innovative treatment modalities. From conventional approaches such as surgery, chemotherapy, and radiation therapy to groundbreaking immunotherapies and targeted therapies, the armamentarium against cancer continues to expand, offering new hope to patients. However, despite these advancements, challenges persist. Drug resistance, treatment toxicity, and disparities in access to care remain significant hurdles

in the fight against cancer. Addressing these challenges requires a multidisciplinary approach, encompassing basic science research, clinical trials, healthcare policy reforms, and community engagement. Looking ahead, the future of cancer research and treatment holds tremendous promise. Emerging technologies such as precision medicine, genomics, and immunotherapy offer unprecedented opportunities to tailor treatments to individual patients, optimize therapeutic efficacy, and minimize adverse effects. Furthermore, collaborative efforts among researchers, clinicians, policymakers, and patient advocates are essential for translating scientific discoveries into tangible improvements in cancer outcomes. In closing, while the battle against cancer is far from over, the collective efforts of the global cancer community continue to drive progress towards a future where cancer is no longer a devastating diagnosis but a manageable chronic condition, and ultimately, a preventable disease.

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