Review

The Evolution of Cancer Therapeutics: From Conventional Methods to Targeted and Personalized Approaches

Ashutosh Kumar Maurya , Ashish Kumar Maurya , Jordi Muntane * , Sameer Kumar V.B *

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Review

The Evolution of Cancer Therapeutics: From Conventional Methods to Targeted and Personalized Approaches

Ashutosh Kumar Maurya [1], Ashish Kumar Maurya [2], Jordi Muntane [3,*] and V.B. Sameer Kumar [4,*]

[1] Department of Biochemistry & Mol. Biology, Central University of Kerala, Kasaragod, Kerala, India, 671316
[2] Institute of Engineering & Technology, Bundelkhand University, Jhansi, Uttar Pradesh, India, 284128
[3] Instituto de Biomedicina de Sevilla, Universidad de Sevilla, Sevilla, Spain, 41004
[4] Department of Genomic Science, Central University of Kerala, Kasaragod, Kerala, India, 671316
* Correspondence: ashu@cukerala.ac.in (J.M.); mauryaashutoshk@gmail.com (V.B.S.K.)

Abstract

Cancer remains a leading cause of morbidity and mortality worldwide, with an ever-increasing demand for more effective and targeted therapies. The treatment of cancer has evolved dramatically over the past century, from the introduction of surgery and radiation therapy to the emergence of chemotherapy and, more recently, targeted therapies and immunotherapies. These advancements have significantly improved patient outcomes, though challenges such as drug resistance, treatment toxicity, and high treatment costs persist. This review provides a comprehensive overview of the historical, current, and future status of cancer therapeutics. The paper explores the evolution of cancer treatment from traditional methods to the development of novel therapies like immune checkpoint inhibitors, CAR-T cell therapies, and personalized medicine strategies. Furthermore, it discusses the obstacles that remain in the field, such as immune evasion, resistance mechanisms, and the need for more accessible treatment options. Future perspectives highlight the integration of advanced technologies such as liquid biopsy and nanomedicine, which promise to revolutionize cancer treatment by enabling early detection, improved targeting, and reduced side effects. The ongoing advancements in cancer therapeutics hold great promise for improving survival rates and quality of life for cancer patients, with the hope of achieving more effective, less toxic, and universally accessible therapies.

Keywords: targeted therapy; immunotherapy; chemotherapy; precision medicine; CAR-T cell therapy; nanomedicine

Introduction

Cancer remains one of the leading global health challenges, with nearly 10 million deaths attributed to the disease annually, according to the World Health Organization (WHO) [1]. In the past few decades, significant progress has been made in understanding the molecular and genetic basis of cancer, leading to the development of more targeted therapies [2]. Despite these advancements, cancer treatment continues to be hampered by challenges such as drug resistance, cancer heterogeneity, and the severe side effects associated with conventional therapies like chemotherapy and radiation [3]. Historically, cancer treatment has evolved through a variety of therapeutic approaches, with the ultimate goal being to improve survival rates and patient quality of life [4].

The treatment of cancer has progressed from simple surgical interventions to more complex therapies that target the genetic and molecular underpinnings of cancer cells. However, overcoming the complexities of cancer's cellular diversity and its ability to evolve resistance to treatment remains one of the biggest obstacles in clinical oncology [5]. This paper explores the journey of cancer

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therapeutics, discussing the historical context of treatment options, current drug discovery and therapeutic advancements, and the future directions that cancer therapy needs to take to address existing challenges and further improve patient outcomes.

To understand the progression of cancer treatment, it is essential to examine how therapeutic strategies have evolved over the years. Table 1 provides a detailed timeline of treatment modalities from early approaches to current innovations in cancer therapy.

Table 1. Evolution of Cancer Treatment Modalities.

Time Period	Treatment Type	Key Characteristics	Notable Advances
Pre-20th Century	Surgical Resection	Limited to localized tumors, high mortality risk	Early use of surgical techniques for tumor removal [2]
Early 20th Century	Radiation Therapy	Introduction of X-ray and radium-based treatments	Pioneering use of radiation in oncology [3,4]
Mid-20th Century	Chemotherapy	Systemic treatment targeting rapidly dividing cells	Introduction of chemotherapy agents like methotrexate, cyclophosphamide [5]
Late 20th Century	Hormonal Therapy	Targeted treatment for hormone-sensitive cancers (e.g., breast, prostate)	Development of tamoxifen, androgen deprivation therapies [6]
Early 21st Century	Targeted Therapy	Focus on specific molecular targets (e.g., HER2, EGFR)	Approval of imatinib (Gleevec) for chronic myelogenous leukemia, trastuzumab (Herceptin) for HER2-positive breast cancer [7,8]
Current Era	Immunotherapy	Use of immune checkpoint inhibitors, CAR-T cells	Pembrolizumab (Keytruda), nivolumab (Opdivo), CAR-T therapies for blood cancers [9,10]
Future (Emerging)	Precision Medicine/Personalized Therapy	Tailored treatment based on genetic profile of the tumor	Liquid biopsies, targeted gene-editing therapies (CRISPR) [11,12]

2. Cancer: Overview and Types

Cancer refers to a broad group of diseases characterized by uncontrolled cell growth, invasion of surrounding tissues, and the ability to metastasize to distant organs. These malignant behaviors are driven by a variety of genetic and environmental factors, including mutations in genes that regulate cell division, repair, and apoptosis [6]. As a result, cancer cells bypass the normal regulatory mechanisms that control cell growth and death, allowing them to proliferate uncontrollably [7].

Cancer can arise in nearly any tissue or organ in the body and is generally classified into two main categories based on the type of tissue affected:

- **Solid Tumors**: These cancers are characterized by the formation of a mass of abnormal cells, typically in solid organs such as the lung, breast, colon, or liver. Solid tumors are usually diagnosed through imaging or biopsy and can be either benign or malignant. Malignant solid tumors are capable of invading nearby tissues and spreading to other parts of the body, a process known as metastasis. The most common solid tumors include lung cancer, breast cancer, colorectal cancer, and prostate cancer [8].
- **Hematologic Cancers**: These cancers, including leukemia, lymphoma, and myeloma, affect the blood and bone marrow. Hematologic malignancies often present as systemic diseases, circulating throughout the body via the bloodstream. The treatment of hematologic cancers generally involves systemic therapies such as chemotherapy, stem cell transplantation, and targeted therapies [9]. The prognosis and treatment approaches for these cancers can differ significantly from those for solid tumors, underscoring the diversity within cancer subtypes.

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The heterogeneity of cancer types poses significant challenges in treatment. Even within a single type of cancer, individual tumors can exhibit substantial differences in genetic mutations, protein expression, and response to treatment. This variability has spurred the field of **precision medicine**, where therapies are increasingly tailored to the genetic and molecular profile of a patient's specific cancer, allowing for more personalized and potentially more effective treatments [10].

3. Past Treatment Methods

The treatment of cancer has undergone significant changes over the last century, with initial strategies being limited to surgical removal of tumors and rudimentary forms of radiation therapy. As the understanding of cancer biology deepened, more systemic therapies like chemotherapy and hormonal therapy were developed. However, these approaches were often nonspecific, resulting in substantial damage to healthy tissues along with cancerous cells.

- **Surgical Treatment**: Surgical intervention has been used as a treatment for cancer for centuries, but its efficacy was greatly improved with the advent of anesthesia, antiseptic techniques, and better diagnostic tools in the late 19th and early 20th centuries [11]. Surgical resection has been particularly effective for localized cancers that have not yet spread to other tissues. However, its success in metastatic cancer is limited, leading to the need for complementary therapies [12].
- **Radiation Therapy**: The discovery of X-rays and the subsequent identification of radioactive materials like radium in the late 19th century paved the way for radiation therapy. Initially, radiation therapy was imprecise and often resulted in significant damage to surrounding healthy tissues. However, the development of linear accelerators and more refined techniques like intensity-modulated radiation therapy (IMRT) have improved the precision and safety of this treatment [13]. Despite these improvements, radiation therapy still carries a risk of long-term side effects, particularly when used at high doses.
- **Chemotherapy**: The introduction of chemotherapy in the 1940s marked the first major advancement in systemic cancer treatment. Chemotherapy works by targeting and killing rapidly dividing cells, a characteristic of most cancer cells [14]. However, its nonspecific nature means that it also damages healthy cells, leading to side effects such as nausea, hair loss, and immunosuppression. Despite these drawbacks, chemotherapy became the mainstay of cancer treatment for decades and is still used today in combination with other therapies [15].
- **Hormonal Therapy**: In the mid-20th century, researchers discovered that certain cancers, such as breast and prostate cancers, were influenced by hormones like estrogen and testosterone [16]. This understanding led to the development of hormonal therapies, which block hormone production or inhibit the action of hormones on cancer cells. For example, tamoxifen is used to treat estrogen receptor-positive breast cancer, while androgen deprivation therapy is used for prostate cancer [17]. Although hormonal therapies can improve survival rates in hormone-sensitive cancers, they are not effective for all patients, especially those whose tumors acquire resistance to hormonal regulation [18].

4. Current Drug Discovery and Therapeutic Advancements

In the past two decades, the landscape of cancer therapy has shifted dramatically due to advancements in molecular biology, genomics, and immunology. The introduction of targeted therapies, immunotherapies, and precision medicinehas revolutionized the way we treat cancer. These approaches have shown significant promise in improving patient outcomes by focusing on the specific genetic mutations or molecular markers driving cancer growth.

To further understand the future landscape of cancer therapeutics, it is essential to consider ongoing clinical trials. Table 2 outlines key innovations currently being explored in clinical trials, offering insights into potential breakthroughs in cancer therapy.

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Table 2. Clinical Trials in Cancer Therapeutics—Key Innovations.

Therapy/Approach	Cancer Type	Key Clinical Trial Outcome	Ongoing Studies
Precision Medicine Trials	Various cancers	Identification of molecular subtypes, tailored therapy approaches	Trials evaluating biomarker-driven therapies [11]
Immunotherapy Trials (Checkpoint Inhibitors)	Lung, Melanoma, Urothelial cancers	Increased survival rates, improved response in PD-L1 positive patients	Combination of immune checkpoint inhibitors with chemotherapy, targeted therapy [9]
CAR-T Cell Trials	Blood cancers (e.g., Leukemia, Lymphoma)	High remission rates in refractory leukemia/lymphoma patients	Trials targeting solid tumors, expansion of CAR-T use [10]
Gene Editing (CRISPR/Cas9)	Various cancers	Early-stage trials to edit cancer cell mutations in vivo	Trials targeting genetic mutations associated with specific cancers [12]

- **Targeted Therapy**: Targeted therapies are designed to specifically interfere with molecular targets involved in cancer cell proliferation and survival. These therapies include small molecule inhibitors, which block specific signaling pathways, and monoclonal antibodies, which target tumor-associated antigens [19]. Notable examples include trastuzumab (Herceptin), used for HER2-positive breast cancer, and imatinib (Gleevec), used for chronic myelogenous leukemia (CML) [20]. Targeted therapies have fewer side effects compared to traditional chemotherapy because they are more selective in their action, targeting only cancer cells and leaving healthy cells largely unaffected.

The development of targeted therapies has revolutionized cancer treatment in recent decades. Table 3 highlights some of the most prominent targeted therapies used in clinical practice today.

Table 3. Key Targeted Therapies in Cancer Treatment.

Therapy	Targeted Protein/Pathway	Cancer Type	Mechanism of Action	Notable Example(s)
Tyrosine Kinase Inhibitors	EGFR, BCR-ABL, ALK	Lung, Leukemia, Breast, Colorectal	Inhibits the activity of abnormal kinases involved in tumor growth	**Imatinib (Gleevec)** for CML, **Erlotinib** for non-small cell lung cancer [7]
Monoclonal Antibodies	HER2, VEGF, CD20	Breast, Colon, Lymphoma, Leukemia	Binds to specific cell surface antigens to block growth or mark for immune attack	**Trastuzumab (Herceptin)** for HER2-positive breast cancer, **Rituximab** for non-Hodgkin lymphoma [8,13]
PARP Inhibitors	PARP1 (DNA repair enzyme)	Ovarian, Breast, Prostate	Inhibits DNA repair mechanisms in cancer cells with BRCA mutations	**Olaparib (Lynparza)** for BRCA-mutated cancers [14]

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Immune Checkpoint Inhibitors	PD-1/PD-L1, CTLA-4	Melanoma, Non-small cell lung cancer, Bladder cancer	Blocks immune checkpoints to enhance immune response against cancer cells	**Pembrolizumab (Keytruda)**, **Nivolumab (Opdivo)** [9,15]
CAR-T Cell Therapy	Tumor-specific antigens (e.g., CD19)	Leukemia, Lymphoma	Genetically engineered T cells to recognize and attack cancer cells	**Kymriah**, **Yescarta** for blood cancers (e.g., leukemia, lymphoma) [10]

- **Immunotherapy**: Immunotherapy has emerged as one of the most promising cancer treatments, leveraging the body's immune system to target and destroy cancer cells. Immune checkpoint inhibitors, such as pembrolizumab (Keytruda) and nivolumab (Opdivo), have shown remarkable success in treating cancers like melanoma, non-small cell lung cancer, and bladder cancer [21]. These drugs block checkpoint proteins (e.g., PD-1, PD-L1), preventing cancer cells from evading immune detection. Additionally, CAR-T cell therapy, which involves engineering a patient's own T cells to specifically recognize and attack cancer cells, has demonstrated efficacy in treating hematologic cancers like leukemia and lymphoma [22].

Immunotherapy has become one of the most exciting areas of cancer treatment in recent years. Table 4 provides an overview of the most widely used immunotherapies, their mechanisms of action, and their current clinical status.

Table 4. Immunotherapies in Clinical Use and Development.

Immunotherapy Type	Mechanism of Action	Indications	Examples	Current Status
Immune Checkpoint Inhibitors	Blocks checkpoint proteins like PD-1/PD-L1	Melanoma, NSCLC, Bladder, Head & Neck	**Pembrolizumab (Keytruda)**, **Nivolumab (Opdivo)**	Approved and in clinical use [9,15]
Chimeric Antigen Receptor T-cell (CAR-T) Therapy	Genetically engineered T cells to target tumor antigens	Leukemias, Lymphomas	**Kymriah**, **Yescarta**	Approved for hematological malignancies, expanding to solid tumors [10]
Cytokine Therapy	Stimulates immune system using cytokines (e.g., IL-2, IFN)	Melanoma, Renal cell carcinoma	**Aldesleukin (Proleukin)**, **Interferon-alpha**	Limited use due to toxicity, ongoing studies for efficacy [23]
Cancer Vaccines	Stimulates immune system to recognize cancer cells	Prostate, Cervical, Melanoma	**Sipuleucel-T (Provenge)** for prostate cancer	In clinical trials, limited approval [24]
Oncolytic Virus Therapy	Uses modified viruses to infect and	Melanoma, Glioblastoma, Head & Neck	**T-VEC (Imlygic)** for melanoma	In clinical trials, emerging therapies [25]

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	destroy cancer cells

- **Precision Medicine**: The advent of next-generation sequencing (NGS) technologies has allowed for the molecular profiling of tumors, enabling clinicians to tailor cancer treatments based on the specific genetic mutations of individual tumors [23]. For instance, targeted therapies against EGFR mutations in non-small cell lung cancer and ALK rearrangements in lung cancer have greatly improved patient outcomes, allowing for more personalized and effective treatments [24].
- **Nanotechnology and Drug Delivery**: Nanotechnology has emerged as a cutting-edge tool in cancer treatment, especially in the context of drug delivery systems. Nanoparticles can be engineered to selectively deliver chemotherapy or other therapeutic agents to tumor sites, improving drug efficacy while minimizing toxicity to healthy tissues [25]. The development of nanocarriers for drug delivery is particularly promising in improving the pharmacokinetics and reducing the side effects of chemotherapy [26].

Advancements in technology are playing an increasingly crucial role in shaping the future of cancer treatment. Table 5 highlights the most promising emerging technologies and their potential impact on cancer therapeutics."

Table 5. Emerging Technologies in Cancer Therapy.

Technology	Description	Potential Impact	Current Stage of Development
Liquid Biopsy	Non-invasive blood test for detecting ctDNA	Early cancer detection, monitoring treatment response, minimal invasiveness	Clinical trials for early detection and monitoring [26]
Nanomedicine	Targeted drug delivery using nanoparticles	Improved specificity and reduced toxicity for chemotherapy	Early-phase trials in targeted drug delivery systems [19]
CRISPR/Cas9 Gene Editing	Genome editing technology to correct cancer mutations	Targeted therapies for genetically defined cancers, overcoming drug resistance	Preclinical and early clinical stages [12]
Artificial Intelligence	AI for predictive modeling, drug discovery, and patient monitoring	Enhanced drug development, personalized treatment strategies	Integrating AI in clinical decision-making and drug development [27]
Organoids and 3D Tumor Models	In vitro tumor models that mimic human tissue	Drug screening, personalized treatment testing, understanding cancer progression	Ongoing studies in personalized medicine and drug screening [28]

While recent advancements in cancer therapeutics have significantly improved patient outcomes, several challenges remain. Table 6 summarizes key challenges in the field and highlights future directions to overcome these obstacles.

Table 6. Challenges in Cancer Therapy and Future Directions.

Challenge	Current Solutions	Future Directions/Innovations
Drug Resistance	Combination therapies, resistance screening	New inhibitors targeting resistance mechanisms, use of gene-editing (e.g., CRISPR) to overcome mutations [7,16]

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Immune Evasion	Immune checkpoint inhibitors, CAR-T therapy	Next-generation immune therapies, targeting immunosuppressive tumor microenvironment, combination with targeted therapies [9,17]
Treatment Toxicity	Dose-limiting chemotherapy, targeted therapies	More selective drug delivery methods (e.g., nanomedicine, targeted nanoparticles), improved biomarkers for patient selection [18,19]
Tumor Heterogeneity	Personalized medicine, genomic profiling	Multi-omics approaches (genomics, proteomics, metabolomics), development of universal therapies targeting common tumor hallmarks [20,21]
Cost and Accessibility	Biosimilars, off-label use of drugs	Reducing production costs of biologics, improving global access to cutting-edge therapies through partnerships, government support [22]

5. Future Needs and Challenges in Cancer Therapeutics

While significant strides have been made in cancer treatment, several challenges persist, and overcoming these barriers will be critical for further improving patient survival rates and quality of life.

- **Drug Resistance**: A major obstacle in cancer therapy is the development of resistance to both chemotherapy and targeted therapies. Tumors can evolve and acquire mutations that allow them to evade treatment, making resistance a significant barrier to long-term success [27]. Research is ongoing to identify new therapeutic strategies, including combination therapies that target multiple pathways or overcome resistance mutations [28].
- **Immune Evasion**: Many cancers have evolved mechanisms to evade detection and destruction by the immune system. Cancer cells may express immune checkpoint proteins or secrete immunosuppressive factors that prevent immune cells from effectively targeting them [29]. Overcoming these mechanisms will be essential for improving the effectiveness of immunotherapies.
- **Biomarkers and Early Detection**: Early detection of cancer is crucial for improving survival outcomes. The development of reliable biomarkers that can detect cancer at its earliest stages, as well as the use of liquid biopsies to detect circulating tumor DNA (ctDNA), represents a promising frontier in both early detection and monitoring treatment responses [30].
- **Cost and Accessibility**: While many new cancer treatments have shown promise, their high cost presents a significant barrier to widespread use. Ensuring equitable access to these therapies, especially in low-income countries, will be critical in making advancements in cancer treatment accessible to all [31].

6. Conclusion

The landscape of cancer therapy has undergone substantial evolution, progressing from rudimentary surgical interventions to highly sophisticated, mechanism-based approaches. The emergence of precision medicine, immunotherapies, and molecularly targeted agents has significantly advanced the therapeutic arsenal, offering improved efficacy and reduced toxicity. Nonetheless, critical challenges persist, including the development of therapeutic resistance, mechanisms of immune escape, and inequitable access to care across diverse populations.

Addressing these barriers is essential for enhancing patient outcomes and global cancer control. The continued advancement of cancer therapeutics will depend on sustained innovation in molecular oncology, immunology, and biotechnological platforms, coupled with strategies aimed at ensuring equitable delivery of care. Bridging scientific discovery with clinical implementation will be central to achieving durable responses and improving both survival and quality of life for patients worldwide.

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