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Recent Advances in Molecular Targets and Pharmacological Strategies in Cancer Therapy

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ABSTRACT

Uncontrolled growth of abnormal cells, or cancer, continues to be one of the world's leading causes of illness and death, taking thousands of lives annually. Although they have been successful in the past, traditional/conventional treatments like chemotherapy and radiation therapy frequently lack precision, can have serious side effects and adverse drug effects, and frequently result in recurrent episodes of the disease. Our approach to antitumor treatment has changed in the last year due to advancements in oncology and cancer/tumor treatment.Novel therapies now target specific genetic and protein changes in tumours, which ultimately reduces the side effects and adverse drug effects that conventional treatments generate. This allows for the design of treatments that are tailored to each patient's needs based on their body needs, stage of the disease, and therapy requirements (1,2). Tyrosine kinases, immune checkpoints, angiogenic pathways, and genetic repair mechanisms/DNA repair mechanisms are important molecular targets that have created new and more accurate opportunities for oncology drug development (3,4). Further-more, there are various options for cancer therapy that are more effective than traditional therapy thanks to novel, innovative platforms like antibody–drug conjugates, epigenetic modulators, and delivery systems based on nanotechnology (5,6). With an emphasis on the pharmacological approaches used in the development of novel therapies, as well as their mechanisms of action, clinical applications, limitations, and future directions, this review focusses on these recent developments in molecular-targeted cancer therapy or cancer treatment.

Keywords: Cancer therapy, molecular targets, tyrosine kinase inhibitors, immunotherapy, nanotechnology, pharmacological strategies, precision medicine.

1.INTRODUCTION

The hallmarks of cancer, a complex and multifaceted disease, include unchecked cell growth, apoptosis avoidance, persistent angiogenesis, and the ability to invade and spread (7). According to the World Health Organisation (WHO), cancer is the second leading cause of death globally, taking the lives of nearly 10 million people each year (8). Traditional cytotoxic chemotherapy agents work by permanently destroying DNA or inhibiting cells formation . Despite their effectiveness, their non-specific mechanism of action affects rapidly replacing normal cells, leading to severe toxicity, including peptic ulcers, gastrointestinal disturbances, alopecia, and myelosuppression (9). Additionally, resistance often arises, which restricts long-term effectiveness and speeds up the onset of action (10).The discovery of molecularly targeted therapies, which acknowledge that certain genetic and epigenetic changes are responsible for tumorigenesis, caused a significant paradigm shift in oncology and cancer treatment. Various oncogenic drivers, signalling pathways, and immune escape mechanisms that can be targeted specifically have been discovered thanks to newly development and on going research in genomics, proteomics, and molecular biology (11). These findings paved the way for treatments that target the pathway that promotes cancer while preserving healthy tissues (12). Recent advancements in molecular targets and pharmacological approaches for cancer treatment are highlighted in this review. Key therapeutic classes are covered, such as immune checkpoint inhibitors (ICIs), tyrosine kinase inhibitors (TKIs), angiogenesis inhibitors, PARP inhibitors, antibody–drug conjugates (ADCs), epigenetic modulators, and systems based nanotechnology. Resistance Mode of action combination therapies, and the future of personalised medicine

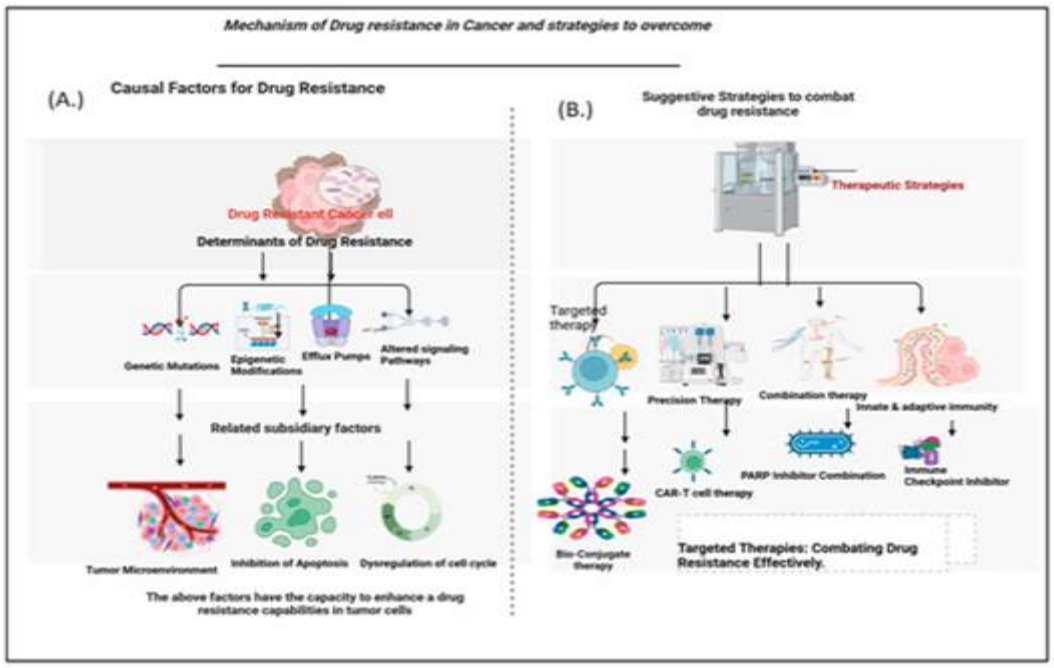

Figure 1 (Drug resistance and suggestive strategies)[6]

2.TYROSINE KINASE INHIBITORS (TKIs)

2.1 Background and Mechanism of Action

A phosphate group is transferred from adenosine triphosphate (ATP) to particular tyrosine residues on target proteins by protein tyrosine kinases (PTKs), a Majority family of enzymes. By acting as a molecular switch, this phosphorylation alters important cellular functions such as migration, survival, differentiation, growth, and proliferation. Oncogenesis is fuelled by aberrant signalling pathways that result from PTK dysregulation, which can be caused by chromosomal translocations, point mutations, or gene amplification. Uncontrolled Abnormal cell division, apoptosis evasion, and increased metastatic potential are all marker of cancer that can arise from hyperactivation of PTK-mediated pathways (13). Micro and Macro molecules known as tyrosine kinase inhibitors (TKIs) specifically block these over-active kinases. The majority of TKIs work by competitively inhibiting the kinase domain's by generating competition site for binding ATP-binding site, which inhibit downstream substrates from being phosphorylated. Important signalling cascades like the phosphatidylinositol 3-kinase–AKT (PI3K-AKT) pathway, which governs or ruled survival and metabolism or bio-transformation, and the mitogen-activated protein kinase (MAPK) pathway, which ruled by cell proliferation, are disrupted by this blockade. TKIs provide a more or localizied targeted therapeutic approach than traditional cytotoxic chemotherapy by specifically inhibiting the growth of cancer cells while preventing the damage to healthy or

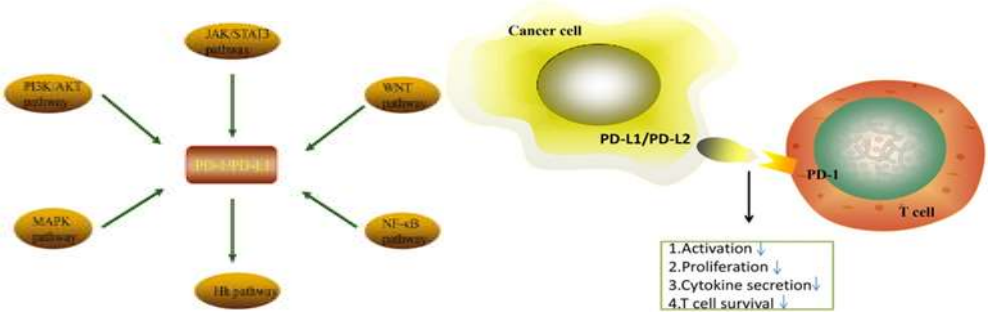

Figure 2 Mechanism of action [68]

2.2 Landmark Example:

One of the example of targeted cancer treatment is imatinib mesylate, the first TKI to be clinically approved for human trials or for human use . It specifically blocks the constitutively active tyrosine kinase, the BCR-ABL fusion protein, which is responsible for long term or chronic myeloid leukaemia (CML) /blood cancer and is caused by the Philadelphia chromosome translocation t(9;22) (15). Imatinib stabilises or inhibit BCR-ABL in an inactive conformation by binding to its ATP-binding site, which stops abnormal down-stream signalling. The advent of imatinib was transformative; in comparison to traditional or conveniental chemo-therapeutics, patients with CML experienced low levels of off-target toxicity and high rates of complete cytogenetic

response, which greatly enhance overall survival rate . The paradigm of precision oncology was Well-known by this achievement, which confirmed the idea that focused inhibition of oncogenic drivers could produce long-lasting clinical responses with fewer side effects (15).

2.3 Expansion of TKIs in Solid Tumors

Following the result of imatinib, tyrosine kinase inhibitors (TKIs) were used to treat solid tumours by targeting kinases specific to cancer. For fast or rapid onset of action, EGFR inhibitors such as gefitinib, erlotinib, and osimertinib are now commonly an more frequently in used to treat patients with non-small cell lung cancer (NSCLC) who have activating EGFR abrupt changes in DNA (mutation). These drugs work by preventing EGFR signalling, which inhibits the growth of tumour cells and triggers apoptosis in cells that rely on this pathway (16). ALK inhibitors, including crizotinib, alectinib, and lorlatinib, target the re-arrangements of the anaplastic lymphoma kinase (ALK) gene that are found in some lung cancers. By preventing aberrant kinase activation, these drugs help stop the spread of tumours (17).Lenvatinib, sunitinib, and sorafenib are examples of VVEGFR inhibitors. They function by blocking or inhibiting vascular endothelial growth factor receptor (VEGFR) signalling, which is required for the formation of new blood vessels in tumours such as hepatocellular carcinoma (HCC) and renal cell carcinoma (RCC). By restricting or by inhibiting the tumor's blood supply, which then restrict the availability of oxygen and nutrients result in necrosis of tumor, these drugs slow the growth of tumours (18). Generally, the development of these TKIs shows the Ability to adjust of targeted therapies by Facilitating treatment customisation based on the exact molecular changes or changes of the tumour rather than just its location.

2.4 Limitations and Resistance Mechanisms

Despite their clinical success, acquired resistance often limits the long-term effectiveness of TKIs. Resistance mechanisms consist of secondary kinase domain mutations or sudden changes that decrease drug binding. For example, the T790M mutation in EGFR results in resistance or inhibition to first-generation EGFR inhibitors, which makes the establishment of third-generation medications like osimertinib (20) Appropriate. alternative growth or survival pathways (e.g., MET, HER2) that are upregulated to sustain Expansion in spite of TKI treatment are known as overcome signalling pathways. When cancerous cells/tumour cells undergo phenotypic or histological transformation, they alter their cellular identity, making the initial TKI ineffective (19). Next-generation TKIs with increases selectivity and the capacity to localizied or target resistance mutations have been created in order to get around these restrictions or inhibition.To overcome these Challenges , next-generation TKIs have been developed that have improved localizied and the ability to target resistance mutations. In order to improve long-term efficacy and postpone or prevent resistance, combination therapies that target several pathways are also being researched (19,20).

3.IMMUNE CHECKPOINT INHIBITORS (ICIS)

3.1 Immune Evasion in Cancer

The immune system plays a crucial role in detecting and excreting malignant cells or cancerous cells through processes collectively referred to as immune surveillance. Cytotoxic T lymphocytes (CTLs), natural killer (NK) cells, and antigen-presenting cells Identify abnormal antigens expressed by tumor cells or by cancerous cells and initiate immune-mediated destruction. However, cancer cells often develop process to evade immune recognition, allowing them to Expand and Spread to other parts of the body unchecked. One major strategy involves the stimulating of immune checkpoint pathways, which are negative regulators of T-cell activity that normally Preserve self-tolerance and prevent autoimmunity. Key checkpoint pathways Utilized by tumors include programmed cell necrosis protein 1 (PD-1) and its ligand PD-L1, as well as cytotoxic T-lymphocyte–linked too antigen 4 (CTLA-4) (21). By involving these Control pathway, tumor cells inhibit T-cell activation and cytotoxicity, inhibiting an immuno-suppressive microenvironment that stimulates cancer growth.

3.2 Mechanism of Action

Immune checkpoint inhibitors (ICIs) are monoclonal antibodies designed to obstructing these inhibitory signals, effectively releasing the "brakes" on the immune system and restoring antitumor immunity (22). Anti–PD-1/PD-L1 antibodies (e.g., nivolumab, pembrolizumab, atezolizumab) combines with to PD-1 on T-cells or PD-L1 on cancerous cells, preventing their interaction. This recovers newly generation of T-cell activation, proliferation, and cytotoxic activity against cancerous/tumor cells. Anti–CTLA-4 antibody (ipilimumab) functions at an primary stage in the immune response by inducing T-cell priming and activation in lymphoid organs, thus enhancing the pool of effector T-cells capable of targeting cancerous/tumor (23).Through these mechanisms, ICIs can enhance pharmacological durable and systemic antitumor immune response, in some cases leading to long-term remission even in recent cancers.

3.3 Clinical Impact

Because they significantly enhance survival for a different types of cancers, ICIs have transformed tumours/cancer treatment:

Melanoma: Even in patients who has metastatic disease, nivolumab and pembrolizumab have significantly increased overall survival and progression-free survival in advanced melanoma (24) and also help in prevention of cancer . Pembrolizumab, which is approved for first-line treatment for PD-L1-positive cancerous/tumors, has magnified than traditional/conventional chemotherapy for non-small cell lung cancer (NSCLC) (25).

Other cancers: ICIs have shown intensified to triple-negative breast cancer, head and neck squamous cell carcinoma, renal cell carcinoma, and Hodgkin lymphoma, displaying their versatility or adaptability to a various types of cancer (26). ICIs are initial examples of precision medicine in immunotherapy, whereby clinical outcomes are enhanced by patient selection based on immunological or diagnostic biomarkers (e.g., tumor mutational burden, PD-L1 expression).

3.4 Limitations and Challenges

Despite their Revolutionary capacity, ICIs are In conjunction with Multiple drawbacks and Medical hurdles : Immune-related adverse effects (irAEs): By Amplifying overall immune activity, ICIs can induce autoimmune-like Treatment with ICIs can result in autoimmune-mimicking toxicities, often involving the gastrointestinal tract (colitis), skin (dermatitis), lungs (pneumonitis), and endocrine organs (thyroiditis, adrenal insufficiency, hypophysitis) (27). Resistance: Some patients exhibit primary resistance and unsuccessful to respond from the outset, while others develop acquired resistance after an initial response, potentially due to loss of neoantigens, upregulation of sequential checkpoint targeting , or immune-suppressive tumor micro-environments (28).

Economic and accessibility barriers: High costs and the requirement for Widespread implementation is constrained by the requirement for specialized monitoring, particularly in lower per capita an gdp countries(like Africa an Asia) , which may Widen global inequities in cancer care" (29).

Ongoing research an development aims to enhance efficacy, reduce toxicity, an reduce adrevse effect and overcome resistance through combination strategies, biomarker-guided patient selection, and upcoming-generation checkpoint inhibitors.

4.ANGIOGENESIS INHIBITORS

4.1 Rationale

Tumor growth and metastasis are intricately linked to angiogenesis—the process by which new blood vessels form from existing ones. This phenomenon is predominantly regulated by vascular endothelial growth factor (VEGF) and its receptors (VEGFRs), which play pivotal roles in both tumor progression and metastatic spread (30, 31).

VEGF, particularly VEGF-A, is a key secretory factor that maintains endothelial cell function and promotes cell mitosis and vascular permeability. It is involved in cell homeostasis, hematopoietic stem cell survival, tumor cell survival, and invasion through autocrine or paracrine mechanisms. VEGF-A is the most important regulator of angiogenesis and plays an irreplaceable role in tumor growth, proliferation, invasion, metastasis, angiogenesis, and drug resistance (32, 33).

The binding of VEGF to its receptors, primarily VEGFR-2, induces receptor dimerization and activation of downstream signaling pathways that promote endothelial cell proliferation, migration, and new vessel formation. These processes are essential for supplying the growing tumor with oxygen and nutrients, facilitating its expansion and the potential for metastasis (34, 35).

Inhibiting angiogenesis through targeting VEGF signaling pathways effectively starves tumors of essential resources, thereby hindering their growth and metastatic potential. This therapeutic strategy has led to the development of anti-VEGF-based antiangiogenic drugs, which are now widely used in clinical settings to treat various cancers (36, 37).

4.2 Approved Agents

For the treatment of metastatic colorectal cancer, non-squamous non-small cell lung cancer or tumor , recurrent glioblastoma, metastatic renal cell carcinoma, cervical cancer, and ovarian cancer/tumor, bevacizumab, a humanised monoclonal antibody that targets VEGF-A, has been approved (31, 38, 39). VEGFR-targeting small molecule tyrosine kinase inhibitors (TKIs): lenvatinib, sunitinib, and sorafenib have Proven efficacy in treatment of hepatic and renal cancers. Sunitinib is approved for metastatic renal cell carcinoma (32, 41), lenvatinib for advanced hepatocellular carcinoma and metastatic renal cell carcinoma (32, 42), and sorafenib for advanced renal cell carcinoma and hepatocellular carcinoma (32, 40).

4.3 Limitations

Angiogenesis inhibitors show initial clinical effectiveness, but they are long-term applicability is constrained by various challenges:

Adaptive resistance: Tumours can turn on other pro-angiogenic signalling pathways, which can make treatments less effective over time (33).

Toxicity profile: Treatment can cause side effects like hypertension, atherosclerosis ,proteinuria, and slow wound healing, which can make it hard to give the right amount of medicine and keep patients on track (34).

Limited human benefit: Although tumour growth/cancerous suppression occurs, enhancements in overall survival are frequently constrained relative to targeted therapies and immune checkpoint inhibitors (35).___

5.PARP INHIBITORS AND SYNTHETIC LETHALITY

5.1 Background

Poly (ADP-ribose) polymerases (PARPs) are a group of enzymes that play a vital role in repairing DNA, particularly through the base excision repair (BER) pathway. They sense single-strand breaks in DNA and help recruit the cellular repair machinery to fix these damages, thereby preserving genomic stability. In certain cancer cells, especially those with defects in homologous recombination (HR) repair—like mutations in BRCA1 or BRCA2—PARP activity becomes crucial for cell survival. Blocking PARP in these cells leads to the buildup of DNA damage, a process that can trigger synthetic lethality, where the simultaneous failure of two DNA repair pathways selectively kills cancer cells while largely sparing normal cells (36).

This understanding has made PARP inhibitors (PARPi) a key part of precision oncology, allowing treatments to target tumors based on their unique molecular weaknesses rather than just their location or tissue type. This strategy is especially effective in cancers that heavily rely on DNA repair mechanisms, such as ovarian, breast, pancreatic, and prostate cancers with HR deficiencies..---

5.2 Mechanism of Action

PARP inhibitors act by binding to the catalytic domain of PARP enzymes, preventing them from repairing single-strand DNA breaks. This causes DNA damage to accumulate, eventually forming double-strand breaks (DSBs) during DNA replication. Cells with intact HR repair can resolve these DSBs, but HR-deficient cells, such as those with BRCA mutations, cannot, resulting in cell cycle arrest and apoptosis (36).

In addition to blocking PARP activity, some inhibitors trap PARP enzymes at sites of DNA damage, further hindering DNA replication and amplifying cytotoxicity. This dual mechanism—enzyme inhibition plus PARP trapping—explains the potent antitumor effects of these drugs (38).---

5.3 Clinical Applications

Several PARP inhibitors have been FDA-approved and are widely used in oncology:

Olaparib: Approved for BRCA-mutated ovarian, breast, pancreatic, and prostate cancers.

Rucaparib: Used in ovarian and prostate cancers with BRCA or other HR gene mutations.

Niraparib: Indicated for ovarian cancer, regardless of BRCA status, with maintenance therapy benefits.

Talazoparib: Primarily for germline BRCA-mutated breast cancer (37).

The clinical success of PARP inhibitors underscores the therapeutic potential of exploiting synthetic lethality, where cancer cells are selectively targeted based on specific genetic vulnerabilities (38). Combination strategies with chemotherapy, immune checkpoint inhibitors, or angiogenesis inhibitors are also being explored to enhance efficacy and broaden the spectrum of responsive tumors.---

5.4 Limitations and Challenges

Despite promising outcomes, PARP inhibitors face several limitations:

Resistance mechanisms: Cancer cells may restore homologous recombination through secondary mutations, increase drug efflux via transporters, or acquire mutations in PARP itself, diminishing drug effectiveness (39).

Toxicity profile: Common adverse effects include anemia, thrombocytopenia, neutropenia, fatigue, nausea, and gastrointestinal disturbances, which can limit dose intensity and patient compliance (40).

Limited efficacy in HR-proficient tumors: Tumors without DNA repair deficiencies are often less responsive, necessitating biomarker-guided patient selection to maximize benefit.

Combination therapy challenges: While combining PARP inhibitors with chemotherapy or immunotherapy may improve responses, overlapping toxicities and optimal dosing schedules remain areas of ongoing investigation.

Future research aims to overcome these challenges by developing next-generation PARP inhibitors with improved potency and selectivity, identifying predictive biomarkers beyond BRCA mutations, and designing rational combination regimens to prevent or circumvent resistance.

6.) ANTIBODY-DRUG CONJUGATES (ADCs)

6.1 Concept and Mechanism

Antibody–Drug Conjugates (ADCs) are a next-generation class of targeted therapeutics that combine the specificity of monoclonal antibodies with the cytotoxicity of chemotherapeutic drugs (41). The antibody component selectively recognizes tumor-associated antigens, while the conjugated cytotoxic payload is delivered directly into malignant cells, minimizing systemic toxicity (42).

The mechanism of action involves:

1. Antigen binding: The monoclonal antibody binds to tumor-associated antigens such as HER2 or CD30.

2. Internalization: The ADC–antigen complex is internalized via endocytosis into the tumor cell.

3. Payload release: The cytotoxic drug (e.g., auristatins, maytansinoids, or topoisomerase inhibitors) is released within the cell, causing DNA damage or microtubule disruption, ultimately leading to apoptosis (43).

This approach enables precise tumor targeting while reducing off-target effects commonly seen with conventional chemotherapy.__

6.2 Approved ADCs

Several ADCs have achieved clinical approval and demonstrated efficacy in various cancers:Trastuzumab emtansine (T-DM1): HER2-positive breast cancer (44). Brentuximab vedotin: CD30-positive Hodgkin lymphoma and anaplastic large-cell lymphoma (45). Trastuzumab deruxtecan (T-DXd): HER2-positive and HER2-low breast cancers (46). Sacituzumab govitecan: Triple-negative breast cancer, targeting Trop-2 (47) .These agents highlight ADCs as a bridge between targeted therapy and chemotherapy, combining specificity with potent cytotoxicity.

6.3 Challenges and Future Directions

Despite success, ADCs face several limitations:

Heterogeneous antigen expression can reduce efficacy.

Resistance mechanisms include antigen downregulation, impaired internalization, and drug efflux.

Off-target toxicities such as neutropenia, thrombocytopenia, and interstitial lung disease may occur.

High production costs limit accessibility (48).

Future research is focused on:

Novel payloads with increased potency or alternative mechanisms.

Bispecific ADCs targeting multiple antigens simultaneously.

Optimized linker technologies to improve stability in circulation and efficient intracellular release (49).

These innovations aim to enhance efficacy, reduce toxicity, and broaden applicability, ensuring ADCs remain a key component of modern targeted cancer therapy.

7.EPIGENETIC TARGETS IN CANCER THERAPY

7.1 Background

Epigenetic modifications—including DNA methylation, histone modifications (acetylation, methylation), and chromatin remodeling—play a pivotal role in regulating gene expression without altering the underlying DNA sequence (50). Aberrant epigenetic changes can silence tumor suppressor genes or activate oncogenes, contributing to cancer initiation, progression, and metastasis. Unlike genetic mutations, epigenetic alterations are reversible, making them attractive therapeutic targets. By modulating these pathways, it is possible to restore normal gene expression, sensitize tumors to other therapies, and overcome resistance mechanisms (51). Epigenetic therapy is therefore considered a precision oncology strategy that complements conventional chemotherapy, targeted therapy, and immunotherapy.

7.2 Mechanism of Action

DNA methyltransferase inhibitors (DNMTis): Drugs such as azacitidine and decitabine inhibit DNA methyltransferases, leading to hypomethylation of tumor suppressor gene promoters and reactivation of silenced genes. They are primarily used in myelodysplastic syndromes and acute myeloid leukemia, restoring normal differentiation and apoptosis pathways (52).

Histone deacetylase inhibitors (HDACis): Drugs like vorinostat, romidepsin, belinostat, and panobinostat inhibit HDAC enzymes, causing hyperacetylation of histones, relaxation of chromatin, and transcriptional activation of tumor suppressor genes. This induces cell cycle arrest, apoptosis, and differentiation in malignant cells, particularly in cutaneous and peripheral T-cell lymphomas (53).

•)Emerging epigenetic targets:

BET inhibitors (bromodomain and extra-terminal): Block BET proteins that recognize acetylated histones, thereby disrupting oncogenic transcription programs (54).

EZH2 inhibitors: Target EZH2-mediated histone methylation, effective in lymphomas harboring EZH2 gain-of-function mutations (55).

Combination strategies: Epigenetic drugs are increasingly used alongside immune checkpoint inhibitors (ICIs) or chemotherapy, as they can reprogram resistant tumor cells and enhance immune recognition (56).

7.3 Clinical Applications

DNMT inhibitors: Azacitidine and decitabine improve overall survival in myelodysplastic syndromes and are used as maintenance therapy in certain AML cases (52).

HDAC inhibitors: Vorinostat and romidepsin have demonstrated durable responses in T-cell lymphomas, with acceptable safety profiles (53).

Emerging therapies: BET and EZH2 inhibitors are currently under phase I/II clinical trials, showing promising activity in hematologic and solid tumors (54,55).

7.4 Limitations and Challenges

Despite potential, epigenetic therapies face several challenges:

Toxicities: Myelosuppression, fatigue, gastrointestinal symptoms, and cardiac effects can limit dosing and patient compliance (57).

Tumor heterogeneity: Variable epigenetic landscapes across tumor cells reduce uniform efficacy.

Lack of predictive biomarkers: Patient selection remains difficult, and reliable biomarkers to predict response are limited.

Transient effects: Epigenetic reprogramming may require continuous therapy to maintain gene expression changes.

Future directions aim to enhance specificity and minimize toxicity, including:

Development of next-generation DNMTis and HDACis with improved selectivity.

Identification of novel epigenetic targets (e.g., histone methyltransferases, demethylases).

Rational combinatorial regimens with ICIs, TKIs, and chemotherapy to maximize efficacy and overcome resistance.

8. NANOTECHNOLOGY-BASED DRUG DELIVERY SYSTEMS

8.1 Rationale

Conventional chemotherapy is often limited by poor tumor selectivity, rapid systemic clearance, and dose-limiting toxicities. Nanotechnology offers a promising approach to overcome these challenges by improving drug delivery, pharmacokinetics, and tumor accumulation (58). Nanocarriers exploit the enhanced permeability and retention (EPR) effect, which allows nanoparticles to preferentially accumulate in tumor tissue due to leaky vasculature and poor lymphatic drainage. Moreover, nanocarriers enable: Controlled and sustained drug release, reducing peak plasma concentrations and systemic toxicity. Co-delivery of multiple therapeutic agents, including chemotherapeutics, immunomodulators, or gene-editing tools.Surface functionalization for active targeting, using ligands or antibodies to bind tumor-specific receptors.

These advantages make nanotechnology a cornerstone of precision oncology.

8.2 Types of Nanocarriers

1. Liposomes:

Spherical vesicles composed of phospholipid bilayers, capable of encapsulating hydrophilic or hydrophobic drugs.

Example: Liposomal doxorubicin improves tumor delivery and reduces cardiotoxicity (59).

2. Polymeric nanoparticles:

Biodegradable and biocompatible carriers that allow controlled and sustained drug release.

Can be engineered for surface targeting and stimuli-responsive release (60).

3. Dendrimers and micelles:

Nanoscale, highly branched structures enabling precision drug delivery.

Micelles can solubilize hydrophobic drugs, enhancing circulation and tumor accumulation (61).

4. Inorganic nanoparticles:

Includes gold nanoparticles, quantum dots, and silica nanoparticles.

Useful for theranostics, combining therapy and imaging for real-time tracking of drug delivery (62).

8.3 Clinical Applications

Several nanomedicines have received FDA approval, demonstrating the clinical utility of nanocarriers:

Liposomal doxorubicin: Reduced systemic toxicity while maintaining antitumor efficacy.

Albumin-bound paclitaxel (nab-paclitaxel): Improved solubility and tumor uptake.

Liposomal irinotecan: Enhanced pharmacokinetics and reduced gastrointestinal toxicity (63).

Research is expanding to advanced nanotherapeutics, including:

siRNA and mRNA delivery for gene silencing or protein expression.

CRISPR/Cas9 systems for targeted gene editing in cancer cells.

Immunomodulator delivery, enhancing antitumor immune responses (64).

8.4 Limitations and Future Outlook

Despite promise, nanotechnology-based therapies face critical challenges:

Variability in EPR effect among patients limits uniform tumor targeting.

Large-scale manufacturing and reproducibility remain hurdles.

Immune clearance by macrophages can reduce bioavailability.

Regulatory and safety concerns slow clinical translation (65).

•)Future directions aim to overcome these challenges:

Smart nanocarriers: Stimuli-responsive systems that release drugs in response to pH, temperature, or enzymatic activity.

Multifunctional platforms: Integrating chemotherapy, immunotherapy, and gene therapy in a single nanocarrier.

Personalized nanomedicine: Designing nanoparticles tailored to individual tumor biology and microenvironment characteristics (66).

These advances position nanotechnology-based therapies at the forefront of next-generation precision oncology, with the potential to revolutionize cancer treatment by enhancing efficacy, reducing toxicity, and enabling combination strategies.

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