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Review

Frontiers in Cancer and Haematology: Emerging Biomarkers, Therapeutics, and Technologies

Imran Khan Yousafzai[1], Aqsa Mehreen[1,*], Nadia Noreen[2], Amanullah[1], Hawaida Ahmad[1], Noor Fatima[3], Khadija Tariq[4]

[1]Department of Biological Sciences, National University of Medical Science, Rawalpindi, Pakistan

[2]Department of Biological Sciences, Abasyn University, Islamabad, Pakistan

[3]Department of Allied Health Sciences, National University of Medical Sciences, Rawalpindi, Pakistan

[4]Atta-ur-Rahman School of Biological Sciences, National University of Science and Technology, Islamabad, Pakistan

[*]Corresponding author: Aqsa Mehreen, aqsamehreen36@gmail.com

Abstract

Cancer continues to be the leading cause of death globally. This paper discusses the major advances in liquid biopsy, cancer microenvironment biology, AI, and nanomedicine for the period 2015-2025 and their translational implications. Original articles, systematic reviews, and top-quality review articles on PubMed, Scopus, and Web of Science were searched for biomarker development, microenvironment-targeted therapeutics, data-driven decision support, and nanoparticle-based delivery systems. Liquid biopsy (circulating tumor DNA, circulating tumor cells, extracellular vesicles) has the potential to identify minimal residual disease and help select targeted therapies, but issues with analytical sensitivity, pre-analytical variability, and assay standardisation still need to be resolved. The roles of stromal cells, immunological infiltrates, and extracellular matrix in disease progression and therapeutic resistance make them very attractive yet still untested targets. Artificial intelligence applied to multimodal data has the potential to assist in diagnosis and prognosis; however, it requires external validation, transparency, and bias mitigation before routine clinical use. Nanomedicine comes with advanced features such as targeting and multimodal therapy; however, it encounters challenges related to manufacturing, pharmacokinetics, and regulatory standards. To make breakthroughs in the clinic, assay standardisation, prospective multicentre validation, biomarker-driven trial design, and interdisciplinary collaborations are imperative.

Keywords

Hematological malignancies, Liquid biopsy, Circulating tumor DNA, Circulating tumor cells, Predictive biomarkers, Treatment resistance, Tumor immune microenvironment, Nanoparticle drug delivery, Immunological processes

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1. Introduction

Every year millions of people die due to cancer as well as haematological disorders. In 2020, cancer led to the death of about 10 million people, highlighting it as the leading cause of death worldwide [1]. There are some diseases that still result in death even with available treatments due to late diagnosis and therapeutic resistance. Even though the discovery of new biomarkers and treatment options that improve survival rates has been made, the problem of access is still very difficult in developing countries. So, the World Health Organization report indicates that in 2020 cancer caused the death of around 10 million people worldwide. The number of cancer cases is expected to rise by 60% in the next 20 years, mainly in low- and middle-income countries [2].

Hematological malignancies such as leukemia, lymphoma, and multiple myeloma are responsible for only a small percentage of overall cancer deaths but a significant one. Leukemia is estimated to be responsible for about 7% of deaths from cancer worldwide. The lack of biomarkers and high heterogeneity in these cancers make their early detection and treatment very difficult [3]. Table 1 shows data on global cancer and hematological issues, which helps us understand the future burden.

Table 1. Global impact of cancer and haematological malignancies.

Disease Category	Global Mortality (2020)	Projected Increase in Cases (2020-2040)	References
Cancer (all types)	~10 million deaths	60% increase globally	[4]
Leukemia	~1.1 million	50% increase in developing countries	[5]
Lymphoma and Myeloma	~0.5 million	40% increase globally	[6]

2. Un-Met Clinical Needs and Emerging Solutions in Cancer Diagnostics

Although cancer treatment has improved, the global medical system is still struggling to provide the right treatments for patients. High-income countries can afford to use precision and personalized medicines, whereas many developing countries hardly manage early diagnosis and treatment. Leukemia, lymphoma, and multiple myeloma are among the few cancers that have remained problematic over the years due to the lack of accurate biomarkers and the disease's heterogeneity [7]. Hematological malignancies immunotherapy has very positive results; however, resistance to treatment, minimal residual disease (MRD) detection, and recurrence are still problematic. Tailored therapy has brought about better treatment effects, but resistance mechanisms and early detection issues still require being tackled [8]. New biomarkers such as circulating tumor DNA (ctDNA), circulating tumor cells (CTCs), and exosomes are reshaping the diagnosis of cancer and addressing the unmet clinical needs. Liquid biopsy is the method to identify these biomarkers, and it allows for the earliest possible diagnosis, better MRD detection, and real-time tracking of the therapy's effectiveness. Besides being non-invasive, samples can be collected easily and offer observations about the dynamic growth of tumors, which are all the benefits of liquid biopsies over tissue biopsies [9].

Through real-time liquid biopsies, treatment can be evaluated alongside tumor growth tracked by clinicians. ctDNA is a favourable representative of the tumor heterogeneity and its genetic abnormalities, thus aiding in evaluating disease progression and making treatment decisions. When it comes to diagnosing the MRD and the prediction of relapse, ctDNA is way ahead of the established imaging techniques [10]. Non-invasive liquid biopsies minimize the risks involved in cancer diagnosis through traditional biopsies. Blood, as a standard test specimen, can still provide an insight into tumor growth and thus, serve as a more accessible and real-time therapeutic management tool for both patient and doctor [11].

As much as cancer and hematological disease treatment has made progress, the methods for early cancer detection, evaluation of treatment resistance, and monitoring of disease still call for improvement. The novel liquid biopsy techniques that employ ctDNA, CTCs, and exosomes alleviate the issues and make cancer treatment more personalized, efficient, and accessible [12].

2.1 Liquid Biopsies

Liquid biopsy has received an invitation in cancer diagnosis and therapy follow-up due to its non-invasive capability to acquire tumor genetic signature. Biomarkers of liquid biopsy include ctDNA, CTCs, and exosomes [13].

Compared to typical tissue biopsies, liquid biopsies have a great number of benefits. Long-term monitoring of the tumor and the effect of treatment over time is possible with liquid biopsies compared to tissue samples, which in many cases provide a picture of the tumor at a specific time point. This enables physicians to customise treatment after real-time data, which is better in patient outcomes.

2.2 Circulating Tumor DNA

The ctDNA is comprised of small DNA strands that are released into the circulation by tumor cells and that are a reflection of the genetic fingerprint of the tumor. A simple blood sample can be tested to ctDNA providing critical information about tumor genetic make up and behaviour and provide non-invasive real time monitoring of genetic changes and tumor growth [14]. Consequently, the presence of ctDNA in a small fraction of cancer cells after treatment is crucial to locate MRD. Table 2 shows that ctDNA is able to identify tumor-related genetic alterations, which can be used to detect MRD well before the appearance of clinical symptoms. Thus, this technique can aid the figuring out of relapse-prone cancers like leukemia, breast cancer, and colon cancer. Additionally, the use of ctDNA for therapeutic response assessment is justified. A decrease in ctDNA following the response indicates the effectiveness of the treatment. On the other hand, elevated or stable levels of ctDNA may be indicative of pharmaceutical resistance, thus the need for a change in therapy. What is more, real-time assessments provide for the personalization of cancer treatment whereby the drugs can be adapted to the genetic development of the tumor [15].

Another great thing is that high ctDNA levels might well reflect disease relapse at an early stage, thereby enabling preclinical management. Early detection of cancer, evaluation of treatment progress, and prediction of recurrence are some of the big breakthroughs in cancer therapy, as they provide a non-invasive substitute for tissue biopsies along with a comprehensive genetic understanding of the tumor [16]. For the clinical and regulatory use of liquid biopsies in conjunction with immunotherapy treatment, various interrelated stages are obligatory, including biomarker discovery, analytical validation, regulatory approval and treatment decision making. Figure 1 shows a schematic representation of these regulatory and clinical translation paths.

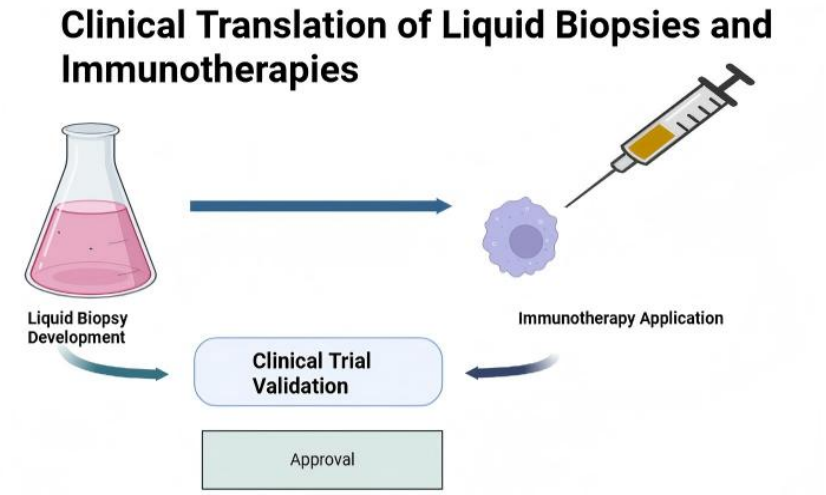

Figure 1. Regulatory pathways for liquid biopsies and immunotherapies–an example of the steps involved in integrating immunotherapy, obtaining regulatory approval, and analyzing liquid biopsies.

2.3 Circulating Tumor Cells

CTCs are cancer cells that break away from the original tumor and get into the circulation. They are the first sign of tumor metastasis and invasion. These cells and the main tumor have the same genetic composition, so they can show the ways of cancer spread and the potential of metastasis. It is essential to detect CTCs in the blood to evaluate how invasive the tumor is. The fact that CTCs are present in the blood means that cancer is spreading or will spread. The amount of CTCs can be used to predict metastasis, which will lead doctors to prevent the development of new cancers [17].

Through the measurement of therapy resistance, the role of CTCs cannot be overestimated. Before treatment, CTCs represent a dynamic picture of a hidden tumor compartment, such as a cell undergoing epithelial-to-mesenchymal transition and escaping treatment. A post-treatment increase in CTCs numbers or acquired mutations would demonstrate the inefficacy of a particular drug and necessitate the consideration of alternate agents [18].

High CTC counts in lung, breast, and prostate cancers have been linked to poor prognosis, higher risk of metastasis, and greater likelihood of recurrence. Tracking tumor cells that circulate in the blood of patients gives clinicians a better understanding of the consequences of the disease and the ability to adjust therapy accordingly. The use of CTCs in post-treatment cancer patients enables the monitoring of cancer progression as well as the detection of MRD in a non-invasive manner. When the imaging results are normal, CTCs can still reveal the presence of hidden metastases, which allows for a quicker diagnosis of relapse [19].

2.4 Exosomes

Exosomes are small vesicles with sizes ranging from 30 to 150 nm. Their main containers are lipids, proteins, and RNA. They are released by many of the body's cells, including cancer cells. The vesicles contain tumor-associated oncogenic proteins and mutations, so they can be very advantageous in studying tumor growth, metastasis, and the tumor

microenvironment (TME). Furthermore, exosomes can be used to diagnose patients non-invasively by isolating them from body fluids such as blood, urine, and saliva. Analysis of exosomes can shed light on immune responses, therapeutic resistance, and tumor proliferation. Tumor exosomes serve as a reflection of the TME, and with their help, metastases can be detected prior to imaging [20].

Exosomes are the carriers of molecules that can help tumor cells to be resistant to immune surveillance, chemotherapy, and targeted therapies. Exosomes will allow healthcare professionals to rapidly identify resistance and switch the treatment in time to prevent failure. Tumor-derived exosomes contribute to the immunomodulatory effects of the TME. For instance, they can carry the immune inhibitory molecule PD-L1 that limits T cell activation and thus helps tumor cells to evade the immune response. By elucidating this role, it is possible to further develop immune checkpoint inhibitors and other immunotherapies aimed at reversing exosome-mediated immune suppression [21].

Table 2 illustrates the enormous potential of exosome profiling to monitor the progress of the disease and predict relapses. By continuously tracking molecular fingerprints and tumor markers in exosomes, it allows for dynamic cancer monitoring, especially MRD post-treatment. This is very helpful for diagnosing relapse at an early stage, particularly when the recurrence is not yet evident by imaging or clinical symptoms [22].

Table 2. This table summarizes the clinical applications of the main liquid biopsy biomarkers.

Biomarker	Clinical Application	Key Advantage	References
ctDNA	Detecting genetic mutations, MRD monitoring	Non-invasive, real-time updates	[23]
CTCs	Monitoring metastasis, predicting treatment failure	Insight into tumor progression	[24]
Exosomes	Tracking therapy response, monitoring relapse	Non-invasive, easy to collect	[25]

3. Immunological and Molecular Mechanisms

In addition to shaping its structure, the TME significantly contributes to therapy resistance and weakens the body's immune responses against the tumor through connected molecular and immune pathways. A deeper understanding of the immunological and molecular pathways that contribute to the development of the tumor is key to the development of targeted therapy and the ability to improve patient outcomes. Accordingly, this section focuses on immunometabolism, epigenetic regulation, and mechanisms of therapeutic resistance within the TME [26].

3.1 Immunometabolism

Immunometabolism is referred to as the metabolic remodeling of immune cells and tumor cells within the TME. Tumor cells experience some metabolic alterations in order to maintain the rapid growth and existence. Some of these changes include an increase in glucose uptake, aerobic glycolysis (Warburg effect) and mitochondrial functional alterations. Similarly, the invading immune cells have to alter their metabolism to respond to the presence of the tumor [27].

Even in the presence of oxygen, tumor cells in most malignancies undergo a switch of oxidative phosphorylation to glycolysis. This transformation is the Warburg effect, allowed to enable tumor cells to obtain energy rapidly and accumulate metabolic intermediates needed to multiply the cells. An illustration of this is the metabolic reprogramming of T cells in the TME as shown in Figure 2. A balance between glycolysis and oxidative phosphorylation regulates the activation, survival and functionality of T cells. The tumor cells often create an immunosuppressive environment which prevents a proper immune response to the tumor. This inhibits the T cell activity, which reduces their ability to develop an effective anti-tumor response [28].

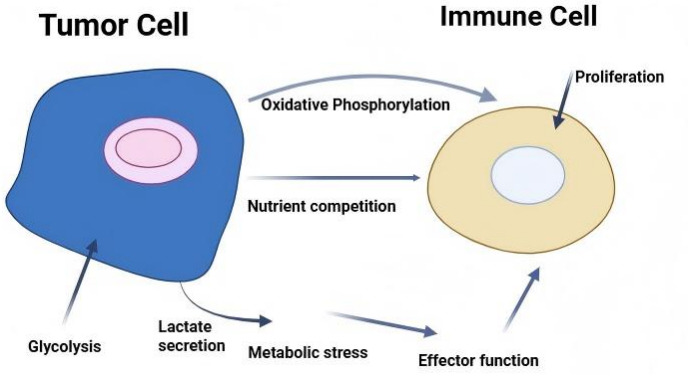

Figure 2. Immunometabolism in tumor cells–Illustration of how tumor cells and immune cells adjust their metabolism within the TME.

3.2 Epigenetic Regulation

Epigenetics is the study of gene expression changes that can be passed down but do not involve any change in the DNA sequence itself. Epigenetic changes, including DNA methylation, histone modification, and non-coding RNA regulation, play vital roles in tumorigenesis, tumor development, and metastasis of cancers. DNA methylation refers to the addition of a methyl group to DNA, leading to the repression of the tumor suppressor genes or oncogene activation, which is shown in Figure 3. Several tumors exhibit the hypermethylation of tumor suppressor genes like p16INK4a, which causes the cells to proliferate uncontrollably [29].

Histone modifications, e.g., acetylation, methylation, and phosphorylation, deeply impact chromatin compaction and gene expression regulation. In many tumor cells, histone deacetylases (HDACs) are overexpressed, which results in the silencing of those genes that normally serve as tumor growth inhibitors. It is worth mentioning that non-coding RNAs such as microRNAs (miRNAs) and long non-coding RNAs (lncRNAs), along with histone modifications, hugely impact gene regulation and cancer progression. Specifically, miRNAs have the ability to suppress tumor suppressor genes or activate oncogenes, thus exerting a potential role in cancer initiation and progression. These molecular mechanisms demonstrate the complexities of gene expression in cancer biology [30].

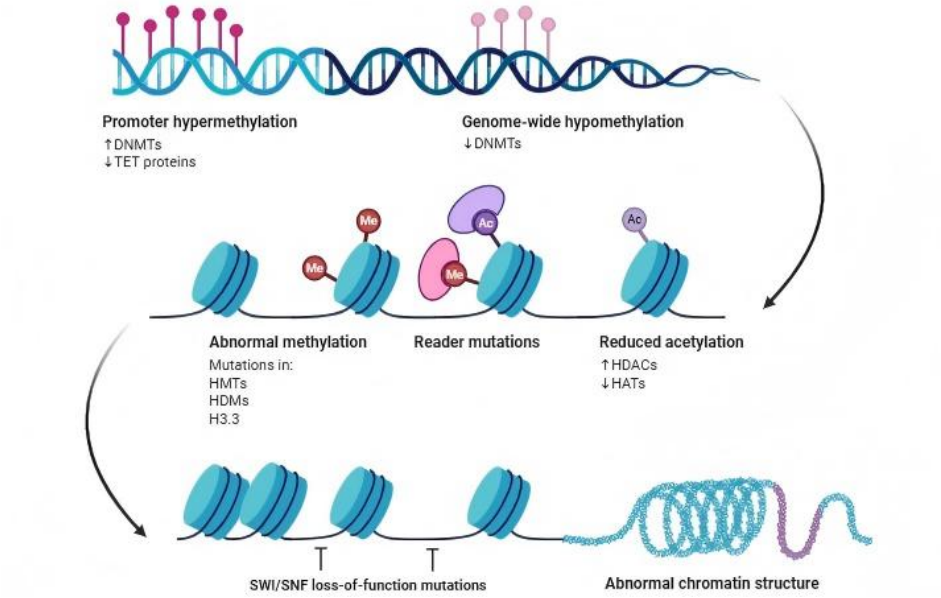

Figure 3. Epigenetic regulation in cancer–overview of epigenetic modifications influencing cancer cell behaviour, including DNA methylation and histone modification.

3.3 Therapy Resistance

Therapeutic resistance remains one of the major challenges in cancer treatment. The primary medication targets mutate, and the cancer cells get signalling pathways from somewhere else, resulting in therapeutic failure. Besides that, understanding the molecular basis of resistance in recent years has opened the way for newer techniques, such as combination therapy, and new drugs to be used to eliminate resistant tumor clones [31].

There are multiple reasons for the development of multidrug resistance against targeted therapy. One of the methods changes the medicine's target genes so that drug binding affinity gets altered. For instance, in the case of lung cancer, mutations in the EGFR gene (epidermal growth factor receptor) lead to resistance to tyrosine kinase inhibitors by reducing their effectiveness. Another method involves the activation of cell survival pathways, which allow tumors to escape targeted therapy. Even when the EGFR pathway is blocked, glioblastoma tumor cells are able to live through the PI3K-AKT pathway. Cancer cells can also escape from immune surveillance by increasing the expression of immune checkpoint inhibitory proteins like PD-L1 that in turn inhibit T cell activity. Although immunotherapies using anti-PD-1 or anti-PD-L1 are quite effective, TME heterogeneity or alterations in the immune checkpoint system often result in resistance, thus making the treatment more difficult [32].

3.4 Tumor Microenvironment and Immune Evasion

Tumor cells, stromal cells, immune cells, and extracellular matrix (ECM) constituents make up a TME, the biotic community that is biologically integrated with the host organism and functionally regulates tumor behaviour. TME plays a crucial role in each of the processes of tumour initiation, progression, metastasis, and therapeutic resistance. For instance, immune checkpoints and cancer-associated fibroblasts (CAFs) may produce an anti-immune state that compromises the body's innate immunity. It is therefore important to explain how these cellular and non-cellular parts work together if we want the development of effective microenvironment-modulating therapies [33]. These factors interact in the TME, which is a dynamic and complicated environment that is not similar to regular tissues, and stimulate tumour development,

immune system evasion, and treatment resistance. The TME does not just play an inactive role in tumour progression, but rather actively takes part in it by promoting angiogenesis, ECM remodelling and cell-to-cell signalling. It is crucial to learn the structure and the role of the TME in order to create more effective treatment methods [34].

4. Bone Marrow and Lymphoid Niches in Haematological Malignancies

4.1 Bone Marrow and Lymphoid Niches

Hematopoietic stem cells, which are the cells responsible for the development of leukaemia or other hematological malignancies, are supported to grow in such milieus. Various cells, such as fibroblasts, endothelial cells, and immune cells, make up the microenvironments in the bone marrow and lymphoid tissue. These cells communicate with tumor cells to promote their growth and survival. Acute myeloid leukemia cells, in particular, seem to have taken advantage of the bone marrow niche to escape treatment-induced cell death [35].

Leukemic cells become more resistant to therapy as a result of the protective signals given by stromal cells within the marrow microenvironment. The crosstalk between the bone marrow niche and leukemic cells deeply influences the development of hematological malignancies. Inside this safe shelter, leukemic cells hide from the immune system, multiply, and acquire resistance to chemotherapy and other treatment interventions for leukemia [36].

4.2 Tumor-Stroma Interactions

Cancer biology research concentrates on understanding the interactions between tumor cells and the surrounding stroma. The stromal environment, which includes CAFs, immune cells, endothelial cells, and ECM, plays a crucial role in the initiation and progression of cancers. Tumor stroma uses CAFs as a means of advancing the growth of solid tumors. Among the different substances they secrete are growth factors such as vascular endothelial growth factor (VEGF) that aid tumors in the formation of blood vessels to receive oxygen and nutrients. Endothelial cells located in the innermost layer of tumor blood vessels initiate angiogenesis, which is the formation of new tumor vasculature through the generation of new blood vessels. Furthermore, neutrophils, T lymphocytes, and macrophages in the TME have been shown to either promote or inhibit tumor growth [37].

Nonetheless, immunosuppressive cells such as regulatory T cells and myeloid-derived suppressor cells in the TME often function to weaken anti-tumor immunity. This mechanism leads to decreased effector immune cell function and, hence, tumor growth. Such interactions, therefore, help tumors evade immune surveillance and enhance their survival. Tumor cells synthesize and secrete matrix metalloproteinases to remodel the ECM. These proteolytic enzymes degrade ECM and thus enable tumor cells to penetrate into tissues [38].

4.3 Microenvironment-Targeted Therapies

Given its active contribution to tumour progression, the TME has emerged as a therapeutic target rather than a passive bystander, multiple approaches are highlighted in Figure 4. These approaches aim to reprogram the TME to restore anti-tumour immunity and inhibit angiogenesis, invasion, and metastatic dissemination [39].

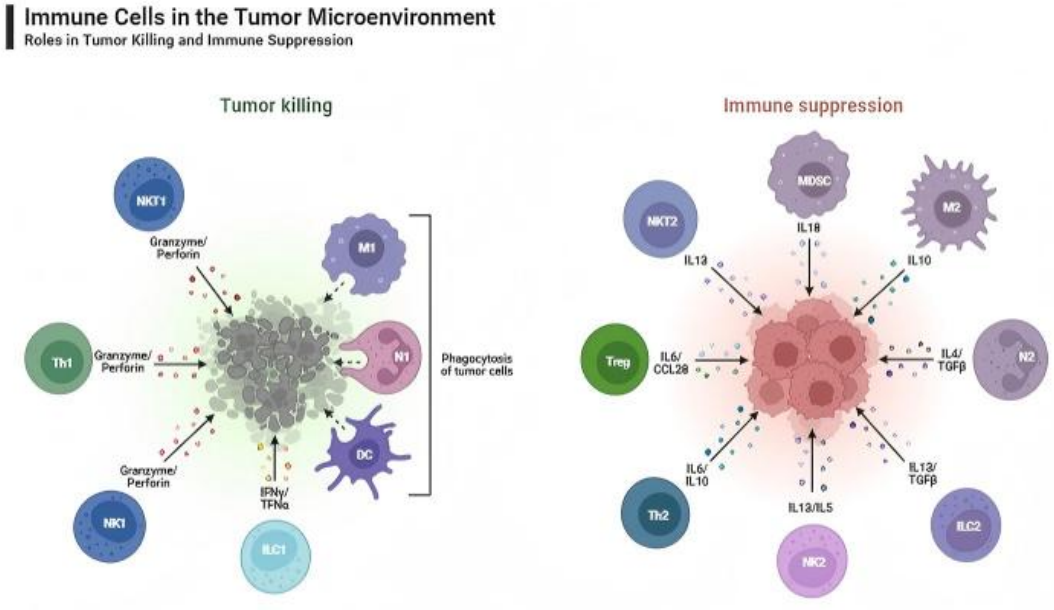

Figure 4. Tumor-stroma interactions–visualizing the interaction between tumor cells, the stroma, and immune cells.

Nowadays, most TME-directed strategies are aimed at breaking the tumour-supportive signalling networks instead of directly attacking the malignant cells. For example, angiogenesis inhibitors such as bevacizumab (an anti-VEGF antibody) cause the tumor's blood supply to be cut off, so the tumor has less oxygen and nutrients, and its growth slows down. Immunotherapeutic methods (Table 3) change the TME to help the immune system clear the tumor more effectively. For example, immune checkpoint inhibitors, such as anti-PD-1/PD-L1, work by lifting the tumour's suppression of the immune system. On the other hand, therapies aimed at the stroma disrupt the communication between tumour and stroma by the triple targeting of CAFs, endothelial cells, and ECM components to curb invasion and drug resistance. LOXO-292 has been effective in treating various cancers by targeting alterations in the oncogenic driven RET's alterations in the tumour cells [40].

Table 3. Types of microenvironment-targeted therapies.

Therapy Type	Example Drug/Target	Mechanism of Action	References
Angiogenesis Inhibition	Bevacizumab (anti-VEGF)	Blocks the formation of new blood vessels in tumors	[41]
Immunotherapy	Anti-PD-1 (Pembrolizumab)	Enhances immune response by inhibiting immune checkpoint proteins	[42]
Stromal-Targeted Therapy	LOXO-292 (RET Inhibitor)	Inhibits the oncogenic-driven RET alterations in cancer cells	[43]

Artificial intelligence (AI), nanomedicine, and gene-editing tools such as CRISPR-Cas9 have paved the way for a new era of cancer treatment. One aspect of cancer diagnostics that AI can revolutionize is the analysis of massive data sets and the prediction of a patient's response to a particular treatment. Furthermore, nanomedicine minimizes the side effects of drugs and provides a wider spectrum of treatment options by very selectively attacking cancer cells. Combining these breakthroughs with personalized medicine is a very promising opportunity to entirely change cancer treatment in the future.

Oncology and haematology are benefiting from the rapid advances of technology, opening up therapeutic options for patients. Diagnosis is made more accurate with the help of AI, while nanomedicine optimizes therapy to the individual patient's needs. Moreover, the use of theranostic approaches that combine diagnostics and therapeutics to provide enhanced and personalized treatment is on the rise [44]. This section presents a few of the most significant findings from cancer and hematological research.

5. Advancements in Cancer Diagnostics and Treatment: Artificial Intelligence, Nanomedicine, and Theranostics

5.1 Artificial Intelligence in Hematopathology

AI in hematopathology pertains to the medical specialty that diagnoses diseases related to blood, bone marrow, and lymph nodes. The field encompasses the use of AI technologies, including automated smear and marrow morphology, as well as multimodal histomorphology-molecular models, their genomic data and the discovery of image-derived biomarkers (Figure 5). It is technically promising, but it is still not sufficiently validated for routine care: most of the evidence is from backward-looking studies or product-centric and therefore lacks prospective and external confirmations [45]. Among the major issues of contention are those that have not been solved, and that should include domain-shift effects (scanner, stain, and center variation) that lead to calibration degradation and change failure modes in external deployments; the discord between explanation methods and actionable clinical utility; and the risk of AI reinforcement of demographic or technical biases when training sets are unrepresentative [46].

The gap in validation is tangible because hardly any model has been subjected to multicenter, prospective external validation with prespecified clinical endpoints, calibration reporting, and subgroup/failure-mode analyses; consequently, high in-center accuracy frequently is not reflected in practice [47]. Translational barriers of a practical nature are just as significant: the public evidence for commercial pathology AI varies, regulatory pathways and reporting standards still feature heterogeneity, and there are outstanding operational issues (data governance, IT integration, monitoring, reimbursement, and medicolegal responsibility); all of these issues point to the necessity of a human-in-the-loop mode of deployment accompanied by continuous logging, periodic recalibration, and predefined performance thresholds that will be enforced through prospective trials and early regulatory engagement [48].

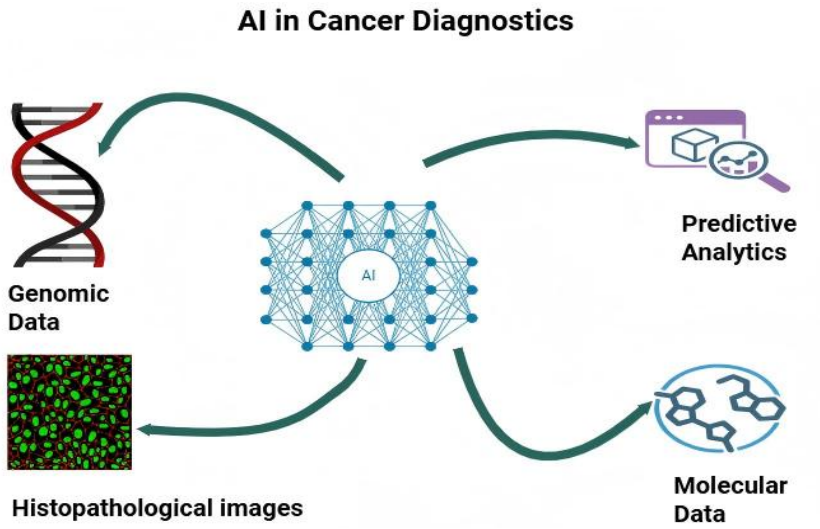

Figure 5. AI in cancer diagnostics—depiction of AI's role in analysing histopathological, genomic, and molecular data for cancer diagnosis.

5.2 AI applications in Haematopathology Include

Applications of AI in haematopathology such as automatic tumour classification, image-derived biomarker discovery, and prediction of prognosis or treatment response from histological and multi-omic data, are still at the preclinical studies or trials stage, although the technical demonstrations have been brilliant. Most of the performance metrics published are based on data from retrospective single-center studies and do not thoroughly consider domain shift due to the staining protocols, scanner variability, or population heterogeneity; that is why the reproducibility of the results from extrinsic cohorts is poor [49]. Moreover, a lot of deep-learning algorithms use correlations between hidden morphological features and clinical variables rather than true biologically causal features; thus, there is a risk of creating false biomarkers, and the predictions will be unstable if the models are used outside of the training environment [50]. The absence of prospective, multicenter validation studies with prespecified clinical endpoints, calibration assessment, and subgroup performance analysis is a big issue, and only a handful of the tools have been able to show their impact on diagnostic accuracy, treatment selection, or patient outcomes [51]. Some other challenges in using AI in healthcare include the difficulty in understanding how the models work, unresolved biases in different demographic and technical groups, lack of clear reporting guidelines, and uncertainty about legal responsibility for decisions made with AI assistance. All these factors together support the case for the necessity of human-in-the-loop implementation and strict regulatory oversight before routine clinical adoption [52].

5.3 Nanomedicine for Targeted Therapy

Despite the mechanistic attractiveness of nanomedicine strategies for targeted delivery, triggered release, and theranostic coupling, their clinical translation has not met expectations: several platforms show a strong preclinical efficacy, but when it comes to the benefit in humans, they fail to deliver [53]. A major dispute that is yet to be resolved is the extent to which the enhanced permeability and retention effect is clinically relevant and varied. The presence and size of the EPR effect vary greatly between different types of tumors, their locations in the body, and individual patients, leading to doubts about whether passive accumulation can be relied upon [54]. On top of that, immunological interactions add further complexity to translation: the clearance of nanoparticles, complement activation (including CARPA), as well as nanoparticle–antibody binding can interfere with on-target delivery, cause infusion reactions, and critically modulate antitumour immunity.

It is a known fact that preclinical models often fail to anticipate the human biodistribution and therapeutic index, and in fact, there are no validated predictive biomarkers for patient selection–which results in trial cohorts being heterogeneous and the benefits not significant enough to be noticed [55]. Besides the biological aspect, the major definitive translation obstacles are practical ones: reproducible scale-up and very strict control of critical quality attributes (size, surface chemistry, and payload stability) are among the difficulties faced; theranostic constructs cause regulatory complexity (combined drug/device pathways); and the data required for patient stratification and reimbursement are most frequently missing. Among the various measures that might be taken by the field to bridge these gaps are the adoption of standardized physicochemical and in-vitro/in-vivo characterization frameworks; patient selection being guided by imaging and molecular biomarkers; early-phase trials running prospectively, even multicenter, with predefined pharmacodynamic and accumulation parameters; early dialogue with regulators to agree on quality and endpoint expectations; and finally, an investment in GMP-scalable manufacturing and post-market surveillance so that clinical performance can be reproducible [56].

5.4 Imaging and Theranostics

A platform is used in the relatively young discipline of theranostics to diagnose and treat patients. Molecular imaging techniques like Positron Emission Tomography and Magnetic Resonance Imaging can be utilised in conjunction with therapeutic groups like nanoparticles to simultaneously diagnose and treat cancer. This dual-purpose strategy has a number of benefits [57].

Theranostics, a therapy strategy that blends medicines with diagnostics, has several advantages when it comes to cancer diagnosis. Due to the real time monitoring of the drugs, the doctors will be able to monitor the tumors as treatment is administered. As an example, the imaging equipment will be able to track drug-carrying nanoparticles that are already therapeutic and determine how they penetrate their targets. It is also a technique that enhances personalized medicine as the treatment regimen can be tailored to the molecular profile of the tumor and it is ensured that the patient receives the best treatment possible. The specific tumor targeting of theranostic medications lowers the chances of off-target effect, the side effects and the overall safety of cancer therapy is enhanced [58]. Even though significant progress has been made in developing new biomarkers and therapeutic approaches, there are various issues that still stand on the path of ensuring their successful application in medical practice.These technologies must be standardised, sensitive, particular, and regulated in order to be extensively employed. To guarantee that the advantages of such developments are distributed evenly across all groups of people, the ethical concerns of patient information privacy and equitable access to novel treatment alternatives should also be adequately considered [59].

It is a difficult and complicated process to move novel technology and biomarkers from the research setting into traditional clinical practice. Although liquid biopsies, immunotherapies, and improved imaging technologies offer a promising future, a number of issues need to be resolved before they can be routinely used in clinical settings [60].

6. Limitations in Emerging Cancer Technologies and Therapies

6.1 Sensitivity and Specificity

When introducing or implementing new biomarkers in a clinical setting, it may be difficult to figure out if these markers have sufficient sensitivity and specificity. Specificity measures a test's ability to correctly recognize patients who do not have the condition, whereas sensitivity speaks to a test's ability to correctly detect those who have the condition. Improper functioning of either process can result in a false positive or a false negative that may have a considerable effect on the patient's treatment and progression [61].

Liquid biopsies (ctDNA, CTCs, extracellular vesicles) have proven clinical advantages; however, their diagnostic accuracy varies and depends on the context (Table 4). Small or early-stage tumours may produce low ctDNA levels; therefore, limited sample volume and assay sensitivity constraints can lead to false-negative results. On the other hand, the presence of CTCs or tumour-associated DNA fragments in benign inflammatory conditions or as a consequence of clonal haematopoiesis can result in false-positive findings [62]. Reported sensitivity and specificity thus vary according to tumour type, disease stage, pre-analytical factors (collection, processing, storage), analytical platform (enrichment strategy, sequencing depth), and bioinformatic thresholds. To reduce misclassification, studies should present representative ranges rather than single-point estimates and, if possible, use orthogonal or combined biomarker approaches (e.g., ctDNA plus protein markers), serial sampling, and standardised assay procedures; these mitigation strategies and the contextual performance ranges are summarised in Table 4 and elaborated upon in the Limitations section.

Immunotherapy is a method that activates the immune system to recognize and destroy cancer cells; therefore, it is considered one of the most promising cancer treatments [63]. It has shown remarkable effectiveness in the treatment of cancers like non-small cell lung cancer and melanoma. However, to some extent, it is still a challenge to decide if a patient will benefit from immunotherapy. To this end, biomarker research is being given more and more attention as a way of predicting patient responses to therapies such as immune checkpoint inhibitors more accurately [64].

Table 4. Representative ranges of sensitivity and specificity reported for liquid biopsy components (ctDNA, CTCs, and exosomes) across selected studies.

Biomarker	Sensitivity (%)	Specificity (%)	References
ctDNA	75-80%	85-90%	[65]
CTCs	70-85%	80-95%	[65]
Exosomes	70-85%	85-90%	[66]

6.2 Standardization and Regulatory Hurdles

The only major thing limiting the use of new biomarkers and technologies in medical settings is a lack of standard protocols and laws. New diagnostic tests, therapies, and devices are to be accredited by authorities like the U.S. Food and

Drug Administration and the European Medicines Agency, among others. However, incorporating these technologies requires constant effort [67].

One of the main issues with liquid biopsies is the lack of standardised methods for sample collection, processing, and analysis. Differences in blood drawing methods, storing of samples, and interpretation of results can lead to inconsistent findings, thus making it difficult to obtain reliable results. Therefore, standardised protocols need to be developed to ensure consistent results in various laboratories and clinical settings. Immunotherapy is one of the most effective cancer treatments, using the patient's immune system to identify and kill cancer cells. However, it is still difficult to determine which patients will benefit from it. Immunotherapy has given outstanding results in melanoma and non-small cell lung cancer, but the use of biomarkers is now increasing among researchers to identify the ones who will benefit the most from immune checkpoint inhibitors [68].

6.3 Ethical Considerations

Table 5 describes how cancer treatment innovations bring about ethical problems such as the potential misuse of patients' genomic data and data confidentiality. Therefore, we should strictly guard information from genetic profiling and liquid biopsy of patients against possible exploitations. For example, low-income groups normally do not have access to state-of-the-art diagnostic devices or new therapies, which hence makes fair access a key concern. Genetic testing, data privacy, and equal access to the latest treatments are three ethical issues of any new medical technology [69]. Additionally, these therapies cost a lot, and, depending on the location, type of healthcare facility, and socioeconomic status, they can be out of reach. Facilitating equitable access to this kind of therapy is the most significant hurdle for healthcare systems globally, especially in low- and middle-income countries.

Among the most important ethical issues are: Big Data Large volumes of sensitive genetic data are produced via liquid biopsies and genomic profiling, and data privacy is a major concern. Liquid biopsies and genomic profiling generate massive amounts of highly sensitive genetic data, which raises issues of data privacy. Patients need to be guaranteed the ethical handling of their data and the protection of their privacy, as genetic information can be used for purposes outside the healthcare sphere, such as insurance and job discrimination. Furthermore, new methods of diagnosis, such as liquid biopsy, make it more difficult to obtain informed consent because of information gaps. Specifically, a patient has to understand the implications of genetic testing, the risks, the benefits, and the uncertainties of the treatment, especially when the genomic information is so complex and the results are not obvious. Immunotherapy is part of innovative medicines [70].

Table 5. Ethical issues in emerging cancer therapies.

Ethical Issue	Impact on Clinical Practice	Example	References
Data Privacy	Risk of unauthorized data use	Genetic data used for non-medical purposes	[71]
Informed Consent	Ensuring patient understanding of risks	Risks associated with genetic testing	[71]
Access to Therapies	Inequitable distribution of new treatments	High cost of immunotherapies in low-income regions	[72]

6.4 Clinical Trial Design and Real-World Data

A significant challenge in using new technology in clinical practice is the necessity for robust clinical trials to validate its efficacy. For instance, new technologies, like liquid biopsies or immunotherapies, are often difficult to assess using traditional trial designs, such as randomised controlled trials [73]. Today, we understand that adaptive trial designs, which incorporate real-world data and biomarker-driven objectives, represent more effective methodologies. These adaptive trials present a flexible methodology for research, which accommodates changes based on interim results. This flexible feature permits the immediate implementation of new treatment approvals by changing them in accordance with patient feedback, thus making the treatment more interactive and data responsive. Moreover, empirical data that can be derived from real-world sources like patient registries, electronic health records, and outcomes-based research might be used to complement traditional clinical trial results. Real-world data presents a deeper insight into treatment effectiveness by using bigger and more varied population groups, and thus it provides valuable information on the effectiveness and safety of therapies in a non-controlled trial setting [74].

Personalised treatment, multi-omics, and new developments such as gene preservation and AI will be some of the key elements in cancer therapies in the future. These developments will lead to a higher chance of patient recovery as a result of more accurate diagnostics and personalised treatment options. It is through current research and interdisciplinary collaboration that we will be able to address the issues that still exist, such as therapeutic resistance, biomarker validation and equitable patient access to therapy. The future appears promising, with the ongoing struggle to transform cancer into a manageable disease and significantly boost survival rates [75].

7. Future Directions in Cancer Treatment

With the development of personalised medicine, new technologies, and a deeper comprehension of the molecular pathways behind disease, cancer therapy is changing quickly. To improve patient outcomes, develop more potent medicines, and tackle the issues mentioned above, there are a number of important areas that will need to be improved in the future. The integration of biomarkers and novel treatments, integrated approaches in disease profiling, and the present spread of personalised medicine are a few of these themes [76].

7.1 Integrative Approaches in Disease Profiling

For future studies, multi-omics approaches will be needed that combine genomics, transcriptomics, proteomics, and epigenomics. Such a combined approach provides a full picture of health and disease; hence, it unlocks the potential for discovering new biomarkers, mechanisms of treatment resistance, and therapeutic targets. High-throughput sequencing technology has enabled cancer genome profiling through sequencing whole genomes or specific cancer genes. The technique then detects somatic mutations, copy-number alterations, and gene fusions that can be used to design personalized therapy [77].

By looking at the genetic differences of cancer, doctors can choose the best medicines for individual cancer profiles, thus gradually increasing patient outcomes and treatment effectiveness. Insights into cancer biology from proteomics and transcriptomics provide a deeper layer to genomic profiling. Proteomics focuses on the study of proteins' covalent modifications, mutual bindings, and signalling pathways, which might be responsible for cancer behaviour. As a result, it might identify the major chemicals that lead to tumor progression and drug resistance. The transcriptome, consisting of RNA molecules, offers new perspectives on gene expression. This provides better cancer diagnosis and treatment through the explanation of tumour growth and metastasis [78]. Both cancer and normal development require epigenomic changes like DNA methylation, histone modification, and non-coding RNA control. Epigenetic alterations regulate gene expression and thus play a major role in cancer progression without changing the DNA sequence. By combining epigenomic, genomic, and transcriptomic data, researchers and physicians are able to better understand cancer biology and discover new potential targets for therapy. It also facilitates the production of genetically- and epigenetically-informed personalized medicines [79].

7.2 Combining biomarkers with novel therapies

As we deepen our understanding of cancer biology, the role of biomarker-guided drug development is gaining momentum. By associating certain biomarkers with targeted therapies, doctors can tailor cancer treatment more effectively and increase the treatment's effectiveness while avoiding side effects. Biomarker-directed therapy has drastically transformed the lives of patients with different types of cancer, such as breast cancer, lung cancer, and colorectal cancer. These drugs are highly selective, as they concentrate on specific changes, like HER2 amplification in breast cancer or EGFR mutations in lung cancer. With a further understanding of cancer biology, the number of treatments based on biomarkers is expected to rise, thus improving the use of targeted therapy and making the patient's treatment personalised and more effective [80].

As knowledge of cancer biology expands, the development of biomarker-based therapies is increasingly pertinent. By correlating specific biomarkers with targeted therapies, clinicians can optimise cancer treatment, thereby increasing efficacy and minimising adverse effects. The use of biomarker-directed therapy has helped patients with a variety of malignancies, such as breast, lung, and colorectal cancers. These drugs can be very precise because they target the specific abnormalities, like EGFR mutations in lung cancer or HER2 amplification in breast cancer, making them highly focused, as illustrated in Table 6. As we continue to unravel the complexities of cancer biology, more biomarker-driven therapy options will become available. These options will continue to utilise targeted therapies and provide a patient care model that is both more effective and personalised [81].

Table 6. Combining biomarkers with targeted therapies.

Biomarker	Associated Therapy	Cancer Type	Potential Impact	References
HER2	Trastuzumab (Herceptin)	Breast Cancer	Increases survival in HER2-positive breast cancer	[82]
EGFR mutations	Erlotinib, Gefitinib	Non-Small Cell Lung Cancer	Improved progression-free survival in EGFR-mutant lung cancer	[82]
BRAF mutations	Dabrafenib, Trametinib	Melanoma	Increases survival in BRAF-mutant melanoma	[83]

7.3 Personalized Medicine

The customised medicine is a significant change in cancer treatment. Personalised medicine increases the effectiveness and precision of a treatment that is tailored to each patient based on their genetic, molecular, and clinical profiles. AI has given diagnostics, liquid biopsies, and genomic sequencing a boost, thereby facilitating the move to more personalised

therapy [84]. Personalised genomic profiling will be an essential part of cancer management very soon. Through tumour sequencing and the identification of specific genetic abnormalities, clinicians can provide treatments that are most suitable to their patients. This process has enabled precision medicine, which is the most effective way to adapt the treatments to the original genetic signature of each cancer, and it has been successful in minimising the side effects that are not necessary [85]. AI is crucial in drug discovery. The implementation of AI systems to evaluate large molecular datasets may be instrumental in finding candidates, estimating their effectiveness, and designing clinical trials. Continued technological innovations expedite the emergence of progressive treatments and acquisition, as well as the establishment of alternative approaches in clinical practice. In addition, several liquid biopsy techniques, including CTCs and ctDNA, are gradually becoming very useful tools for monitoring the progression of the disease, predicting relapse, and evaluating response to therapy. They are the least invasive procedures and offer an ever-changing and immediate method of monitoring tumour behaviour and modifying treatment plans as necessary. Liquid biopsies help increase the effectiveness of cancer treatments by allowing changes in therapy through constant monitoring [86].

7.4 How Emerging Technologies Are Shaping the Future of Cancer Treatment

Several emerging technologies have the potential to completely transform cancer therapy. One such technical breakthrough is the gene editing tool CRISPR-Cas9, which can directly modify the genes responsible for cancer. Furthermore, there is hope that new technology could help fix the genetic defects that cause cancer or maybe even prevent it at the genetic level. This discovery would also lead to the treatment of cancers due to genetic mutations. Among other uses, scientists are testing CRISPR-Cas9 in trials to see if it can fix mutations in cancer suppressor genes or boost the function of immune cells, which might have a beneficial effect on cancer therapy [87].

Another promising technological innovation, CAR-T cell therapy, has already demonstrated remarkable results in treating blood cancers such as leukaemia and lymphoma. By reprogramming T cells to attack specific cancer cells, CAR-T therapy has revealed how various types of cancer, including solid tumours, can be treated. Whereas CAR-T cell therapy has mainly been used in haematological cancers, it is now being tested in the treatment of solid tumours, such as brain and pancreatic cancers [88].

Scientists are working on a combination of CAR-T, along with checkpoint inhibitors or other immunomodulatory drugs, to get the most out of it and thus be able to tackle the most difficult tumours. Nanotechnology will greatly impact drug delivery systems in the future. With the help of nanotechnology, drug delivery systems can be engineered to be "smart" so that they will only attack cancer cells and leave healthy cells alone, thereby reducing side effects. The eventual goal of these customised therapies is to increase treatment effectiveness and reduce the toxicity that comes with traditional cancer treatments [89]. Eventually, clinical decision assistance via AI will be one of the most powerful tools for personalising cancer treatment. Clinicians will receive support from AI in making more logical and data-driven decisions, as it will be capable of evaluating large datasets, including genomes, imaging, and patient histories. The technology is thought to simplify treatment, allowing for better, more precise, and more personalised care [90].

8. Conclusion

New developments in liquid biopsy, tumour microenvironment biology, AI, and nanomedicine promise the delivery of cancer care that is more precise and biomarker-guided as well as advanced tools for monitoring disease. To fully realize this potential, we will need assay standardization, prospective multicenter validation, biomarker-driven trial designs, manufacturing and regulatory harmonization, and data governance and equitable access safeguards all of these are challenges that need to be solved through interdisciplinary collaboration before we can get to routine clinical adoption.

Conflict of Interest

The authors declare no conflict of interest.

Generative AI Statement

The authors declare that no Gen AI was used in the creation of this manuscript.

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