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Precision Medicine Approaches for Cancer Therapy Recent and Advance

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Abstract

Recent advances in biotechnology have made it possible to identify intricate and distinctive biological characteristics linked to carcinogenesis. Proteomic and RNA studies, immunological markers, tumor and cell-free DNA profiling, and other methods are utilized to find these traits to optimize anticancer treatment for specific patients. In recent years, the focus of clinical trials has shifted considerably to enhance treatment outcomes in cancer therapy. Rather than being primarily centered on tumor type, trials are increasingly designed to be gene-directed and histology-agnostic. This approach allows for a more personalized treatment strategy that is tailored to the genetic and molecular profile of the tumor rather than its anatomical location. Additionally, clinical trial designs have embraced innovative and adaptive methodologies, particularly those that integrate biomarker profiling to identify patients who are most likely to benefit from specific treatments. A growing body of evidence from precision medicine trials supports the effectiveness of this approach. These trials have consistently demonstrated that therapies matched to the molecular characteristics of the tumor are associated with improved patient outcomes, including higher response rates and extended progression-free survival, compared to non-matched therapies. This paradigm shift marks a significant advancement in oncology, providing hope for more effective, individualized treatments for a variety of cancers.

Keywords: ctDNA, personalized, precision, molecular profile, matched therapy, genomic landscape

INTRODUCTION

Anywhere in the body, aberrant cells can develop out of control and cause cancer. We refer to these aberrant cells as tumor cells, malignant cells, or cancer cells. These cells can penetrate healthy bodily tissues. The tissue from which the abnormal cells originate plays a key role in identifying various cancers and the unusual cells that form the cancerous tissue (e.g., breast cancer, lung cancer, and colorectal cancer). A mass of cancer cells forms when injured or unrepaired cells do not die and instead divide and expand uncontrollably to become cancer cells. It is common for cancer cells to separate from this initial mass of cells, move through the lymphatic and circulatory systems, and settle in other organs where they can resume the unchecked growth cycle [1].

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Cancer is a hereditary condition. One significant occurrence in the early phases of tumor formation is the manifestation of oncogenesis. Tumor virus infection or the conversion of normally normal cellular proto-oncogenes to oncogenes are the two ways that oncogenes are activated. Then, a single cell undergoes oncogenic transformation to become a tumor. Certain tumors develop the capacity to spread beyond their original location and invade other bodily regions. We refer to this process as

metastasis. The Rous sarcoma virus could spread solid tumors, or sarcomas, from one animal to another. Either the expression of genetic material – in this case, viral DNA – or its addition to healthy cells could result in tumors. Rous received a Nobel Prize [2].

RISK FACTORS

1. Heredity.
2. Ionizing radiation.
3. Chemical substance.
4. Dietary factors – meat, energy balance, fat, protein, alcohol, nitrate.
5. Estrogen.
6. Viruses.
7. Stress.
8. Age.

HEREDITY

These include the following genes: ovarian, colorectal, prostate, skin, melanoma, and breast. An individual is more likely to get cancer if they are exposed to higher levels of elements that cause cancer. Furthermore, those who have a genetic predisposition to cancer might not get it for the same reasons (insufficient stimulation to activate the genes). A heightened immune response in certain individuals may also regulate or eradicate cancerous or possibly cancerous cells [3].

IONIZING RADIATIONS

Ionizing radiation is a significant environmental risk factor for cancer. It describes radiation that has sufficient energy to liberate atoms' firmly bonded electrons, forming ions in the process. Living tissue, especially DNA, can be harmed by this radiation, which can result in mutations and the emergence of cancer. Here are key facts about ionizing radiation and its role in increasing the risk of cancer [4].

TYPES OF IONIZING RADIATION

There are various types of ionizing radiation, and each has unique characteristics.

Alpha Particles

These are heavy, positively charged particles that are dangerous to breathe in or consume but cannot pass through the skin.

Beta Particles

These are tiny, skin-piercing electrons that are often less dangerous than alpha particles.

Gamma Rays

These high-energy electromagnetic radiations are employed extensively in cancer therapies and medical imaging because they can enter the body deeply.

The fourth type of electromagnetic radiation is X-rays, which are like gamma rays but usually have less energy.

Neutrons are extremely penetrating, high-energy particles that are frequently created in nuclear reactions and have the potential to cause greater harm than other types [5, 6].

CHEMICAL SUBSTANCES

1. *Tobacco smoke:* Contains hundreds of harmful chemicals, including carcinogens like benzene, formaldehyde, and polycyclic aromatic hydrocarbons.
2. *Asbestos:* A mineral fiber commonly used in construction materials, recognized for its link to lung cancer and mesothelioma.

3. *Aflatoxins:* Toxic substances produced by certain molds that grow on food products like peanuts and grains; these can cause liver cancer.
4. *Benzene:* A solvent found in industrial settings and cigarette smoke, associated with leukemia and other cancers.
5. *Formaldehyde:* A chemical used in manufacturing and as a preservative in some consumer products, linked to nasopharyngeal cancer and leukemia.
6. *Arsenic:* Found in contaminated water and some pesticides, known to increase the risk of skin, lung, and bladder cancers.
7. *Radiation (ionizing):* Although not a chemical, radiation exposure from sources like radon gas or X-rays can damage DNA and lead to cancer.

DIETARY FACTORS

The World Health Organization (WHO) classifies processed meats, such as hot dogs, sausages, bacon, and deli meats as Group 1 carcinogens, which means there is sufficient evidence to suggest they cause cancer. Although stomach and pancreatic cancers are also linked, colorectal cancer is the main culprit [7].

Red Meat

The WHO classifies red meat (beef, lamb, and pork) as a Group 2A carcinogen, which indicates that it is most likely harmful to people. Red meat's ability to raise the risk of colorectal cancer is the main worry, while there may also be connections to pancreatic [8].

FATS THAT ARE SATURATED

Increased Risk

Diets heavy in saturated fats, which are present in foods like red meat, butter, full-fat dairy, and processed foods, have been associated with a higher risk of developing some types of cancer, such as colorectal, breast, and prostate cancer [9].

Mechanisms

Saturated fats may enhance oxidative stress, change hormone levels (such as estrogen), and encourage inflammation, all of which can lead to the development of cancer.

TRANS FATS

Increased Risk

Trans fats, which are frequently included in baked products, processed meals, and fried foods, have been connected to an increased risk of developing cancer, especially breast and colorectal cancer. It is well known that trans fats can lead to inflammation and even damage to cells [10].

What Are the Different Types of Cancer?

Carcinoma

This type of cancer is the most common and includes subtypes such as basal cell carcinoma, squamous cell carcinoma, adenocarcinoma, and transitional cell carcinoma, affecting organs like the skin, lungs, breasts, prostate, and digestive tract.

For Instance

Cancer of the Lung

Lung cancer is a type of cancer that begins in the lungs and is one of the most common and aggressive forms of cancer. There are two main types of lung cancer. Non-small cell lung cancer (NSCLC) is the most common, accounting for about 85% of cases, and includes subtypes like adenocarcinoma, squamous cell carcinoma, and giant cell carcinoma. Small cell lung cancer (SCLC), though less common, is more aggressive and tends to grow and spread more rapidly. SCLC is strongly associated with smoking [11].

Lung Cancer Risk Factors

Although non-smokers can also get lung cancer, smoking is the main cause of the disease.

a. *Secondhand smoke exposure:* The danger is increased by being around smokers.
b. *Exposure to radon gas:* Radon is a naturally occurring radioactive gas that poses concern and can accumulate in dwellings.
c. *Occupational hazards:* Risk can be raised by exposure to carcinogens, such as arsenic and asbestos.

Cancer of the Breast

Breast cancer is a type of cancer that originates in the cells of the breast, typically in the milk ducts (ductal carcinoma) or the milk-producing glands (lobular carcinoma). While it can affect both men and women, it is much more common in women [12].

Types of Breast Cancer

1. *Ductal Carcinoma in Situ (DCIS):* A non-invasive cancer, meaning the cancer cells are confined to the ducts and have not spread to surrounding tissue.
2. *Invasive Ductal Carcinoma (IDC):* The most common form of breast cancer, where the cancer cells break out of the milk ducts and invade surrounding tissue.
3. *Invasive Lobular Carcinoma (ILC):* Cancer that begins in the milk-producing lobules and spreads to nearby tissue.
4. *Inflammatory Breast Cancer (IBC):* A rare and aggressive type of breast cancer in which the breast becomes red, swollen, and warm because cancer cells block the lymph vessels in the skin [13].

CANCERS OF THE CENTRAL NERVOUS SYSTEM (CNS)

Cancers that begin in the brain or spinal cord are uncommon but tend to be highly aggressive. They can grow quickly, be resistant to standard treatments, and significantly impair neurological function. For example, NTRK fusions in certain tumors offer potential targets for precision therapies [14, 15].

Glioma

Glioma is a type of cancer that begins in the glial cells of the brain or spinal cord. Glial cells are the supportive cells that surround and protect neurons. Gliomas are a varied group of tumors, differing significantly in severity, location, and treatment options. They are classified according to the specific type of glial cells affected [16].

TYPES OF GLIOMAS

Astrocytomas

These tumors arise from astrocytes, a type of glial cell. They can be benign (slow growing) or malignant (fast-growing).

Grade I & II

Low-grade astrocytomas (benign or slow growing).

Grade III

Malignant, but not the most aggressive.

Grade IV (Glioblastoma)

Multiforme (GBM) is the most common and aggressive form of malignant glioma. Glioma is a type of cancer that begins in the glial cells of the brain or spinal cord. The protective cells that envelop and shield neurons (nerve cells) are called glial cells. Gliomas are a broad category of tumors with wide variations in location, intensity, and available treatments [17].

The kind of glial cells involved determines their classification.

Cancers of the Endocrine System

Endocrine system cancer describes cancers that arise in the glands of the endocrine system, which release hormones that control different bodily processes. Among other organs, the thyroid, pituitary, adrenal, and pancreatic glands may be impacted by these malignancies. An outline of the several kinds of endocrine malignancies is provided below [18].

Thyroid Cancer

Thyroid cancer is the most common type of cancer that affects the thyroid gland. It can be divided into four main types: anaplastic, medullary, follicular, and papillary. Risk factors include radiation exposure and a family history of thyroid issues. Symptoms may include a lump in the neck, hoarseness, trouble swallowing, and swelling [19].

Adrenal Cancer

Adrenal cancer affects the adrenal glands, which are located above the kidneys and produce hormones, such as cortisol, adrenaline, and aldosterone. This type of cancer can lead to an overproduction of hormones, causing symptoms like weight gain, high blood pressure, and excessive body hair growth. Adrenal tumors can be either benign (non-cancerous) or malignant (cancerous), with malignant tumors being more aggressive [20].

Tumors of the Pituitary

At the base of the brain, the pituitary gland regulates growth, metabolism, and reproductive health, among other important processes.

Hormone abnormalities may result from pituitary tumors. Although they can impact hormone production, they are usually benign.

Headaches, eyesight issues, and inexplicable changes in bodily processes brought on by hormone imbalances are some of the symptoms.

Endocrine-Type Pancreatic Cancer

The pancreas performs both exocrine and endocrine functions. The endocrine system is made up of the islets of Langerhans, which produce insulin and other hormones.

These hormone-producing cells can develop into malignant growths known as pancreatic neuroendocrine tumors (PNETs).

Some of the symptoms include unexplained weight loss, stomach pain, and fluctuations in blood sugar levels.

Cancer of the Parathyroid

The body’s calcium levels are controlled by the parathyroid glands. Rarely do these glands develop cancer.

It may result in hypercalcemia, or elevated blood calcium levels, which can cause bone pain, kidney stones, and exhaustion.

Risk Elements

Many endocrine tumors have established risk factors, including radiation exposure, genetic alterations, and a family history of endocrine cancers.

The chance of developing endocrine system malignancies can also be increased by some hereditary disorders, such as Multiple Endocrine Neoplasia (MEN) syndromes [21].

THERAPY

Depending on the cancer's nature, location, and stage, treatment options may include hormone therapy, radiation therapy, chemotherapy, or surgery.

For instance, surgery and thyroid hormone replacement may be used to treat endocrine system cancers to have better results, early detection and routine monitoring are essential.

These tumors begin in the endocrine system's glands, which generate hormones that control the bodies [22].

KEY ADVANCES IN PRECISION MEDICINE FOR CANCER

Genomic Profiling and Molecular

The creation and broad application of next-generation sequencing (NGS) technologies is one of the most important developments in precision medicine. These enable the identification of certain mutations, gene rearrangements, and changes in DNA copy numbers through thorough genomic profiling of cancerous tumors. Clinicians can find actionable mutations and choose tailored medicines that are more likely to work for certain patients by examining the genetic composition of both tumor cells and healthy tissue [23].

LIQUID BIOPSY

The identification of genetic mutations and changes from a blood sample is made possible by advancements in liquid biopsy techniques, providing a non-invasive way to track tumor dynamics and therapy response.

Microsatellite instability (MSI) and tumor mutational burden (TMB): By using these biomarkers, it is now possible to identify cancers that are more likely to react to immune checkpoint inhibitors [24].

SPECIFIC TREATMENTS

Because targeted medicines directly target chemicals or processes linked to the growth of cancer, they have emerged as a key component of precision oncology. By interfering with the processes that propel tumor growth without harming healthy cells, these treatments aim to enhance therapeutic results and lower toxicity ALK and EGFR Inhibitors:

Targeted treatments like ALK inhibitors (like alectinib) and EGFR inhibitors (like osimertinib) have greatly enhanced patient outcomes for non-small cell lung cancer (NSCLC).

HER2-targeted therapy: Survival rates for patients with HER2-positive breast cancer have significantly increased thanks to targeted therapies that block the HER2 receptor, such as trastuzumab and more recent medications such trastuzumabemtansine (T-DM1).

IMMUNOTHERAPY INTEGRATION

Immunotherapy has transformed cancer treatment by using the patient's immune system to combat cancer. Precision medicine has been crucial in identifying which patients are most likely to respond to immunotherapies, such as immune checkpoint inhibitors [25].

PD-1/PD-L1 Inhibitors: Drugs like pembrolizumab and nivolumab have shown success in cancers, such as melanoma, lung cancer, and head and neck cancer. The identification of PD-L1 expressions in tumors through biomarkers has enabled better patient selection for these therapies.

Chimeric Antigen Receptor (CAR) T-cell therapy involves modifying a patient's T-cells to target and destroy specific cancer cells. It has shown remarkable success in hematologic cancers, especially acute lymphoblastic leukemia (ALL) and lymphomas.

INTEGRATION OF IMMUNOTHERAPY

Immunotherapy has completely transformed cancer treatment by utilizing the patient's immune system to fight cancer. Precision medicine has been vital in identifying which patients are most likely to benefit from immunotherapies, such as immune checkpoint inhibitors.

PD-1/PD-L1 Inhibitors: Pembrolizumab and nivolumab are two medications that have demonstrated efficacy in treating cancers like melanoma, lung cancer, and head and neck cancer. Better patient selection for these treatments has been made possible by the discovery of biomarkers that identify PD-L1 expressions in malignancies.

The aim of chimeric antigen receptor (CAR) T-cell therapy is to alter a patient's T-cells so they can recognize and attack specific cancer cells. It has demonstrated exceptional efficacy in treating hematologic malignancies, particularly lymphomas and acute lymphoblastic leukemia (ALL).

The possibility for long-lasting effects is a major factor in the clinical excitement surrounding immunotherapy, as seen by the more than 2000 active trials examining antiPD-1/anti-PD-L1 targeted medications alone. 1. Only a small percentage of patients using immune checkpoint inhibitors (ICIs) do well with these medications, though. 2,3. Some of the patients who do respond will have progressive, refractory disease later. 4. Novel agents and combinations are required to address primary and acquired resistance (Figure 1).

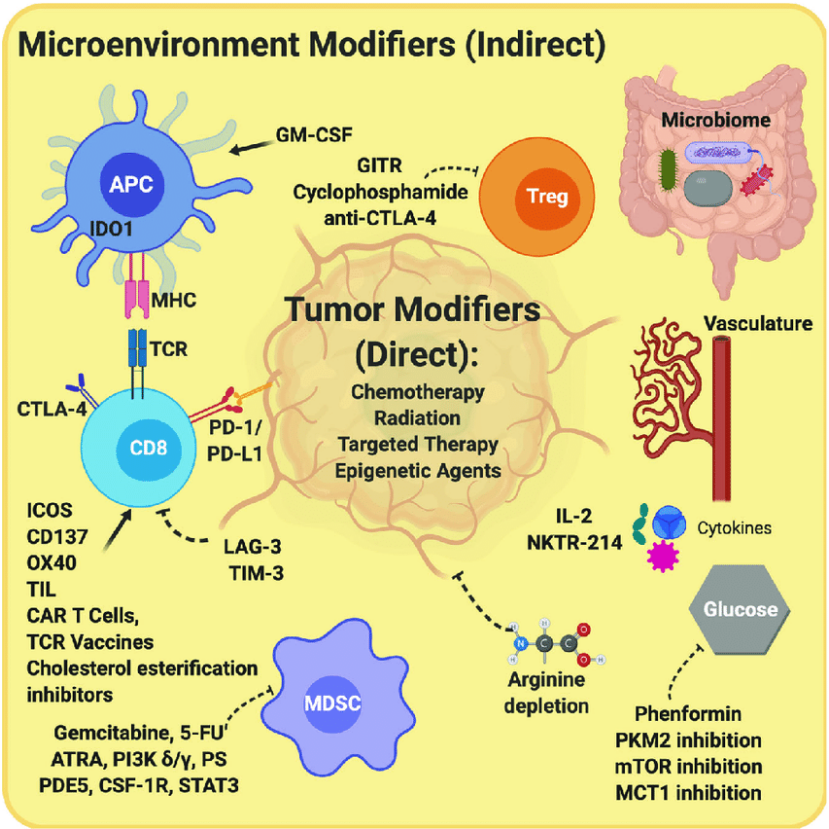

Figure 1. Shows a schematic depiction of how direct tumor modifiers and indirect tumor microenvironment modifiers interact.

An Overview of Artificial Intelligence and Machine Learning in Cancer

Artificial Intelligence (AI) and Machine Learning (ML) are quickly changing the field of cancer diagnosis, treatment, and research. These technologies leverage vast datasets, including medical imaging, genomics, clinical records, and other molecular data, to uncover insights that were previously

unattainable using traditional methods. In oncology, AI and ML are being applied to enhance early detection, tailor treatments, predict patient outcomes, and speed up drug discovery, among other uses. This review explores recent advancements in AI and ML in cancer, highlighting their clinical implications and the challenges faced in their integration into cancer care.

The fields of cancer diagnosis, therapy, and research are quickly changing because of artificial intelligence (AI) and machine learning (ML). These technologies make use of enormous datasets, such as genomes, clinical records, medical imaging, and other molecular data, to provide insights that were previously impossible to obtain by conventional means. Among other things, oncology is using AI and ML to speed up drug discovery, predict patient outcomes, enhance early detection, and tailor treatment. The therapeutic implications of current developments in AI and ML in cancer are examined in this study, along with the difficulties in incorporating these technologies into cancer treatment.

EARLY DETECTION AND DIAGNOSIS USING AI AND MI

Outcomes require early cancer identification. Using a range of data sources, AI and ML algorithms are being created to detect cancers early on Medical Imaging: AI-powered image recognition has demonstrated potential in the analysis of medical pictures, including CT scans, MRIs, mammograms, and histopathology slides. This is particularly the case when using deep learning methods, such as Convolutional Neural Networks (CNNs). These technologies can occasionally outperform human radiologists in their ability to identify cancers, categorize lesions, and even measure the development of diseases. For instance, AI has significantly increased the sensitivity and specificity of early detection of colorectal, lung, and breast cancer symptoms (Figure 2).

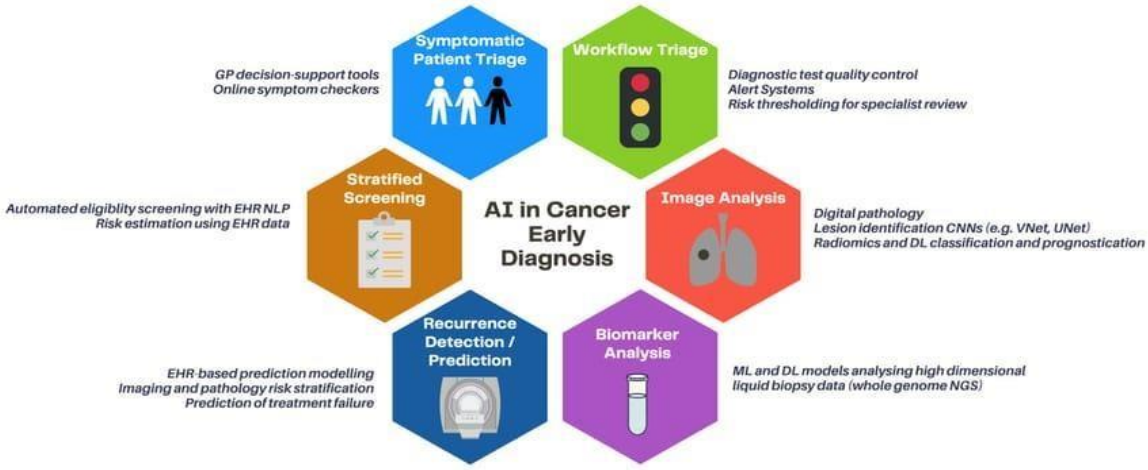

Figure 2. Artificial intelligence and machine learning.

Liver cancer is the fourth leading cause of cancer-related deaths worldwide. The development of algorithms in the context of cancer has been spurred by advances in artificial intelligence (AI) throughout the last ten years. A growing number of recent studies have explored the use of machine learning (ML) and deep learning (DL) algorithms for pre-screening, diagnosis, and treatment of liver cancer patients, utilizing diagnostic image analysis, biomarker identification, and personalized predictions of clinical outcomes. Although these early AI tools showed promise, much effort needs to be done to explain the “black box” of AI and move toward implementation to achieve ultimate clinical translatability. The application of AI, particularly in nano-formulation research and development, may also be advantageous for several new industries, such as RNA nanomedicine for targeted liver cancer therapy, provided that they.

MULTI -OMICS APPROACHES

A complex and multifaceted disease, cancer is brought on by a confluence of metabolic changes, dysregulated protein functions, epigenetic modifications, and genetic abnormalities. While genetics has

been the focus of the traditional approach to studying cancer, recent developments in high-throughput technology have made it possible to use multi-omics to gain a more thorough understanding of tumor biology. A more comprehensive understanding of cancer and its molecular causes is provided by multi-omics, which combines information from several biological levels (such as genomes, transcriptomics, proteomics, metabolomics, and epigenomics).

There is great potential for enhancing cancer diagnosis, prognosis, and treatment approaches with this integrated approach. An outline of the main omics platforms, the advantages of multimers integration, and its use in cancer research and treatment are given here [20–25].

IMPORTANT CANCER OMICS PLATFORMS

Genetics

The study of the entire collection of genetic material (DNA) found in cancer cells is known as genomics. Researchers can find the chromosomal rearrangements, copy number variations (CNVs), and genetic mutations that cause cancer by using whole-genome sequencing (WGS), whole-exome sequencing (WES), and next-generation sequencing (NGS). This comprises alterations in tumor suppressor genes (TP53, BRCA1) and oncogenes (EGFR, KRAS).

Targeted medicines are frequently based on genomic changes.

The Study of Transcriptomics

Gene expression, especially the quantity of mRNA transcripts generated in cancer cells, is the focus of transcriptomics. RNA sequencing (RNA-seq) can identify differentially expressed genes, alternative splicing events, and non-coding RNAs (such as microRNAs and long non-coding RNAs) involved in cancer development. Transcriptomic data helps clarify how these factors contribute.

CHALLENGE IN PRECISION MEDICINE FOR CANCER

1. *Tumor Heterogeneity:* Because tumors are so diverse, they may contain several subclones of cancer cells with various genetic alterations and traits. Because different sections of the same tumor or metastases may respond differently to therapy, it is challenging to establish a one-size-fits-all treatment.
2. *Genetic Complexity:* A variety of genetic mutations contribute to the development of cancer, and not all these mutations are equally significant. It is difficult and calls for sophisticated bioinformatics methods to distinguish between “driver” mutations – those that fuel the cancer – and “passenger” mutations, which could be innocuous bystanders.
3. *Data Integration and Interpretation:* Clinical, transcriptomic, proteomic, and genomic data are among the vast datasets that precision medicine depends on. It is still very difficult to integrate and evaluate these datasets to provide insights that can be use, especially given the complexity of cancer biology.
4. *Cost and Accessibility:* Many patients, especially those in low-resource environments, may not be able to afford the costly procedures that precision medicine frequently entails, such as genome sequencing and sophisticated imaging. The availability of tailored medicines is further restricted by their high cost of development.

CONCLUSIONS

Treatments: As our knowledge of cancer genomics has grown, targeted medicines that target genetic abnormalities or changes in cancer cells have been developed. These treatments, which include monoclonal antibodies and small molecule inhibitors, have completely changed how malignancies including breast, lung, and melanoma are treated. *Immunotherapy Breakthroughs:* Immunotherapy, which includes CAR-T cell therapy and immune checkpoint inhibitors (like pembrolizumab and nivolumab), has become a significant breakthrough, demonstrating effectiveness in treating tumors that were previously challenging to treat. But issues, like side effects, resistance, and the requirement for biomarkers to forecast response, still need to be resolved. *Combination Approaches:* It has been

demonstrated that combining immunotherapy, targeted medicines, and traditional treatments, like radiation and chemotherapy, can improve therapeutic efficacy and overcome resistance. But making these pairings better.

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