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# A brief review: personalised medicine in oncology

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Abstract

Cancer remains one of the most significant global health challenges, consistently ranking as the second leading cause of death worldwide. Each year, millions of new cases and fatalities are reported, emphasizing the urgent need for innovative approaches to diagnosis and treatment. In the field of oncology, personalised medicine has emerged as a groundbreaking paradigm, revolutionising cancer care by tailoring therapies to the unique genetic, molecular, and environmental profiles of individual patients.This review highlights the latest advancements in personalised cancer treatments, particularly focusing on targeted therapies, biomarker discovery, and the integration of genetic sequencing. These innovations are not only transforming cancer care but also paving the way for more precise and effective interventions. The use of genomic data in clinical practice is enabling the development of novel targeted drugs and immunotherapies, which hold the potential to improve therapeutic outcomes significantly.However, the implementation of personalised medicine comes with its own set of challenges. Financial constraints, ethical considerations, and logistical barriers remain critical issues that need to be addressed for wider accessibility. Despite these obstacles, personalised medicine offers immense promise in enhancing cancer screening, prognosis, and prevention. By leveraging advancements in genomics, bioinformatics, and molecular biology, this approach continues to reshape oncology, bringing hope to millions of patients worldwide.

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## INTRODUCTION

Cancer is characterised by uncontrolled cell growth driven by damaged DNA expression. Repeated abnormal cell divisions disrupt normal tissues, giving rise to benign or malignant tumours. Malignant cancers can metastasize, spreading to other organs, while benign cancers remain localised. Tumours, often identified with the suffix "-oma," may arise from diverse origins. Given the heterogeneity of cancers, traditional therapies such as radiation and chemotherapy show limited success due to tumour variability. The advent of personalised and precision medicine (PPM) has

marked a turning point in oncology. PPM involves tailoring treatment strategies to individual patients based on pharmacogenetic, pharmacogenomic, and pharmacoproteomic data. Next-Generation Sequencing (NGS) and polymerase chain reaction (PCR) technologies have enabled the detection of genomic variations through biomarkers like circulating tumour cells, cell-free DNAs (cfDNAs), and microRNAs. This advancement facilitates liquid biopsies—non-invasive tools for diagnosing and monitoring cancers [2].

The World Health Organization (WHO) reported 20 million new cancer cases and 9.7 million deaths globally in 2022. Understanding cancer at the molecular level enables better therapeutic strategies and improves patient outcomes [1].

**Cancer – a short history:**

Edwin Smith Papyrus records eight cases in Egypt circa 1600 B.C. that seem to be breast cancer cases. The "fire drill" was a tool used in the cauterization process of the breast cancers. Percivall Pott discovered in 1775 that chimney sweeps may have a higher risk of developing scrotal cancer due to soot exposure. This was the first proof that cancer might result from chemical exposure. During the late 19th and early 20th centuries, there was overwhelming evidence during the Industrial Revolution that chemical exposure at work might lead to cancer.

However, other factors can also contribute to cancer. In 1898, Marie Curie—awarded the Nobel Prize in chemistry and physics—made the discovery of radium. Radium's green light was used to treat a variety of illnesses, including cancer.

Some cancers are caused by radiation from industrial and medical sources, as well as background radiation that occurs naturally.

**Genetic toxicology and the biology of cancer**

The study of how physical and chemical factors affect genetic material is known as genetic toxicology.

**DNA Mutation**

Investigating the biological alteration that transforms a healthy cell into a malignant cell that divides repeatedly and uncontrollably is essential to understanding cancer. When a cell's DNA structure is altered or there is genetic damage, this transformation takes place. The coding system of life is DNA. The simplicity of DNA is its beauty. The elements adenine (A), guanine (G), thymine (T), and cytosine (C) make up DNA's double helix. Long sequences of AT and CG pairs are coupled to these compounds, which are then held together by sugar molecules. This type of gene that produces the protein when it is "read" A mutation happens when the DNA is incorrectly repaired for whatever cause. A mutation is a slight or not-so-subtle alteration to one of the DNA's constituent letters, A, G, C, or T. A cell may begin to divide uncontrollably, turn into a malignant cell, and eventually result in cancer if a mutation takes place in the wrong location.

**Mutagens**

Mutagens are substances that cause DNA mutations; when these alterations result in cancer, the substance is referred to as a carcinogen. Not every carcinogen is a mutagen, and not every mutagen is a carcinogen. It was demonstrated in 1946 that nitrogen mustards, which were generated from mustard gas, which the military had first employed in 1917 during World War I,

**Table 1 Historical Timeline of Carcinogenic Causes and Associated Cancer Types**

| Year | Cause | Cancer type |
|---|---|---|
| 1775 | Soot | Scrotal cancer |
| 1822 | Arsenic | Skin cancer |
| 1879 | Uranium mining | Lung cancer |
| 1895 | Aniline dyes | Bladder cancer |
| 1902 | X-rays | Skin cancer |
| 1908 | Filterable agents | Leukemia |
| 1914 | Coal tar | Experimental induction of skin cancer |
| 1928 | UV light | Experimental induction of skin cancer |

could cause fruit fly mutations and slow the formation of tumours in mice. Toxic chemicals have the ability to interact with proteins or DNA in cells to create cancerous cells. We refer to this procedure as bioactivation. There is continuous research being done to determine the biology of cancer. The reason why some people are more prone to cancer than others is being explained in part by the genetic sciences [1].

**What causes cancer?**

Constant contact with a variety of man-made and natural chemicals and physical factors can have harmful effects. Cancer can arise from DNA damage caused by exposure to sunshine, artificial and natural chemicals, background radiation, and even oxygen. Among the recognized causes of cancer are

**Table 2 Recognized Causes of Cancer and Their Examples**

| Cause | Example |
|---|---|
| Lifestyle | Tobacco, alcohol consumption diet |
| Ambient environment exposure | Air, drinking water |
| Organic chemicals | Benzo(a)pyrene (in coal tar), Benzene |
| Inorganic chemicals and metals | Arsenic, Cadmium, Nickel |
| Fibers | Asbestos |
| Radiation | Sunlight (Ultra Violet), radioactive material |
| Drugs | Diethylstilbesterol (DES) |
| Viruses | Epstein-Barr, AIDS, Papilloma |
| Genetic | Increased likelihood ( eg: Breast Cancer) |

**Common causes of cancer**

Substances known to raise the risk of cancer are known as carcinogens, and they fall into three basic categories:

Carcinogens in the body: These include ultraviolet (UV) light from the sun and other radiation exposure, both of which can damage skin.

Chemical carcinogens: These can cause cancer and include things like alcohol, asbestos, cigarettes smoke, air pollution, and some chemicals that can be present in tainted food and water.

Biological carcinogens: These include bacteria, viruses, and parasites that have been connected to a higher risk of developing cancer [1].

**Symptoms**

Changes in bowel or bladder habits

Non-healing sores

Unusual bleeding or discharge

Thickening or lump

Wart or mole changes

Nagging cough, breathlessness or hoarseness

Fatigue or unexplained swelling

Weight fluctuations

Skin changes

Persistent indigestion after eating

Unexplained persistent fever or night sweats

Unexplained persistent muscle or joint

**Types of cancer**

Cancer can be classified according to tissue types or according to the primary location of origin. The histology of a malignancy can identify its various forms.

Carcinoma: Carcinomas, or malignancies of the epithelium, account for 80–90% of all cases of cancer and typically attack the organs or glands that secrete, including the bladder, prostate, lung, breast, and colon. Squamous cell carcinoma or adenocarcinoma may be the kind.

Sarcoma: Bones, tendons, cartilage, muscle, and fat are examples of supporting and connective tissues where sarcomas first appear. Sarcomas include osteosarcoma, chondrosarcoma, leiomyosarcoma, and others.

Myeloma: The overproduction of immature white blood cells is associated with myeloma, a disease that starts in the bone marrow plasma cells. Leukemias that are granulocytic or myelogenous, lymphatic, lymphocytic, or lymphoblastic etc.,

Lymphoma: Known colloquially as "solid cancers," lymph nodes are developed by lymphatic system

glands that are involved in the creation of lymphocytes and the purification of body fluids.

Mixed types: Adenosquamous carcinoma, mixed mesodermal tumour, carcinosarcoma, and teratocarcinoma are examples of mixed forms[3].

**Diagnosis of cancer**

Biopsy

Histopathological studies of tissue

Radiography techniques

Computed Tomography (CT)

Magnetic Resonance Imaging (MRI)

Molecular biology techniques

Finding new biomarkers for cancer early detection is unavoidable. Digital PCR, NextGen sequencing, and cfDNA technology are examples of modern genomic technologies that have recently demonstrated significant promise. Other examples include transcriptome analysis and data on methylation and copy number variants from the Cancer Genome Atlas. Because of its favorable physical characteristics, stability, biocompatibility, and magnetic susceptibility, among other qualities, magnetic nanoparticles are used in in vivo cancer diagnostics[3].

**Personalized medicine in cancer**

In personalized medicine, certain tumour features are measured and used to determine the best treatment plan for each patient, with the goal of effectively treating their condition and avoiding recurrence. Many people acquire resistant malignancies and either recur later on or do not respond to initial treatment. Thus, the scientific community moved away from the "one treatment fits all" mentality and understood the need for a tailored medicine strategy. Worldwide, breast cancer is still the most frequent type of cancer. The role of the oestrogen receptor (ER) in breast cancer was one of the most significant findings in the field of cancer research. Tamoxifen, the first endocrine therapy sold commercially, was accessible. Until endocrine therapy, ovarian oblation was the method used by George Beatson in 1896 to stop the use of oestrogen as a treatment for breast cancer. Not every woman saw a discernible improvement. The first molecular test for breast cancer was ultimately made possible by the discovery of the ER.

Endocrine therapy would benefit the women who had detectable ER in their diagnostic biopsies, whereas it would not benefit the others. Not only do all ER-negative patients not benefit from endocrine therapy, but between 30 and 50 percent of ER-positive patients will either relapse or acquire primary resistance while receiving adjuvant medication to avoid relapse[4].

**Cancer treatment**

Currently, surgery, radiation therapy (RT), chemotherapy, and targeted therapy are widely accepted methods for cancer treatment. Traditionally, surgical removal was the primary approach for managing malignant tumors, followed by chemotherapy and radiation therapy. Before the advent of anesthesia and antiseptic techniques, surgery was the most conventional form of cancer treatment, and it remains a key element of cancer care today. Advances such as radiography and CT scanning have enabled precise tumor localization, leading to the surgical removal of tumors with various malignancies. Minimally invasive techniques like laparoscopic, endoscopic, and robotic surgeries have emerged, along with innovative procedures such as high-intensity focused ultrasound (HIFU), microwave ablation, cryosurgery, and radiofrequency ablation.

Radiation therapy (RT) has also become a cornerstone of cancer treatment. RT employs ionizing radiation, including X-rays, gamma rays, and particle radiation, to destroy cancer cells. Brachytherapy, for example, uses radiation emitted from radioactive isotopes like radium-223. RT is often combined with surgery as an adjuvant therapy to improve outcomes and lower the risk of recurrence. However, RT can lead to significant side effects, such as damage to surrounding healthy tissues.

Chemotherapy is the primary treatment for advanced or metastatic cancers, aiming to eliminate tumor cells while minimizing harm to normal tissues. Cisplatin, a well-known platinum-based chemotherapy agent, is used to treat cancers such as testicular, ovarian, lung, bladder, and head and neck cancers.

Cisplatin works by forming crosslinks with purine nucleotides in DNA, leading to DNA damage and apoptosis of cancer cells. To improve efficacy and reduce toxicity, cisplatin is often combined with other drugs such as gemcitabine, doxorubicin, vitamin D, bevacizumab, and vinblastine. Different cancer types are treated using specific drug combinations: methotrexate, vincristine, doxorubicin, and cisplatin for bladder cancer; cyclophosphamide, vincristine, and doxorubicin for lung cancer; and epirubicin, cisplatin, and 5-fluorouracil for stomach cancer. Combining chemotherapy with radiation therapy has proven to be more effective than using either treatment alone.

In recent years, the approach to cancer treatment has shifted from traditional cytotoxic drugs toward targeted therapies. Targeted therapy focuses on specific proteins involved in cancer development, making it a more tolerable option for cancers such as leukemia, lung, colorectal, and breast cancers. Molecular pathways like HER2/neu and vascular endothelial growth factor (VEGF) are often targeted, particularly in solid tumors. Targeted therapies include monoclonal antibodies and small molecule inhibitors. Monoclonal antibodies, with a large molecular weight (~150,000 Da), are water-soluble and specifically target extracellular components, such as receptor-binding domains and ligands. In contrast, small molecule inhibitors (~500 Da) are small enough to penetrate cells and disrupt intracellular signaling pathways. Despite their efficacy, these therapies can cause severe side effects, including proteinuria, thrombosis, heart failure, hypertension, and acneiform rash [2].

**Problems associated with cancer treatment**

Chemoresistance causes the disease to worsen and raises the death rate from cancer. Moreover, the emergence of "multidrug resistance (MDR)" in cancer cells, which is resistance to chemotherapeutic drugs. Multiple drug resistance (MDR) mechanisms include decreased absorption of water-soluble medications, improved repair of DNA damage, increased efflux of hydrophobic pharmaceuticals, inhibition of apoptosis, changes in drug metabolism, and cell cycle disruption [2].

**The power of multi omics technologies: a new era in personalized medicine:**

The field of omics sciences has transformed translational medicine in the past ten years. The term "omics" (X-omics) refers to high-throughput experimental methods that offer the techniques that utilize big data to track the progression of diseases extensively at the molecular level. One of the biggest advances in the field of omics research to far was the release of the whole human genome sequence. A comprehensive range of biological sciences, including transcriptomics, proteomics, metabolomics, and genomics, are included in the suffix -ome-, which is derived from the word "chromosome." The "omics" method suggests a large range of molecules for examination. Omics sciences, which are based on high-throughput analytical techniques, have shown to be more precise and efficient than traditional molecular approaches, saving time and improving understanding of the genetic makeup of prevalent illnesses. Precision medicine can greatly benefit from the neologism known as "multi-omics" (X-omics).

With the use of precision medicine (PM), clinical techniques that provide accurate prevention, diagnosis, and treatment may be changed. Precision medicine is become more appealing and useful as Next Generation Sequencing (NGS) and RNA sequencing (RNASeq) technologies advance.

These advancements have enormous potential for the field of medicine. A deeper comprehension of the pathophysiology of the illness will result from the integration of metabolomics, genomics, transcriptomics, proteomics, and epigenomics research. Therefore, this point of view is seen as a significant advancement in precision medicine. In essence, multi-omics data are useful for drug discovery if they reveal novel targets for drugs or disease indicators that are linked to treatment outcomes or the course of the disease[5].

**Genomics:**

The systematic study of an organism's entire genome and its activities is known as genomics. There are two types of genomics: structural and functional. Genomics serves as a foundation for other therapeutic omics approaches and is relatively quick and easy to use. Genomics is the most important form of omics technique among them all. A useful framework for gene mapping and the identification of genetic variations causing

single-gene and multifactorial disorders was made possible by genomics research.

Three billion DNA base pairs (bp) make up the whole haploid human genome, which codes for about 20,000 genes. Exomes, another name for these protein-coding sections of the genome, comprise 1%–2% of the total, with the rest portion containing structural importance. Less than 1% of the human genome sequence varies across individuals, and an organism's genome is generally consistent throughout time aside from genetic variants. Precision medicine is centered on genomic medicine. In the field of genomics, Whole Exome Sequencing (WES) and Genome Wide Association Studies (GWAS) are novel techniques for comprehending linked variations of prevalent multifactorial disorders. Scientific progress in genomics has the potential to transform public health and medicine [5].

**Transcriptomics:**

Using advanced techniques such as microarray analysis, transcriptomics is the study of the transcriptome, which is the whole collection of RNA transcripts generated by the genome in a particular cell under certain conditions. Genes that are differently expressed in various cell groups or in response to various treatments can be identified using transcriptome comparison. Transcriptomes assess RNA levels across the whole genome in a quantitative and qualitative manner. The primary regulating stage of gene expression is transcription. Because transcriptomics may reflect the potential of genome expression, it has emerged as an exciting area of molecular sciences study in the post-genome age. In the 1990s, the word "transcriptome" was coined. The term "transcriptome" refers to the whole collection of ribonucleic acid (RNA) transcripts, which includes the transfer RNAs (tRNA), ribosomal RNAs (rRNA), and classical messenger RNAs (mRNA) that are encoded by a particular cell type or tissue's genome. Through the ribosome machinery (which includes ribosomal proteins and rRNA), the mRNA sequence encodes proteins. Non-coding RNAs (ncRNAs) are RNAs that have been identified as existing but do not encode proteins. These non-coding RNAs (ncRNAs) include microRNAs and long ncRNAs. They have been shown in more recent research to have regulatory roles in protein function and gene expression. Thus, in many biological processes, total RNAs play crucial roles in the regulation and expression of genes. Only 2% of the transcribed RNAs from the human genome come from the coding region, with the remaining 90% coming from other parts of the genome. Transcriptome analysis enables us to determine the genome's transcriptional expression following the completion of the Human Genome Project. The analysis of transcriptome data will ultimately provide some direction for the prediction and prevention of disease by illuminating the regulatory network of biological processes [5].

**Epigenomics:**

The epigenome is defined by chemical changes to nuclear RNA, histones, non-histone chromatin proteins, and DNA. Without changing the base sequence, these modifications impact gene expression. Generally speaking, structural adaptation of chromosomal regions is referred to as epigenetics. These epigenetic modifications might be inherited during cell division or be temporary. They result from environmental exposures throughout the course of a lifetime at different developmental stages. The four primary players in the epigenetic apparatus are chromatin condensation, production and processing of microRNA (miRNA), histone modification, and DNA methylation. Epigenomic changes are depend on temporal and geographical variables. As a result, they may react differently depending on the tissue to environmental or illness-related modifiers. These alterations may have an impact on cell homeostasis by controlling gene expression. It has been claimed that the epigenetic composition of several cell types and tissues has been thoroughly mapped. Various approaches have been devised to evaluate the epigenome. Histone modification ChIP-seq (chromatin immunoprecipitation sequencing) is one epigenomics technique that focuses on chromatin structure and helps identify DNA-associated protein-binding sites. DNase-seq uses HTS and DNase I chromatin digestion to find genomic regulatory areas. The mapping of chromatin accessibility across the genome is made possible by DNA methylation and ATAC-seq, an assay for transposase-accessible chromatin sequencing. Highly-density lipoprotein (HDL) particle metabolism may vary across individuals

depending on epigenome alterations, according to recent epigenome-wide research [6].

**Proteomics:**

Proteomics is the large-scale study of the function, structure, and physiological importance of the entire proteome, which is the total amount of proteins from an organism, tissue, cell, or biofluid. Identifying and classifying every protein in a biological system as well as the relationships among them is known as proteomics.

The information obtained from proteomic measurements includes protein-protein interactions, protein production and degradation rates, and information on protein structure, concentrations, and cellular locations. Identifying patterns of illness and comprehending how the proteome evolves during various biological activities are made possible by this knowledge. PPM may benefit from information on post-transcriptional alterations or the quantity of proteins in a tissue for the diagnosis, advancement, and management of the illness. The primary method for gathering proteomic data during the previous 20 years has been mass spectrometry (MS), specifically for measuring protein expression, locating protein modification sites, and looking into protein–protein interactions. Top-down and bottom-up proteomics are the two main approaches used to produce proteome data.

**Metabolomics:**

Metabolomics, also referred to as metabolic profiling, has long been applied in practice. Historically, the taste, odor, and color of urine have been used to identify various medical conditions. The metabolome refers to the collection of metabolites within a biological system, fluid, cell, or tissue at a specific moment in time. Metabolomics, an "omics" approach, focuses on describing the biochemical nature of metabolites and understanding how their variations are influenced by internal (genetic) and external (environmental) factors. This method has been widely utilized in disease research.

The primary analytical techniques in metabolomics are mass spectrometry (MS) and nuclear magnetic resonance (NMR), with MS already being integrated into clinical laboratories. Advances in analytical technologies, such as ion mobility spectrometry (IMS) and high-resolution mass spectrometry, have expanded the coverage of the metabolome. Metabolomics is particularly recommended for assessing inborn errors of metabolism (IEM), as these disorders result from disruptions in metabolic pathways. Quantitative metabolic profiling of multiple metabolites in biological fluids is critical for the future diagnosis and management of IEM. Globally, MS-based metabolomics has been extensively employed in national newborn screening programs for IEM, with untargeted approaches showing promising results.

Recently, Miller et al. introduced an integrated approach for IEM evaluation that combines targeted and untargeted metabolomics, providing practical and valuable diagnostic information. Using plasma metabolite assays and metabolomics, they successfully identified 21 IEM disorders. Similarly, Aygen et al. conducted a multi-center clinical study across 14 centers in Turkey utilizing NMR-based platforms. Urine samples from 989 neonates were analyzed, identifying specific metabolites that differed between patients and healthy controls. Predictive models were developed, and a reference NMR database was established. For a comprehensive understanding of metabolomics' potential in IEM studies, including its underlying technologies, advantages, limitations, and applications, a recent review provides an in-depth exploration [6].

**ct-DNA**

Cell free DNA (cfDNA) is also known as circulating tumour DNA. It is made up of fragments of tumour DNA that are released into the bloodstream by primary tumour or metastatic cells. These fragments are about 166,332 or 498 base pairs long and display characteristics unique to tumours, such as point mutation, chromosomal rearrangement, copy number variation (CNV), and DNA methylation. The active secretion of cell microvesicles, which results in the apoptosis or necrosis of tumour cells with a half-life of around 114 minutes, releases these chemicals into the circulation. There is great promise for circulating cell-free tumour DNA (ctDNA) as an oncology biomarker.

After curative therapy, the presence of limited residual illnesses is indicated by the detection of ctDNA in cancer patients, and this finding is believed to be a prognostic sign of relapse.

Applications for ctDNA were created using tests that target mutation(s) that were previously found by genomically characterizing each patient's tumour—a biopsy of which might not be available. The de novo detection of somatic mutations, especially those that have been demonstrated to be predictive of response or resistance to targeted therapy, is another possible application of ctDNA that could replace solid tissue biopsies as a source of tumour DNA. Because ctDNA collection techniques have improved in sensitivity, they can be useful in liquid biopsies. Because the ctDNA is at low leels compared to cfDNA, very sensitive technologies are needed to identify it. A particular mutation found in cancer aids in separating ctDNAs from healthy cfDNAs. Currently, uncommon mutations in cfDNAs with allele fractions as low as 0.001% in a wild-type background can be found thanks to digital PCR. Genomic data determines modifications for focused treatment. Targeted therapies include activating EGFR mutation for EGFR tyrosine kinase inhibitors (TKIs) in non-small lung cancer (NSCLC) and amplifying human epidermal growth factor receptor 2 (HER2) for HER2 antibody in breast and gastric cancer. One benefit of ctDNA testing over tissue biopsies is that it is less intrusive and enables repeated blood collection. Since ctDNAs originate from numerous tumour sites, they are superior diagnostic samples in a metastatic scenario than single-site biopsied tissue. The half-lives of ctDNAs are perfect indicators of the response to treatment and the appearance of secondary mutations linked to treatment resistance, exposing heterogeneity and clonal evolution in the course of cancer. For this reason, ctDNA testing is a tempting method for genotyping individual tumours[7].

**Use of ctDNAs in cancer management**

Nearly 50% of patients with advanced non-small cell lung cancer (NSCLC) exhibit EGFR mutations, which are common in this type of cancer. The key activating EGFR mutations include exon 19 deletions and the L858R point mutation in exon 21, which are critical for selecting EGFR tyrosine kinase inhibitors (TKIs) and serve as significant predictive markers for EGFR TKI sensitivity. First-generation TKIs, such as erlotinib and gefitinib, bind reversibly to the tyrosine kinase domain, whereas second-generation TKIs, like afatinib, form covalent bonds with the target.

In terms of specificity, ctDNA testing for detecting activating EGFR mutations in NSCLC shows strong concordance with tissue biopsy results. Monitoring active EGFR mutations is considered a potential prognostic indicator for EGFR TKI efficacy. However, tissue biopsies often yield insufficient or poor-quality material for genotyping, particularly at the time of disease progression. In real-world settings, ctDNA testing has demonstrated high performance in identifying EGFR mutations.

Acquired resistance to first- and second-generation EGFR TKIs is frequently associated with the replacement of methionine for threonine at amino acid position 790 in exon 20 of the EGFR gene (T790 mutation). This alteration reduces TKI binding to the ATP-binding pocket of EGFR, thereby decreasing drug responsiveness. Mutations in T790 account for approximately 50–60% of acquired resistance mechanisms in patients receiving EGFR TKI therapy

. The low abundance of T790M mutations in blood prior to the start of treatment has made ctDNA testing difficult to perform. However, it has been documented that T790M mutations are discovered during treatment by ctDNA testing. Third-generation TKIs, including osimertinib and rociletinib, target T790M mutations as well as activating EGFR mutations. A new major driver of osimertinib resistance was found to be the C797S mutation, whereas the L789I mutation was linked to rociletinib resistance. These investigations demonstrated that ctDNA testing might identify resistance to treatments and clonal evolution, indicating that ctDNA testing for lung cancer therapy will likely be used more often in clinical settings soon[8].

**Organoids**

Preclinical models in cancer have typically depended on mouse models and two-dimensional cell culture [9]. The inherent limitations of current animal models and two-dimensional cancer cultures may be the cause of the failure of new cancer therapies. Genetic drift that happens during long-term culture also causes tumour-specific heterogeneity to disappear in two-dimensional cultures. Organoids are artificially

created three-dimensional (3D) structures derived from stem cells that mimic a primary organ [10]. Organoids are composed of many cell types produced from native tissues or stem cells taken from mice, patients, or other sources. Organoids provide a more realistic depiction of this dynamic niche, and there is evidence that patient-derived tumour organoids can share essentially identical genetic and functional characteristics with their original specimens. Weeber and Collegues, who successfully reported 90% preservation of somatic mutation and DNA copy number profile between the generated tumour organoids and patient original biopsies, can be credited with the original success of tumour organoid culture. This was accomplished in 14 patients with metastatic colorectal cancer, encompassing 1,977 cancer-related genes. Understanding organoids and/or spheroids through the use of cell cultures, including ES cells, induced pluripotent stem (iPS) cells, adult stem cells, and primary cultured cells originating from human tissues, has advanced dramatically in recent years. Comparing in vitro organoids to traditional models, there are numerous benefits. Initially, the growth and morphological characteristics of an organoid in 3D culture can be mimicked in vivo. Second, without any genetic or physiological alterations, an organoid generated for a particular organ can sustainably retain its pure in vivo features even after numerous generations. Third, it is simple to create gastrointestinal (GI) organoid models by separating epithelial crypts from a human GI biopsy or a mouse GI tract. In about ten days, the crypts will grow into a crypt-villus structure. Currently, organoids are grown utilizing animal-derived hydrogels, such as collagen and matrigel, to support organoid shape and a strong extracellular matrix to enable cell adhesion and proliferation. To create intestinal organoids, for instance, Lgr5+ stem cells or crypts were coated in Matrigel and cultivated in a mixture containing noggin, R-Spondin, and EGF. Histological examination revealed that the parental tissues of HCC-derived organoids were pseudo glandular rosettes, while the organoids produced from CC showed glandular lumens. comparable to the initial patient's clinical morphology, suggesting stability even following a protracted enlargement, and capable of recapitulating the relevant organs' physiological activity. Furthermore, organoids have the ability to simulate brain activity, filtration, and contraction processes. The intricate and interrelated process of organogenesis is facilitated by interactions across borders. The availability of embryonic or fetal tissues and ethical considerations have hampered research on it. Organoids have aided in the demonstration of how the start of multi-organ structures is coordinated by individual surrounding tissues. Organoids play a critical role in customized therapy and cancer research. In theory, organoids enable the enlargement of samples obtained from the tumour tissues of specific patients suffering from various types of carcinomas. Through the introduction of oncogenic mutations, CRISPR-based genetic modifications enable the manufacture of non-cancerous organoids, opening up new avenues for the study of tumour genesis and progression—a crucial area of research in personalized medicine and cancer research. In this study, we outlined the current uses of organoids for personalized medicine and examined the numerous applications of tumour organoids employing tumour biobanks and known genetic alteration of organoids. Organoids therefore have enormous potential to be important players in the creation of PPM cancer treatments [11].

**Monoclonal antibodies:**

Monoclonal antibodies are lab-engineered proteins designed to mimic the body's natural antibodies, which help the immune system recognize and eliminate pathogens such as bacteria and viruses. Like naturally occurring antibodies, monoclonal antibodies are highly specific and can recognize particular targets. Many monoclonal antibodies are utilized in cancer treatment as a form of targeted therapy, specifically designed to interact with certain molecules or proteins.

Some monoclonal antibodies also function as immunotherapy by directing the immune system to recognize and destroy cancer cells. For example, certain monoclonal antibodies tag cancer cells, making them more visible to the immune system. Rituximab is one such drug; it binds to a protein called CD20 on the surface of B cells (a type of white blood cell) and cancer cells, prompting the immune system to eliminate them.

Other monoclonal antibodies enhance the immune response by bringing T cells closer to cancer cells. For instance, blinatumomab (Blincyto®) is a monoclonal antibody that connects CD3, a protein on T cells, with CD19, a protein found on leukemia cells. This dual binding helps activate T cells to attack and destroy the cancer cells effectively.Among the several molecular-based approaches (such as small compounds, monoclonal antibodies, and vaccines), monoclonal antibodies (mAbs) have shown great promise for cancer therapies because of their high selectivity, low cytotoxicity, and scalability90–92. Monoclonal antibodies (mAbs) are Y-shaped proteins that can attach to a particular molecular target. They can be made synthetically or by B lymphocytes. mAbs are among the immunotherapies with the greatest rate of growth; over 22 oncology-related mAb-based medications have received FDA approval. Compared to conventional treatments (such as surgery, radiation, and/or chemotherapy), monoclonal antibodies (mAbs)-based therapies are more likely to be successful because they target specific molecular markers that a certain tumour expresses. For example, human epidermal growth factor receptor 2 (HER2) positive breast tumours benefit more clinically from HER2-targeted monoclonal antibodies (mAbs). Furthermore, KRAS wild-type colorectal cancers are frequently treated with epidermal growth factor receptor (EGFR) monoclonal antibodies (mAbs); however, only about half of treated patients have seen any clinical benefit . It's interesting to note that cancers can even change and develop primary resistance to the targeted molecule95 in certain circumstances. The final decision on the mAb (or combination of mAbs) will frequently depend on the kind and subtype of the malignancy as well as the overall effectiveness and side effects from additional clinical and preclinical research[12].

**Immune check point inhibitors:**

Substantial advancements have been made recently, especially in the areas of cancer therapies and customized medicine. Utilizing immune system components to combat tumour cells, immunotherapy, such as immune checkpoint inhibitors, is one kind of cancer treatment Immune system checkpoints are a typical component [13]. The role of immune checkpoints is to prevent the immune system from overreacting and attacking the body's healthy cells. These checkpoints are regulated by specific proteins on the surface of immune cells, particularly T cells. When T cell proteins bind to partner proteins on other cells, such as tumor cells, immune checkpoints are activated. This interaction sends an "off" signal to T cells, which can suppress the immune response and allow the tumor to evade destruction by the immune system.

Immune checkpoint inhibitors, a class of immunotherapy drugs, work by blocking the interaction between checkpoint proteins and their partner proteins. By preventing this binding, the "off" signal is disrupted, allowing T cells to remain active and initiate cell death in the cancer cells [14].

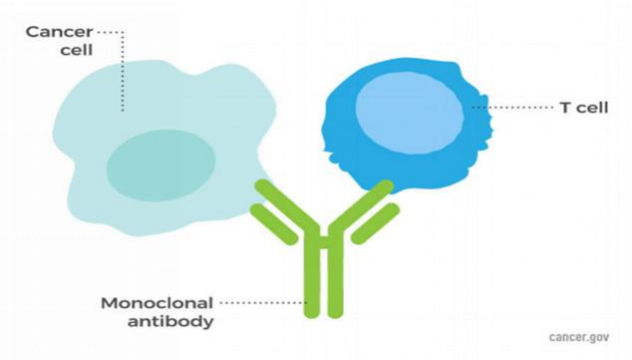


**Figure 1 A Schematic representation showing the interaction between a cancer cell and a T-cell facilitated by a monoclonal antibody**

**Mechanism:**

Cytotoxic T lymphocytes (CTLs) play a central role in the immune response against tumors. For CTLs to recognize and eliminate cancer cells effectively, two activation signals are required during the initial "priming" phase of the immune response, which primarily occurs in the lymph nodes.

**First Signal**:

CD8+ T cells recognize antigenic peptides presented by major histocompatibility complex (MHC) class I molecules on the surface of cancer cells using their T cell receptors (TCRs).

**Second Signal**:

A costimulatory signal occurs through the interaction of CD28 on T cells with B7-1/B7-2 ligands expressed on antigen-presenting cells

(APCs). This costimulatory interaction triggers T cell activation and differentiation.

In addition to these signals, a

**third signal**

regulates T cell tolerance and prevents uncontrolled activation or cell death. During this phase, T cells express surface coinhibitory receptors, also known as immune checkpoints, to negatively regulate the immune response:

**Programmed cell death-1 (PD-1)**

**Cytotoxic T lymphocyte-associated protein 4 (CTLA-4)**

The binding of CTLA-4 to B7-1/B7-2 ligands on APCs counteracts the stimulatory effects of CD28, thereby inhibiting T cell activation. Similarly, when PD-1 on T cells interacts with PD-L1 on tumor cells, it suppresses T cell activation and function, enabling tumors to evade the immune response.Immune checkpoint inhibitors (ICIs), such as anti-CTLA-4, anti-PD-1, and anti-PD-L1 therapies, disrupt these inhibitory interactions. By binding to these coinhibitory receptors, ICIs block the suppression of T cell activity, effectively reactivating the immune system's ability to attack and destroy tumor cells [15].

**Table 3 FDA-Approved Immune Checkpoint Inhibitors and Their Indications**

| Drugs | Target | FDA- approved indications |
|---|---|---|
| Nivolumab | PD-1 | Stage 3B or 4 squamous NSCLC |
| Pembrolizumab | PD-1 | Stage4 non squamous and squamous NSCLC |
| Atezolizumab | PD-L1 | Metastatic cutaneous squamous cell carcinoma |
| Cemiplimab | PD-1 | Stage 3 or 4 malignant melanoma |
| Ipilimumab | CTLA-4 | Metastatic merkel cell carcinoma |
| Avelumab | PD-L1 | Stage 3 NSCLC |
| Durvalumab | PD-L1 | Non squamous NSCLC |

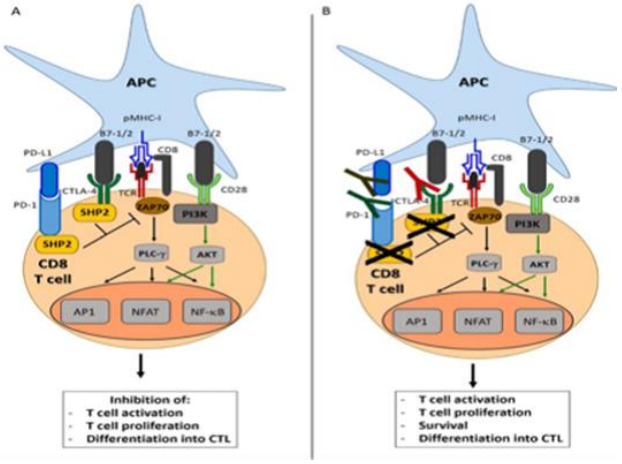


**Figure 2 Rationale for the use of immune checkpoint inhibitors in cancer therapy**

(A) Engagement of CTLA-4 or PD-1 triggers signals that inhibits activation signaling pathways in the Tcell, leading to T cell anergy or exhaustion, thus inhibiting the T cell immune response. (B) The administration of CTLA-4, PD-1 or PD-L1 blocking antibodies releases the brakes on the T cell-mediated antitumour immune response and allows for the generation of functional tumour-specific CTLs capable of killing tumour cells. Ag: Antigen; AP1: Activator protein 1; APC: Antigenpresenting cell; CTLA-4: Cytotoxic T lymphocyte antigen 4; NFAT: Nuclear factor of activated T cells; NF-kB: Nuclear factor kappa B; PD-1: Programmed cell death protein 1; PD-L1: Programmed death ligand 1; PI3K: Phosphoinositide 3-kinase; PLC-g: Phospholipase C gamma; pMHC-I: peptide-MHC class I complex; SHP2: Src homology phosphatase 2; TCR: T cell receptor; ZAP70: Zeta-chain-associated protein kinase [15].

**Cancer vaccines:**

Immunotherapy, in the form of cancer treatment vaccines, strengthens the body's ability to fight cancer. Unlike preventive vaccines, treatment vaccines are administered to individuals who already have cancer. They target cancer cells rather than the agents that cause cancer. The approach is based on the principle that cancer cells express molecules known as tumor-associated antigens, which are either absent or found in very low concentrations on normal cells. These vaccines help the immune system recognize and respond to these antigens, enabling it to destroy the cancer cells that harbor them.

There are three main strategies for developing cancer treatment vaccines:

**Using the Patient's Own Tumor Cells**:

These vaccines are personalized to trigger an immune response against unique characteristics specific to an individual's cancer.

**Using Tumor-Associated Antigens**:

These antigens are found on cancer cells in many patients with a specific type of cancer. Vaccines targeting these shared antigens can potentially benefit any patient whose cancer expresses the antigen. Such vaccines are still under investigation.

**Using Dendritic Cells**:

These vaccines are created using the patient's dendritic cells, a type of immune cell. Dendritic cell vaccines stimulate the immune system to respond to tumor-specific antigens. The only FDA-approved dendritic cell vaccine is sipuleucel-T, which is used to treat certain men with advanced prostate cancer.Another form of cancer treatment, known as oncolytic virus therapy, is sometimes categorized as a cancer treatment vaccine. This therapy uses oncolytic viruses—viruses that selectively infect and break down cancer cells without harming normal cells. The first FDA-approved oncolytic virus therapy is talimogene laherparepvec (T-VEC or Imlygic), derived from herpes simplex virus type 1. While T-VEC can infect both cancerous and normal cells, normal cells can eliminate the virus, whereas cancer cells cannot.

T-VEC is administered directly into the tumor. Once inside, the virus replicates, causing the cancer cells to burst and die. This process releases additional viral particles and other substances, which can stimulate an immune response against cancer cells throughout the body [16].

**Cancer vaccines in personalized medicines**

Therapeutic cancer vaccines aim to induce an adaptive immune response against tumour antigens, leading to tumour regression. The efficacy of cancer vaccines depends on four factors [17] :

The optimized delivery of dendritic cells

Activation of effector T cells

Trafficking activated T cells into tumour microenvironment

Induction of durable memory response

**Target antigens for therapeutic cancer vaccine** :

Tumour associated antigens, or TAAs, have historically been thought of as targets for therapeutic cancer vaccinations. Self antigens known as TAA are expressed on tumour cells alone. On the other hand, the tumour response of high affinity T lymphocytes against TAA is impeded by the presence of central tolerance. Conversely, oncoviral antigens, private neoantigens, and shared neoantigens are examples of tumour-specific antigens (TSA). High affinity T cells are adept in identifying TSA, and central tolerance has a significant impact on them as well. Research has demonstrated the importance of tumour neoantigens, which are encoded by altered genes unique to tumours, in therapeutic immunization. Tumour neoantigens resulting from somatic mutations have been systematically discovered thanks to recent advances in gathering omics data using NGS. Due to its specificity, a variety of tumour neoepitopes—peptides that result from somatic mutations and are identifiable as distinct from one another across individuals—can exist. The creation of tailored cancer vaccines is facilitated by the identification of these possible tumour neoantigens for individual patients. The quantity of gene mutations present in cancer cells determines the tumour mutation burden (TMB). It demonstrates a substantial relationship with the efficacy of vaccines based on neoantigens. Neo antigen-based vaccination treatment may be a suitable option for patients with elevated TMB. Vaccines based on TAA can improve the treatment of patients with low TMB [17].

**CAR -T cell therapy:**

" A living drug ". This kind of treatment involves genetically modifying a patient's T cells, which are immune system cells, in a lab so they will target cancer cells. Blood from a patient is used to extract T lymphocytes. The T cells in the lab are then given the gene for a unique receptor that attaches to a specific protein on the cancer cells of the patient. The unique receptor known as the CAR (chimeric antigen receptor). A sizable quantity of CAR T cells are grown in a lab and infused into the patient.

chimeric antigen receptor. T cell therapy is being researched for the treatment of additional cancer types and is now being utilized to treat some blood malignancies [18] .


**Figure 3 Simplifies the relationship as: T Cell + CAR = CAR T Cell**

**Table 4 CAR T- cell therapies Targeting Specific Antigens for Various Diseases:**

| Generic name | Target antigen | Targeted disease |
|---|---|---|
| Tisagenlecleucel | CD19 | B cell acute lymphoblastic leukemia<br>B cell non Hodgkin lymphoma |
| Brexucabtagene autoleucel | CD19 | Mantle cell lymphoma<br>B cell acute lymphoblastic leukemia |
| Axicabtagene ciloleucel | CD19 | B cell non Hodgkin lymphoma<br>Follicular lymphoma |
| Lisocabtagene maraleucel | CD19 | B cell non Hodgkin lymphoma |
| Idecabtagene vicleucel | BCMA | Multiple myeloma |
| Ciltacabtagene autoleucel | BCMA | Multiple myeloma |

The extracellular domain (transmembrane domain and intracellular domain) of chimeric antigen receptors often binds to a particular antigen on tumour cells, triggering T cell activation to target the tumour cells. Tisagenlecleucel is a genetically engineered autologous T cell immunotherapy that targets CD19-directed cluster of differentiation. The treatment entails reprogramming the patient's own T cells using CAR to recognize and eradicate CD19-expressing cells, both malignant and normal. CAR identifies and attaches to cells that express CD19. The CD3 zeta component of CAR is in charge of starting the antitumour and T cell activation processes. Tisagenelecleucel's growth and persistence are enhanced by 41BB. Following anti-CD19 CAR T cell-CD19 target cell, cells become activated and secrete chemokines and inflammatory cytokines. Tumour cells die as a result of this [19].

## Conclusion

You cannot cure until you know you. Precision oncology seeks to identify genetic, epigenetic and transcriptomic inter and intra tumoural changes and match cancer therapy based on individual's distinctive cancer biology. This translational paradigm is dependent on the co-ordination between clinicians and researchers, both use their expertise to evaluate potential drug therapies using patient-specific cancer modelling system.

## Author Contribution

All authors made substantial contributions to the conception, design, acquisition, analysis, or interpretation of data for the work. They were involved in drafting the manuscript or revising it critically for important intellectual content. All authors gave final approval of the version to be published and agreed to be accountable for all aspects of the work, ensuring its accuracy and integrity.

## Conflict of Interest

The authors declare no conflict of interest, financial or otherwise.

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