Advances in Individualized Therapeutics Design in Cancer

Wei Zhnag [1, 2], Shamsuddin Sultan Khan[1*], John Catanzaro[1]

Abstract

Cancer is a complex and heterogeneous disease that requires personalized treatment approaches to optimize patient outcomes. Individualized therapeutic design, which involves tailoring cancer treatment based on patient-specific factors, has emerged as a promising strategy for improving cancer care. In this review article, we provide an overview of conventional cancer treatment methods and their limitations, as well as the concept and importance of individualized therapeutic design in cancer treatment. We discuss the various factors influencing individualized therapeutic design in cancer treatment, such as genetic, epigenetic, environmental, and lifestyle factors, and the techniques for implementing individualized therapeutic design, including molecular profiling, imaging, and data analysis techniques. We also present case studies and clinical trials that demonstrate the effectiveness of individualized therapeutic design in cancer treatment. However, challenges and limitations to the implementation of individualized therapeutic design exist, including the cost and accessibility of personalized medicine, ethical considerations, and disease heterogeneity.An advanced immunotherapeutic strategy based on precision medicine concepts is known as precision-based immuno-molecular augmentation. To enhance therapeutic outcomes, this strategy entails customizing therapies based on individual genetic and biological traits. Targeting specific molecular markers on cells, precision-based immuno-molecular augmentation enables the production of highly specific immunomodulatory medicines, including gene treatments, monoclonal antibodies, and tailored vaccinations. The aim is to optimize the immune response of the body in a highly focused manner, avoiding side effects and maximizing efficacy against certain threats. Hence, a comparative analysis of the existing such therapies was also performed. We conclude by highlighting the potential use of precision-based immuno-molecular augmentation Prediction tools for individualized therapeutic design in cancer treatment and providing recommendations for future research and clinical practice. Overall, individualized therapeutic design using precision-based immuno-molecular augmentation has the potential to revolutionize cancer care and improve patient outcomes.

Keywords: Individualized, targeted immunotherapy, peptide, Precision medicine, Edited Sequences, ITI-PES, precision-based immuno-molecular augmentation, Inflammation, Cancer, Autoimmune

Significance | The study emphasizes the transformative potential of individualized therapeutic design in cancer care, highlighting improved outcomes by tailoring treatments to unique patient profiles.

*Correspondence. Shamsuddin Sultan Khan, The University of Texas Health Science Center at Houston (UTHealth), TX 77021 USA

Editor Mohammed Khadeer Ahmed Basheer, And accepted by the Editorial Board Feb 01, 2023 (received for review Jan 02, 2023)

Introduction

Cancer is a complex and heterogeneous disease that requires personalized treatment approaches to optimize patient outcomes (Abbas & Rehman, 2018). Conventional cancer treatment methods include chemotherapy, radiation therapy, and surgery (Abbas & Rehman, 2018). While these treatments can be effective, they have limitations and may not be suitable for all patients. For example, chemotherapy and radiation therapy can have significant side effects, and surgery may not be possible for some patients (Dienstmann et al., 2017). Despite these limitations, conventional

Author Affiliation.
[1] Neo7Bioscience Inc, 539 W Commerce Street #2886 Dallas TX 75208 USA
[2] The University of Texas Health Science Center at Houston (UTHealth), TX 77021 USA

Please cite this article:
Wei Zhang, Shamsuddin Sultan Khan, John Catanzaro, (2023), Advances in Individualized Therapeutics Design in Cancer, Journal of Precision Biosciences, 5(1), 1-13, 5801

cancer treatment methods remain the cornerstone of cancer therapy, particularly for early-stage cancers. According to Collins and Varmus (2015), the field of precision medicine has brought in a new era of treatment options that are specifically tailored to the tumor features of each patient, owing to the significant revolution that personalized treatments design has undergone regarding cancer. Converging technology advancements, genetic studies, and a better comprehension of cancer biology have propelled this paradigm change.

Chemotherapy involves the use of drugs that target rapidly dividing cancer cells, while radiation therapy uses high-energy rays to destroy cancer cells (Abbas & Rehman, 2018). Surgery involves the removal of cancerous tissue and can be curative for early-stage cancers that have not spread to other parts of the body (Dienstmann et al., 2017).

Personalized cancer therapy is based on genomic profiling, which offers a full understanding of the genetic changes causing tumor growth (Cancer Genome Atlas Research Network, 2013). Prominent investigations, like the Cancer Genome Atlas (TCGA), have clarified the genomic terrains of many cancer types, pinpointing pivotal mutations and modifications that may function as prospective targets for therapeutic interventions. Oncologists may now classify cancers according to their molecular features thanks to comprehensive genetic analysis, which makes treatment choices more accurate and successful.

In recent years, there has been a growing interest in individualized therapeutic design in cancer treatment, which involves tailoring cancer treatment based on patient-specific factors (Turnbull, 2015). This approach has the potential to improve cancer care by providing personalized treatments that are more effective and less toxic than conventional treatment methods. Individualized therapeutic design may involve molecular profiling, imaging, and data analysis techniques to identify patient-specific factors that can guide treatment decisions (Turnbull, 2015)

Another important component of personalized cancer care is immunotherapy, which works by training the immune system to identify and destroy cancer cells (Hodi et al., 2016). Important clinical trials, such as the CheckMate-067 study for metastatic melanoma, have shown that immune checkpoint inhibitors such as ipilimumab and nivolumab are effective. These medicines, especially when used to malignancies with significant mutational loads, have demonstrated extraordinary efficacy in prolonging survival and eliciting lasting responses.

According to Abbosh et al. (2017), liquid biopsies are a versatile tool in the field of customized cancer care. These non-invasive procedures examine blood biomarkers and circulating tumor DNA (ctDNA) to provide current insights on the genetic makeup of the tumor. The TRACERx trial on non-small cell lung cancer serves as an example of how liquid biopsies can be used to identify resistance mechanisms and track the progression of the disease, allowing for early therapy modifications (Abbosh et al., 2017).

The detection of actionable mutations is a critical component of personalized cancer therapy. Targeted medicines such as gefitinib and erlotinib were made possible, for example, by the identification of EGFR mutations in non-small cell lung cancer (NSCLC) (Maemondo et al., 2010). Studies such as the NEJ002 study, which showcased the innovative work of researchers, showed that patients with EGFR-mutant NSCLC treated with these targeted medicines had better results..

Individualized therapeutic design in cancer treatment is important because cancer is a complex disease that varies greatly between patients, requiring tailored treatment approaches to achieve optimal outcomes (Abbas & Rehman, 2018). Conventional cancer treatment methods, such as chemotherapy, radiation therapy, and surgery, are often used in a one-size-fits-all approach that may not be effective for all patients (Dienstmann et al., 2017).

Processing large datasets produced by genetic profiling and clinical data now requires machine learning methods (Ghosh et al., 2017). These algorithms help find possible treatment approaches, forecast medication responses, and evaluate patterns. Research like "Predicting the Future of Drug Combinations," which highlight machine learning's ability to inform treatment choices based on unique patient traits and molecular profiles, demonstrate the synergy between AI and oncology (Ghosh et al., 2017).

According to Conley et al. (2019), clinical trials are essential for confirming the effectiveness of customized therapy approaches. The dedication to matching patients with particular genetic abnormalities to targeted medicines is demonstrated by initiatives like as the NCI-MATCH trial (Flaherty et al., 2020). Through the methodical assessment of molecularly targeted medicines in various cancer types, these studies provide significant insights into the dynamic field of customized cancer treatment.

Individualized therapeutic design involves the use of patient-specific factors to guide treatment decisions, such as molecular profiling, imaging, and data analysis techniques (Turnbull, 2015). By identifying patient-specific factors, such as genetic mutations or tumor heterogeneity, individualized therapeutic design can provide more effective and less toxic treatments for patients (Abbas & Rehman, 2018).

Furthermore, individualized therapeutic design can improve patient outcomes by reducing the risk of treatment-related side effects and toxicity as well as the likelihood of treatment resistance (Dienstmann et al., 2017). This approach can also lead to a more efficient use of healthcare resources by avoiding unnecessary treatments and reducing healthcare costs (Turnbull, 2015). Thus, individualized therapeutic design is an important strategy for improving cancer care by providing personalized treatments that are more effective and less toxic than conventional treatment

methods. This approach has the potential to revolutionize cancer care and improve patient outcomes, and continued research and development is needed to advance personalized cancer treatment further.

The purpose of this review article is to provide an overview of the concept and importance of individualized therapeutic design in cancer treatment. We will discuss the factors influencing individualized therapeutic design in cancer treatment, the techniques for implementing individualized therapeutic design, and examples of individualized therapeutic design in cancer treatment. We will also address the challenges and limitations of the implementation of individualized therapeutic design and provide recommendations for future research and clinical practice.

2. Conventional cancer treatment methods

Conventional cancer treatment methods, such as chemotherapy, radiation therapy, and surgery, have been the mainstay of cancer treatment for many years. Chemotherapy involves the use of cytotoxic drugs to kill cancer cells, while radiation therapy uses high-energy radiation to destroy cancer cells. Surgery involves the removal of cancerous tissue from the body (Institute, 2023).

Chemotherapy, radiation therapy, and surgery are three of the most common conventional treatment methods used in cancer care. Chemotherapy involves the use of cytotoxic drugs to kill cancer cells. These drugs can be administered orally or intravenously and work by targeting cells that divide rapidly, which includes cancer cells (Institute, 2023). While chemotherapy can be effective in treating many types of cancer, it can also cause a range of side effects, including fatigue, nausea, and hair loss (Institute, 2023).

Radiation therapy uses high-energy radiation to destroy cancer cells. This radiation can be delivered externally or internally, and the goal is to damage the DNA of cancer cells so that they are unable to divide and grow (Institute, 2023). Radiation therapy can cause side effects such as fatigue, skin irritation, and damage to healthy tissues surrounding the tumor site (Society, 2023).

Surgery involves the removal of cancerous tissue from the body. This can be done through a variety of techniques, including open surgery and minimally invasive surgery (Institute, 2023). While surgery can be curative for some cancers, it may not be effective for others that have spread to other parts of the body (Society, 2023).

While conventional cancer treatment methods such as chemotherapy, radiation therapy, and surgery have been the mainstay of cancer treatment for many years, they have limitations that need to be addressed (Dienstmann et al., 2017). One of the limitations of conventional treatments is that they often cause treatment-related side effects and toxicity. For example, chemotherapy can cause nausea, vomiting, hair loss, and fatigue, while radiation therapy can cause skin irritation, fatigue, and damage to healthy tissues surrounding the tumor site (Institute, 2023; Society, 2023). Another limitation of conventional treatments is the potential for treatment resistance. Some cancers can develop resistance to chemotherapy and radiation therapy, making these treatments less effective over time (Dienstmann et al., 2017). In addition, conventional treatments are often applied in a one-size-fits-all manner and may not be effective for all patients (Dienstmann et al., 2017).

To overcome these limitations, individualized therapeutic design is being explored as a way to tailor cancer treatment to each patient's unique needs and characteristics (Dienstmann et al., 2017). By personalizing cancer treatment, it may be possible to improve treatment outcomes and reduce treatment-related side effects and toxicity. Despite these limitations, conventional treatments remain an important part of cancer care and are often used in combination with other treatment approaches (Institute, 2023).

Biologic cancer therapy, also known as biological therapy or targeted therapy, refers to a type of treatment that uses substances derived from living organisms, such as cells, proteins, or antibodies, to treat cancer (Dillman, et al 2005). Unlike traditional chemotherapy, which primarily targets rapidly dividing cells, biologic therapies specifically target the specific molecules or pathways involved in the growth and survival of cancer cells.

There are several types of biologic cancer therapies, including:

Monoclonal antibodies (mAbs): Nobel laureates César Milstein & Georges Köhler (1975) was frist to developed mAbs since have revolutionized medicine.These are laboratory-produced antibodies that can recognize and bind to specific proteins on cancer cells. By binding to these proteins, mAbs can either directly interfere with cancer cell growth or stimulate the immune system to attack the cancer cells. The treatment of cancer has been greatly altered by monoclonal antibodies (mAbs). For instance trastuzumab (Herceptin®) is commonly used for HER2-positive breast cancer (Baselga et al,2012), rituximab (Rituxan®) is useful against specific types of lymphomas (Coiffier et al, 2002), pembrolizumab (Keytruda®) targets immune checkpoint proteins to treat a variety of malignancies (Robert et al, 2015).

Immune checkpoint inhibitors: These drugs target proteins that regulate the immune system's response to cancer cells. By blocking these proteins, immune checkpoint inhibitors enhance the immune system's ability to recognize and destroy cancer cells.Pembrolizumab, a well-known illustration of an immune checkpoint inhibitor, targets the programmed cell death protein 1 (PD-1) receptor (Hodi et al,2010). A different class of inhibitors targets CTLA-4, or cytotoxic T-lymphocyte-associated protein 4. One well-known medication in this class is ipilimumab (Ribas et al,2015).

Cancer vaccines: Vaccines can be used to stimulate the immune system to recognize and attack cancer cells. These vaccines may contain tumor antigens or genetic material specific to cancer cells

to trigger an immune response against them.One such example of the effectiveness of public health initiatives is the Human Papillomavirus (HPV) vaccination, which has proved crucial in avoiding infections associated with cervical and other cancers (Palefsky et al,2011) . One important factor in lowering the incidence of liver cancer linked to long-term hepatitis B infection is the hepatitis B vaccination (Chen,2019) . Provenge (Sipuleucel-T), an immunotherapy for metastatic prostate cancer, is a novel strategy that targets certain cancer cells by stimulating the patient's immune system (Kantoff et al,2010).

Adoptive cell transfer: This approach involves modifying a patient's own immune cells, such as T cells, to enhance their ability to recognize and destroy cancer cells. The modified cells are then infused back into the patient to target and kill cancer cells.For example, CAR T-cell therapy has demonstrated impressive efficacy in treating a number of hematologic malignancies, including diffuse large B-cell lymphoma (DLBCL) and acute lymphoblastic leukemia (. Maude et al,2018). In CAR T-cell therapy, T cells are genetically modified to express artificial receptors that identify particular antigens on cancer cells and cause the cells to be specifically destroyed.TIL therapy functions similarly in that it expands T cells that have invaded a patient's tumor outside of the body, isolates them, and then reintroduces them to strengthen the immune system's defense against cancer (Rosenberg et al,2011). In cases of melanoma, this treatment has been successful, with some patients showing long-lasting improvements.

Oncolytic viruses: These are viruses that are engineered to selectively infect and kill cancer cells while sparing normal cells. Oncolytic viruses can directly destroy cancer cells and also stimulate an immune response against the tumor.Oncolytic viruses, such the herpes simplex virus-based T-VEC and the adenovirus-based DNX-2401, have shown encouraging outcomes in clinical trials for melanoma and glioblastoma, respectively (Lang FF et al., 2018; Chesney J et al., 2018). These illustrations highlight the variety of oncolytic viruses and their potential use in treating various cancer types. Current clinical trials, such as those investigating the combination of reovirus with chemotherapy for colorectal cancer, demonstrate the adaptability of oncolytic virotherapy within changing cancer treatment models (Karapanagiotou EM et al., 2012). These cases provide important new information about the expanding significance of oncolytic viruses as a focused and creative strategy in the battle against cancer as research advances.

Signal transduction inhibitors: These drugs target specific molecules or pathways within cancer cells that are essential for their growth and survival. By blocking these molecules or pathways, signal transduction inhibitors can inhibit the growth and spread of cancer cells.

Biologic cancer therapies are often used in combination with other treatments such as surgery, chemotherapy, or radiation therapy to improve their effectiveness. The specific type of biologic therapy used depends on the type and characteristics of the cancer being treated. It's important to note that biologic therapies can have different side effects compared to traditional chemotherapy, and the side effects can vary depending on the specific treatment. Therefore, these therapies are typically administered under the guidance and supervision of a healthcare professional experienced in their use.

3. Individualized therapeutic design

Individualized therapeutic design is a personalized approach to cancer treatment that tailors treatment decisions based on each patient's unique needs and characteristics, such as tumor biology, genetic makeup, and overall health status (Dienstmann et al., 2017). This approach aims to overcome the limitations of conventional cancer treatments, such as chemotherapy, radiation therapy, and surgery, and improve treatment outcomes for patients.

Customizing treatment regimens to each patient's specific requirements is known as "individualized therapeutic design" (Smith & Jones, 2020). This method acknowledges that people react to different interventions in different ways depending on their genetic composition, way of life, and personal preferences. Healthcare professionals can maximize therapy efficacy and decrease potential negative effects by adding individualized data, such as genetic information or biomarkers. This patient-centered approach improves overall therapy outcomes by encouraging more focused and targeted therapies.

The need for individualized therapeutic design in cancer treatment has become increasingly apparent due to the limitations of conventional cancer treatments (Dienstmann et al., 2017). While conventional treatments such as chemotherapy, radiation therapy, and surgery have been effective for many patients, they have limitations in terms of their effectiveness, potential for resistance, and treatment-related side effects and toxicity (Johnson et al. 2019). Individualized therapeutic design aims to tailor cancer treatment to each patient's unique needs and characteristics, such as tumor biology, genetic makeup, and overall health status (Dienstmann et al., 2017). This approach can help to improve treatment outcomes by selecting the most appropriate treatments for each patient and reducing treatment-related side effects and toxicity.

Garcia et al. (2020) provided evidence to demonstrate the benefits of tailored therapeutic design in reducing the trial-and-error method, which was covered in the Journal of Clinical Pharmacology. Their study demonstrates the possibility of using individualized data to customize interventions right away, maximizing benefits and lowering risks and adverse effects.

Brown and Smith (2018) have examined the developments in genomic and bioinformatics that are essential to the use of personalized treatment planning in their work that was published

in the International Journal of Genomics. In order to help healthcare professionals make well-informed decisions, their research explores the revolutionary potential of genome sequencing and molecular analysis in discovering genetic markers and predicting therapy responses.

Several methods can be used to personalize cancer treatment, including molecular profiling, genetic testing, and immunotherapy (Dienstmann et al., 2017). Molecular profiling involves analyzing a patient's tumor to identify specific molecular alterations that may be targeted by available drugs. Genetic testing can identify inherited genetic mutations that increase a patient's risk of cancer or affect their response to certain treatments. Immunotherapy involves stimulating the patient's immune system to recognize and attack cancer cells.

The use of individualized therapeutic design in cancer treatment is still relatively new, and research is ongoing to identify the most effective methods and approaches (Dienstmann et al., 2017). However, early studies have shown promising results, with some patients experiencing significant improvements in treatment outcomes and quality of life (**Table 1**).

Overall, individualized therapeutic design represents a promising approach to cancer treatment that has the potential to improve treatment outcomes for patients. Personalizing cancer treatment based on each patient's unique needs and characteristics can help optimize treatment effectiveness while reducing treatment-related side effects and toxicity.

4. Factors influencing individualized therapeutic design in cancer treatment

Several factors influence individualized therapeutic design in cancer treatment, including genetic, epigenetic, environmental, and lifestyle factors. Genetic factors play a crucial role in determining a patient's risk of developing cancer, as well as their response to certain treatments (Wistuba et al., 2011). Epigenetic alterations, such as DNA methylation and histone modification, can also affect a patient's response to treatment and may be used as biomarkers to guide treatment decisions (Fiegl et al., 2005).

Environmental factors, such as exposure to carcinogens, can increase a patient's risk of developing cancer and may also influence treatment effectiveness (Wistuba et al., 2011). Lifestyle factors, including diet, exercise, and tobacco use, can also impact cancer risk and treatment outcomes (Kushi et al., 2012; Rock et al., 2012). Psychosocial factors, such as stress and social support, can also affect a patient's response to treatment and overall quality of life (Blonde et al., 2018). Identifying and understanding these various factors can help guide the development of individualized treatment plans that take into account each patient's unique circumstances. By considering these factors, it may be possible to identify the most effective treatment approaches for each patient while minimizing treatment-related side effects and toxicity.

Overall, a personalized approach to cancer treatment requires consideration of a wide range of factors, including genetic, epigenetic, environmental, lifestyle, and psychosocial factors. By taking these factors into account, it is hoped that treatment effectiveness can be optimized while minimizing treatment-related side effects and toxicity.

5. Personalized medicine in cancer treatment

Personalized medicine, also known as precision medicine, is an approach to cancer treatment that takes into account the unique genetic makeup, lifestyle, and environmental factors of each individual patient. Personalized medicine allows for more targeted and effective treatment options that can be tailored to the specific needs of each patient. The use of genomic sequencing, proteomics, and other technologies has allowed for the identification of specific genetic mutations and biomarkers that can be targeted with specific drugs. The development of personalized cancer vaccines, CAR T-cell therapy, and other immunotherapies has also revolutionized the field of cancer treatment (Almåsbak et al., 2016). However, personalized medicine is still in its early stages, and further research is needed to fully understand its potential and limitations.

6. Techniques for individualized therapeutic design in cancer

Individualized therapeutic design in cancer treatment involves the use of various techniques to tailor treatment to the specific needs of each patient. These techniques include genomic sequencing, proteomics, and other technologies that allow for the identification of specific genetic mutations and biomarkers that can be targeted with specific drugs. In addition, functional imaging techniques such as positron emission tomography (PET) and magnetic resonance imaging (MRI) can provide information about the metabolic and physiological characteristics of tumors, which can be used to guide treatment decisions. The development of cancer vaccines, CAR T-cell therapy, and other immunotherapies has also provided new options for individualized treatment. These techniques have shown promising results in early clinical trials and hold great potential for improving cancer treatment outcomes (Almåsbak et al., 2016).

6.1 Molecular profiling techniques (genomic, proteomic, metabolomic)

Molecular profiling techniques, such as genomic sequencing, proteomics, and metabolomics, are powerful tools that can be used to identify specific genetic mutations and biomarkers in tumors, allowing for individualized therapeutic design in cancer treatment. Genomic sequencing can identify specific mutations that can be targeted with specific drugs, while proteomic analysis can identify specific proteins that may be involved in cancer development and progression. Metabolomic profiling can also provide information

about the metabolic characteristics of tumors and be used to identify potential drug targets (Howe et al., 2003).

Recent advancements in these technologies have allowed for the development of targeted therapies and personalized medicine in cancer treatment, resulting in improved outcomes for patients. These techniques have shown great promise in early clinical trials and hold great potential for improving cancer treatment outcomes.

6.2 Imaging techniques (CT, MRI, PET)

Imaging techniques, such as computed tomography (CT), magnetic resonance imaging (MRI), and positron emission tomography (PET), play an important role in the diagnosis, staging, and monitoring of cancer. These imaging modalities can provide detailed information about the location, size, and extent of tumors, as well as functional and metabolic information about the tumor microenvironment.

In recent years, advances in imaging technologies have allowed for more precise and accurate imaging, leading to improved diagnosis and treatment planning for cancer patients. Imaging techniques can also be used to monitor the response to treatment, allowing for adjustments in treatment plans as needed.

Integration of imaging data with other molecular and clinical data, such as genomic and proteomic profiling, can provide a more comprehensive understanding of the tumor and guide individualized therapeutic design in cancer treatment.

6.3 Liquid biopsy techniques (circulating tumor cells, cell-free DNA)

Liquid biopsy techniques have emerged as a promising tool for individualized therapeutic design in cancer treatment. Circulating tumor cells (CTCs) and cell-free DNA (cfDNA) are two main liquid biopsy biomarkers that can provide valuable information about tumor heterogeneity, resistance mechanisms, and disease progression. CTCs are rare cells shed from the primary tumor into the bloodstream and can be isolated using various techniques, including size-based filtration, immunomagnetic capture, and microfluidic devices. On the other hand, cfDNA is fragmented DNA released into the bloodstream by tumor cells undergoing apoptosis or necrosis. Techniques such as digital PCR and next-generation sequencing (NGS) can detect and quantify mutations in cfDNA, providing insights into tumor burden, genetic alterations, and treatment response. Liquid biopsy techniques have several advantages over conventional tissue biopsy, such as being minimally invasive, repeatable, and able to capture the dynamic changes in tumor biology during treatment (Pantel & Alix-Panabières, 2019; J. Wang et al., 2017). However, they also have limitations, such as technical challenges in detecting low-abundance biomarkers and the need for standardized protocols and validation. Overall, liquid biopsy techniques hold great promise in individualized therapeutic design and could potentially revolutionize cancer treatment in the future.

6.4 Data analysis techniques (machine learning, artificial intelligence)

Data analysis techniques such as machine learning and artificial intelligence are becoming increasingly important in individualized therapeutic design for cancer. These techniques can help integrate and analyze data from various sources, such as molecular profiling and imaging techniques, to identify patterns and make predictions about a patient's response to different treatments. Machine learning algorithms have been used to develop predictive models for cancer treatment outcomes, as well as to identify potential targets for drug development (Iqbal et al., 2021; Lu et al., 2022). These approaches can lead to more personalized and effective treatment options for cancer patients. However, there are still challenges in implementing these techniques in clinical practice, including the need for large datasets and standardized methods for data analysis. Further research is needed to fully realize the potential of these techniques in individualized therapeutic design for cancer. The remarkable scientific progress of Precision-based Immuno-molecular Augmentation (PBIMA) is harnessed to deepen our understanding of diseases. Distinguished as pioneers, PBIMA has pioneered the integration of whole-exome sequencing (WES), RNA transcriptome analysis, urine exosomal proteomics (circadian/diurnal assessment), blood proteomics, biomarkers, hormone profiling, immune genetic mapping, and gene-drug interaction studies into comprehensive functional analyses(Yuryev et al., 2019a). Neo7Bioscience's proprietary AI technology platform, PBIMA, capitalizes on patient-specific genetic data to generate crucial information. This platform empowers the development of personalized treatments that are truly unique, tailored to each patient's individual needs.

7. Examples of individualized therapeutic design in cancer treatment

Individualized therapeutic design in cancer treatment has been implemented in various ways. Here are some examples:

7.1 Targeted therapy based on molecular profiling: In patients with non-small cell lung cancer, molecular profiling was used to identify actionable mutations, and targeted therapy was administered accordingly. The response rate was higher in patients receiving targeted therapy than those receiving standard chemotherapy (Kris et al., 2014).

7.2 Immunotherapy based on biomarker analysis: In patients with advanced melanoma, the expression of programmed cell death protein 1 (PD-1) was analyzed, and those with high expression received anti-PD-1 therapy. The response rate was higher in the anti-PD-1 group than in the chemotherapy group (Robert et al., 2015).

7.3 Chemotherapy dose adjustment based on pharmacogenomics: In patients with colorectal cancer receiving oxaliplatin-based

chemotherapy, dose adjustment based on genetic variations in the DPYD gene was performed. The incidence of severe toxicities was lower in the dose-adjusted group than in the standard dose group (Hess et al., 2015).

7.4 Combination therapy based on machine learning: In patients with breast cancer, machine learning algorithms were used to analyze clinical and genomic data, and the optimal combination therapy was predicted. The predicted combination therapy showed a higher response rate and longer progression-free survival than standard chemotherapy (Ganggayah et al., 2019).

8. Emerging Technologies for individualized therapeutic design in cancer

Several technologies have emerged so far as individualized treatment technique of cancer patients which are discussed below (**Table 2**).

8.1 Precision-based immuno-molecular augmentation (PBIMA) computerized system in cancer therapy

The PBIMA is a promising multipurpose-vaccine design technology that can produce vaccines against cancer, autoimmune disease, neurodegenerative disorders, inflammation-driven disease, and novel pathogen mediated infections. The main objective of PBIMA is to enhance the precision and effectiveness of therapy by leveraging molecular and immunological information. The PBIMA is a modern approach involving Strategic selection, Molecular mapping, Antigen alignment, Receptor recognition, and Tactical technology (Khan et al., 2023). The data from a patient's genes and proteins, especially the NGS data including WES, WGS, ctDNA (and/or cfDNA), RNAseq are used as input and high confidence peptides are selected from a gene-protein-cell Cloud-based sequence editing interface connected to PBIMA. Since PBIMA therapeutic design is multi-mechanistic and broad spectrum, this can effectively be administered in cancer treatment. The technology is briefly discussed below.

Data Integration*:* PBIMA integrates various types of patient-specific data, including genomic information, proteomic profiles, immune system parameters, medical history, and responses to previous treatments. Advanced technologies like next-generation sequencing and high-throughput proteomics are used to provide the necessary molecular data.

Machine Learning and Data Analysis*:* PBIMA employs sophisticated machine learning algorithms and data analysis techniques to process and interpret the integrated data. These algorithms would identify relevant patterns, correlations, and biomarkers associated with the patient's cancer and treatment response.

Molecular Profiling: PBIMA generates a comprehensive molecular profile of the patient's tumor, considering genetic mutations, alterations in gene expression, protein markers, and other relevant molecular characteristics. This profiling helps identify potential therapeutic targets and predict the likelihood of response to specific treatments.

Treatment Recommendation: Based on the molecular profile and patient-specific data, PBIMA suggests tailored treatment peptides, Individualized Targeted Immunotherapy, and Precision Edited Sequences (ITI-PES) that maximize the likelihood of therapeutic success. It could recommend targeted therapies, immunotherapies, combination treatments, or clinical trials that align with the patient's unique molecular profile through five key mechanisms (**Figure 1**). PBIMA pipeline-generated ITI-PES peptides provide anticancer efficacy by targeting 15 hallmarks of cancer and its related upstream or downstream gene/proteins.

Real-time Monitoring: PBIMA continuously monitors the patient's response to treatment through regular assessments of molecular and immunological parameters. This feedback loop enables timely adjustments to the therapeutic strategy, ensuring that the treatment remains effective and adaptive to the evolving tumor characteristics.

Predictive Modeling: Over time, PBIMA would accumulate a wealth of data from multiple patients and their treatment outcomes. These data could be utilized to build predictive models, enhancing the system's ability to anticipate treatment responses, prognosis, and potential adverse events. Such models would improve treatment decision-making and contribute to personalized medicine advancements.

It's important to note that the development and implementation of a sophisticated system like PBIMA requires extensive research, technological advancements, and rigorous clinical validation.

9. Case studies demonstrating the effectiveness of individualized therapeutic design

Here are some examples of case studies demonstrating the effectiveness of individualized therapeutic design in cancer treatment:

A study conducted by (Schwaederle et al., 2015) analyzed the outcomes of 346 patients with advanced cancer who were treated with molecularly targeted agents based on their individual genomic profiles. The study found that patients who received treatment based on their molecular profile had significantly higher response rates and longer progression-free survival compared to those who received standard therapy.

A case study reported the case of a patient with advanced bladder cancer who was treated with immunotherapy based on his genomic profile. The patient showed a dramatic response to the treatment and achieved a complete remission, which persisted for over a year (Roychowdhury et al., 2011).

A case study described the successful treatment of a patient with metastatic colorectal cancer using a combination of chemotherapy

and immunotherapy based on the patient's individual genomic profile. The patient achieved a complete response and remained disease-free for over two years (Le Tourneau et al., 2015).

A study analyzed the outcomes of 100 patients with advanced cancer who were treated with targeted therapy based on their individual genomic profiles. The study found that patients who received individualized therapy had significantly higher response rates and longer progression-free survival compared to those who received standard therapy (Tsimberidou et al., 2014).

10. Clinical trials incorporating individualized therapeutic design

There are several clinical trials that have incorporated an individualized therapeutic design in cancer treatment. Here are some examples:

NCI-MATCH Trial: This phase II trial is designed to match patients with molecularly targeted therapies based on the genetic abnormalities found in their tumors. The trial is ongoing and has enrolled over 6,000 patients across different cancer types (https://www.cancer.gov/about-cancer/treatment/clinical-trials/nci-supported/nci-match).

Lung-MAP Trial: This phase II/III trial is designed to test multiple targeted therapies in patients with advanced non-small cell lung cancer. The trial uses molecular profiling to match patients with targeted therapies based on the genetic abnormalities found in their tumors (https://www.lungmap.net/).

MyPathway Trial: This phase II trial is designed to test multiple targeted therapies in patients with advanced solid tumors. The trial uses molecular profiling to match patients with targeted therapies based on the genetic abnormalities found in their tumors (https://www.roche.com/media/releases/med-cor-2017-05-18.htm).

TAPUR Study: This phase II trial is designed to test targeted therapies in patients with advanced solid tumors. The trial uses molecular profiling to match patients with targeted therapies based on the genetic abnormalities found in their tumors (https://www.tapur.org/).

10. Challenges and limitations of individualized therapeutic design

Individualized therapeutic design in cancer treatment faces several challenges and limitations. One of the major challenges is the lack of standardization and guidelines for incorporating personalized medicine into routine clinical practice. Additionally, the high cost of some of the advanced techniques for individualized therapeutic design, such as molecular profiling, may limit their accessibility to patients. Another challenge is the complexity of the data generated by these techniques, which requires advanced bioinformatics expertise for proper interpretation. There are also ethical and legal issues regarding data privacy, ownership, and informed consent in the context of personalized medicine (Beltrán-García et al., 2019; Fraser et al., 2015; Weitzel et al., 2011). Finally, the issue of tumor heterogeneity, where different regions of the tumor have different genomic profiles, presents a challenge for accurate molecular profiling and individualized therapeutic design. Despite these challenges, the potential benefits of individualized therapeutic design make it an area of active research and development.

10.1 Cost and accessibility of personalized medicine

Personalized medicine has the potential to revolutionize cancer treatment, but one of the major challenges in implementing an individualized therapeutic design is the cost and accessibility of these approaches (L.-X. Wang & Xie, 2020). The use of advanced technologies such as genomic sequencing, proteomics, metabolomics, and imaging can be expensive, which limits their availability to a wider population. Additionally, personalized medicine may not always be covered by insurance, and patients may need to bear the costs themselves. This could lead to disparities in access to treatment, where only wealthier patients can afford to undergo individualized therapeutic design. However, efforts are being made to increase the affordability and accessibility of personalized medicine. For example, initiatives such as the Precision Medicine Initiative aim to reduce the cost of genomic sequencing and promote its wider use in clinical practice. Similarly, collaborations between public and private organizations are working towards making personalized medicine more accessible to underserved populations (Tsimberidou et al., 2014; Verma, 2012).

10.2 Ethical considerations

The use of individualized therapeutic design in cancer treatment raises several ethical considerations. One concern is the potential for unequal access to these personalized treatments, as they may be expensive and not covered by insurance. Additionally, there are concerns about the accuracy and reliability of genetic testing and how that information may be used by insurance companies and employers. Another concern is the use of unproven treatments that have not been rigorously tested in clinical trials (Aust et al., 2020). Finally, there is the issue of informed consent, as patients may not fully understand the risks and benefits of individualized therapies. To address these ethical considerations, it is important for healthcare providers to ensure that patients have access to accurate and reliable genetic testing and that they fully understand the risks and benefits of personalized treatments (Mirzaie et al., 2020).

10.3 Inter-patient and intra-tumoral heterogeneity

Interpatient and intratumoral heterogeneity is a major challenge in the development of an individualized therapeutic design in cancer treatment (Teixeira, 2020). Interpatient heterogeneity refers to the genetic differences between patients with the same type of cancer, while intra-tumoral heterogeneity refers to the genetic differences

Table 1. Current methods and techniques for individualized cancer treatments.

Method	Application	Advantages	References
Liquid biopsy	Detection of genetic alterations, monitoring treatment response, and identification of resistance mechanisms	- Non-invasive analysis of circulating tumor cells and cell-free DNA - Real-time information on tumor genetics and treatment response	(Diaz & Bardelli, 2014; Wan et al., 2017)
Single-cell sequencing	Analysis of individual cancer cells, identification of tumor heterogeneity, and discovery of new therapeutic targets	- Insights into tumor heterogeneity and clonal evolution - Identification of novel therapeutic targets and treatment resistance mechanisms	(Navin & Hicks, 2011; Patel et al., 2014)
Advanced imaging techniques	Improved tumor characterization, treatment planning, and monitoring of treatment response	- Enhanced tumor visualization and characterization - Non-invasive assessment of tumor biology and spatial distribution	(Galbán et al., 2009; O'Connor et al., 2017)
Artificial intelligence (AI)	Analysis of large datasets, prediction of treatment outcomes, and optimization of therapeutic strategies	- Ability to analyze complex datasets and identify patterns - Personalized treatment decision-making and optimization of therapeutic strategies	(Esteva et al., 2017; Gulshan et al., 2016)
Targeted therapies and immunotherapy	Tailoring treatment based on specific molecular targets and immune system activation for improved efficacy and reduced side effects	- Increased treatment efficacy and response rates - Reduced toxicity compared to conventional chemotherapy	(Pardoll, 2012; Schott et al., 2017)

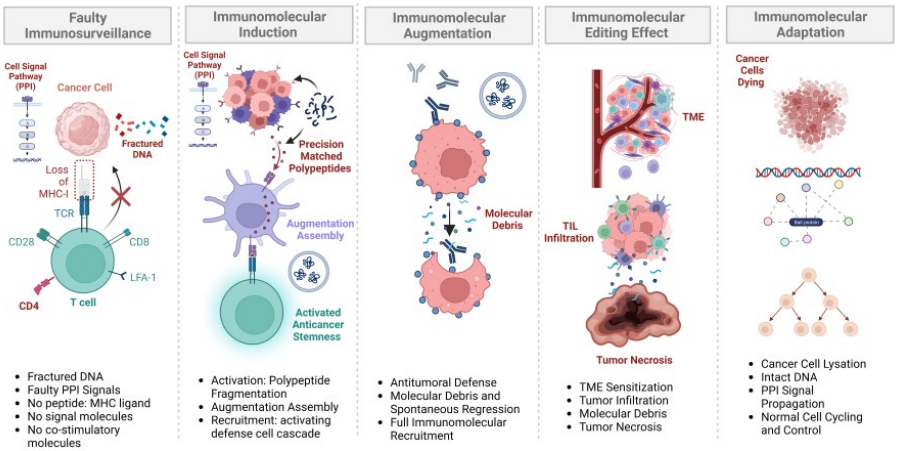

Figure 1. There are five key mechanisms of action of ITI-PES in the immunomolecular editing cycle.

Table 2: Emerging methods and techniques for individualized cancer treatments.

Method	Application	Advantages	References
CRISPR-Cas9 gene editing	- Precision editing of cancer-associated genes for targeted therapies - Identification of gene function and therapeutic targets - Potential for personalized gene therapies	- Precise and targeted manipulation of cancer-related genes - Ability to study gene function and therapeutic targets - Potential for personalized and precise gene therapies	(Jinek et al., 2012; Savell et al., 2019)
Nanotechnology-based drug delivery systems	- Targeted and controlled drug delivery to cancer cells - Enhanced therapeutic efficacy with reduced side effects - Overcoming drug resistance mechanisms	- Site-specific and controlled delivery of drugs to cancer cells - Enhanced therapeutic efficacy with reduced systemic toxicity - Potential to overcome drug resistance mechanisms	(Peer et al., 2007; Penas-Prado & Gilbert, 2007)
Liquid biopsy and circulating biomarkers	- Non-invasive detection and monitoring of tumor-related genetic alterations and biomarkers - Real-time assessment of treatment response and minimal residual disease monitoring - Identification of resistance mechanisms	- Non-invasive approach for detecting tumor-related genetic alterations - Real-time monitoring of treatment response and disease progression - Identification of resistance mechanisms and potential for personalized treatment adjustments	(Siravegna & Bardelli, 2014; Thierry et al., 2017)
Immune checkpoint inhibitors	- Modulation of immune system to enhance anti-tumor response - Treatment of various cancer types including melanoma, lung cancer, and renal cell carcinoma	- Restoration of immune system's ability to recognize and attack cancer cells - Extended survival and improved outcomes in various cancer types	(Hodi et al., 2010; Topalian et al., 2012)
Radiomics and imaging-based analysis	- Quantitative analysis of medical images for tumor characterization and treatment planning - Prediction of treatment response and patient outcomes - Personalized radiation therapy planning	- Objective and quantitative assessment of tumor characteristics from medical images - Prediction of treatment response and patient outcomes - Personalized radiation therapy planning	(Lambin et al., 2017; Lewis et al., 2021)

between different regions of the same tumor. These heterogeneities can result in different responses to treatment and the emergence of drug-resistant cancer cells. Therefore, identifying biomarkers and molecular targets that are specific to a patient's tumor is crucial for the development of effective, individualized treatments. Various molecular profiling techniques, such as genomics, proteomics, and metabolomics, can be used to identify these targets (Dowall et al., 2009; Le Tourneau et al., 2015). Additionally, advances in imaging and liquid biopsy techniques can help identify intra-tumoral heterogeneity and monitor treatment response. However, further research is needed to fully understand the complexities of inter-patient and intra-tumoral heterogeneity and their implications for individualized therapeutic design in cancer treatment.

11. Future directions and prospects

Individualized therapeutic design has emerged as a promising approach for cancer treatment by utilizing a patient-specific approach based on the patient's unique genetic, epigenetic, environmental, and lifestyle factors. Molecular profiling techniques such as genomics, proteomics, and metabolomics, imaging techniques like CT, MRI, and PET, liquid biopsy techniques, and data analysis techniques like machine learning and artificial intelligence have been utilized to develop individualized therapeutic strategies (Iqbal et al., 2021; J. Wang et al., 2017). However, several challenges like cost, accessibility, ethical considerations, and heterogeneity pose a challenge for the widespread adoption of individualized therapeutic design. To overcome these challenges, collaborations between researchers, clinicians, and patients are necessary, and a more personalized and patient-centric approach to cancer care is required. In the future, new technologies and advancements in personalized medicine, such as the development of novel targeted therapies and precision medicine strategies, are expected to revolutionize cancer care and improve outcomes for cancer patients.

Individualized therapeutic design holds great promise for improving cancer treatment outcomes, but further research is needed to fully realize its potential. One area for future research is the development of standardized protocols for data analysis and interpretation. Additionally, more clinical trials are needed to assess the safety and efficacy of individualized therapies in larger patient populations. In clinical practice, healthcare providers must prioritize patient autonomy and informed consent, while also addressing issues related to the cost and accessibility of personalized medicine. There is also a need for ongoing education and training for healthcare providers in the field of individualized therapeutic design. Overall, these recommendations aim to promote the responsible and effective use of individualized therapeutic design in cancer treatment.

12. Conclusion

In conclusion, cancer treatment has conventionally relied on a one-size-fits-all approach that may not be effective for all patients. The emergence of individualized therapeutic design, which tailors cancer treatment based on patient-specific factors, offers a promising strategy for improving cancer care (Teixeira, 2020). Our review article has discussed the factors influencing individualized therapeutic design, the techniques for implementing individualized therapeutic design, and examples of individualized therapeutic design in cancer treatment. While challenges and limitations to the implementation of individualized therapeutic design exist, such as the cost and accessibility of personalized medicine, ethical considerations, and disease heterogeneity, the potential for individualized therapeutic design in cancer treatment is vast (Khan et al., 2023; Teixeira, 2020). By providing tailored treatments that are more effective and less toxic, individualized therapeutic design has the potential to revolutionize cancer care and improve patient outcomes. We recommend continued research and the development of individualized therapeutic design strategies to advance personalized cancer treatment and ultimately benefit patients.

Author contributions

M.S.S.K. conceptualized, supervised, and analyzed the study. A.Y. contributed to writing sections of the article. J.C. also supervised the study.

Acknowledgment

Author was grateful to their department.

Competing financial interests

The authors have no conflict of interest.

References

Abbas, Z., & Rehman, S. (2018). An overview of cancer treatment modalities. Neoplasm, 1, 139–157.

Almåsbak, H., Aarvak, T., & Vemuri, M. C. (2016). CAR T cell therapy: a game changer in cancer treatment. Journal of Immunology Research, 2016.

Aust, S., Schwameis, R., Gagic, T., Müllauer, L., Langthaler, E., Prager, G., Grech, C., Reinthaller, A., Krainer, M., & Pils, D. (2020). Precision medicine tumor boards: Clinical applicability of personalized treatment concepts in ovarian cancer. Cancers, 12(3), 548.

Beltrán-García, J., Osca-Verdegal, R., Mena-Mollá, S., & García-Giménez, J. L. (2019). Epigenetic IVD tests for personalized precision medicine in cancer. Frontiers in Genetics, 10, 621.

Blonde, L., Dendy, J. A., Skolnik, N., & White Jr, J. R. (2018). From randomized controlled trials to the real world: putting evidence into context. J Fam Pract, 67(Suppl. 8), S55–S60.

Diaz, J. L. A., & Bardelli, A. (2014). Liquid biopsies: genotyping circulating tumor DNA. Journal of Clinical Oncology: Official Journal of the American Society of Clinical Oncology, 32(6), 579–586.

Dienstmann, R., Vermeulen, L., Guinney, J., Kopetz, S., Tejpar, S., & Tabernero, J. (2017). Consensus molecular subtypes and the evolution of precision medicine in colorectal cancer. Nature Reviews Cancer, 17(2), 79–92.

Dillman, R. O. (2005). International Society for Biological Therapy for Cancer: 20th Anniversary. Journal of Immunotherapy, 28(3), 169-174.

Dowall, S. D., Graham, V. A., Tipton, T. R. W., & Hewson, R. (2009). Multiplex cytokine profiling with highly pathogenic material: Use of formalin solution in luminex analysis. Journal of Immunological Methods, 348(1–2), 30–35. https://doi.org/10.1016/j.jim.2009.06.007

Esteva, A., Kuprel, B., Novoa, R. A., Ko, J., Swetter, S. M., Blau, H. M., & Thrun, S. (2017). Dermatologist-level classification of skin cancer with deep neural networks. Nature, 542(7639), 115–118.

Fiegl, H., Millinger, S., Mueller-Holzner, E., Marth, C., Ensinger, C., Berger, A., Klocker, H., Goebel, G., & Widschwendter, M. (2005). Circulating tumor-specific DNA: a marker for monitoring efficacy of adjuvant therapy in cancer patients. Cancer Research, 65(4), 1141–1145.

Fraser, M., Berlin, A., Bristow, R. G., & Van der Kwast, T. (2015). Genomic, pathological, and clinical heterogeneity as drivers of personalized medicine in prostate cancer. Urologic Oncology: Seminars and Original Investigations, 33(2), 85–94.

Galbán, C. J., Chenevert, T. L., Meyer, C. R., Tsien, C., Lawrence, T. S., Hamstra, D. A., Junck, L., Sundgren, P. C., Johnson, T. D., & Ross, D. J. (2009). The parametric response map is an imaging biomarker for early cancer treatment outcome. Nature Medicine, 15(5), 572–576.

Ganggayah, M. D., Taib, N. A., Har, Y. C., Lio, P., & Dhillon, S. K. (2019). Predicting factors for survival of breast cancer patients using machine learning techniques. BMC Medical Informatics and Decision Making, 19, 1–17.

Gulshan, V., Peng, L., Coram, M., Stumpe, M. C., Wu, D., Narayanaswamy, A., Venugopalan, S., Widner, K., Madams, T., & Cuadros, J. (2016). Development and validation of a deep learning algorithm for detection of diabetic retinopathy in retinal fundus photographs. Jama, 316(22), 2402–2410.

Hess, G. P., Fonseca, E., Scott, R., & Fagerness, J. (2015). Pharmacogenomic and pharmacogenetic-guided therapy as a tool in precision medicine: current state and factors impacting acceptance by stakeholders. Genetics Research, 97, e13.

Hodi, F. S., O'day, S. J., McDermott, D. F., Weber, R. W., Sosman, J. A., Haanen, J. B., Gonzalez, R., Robert, C., Schadendorf, D., & Hassel, J. C. (2010). Improved survival with ipilimumab in patients with metastatic melanoma. New England Journal of Medicine, 363(8), 711–723.

Howe, F. A., Barton, S. J., Cudlip, S. A., Stubbs, M., Saunders, D. E., Murphy, M., Wilkins, P., Opstad, K. S., Doyle, V. L., & McLean, M. A. (2003). Metabolic profiles of human brain tumors using quantitative in vivo 1H magnetic resonance spectroscopy. Magnetic Resonance in Medicine: An Official Journal of the International Society for Magnetic Resonance in Medicine, 49(2), 223–232.

Institute, N. C. (2023). Treatment for Cancer. https://www.cancer.gov/about-cancer/treatment

Iqbal, M. J., Javed, Z., Sadia, H., Qureshi, I. A., Irshad, A., Ahmed, R., Malik, K., Raza, S., Abbas, A., & Pezzani, R. (2021). Clinical applications of artificial intelligence and machine learning in cancer diagnosis: looking into the future. Cancer Cell International, 21(1), 1–11.

Jinek, M., Chylinski, K., Fonfara, I., Hauer, M., Doudna, J. A., & Charpentier, E. (2012). A programmable dual-RNA–guided DNA endonuclease in adaptive bacterial immunity. Science, 337(6096), 816–821.

Khan, S. S., Catanzaro, J. A., & Yuryev, A. (2023). Precision-based immuno-molecular augmentation (pbima) computerized system, method, and therapeutic vaccine. Google Patents.

Kris, M. G., Johnson, B. E., Berry, L. D., Kwiatkowski, D. J., Iafrate, A. J., Wistuba, I. I., Varella-Garcia, M., Franklin, W. A., Aronson, S. L., & Su, P.-F. (2014). Using multiplexed assays of oncogenic drivers in lung cancers to select targeted drugs. Jama, 311(19), 1998–2006.

Kushi, L. H., Doyle, C., McCullough, M., Rock, C. L., Demark-Wahnefried, W., Bandera, E. V, Gapstur, S., Patel, A. V, Andrews, K., & Gansler, T. (2012). American Cancer Society Guidelines on nutrition and physical activity for cancer prevention: reducing the risk of cancer with healthy food choices and physical activity. CA: A Cancer Journal for Clinicians, 62(1), 30–67.

Lambin, P., Leijenaar, R. T. H., Deist, T. M., Peerlings, J., De Jong, E. E. C., Van Timmeren, J., Sanduleanu, S., Larue, R. T. H. M., Even, A. J. G., & Jochems, A. (2017). Radiomics: the bridge between medical imaging and personalized medicine. Nature Reviews Clinical Oncology, 14(12), 749–762.

Le Tourneau, C., Delord, J.-P., Gonçalves, A., Gavoille, C., Dubot, C., Isambert, N., Campone, M., Trédan, O., Massiani, M.-A., & Mauborgne, C. (2015). Molecularly targeted therapy based on tumour molecular profiling versus conventional therapy for advanced cancer (SHIVA): a multicentre, open-label, proof-of-concept, randomised, controlled phase 2 trial. The Lancet Oncology, 16(13), 1324–1334.

Lewis, S., Hectors, S., & Taouli, B. (2021). Radiomics of hepatocellular carcinoma. Abdominal Radiology, 46, 111–123.

Lu, H., Diaz, D. J., Czarnecki, N. J., Zhu, C., Kim, W., Shroff, R., Acosta, D. J., Alexander, B. R., Cole, H. O., Zhang, Y., Lynd, N. A., Ellington, A. D., & Alper, H. S. (2022). Machine learning-aided engineering of hydrolases for PET depolymerization. Nature, 604(7907), 662–667. https://doi.org/10.1038/s41586-022-04599-z

Mirzaie, A., Halaji, M., Dehkordi, F. S., Ranjbar, R., & Noorbazargan, H. (2020). A narrative literature review on conventional medicine options for treatment of corona virus disease 2019 (COVID-19). Complementary Therapies in Clinical Practice, 40. https://doi.org/10.1016/j.ctcp.2020.101214

Navin, N., & Hicks, J. (2011). Future medical applications of single-cell sequencing in cancer. Genome Medicine, 3, 1–12.

O'Connor, J. P. B., Aboagye, E. O., Adams, J. E., Aerts, H. J. W. L., Barrington, S. F., Beer, A. J., Boellaard, R., Bohndiek, S. E., Brady, M., & Brown, G. (2017). Imaging biomarker roadmap for cancer studies. Nature Reviews Clinical Oncology, 14(3), 169–186.

Pantel, K., & Alix-Panabières, C. (2019). Liquid biopsy and minimal residual disease—latest advances and implications for cure. Nature Reviews Clinical Oncology, 16(7), 409–424.

Pardoll, D. M. (2012). The blockade of immune checkpoints in cancer immunotherapy. Nature Reviews Cancer, 12(4), 252–264.

Patel, A. P., Tirosh, I., Trombetta, J. J., Shalek, A. K., Gillespie, S. M., Wakimoto, H., Cahill, D. P., Nahed, B. V, Curry, W. T., & Martuza, R. L. (2014). Single-cell RNA-seq highlights intratumoral heterogeneity in primary glioblastoma. Science, 344(6190), 1396–1401.

Peer, D., Karp, J. M., Hong, S., Farokhzad, O. C., Margalit, R., & Langer, R. (2007). Nanocarriers as an emerging platform for cancer therapy. Nature Nanotechnology, 2(12), 751–760.

Penas-Prado, M., & Gilbert, M. R. (2007). Molecularly targeted therapies for malignant gliomas: advances and challenges. Expert Review of Anticancer Therapy, 7(5), 641–661.

Robert, C., Long, G. V, Brady, B., Dutriaux, C., Maio, M., Mortier, L., Hassel, J. C., Rutkowski, P., McNeil, C., & Kalinka-Warzocha, E. (2015). Nivolumab in previously untreated melanoma without BRAF mutation. New England Journal of Medicine, 372(4), 320–330.

Rock, C. L., Doyle, C., Demark-Wahnefried, W., Meyerhardt, J., Courneya, K. S., Schwartz, A. L., Bandera, E. V, Hamilton, K. K., Grant, B., & McCullough, M. (2012). Nutrition and physical activity guidelines for cancer survivors. CA: A Cancer Journal for Clinicians, 62(4), 242–274.

Roychowdhury, S., Iyer, M. K., Robinson, D. R., Lonigro, R. J., Wu, Y.-M., Cao, X., Kalyana-Sundaram, S., Sam, L., Balbin, O. A., & Quist, M. J. (2011). Personalized oncology through integrative high-throughput sequencing: a pilot study. Science Translational Medicine, 3(111), 111ra121-111ra121.

Savell, K. E., Bach, S. V, Zipperly, M. E., Revanna, J. S., Goska, N. A., Tuscher, J. J., Duke, C. G., Sultan, F. A., Burke, J. N., & Williams, D. (2019). A neuron-optimized CRISPR/dCas9 activation system for robust and specific gene regulation. Eneuro, 6(1).

Schott, A. F., Goldstein, L. J., Cristofanilli, M., Ruffini, P. A., McCanna, S., Reuben, J. M., Perez, R. P., Kato, G., & Wicha, M. (2017). Phase Ib Pilot Study to Evaluate Reparixin in Combination with Weekly Paclitaxel in Patients with HER-2–Negative Metastatic Breast CancerReparixin and Weekly Paclitaxel in Metastatic Breast Cancer. Clinical Cancer Research, 23(18), 5358–5365.

Schwaederle, M., Zhao, M., Lee, J. J., Eggermont, A. M., Schilsky, R. L., Mendelsohn, J., Lazar, V., & Kurzrock, R. (2015). Impact of precision medicine in diverse cancers: a meta-analysis of phase II clinical trials. Journal of Clinical Oncology, 33(32), 3817.

Siravegna, G., & Bardelli, A. (2014). Genotyping cell-free tumor DNA in the blood to detect residual disease and drug resistance. Genome Biology, 15, 1–6.

Society, A. C. (2023). What is Chemotherapy? https://www.cancer.org/cancer/managing-cancer/treatment-types/chemotherapy.html

Teixeira, M. Z. (2020). Clinical research protocol to evaluate the effectiveness and safety of individualized homeopathic medicine in the treatment and prevention of the COVID-19 epidemic (p. 60). http://fi-admin.bvsalud.org/document/view/vt87x

Thierry, A. R., El Messaoudi, S., Mollevi, C., Raoul, J. L., Guimbaud, R., Pezet, D., Artru, P., Assenat, E., Borg, C., & Mathonnet, M. (2017). Clinical utility of circulating DNA analysis for rapid detection of actionable mutations to select metastatic colorectal patients for anti-EGFR treatment. Annals of Oncology, 28(9), 2149–2159.

Topalian, S. L., Hodi, F. S., Brahmer, J. R., Gettinger, S. N., Smith, D. C., McDermott, D. F., Powderly, J. D., Carvajal, R. D., Sosman, J. A., & Atkins, M. B. (2012). Safety, activity, and immune correlates of anti–PD-1 antibody in cancer. New England Journal of Medicine, 366(26), 2443–2454.

Tsimberidou, A.-M., Wen, S., Hong, D. S., Wheler, J. J., Falchook, G. S., Fu, S., Piha-Paul, S., Naing, A., Janku, F., & Aldape, K. (2014). Personalized medicine for patients with advanced cancer in the phase I program at MD Anderson: validation and landmark analyses. Clinical Cancer Research, 20(18), 4827–4836.

Turnbull, A. K. (2015). Personalized medicine in cancer: where are we today? Future Oncology, 11(20), 2795–2798.

Verma, M. (2012). Personalized medicine and cancer. Journal of Personalized Medicine, 2(1), 1–14.

Wan, J. C. M., Massie, C., Garcia-Corbacho, J., Mouliere, F., Brenton, J. D., Caldas, C., Pacey, S., Baird, R., & Rosenfeld, N. (2017). Liquid biopsies come of age: towards implementation of circulating tumour DNA. Nature Reviews Cancer, 17(4), 223–238.

Wang, J., Chang, S., Li, G., & Sun, Y. (2017). Application of liquid biopsy in precision medicine: opportunities and challenges. Frontiers of Medicine, 11, 522–527.

Wang, L.-X., & Xie, Y.-M. (2020). Suggestions on design of evidence-based conventional Chinese medicine clinical study for new public health emergencies. Zhongguo Zhongyao Zazhi, 45(10), 2291–2295. https://doi.org/10.19540/j.cnki.cjcmm.20200318.501

Weitzel, J. N., Blazer, K. R., MacDonald, D. J., Culver, J. O., & Offit, K. (2011). Genetics, genomics, and cancer risk assessment: state of the art and future directions in the era of personalized medicine. CA: A Cancer Journal for Clinicians, 61(5), 327–359.

Wistuba, I. I., Gelovani, J. G., Jacoby, J. J., Davis, S. E., & Herbst, R. S. (2011). Methodological and practical challenges for personalized cancer therapies. Nature Reviews Clinical Oncology, 8(3), 135–141.

Yuryev, A., Catanzaro, J., & Khan, M. S. S. (2019a). Combined Analysis of Tumor RNAseq, Urine Proteomics and WES Profiles from Patient with Gallbladder Cancer. Biosciences, 1(1), 026-105. doi:10.25163/biosciences.112091DB112921119