# Mini Review Article: The Role of Precision Medicine in Personalized Cancer Treatment

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**ABSTRACT**

Recent advancements in CRISPR (Clustered Regularly Interspaced Short Palindromic Repeats) technology have revolutionized the field of gene therapy, particularly in the context of cancer treatment. CRISPR-Cas9, a powerful genome-editing tool, enables precise modifications to the DNA of cancer cells, offering new avenues for targeted therapy. This technology allows for the knockout of oncogenes, activation of tumor suppressor genes, and engineering of immune cells to enhance their anti-tumor activity. Additionally, CRISPR-based screens have facilitated the identification of novel therapeutic targets and resistance mechanisms in various cancer types. Despite its potential, challenges such as off-target effects, delivery efficiency, and immune responses remain significant hurdles. Recent innovations, including base editing, prime editing, and CRISPR interference (CRISPRi), are addressing these limitations, enhancing the specificity and safety of CRISPR applications. Furthermore, the integration of CRISPR with other therapeutic modalities, such as immunotherapy and chemotherapy, holds promise for synergistic effects in combating cancer. This review highlights the transformative impact of CRISPR technology on cancer gene therapy, discusses current advancements, and explores future directions to overcome existing barriers, ultimately paving the way for more effective and personalized cancer treatments.

## Introduction

Researchers have taken a major step forward in cancer treatment using CRISPR technology [1]. This method significantly increases the body's ability to fight cancerous tumors by genetically modifying immune cells. CRISPR technology [2], which is known as a powerful tool for editing genes, is now being used as a new method in cancer treatment. In a new study [3], American researchers have used this technology to genetically modify immune cells to increase their ability to recognize and destroy cancer cells [4].

The method, called CRISPR-based immunotherapy, involves changing specific genes in T cells, a type of immune cell, so that they can attack tumors more effectively. Initial results from clinical trials suggest that this method can lead to a reduction in the size of tumors and improve the quality of life of patients [5].

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This scientific breakthrough has not only brought new hope to cancer patients, but also paved the way for the development of personalized treatments based on each person's genetic characteristics (Figure 1). With continued research, this technology could make a huge difference in the fight against cancer [6].

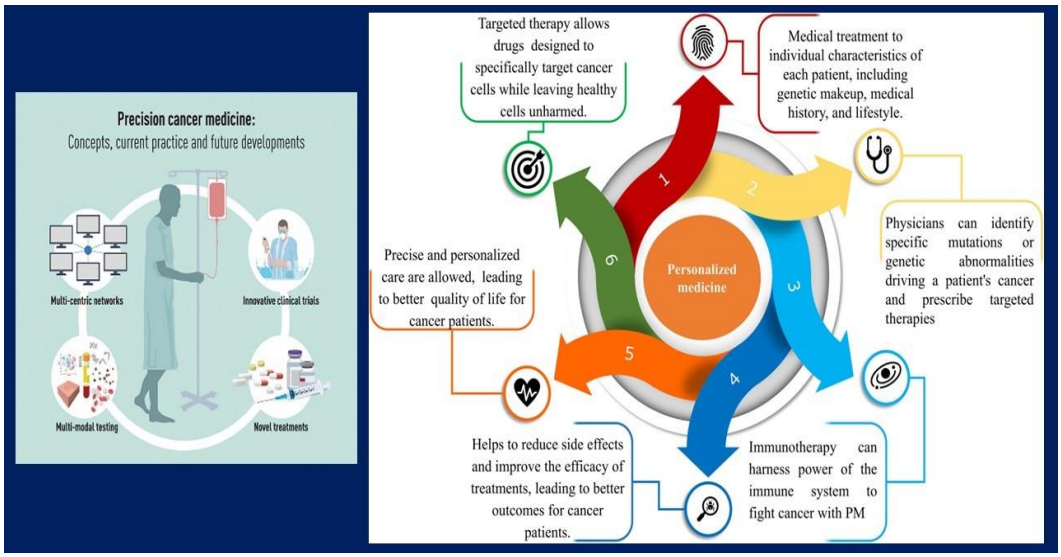


**Figure 1.** The Role of Precision Medicine in Personalized Cancer Treatment

## A review of 9 important achievements of CRISPR in the path of treating diseases in 2017

CRISPR technology allows researchers to modify the content of the genome. Part of this activity is carried out with the help of a protein called cas9, and the result will be cheaper, faster and more accurate than other methods. Researchers have made many achievements in the past few years using this technology. This year alone, there has been a lot of news about the success of CRISPR in treating various diseases, combating antibiotic-resistant bacteria or disease-carrying insects. Here are 9 important achievements of CRISPR/cas9 in 2017:

1- For the first time, researchers have succeeded in using the gene editing technique to clear the HIV virus from a living organ. This method has worked on 3 different species of animals. With the help of CRISPR, the research team separated the DNA of the HIV virus from the DNA of the body and succeeded in eliminating infections.

2- The development of the first semi-synthetic living organism took place with the help of CRISPR technology. This method was achieved by cultivating a type of bacteria called E. coli with a six-letter genetic code. Genetic information is normally written with 4 letters. Using CRISPR, researchers monitored the formation of invasive DNA by bacteria [7].

3- Using the genome content editing method, scientists succeeded in eliminating cancer cells by targeting the command center of cancer cells. In this experiment, human liver and prostate cancer cells were transferred to mice, and with the help of the CRISPR/cas9 method, scientists succeeded in eliminating the fused cells.

4- In other research, the growth rate of cancer cells has been reduced using CRISPR. In this study, researchers attacked a protein called

Tudor-SN, which plays an important role in cell division [8].

5- Using CRISPR, researchers succeeded in eliminating antibiotic-resistant bacteria. In this method, bacteriophages became so powerful that they forced resistant bacteria to destroy themselves. By equipping microphage viruses with a genetic sequence that includes antibiotic resistance genes, scientists created a kind of self-destruction mechanism in the bacteria.

6- The spread of diseases transmitted from mosquitoes to humans, such as Zika or malaria, was limited using the CRISPR/cas9 gene editing technique. In this method, scientists have succeeded in using Crispr to cleave mosquito reproductive genes and change multiple genetic codes simultaneously [9].

7- Symptoms of Huntington's disease have been successfully managed and partially improved in mice. Using this technique in mice to treat this rare disease that destroys brain cells could raise hopes for its treatment in humans.

8- Crispr technology is not only used in the medical world. Recently, a group of scientists have succeeded in genetically modifying and engineering algae using this method. As a result, up to twice as much algae-based biofuels can be obtained [10].

9- In the latest research, scientists have managed to store a moving image in the DNA of a living E. coli bacterium cell thanks to CRISPR. This experiment is considered the first step towards understanding the limitations and creating biological storage spaces.

In addition to this research, other experiments can be mentioned, such as genetic editing of human embryos, which increases hopes for reducing and controlling diseases in the future. Of course, one should not think that CRISPR does not have side effects. The use of CRISPR causes unwanted genetic mutations. Recently, scientists have succeeded in developing a new method that improves the efficiency and accuracy of DNA editing and prevents the creation of unwanted scars. This new method, known as "scarless editing", allows scientists to make genetic changes without leaving visible marks in the DNA structure.

This development is especially important for medical and therapeutic applications. Because reducing the risk of unwanted changes and side effects can lead to increased safety and effectiveness of genetic therapies. One of the key applications of this technology is in the treatment of genetic diseases such as Duchene muscular dystrophy, sickle cell anemia and some types of cancer. Using CRISPR, researchers can correct the genetic mutations that cause these diseases and create healthier cells [11].

In addition, CRISPR can also be used in agriculture, so that more resistant and higher-yielding crops are produced. By reducing the risks associated with unwanted changes in the genome, this technology can quickly move to the clinical trial stage and eventually to more widespread treatments. Researchers hope that these advances can help treat chronic and fatal diseases and improve the quality of life of patients. One successful example in this field is the use of CRISPR to treat sickle cell anemia.

In this method, stem cells from the patient's blood are taken and their defective gene is corrected using CRISPR. These modified cells are then returned to the patient's body to start producing healthy blood cells. The

method has shown promising results in clinical trials and could become a permanent cure for the disease. In addition, researchers are exploring the use of CRISPR in treating cancers that are resistant to conventional treatments [12].

Using this technology, they are able to identify and inactivate drug resistance genes in cancer cells, which could lead to increased effectiveness of chemotherapy treatments. Overall, recent advances in CRISPR technology, and especially new wound-free editing methods, represent a major step towards a future in which genetic diseases can be treated precisely and without unwanted risks.

These scientific developments could help improve public health and reduce the burden of chronic diseases, ultimately improving people's quality of life. In this system, CRISPR acts as a guide and identifies the target region in the genome of a microbe. The Cas9 enzyme then cuts the DNA at a specific location and the desired genes are deleted or modified. One of the main advantages of this technology is its high speed and accuracy. This method has not only greatly reduced the time for gene modification, but also minimized the error rate. Editing the genome of microbes using CRISPR-Cas technology is used in various fields [13].

In the pharmaceutical industry, this method has helped to produce drugs and vaccines faster and more accurately. For example, by genetic changes in bacteria and yeast, biological products such as insulin or antibiotics can be produced with greater efficiency and quality. Also in the medical field, scientists use this technology to develop new treatments for genetic diseases. Another important field of application of this technology is in agriculture. By editing the genome of soil microbes, the quality of the soil can be improved and, in this way, the growth of plants can be enhanced. Microbes have also been created with the ability to fight agricultural pests and plant diseases, reducing the need for chemical pesticides.

Other advances in this area include the development of more advanced versions of CRISPR, such as CRISPR-Cas12 and CRISPR-Cas13. In addition to editing DNA, these systems also have the ability to edit RNA, which has opened up new horizons in genetics. For example, using these systems, it is possible to target genes associated with microbial resistance to antibiotics and prevent the spread of this resistance [14].

Another new technology is Prime Editing. Unlike CRISPR-Cas, which relies on DNA cutting, this method makes small and precise changes at the genome level. Prime Editing has fewer errors than previous methods and can be used to correct small genetic mutations and make precise changes. Along with these advances, there are also challenges. One of the most significant challenges is the ethical and security concerns associated with genome editing. Although editing the genome of microbes has many benefits, there are concerns about the technology being misused for irresponsible purposes or creating dangerous microbes.

In general, new advances in microbial genome editing technology have allowed scientists to work more precisely and efficiently in various fields than before. These advances can help solve many medical, agricultural and environmental problems and improve the quality of human life.

## Optimizing the CRISPR gene editing system

Among the most important scientific advances in recent years is the discovery and development of new ways to edit the genes of living organisms using a fast and cost-effective technology called CRISPR. Now, scientists at the University of Texas say they have identified a way to improve and enhance this technology that could lead to more precise gene editing with greater safety and pave the way for the use of this technology in human genome editing [15].

A research team of molecular biologists has found that the CAS9 protein, which is much more widely used in CRISPR technology today, is at a lower level in terms of efficiency and safety compared to the lesser-known CAS12a protein. Since Cas9 is likely to edit the wrong parts of the genome and disrupt healthy functions, scientists propose that using Cas12a will make gene editing safer and more effective. "Our goal is to identify the best possible protein for the most beneficial and safe use of CRISPR technology," says Ilya Finkelstein, one of the researchers in the study. CRISPR is expected to lead to the development of new treatments for human diseases, as well as the production of higher-quality, pest-resistant products.

## Personalized medicine or targeted therapy

Personalized medicine or targeted therapy is based on the treatment of diseases based on the molecular characteristics of an individual. This new treatment method can be used in the treatment of cancer. Unfortunately, the number of people with cancer is increasing today, and finding an effective way to treat this disease is very important. One of the new discussions that has become popular in the treatment of diseases in recent years, especially the treatment of chronic diseases such as cancer, is personalized therapy [16].

## Management of Ultra-Precision Diagnosis and Person-Centered Cancer Treatment at the P7SPORT International Center

**History of the Role of Person-Centered Medicine in Cancer Treatment:** About 50 years ago, a controversial change in the philosophy of the role of person-centered medicine in cancer treatment was proposed, and today most doctors have a positive opinion about the effects of this method in the treatment of patients with cancer, to the extent that the World Health Organization has provided guidelines for achieving the goals of person-centered care. Currently, the role of person-centered medicine in cancer treatment is not controversial, but there are still challenges on the way to achieving desired results (Figure 2).

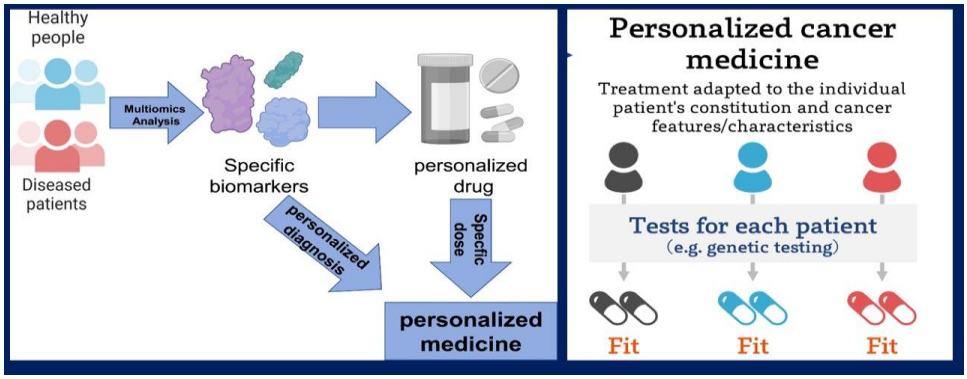


**Figure 2.** Personalized medicine or targeted therapy

## Person-centered treatment or patient-centered cancer care

Another definition that can be considered for the role of person-centered medicine in cancer treatment is to pay attention to the individual symptoms of each patient according to his or her personal history in the past. The treatments that are currently provided to patients are not at all person-centered, but group-centered. In other words, the symptoms and test results of patients are examined according to the symptoms and results that are defined for a normal group. For example, if your test results are within a previously determined range, you are considered healthy, and if they are outside this range, you are considered sick. However, in some cases, these parameters cannot be completely accurate. It is necessary to separate the individual from the group and examine the test results according to the individual's history [17].

## Treatment of the first German cancer patient in Iran by person-centered medicine

Currently, doctors have not received any training to consider an individual with unique biochemical characteristics, but it should be noted that each individual with unique characteristics can have different responses to cancer treatments. Many of us do not know the normal range of our blood pressure and heart rate, but we can recognize when our heartbeat is getting higher or we have low blood pressure.

The normal range of blood pressure and heart rate for each disease may be different, and therefore, the treatment method chosen for cancer patients should be selected according to their other specific and individual symptoms. Person-centered care can have other meanings, but one of the intended ones is respect for the patient's values and preferences in the cancer treatment process. Given that there are various treatment options for cancer treatment, it seems that respecting the patient's opinion in choosing the desired method from among the many treatment options can have a positive effect on the patient's morale. In this approach, the patient can play an active role in different stages of treatment [18].

Given that some patients experience psychological problems and despair after learning about their disease, person-centered medicine can encourage them to actively participate in all treatment periods.

## How is personalized medicine implemented?

Personalized medicine takes into account individual variation in genes, environment, and lifestyle to treat and prevent diseases. The advantage of personalized medicine in complex diseases is the intelligent use of data, especially genetic data, to decide on the course of treatment. Combining and analyzing genetic data with other data at the same time allows specialists to obtain patterns about the likelihood of effectiveness of different treatments.

According to the scientific definition, personalized medicine refers to adapting medical treatment to the individual characteristics of each patient. This does not mean producing unique drugs or medical devices for an individual patient, but rather categorizing people into specific groups who share a set of characteristics related to a single disease [19].

For example, their similar predisposition to a single disease makes them respond differently

to a treatment for that disease than people in other groups. This is why most experts believe that it is more useful to use the term precision medicine instead of personalized medicine [20].

## Definition of some key terms in targeted medicine

Many scientific terms used to describe the progress and challenges of precision medicine have complex specialized definitions that can be redefined in a tangible way to provide acceptable and useful targeted medicine services to patients. Below, we will review the simple definition of some commonly used terms in this field:

**1- Genome and DNA:** The genome refers to the complete set of hereditary material of the structure of a living organism. There is a special part within each of the cells of an organism that contains the hereditary information responsible for development and biological functions, this part is called DNA. DNA transmits hereditary information from one generation to the next [21].

**2- Genes and Genomics:** Genes are parts of the DNA of an organism's body that are associated with creating unique biological characteristics of that organism. These characteristics can include obvious external characteristics such as eye color or blood type, or hidden characteristics such as susceptibility to certain diseases. Genomics is the study of genes and their function. Researchers are still discovering the very complex relationships between genes and disease. Scientists can compare cancer cells with this data to understand where and how specific mutations occur and what their effects might be [22].

**3- Genetic sequencing:** Researchers can use genetic sequencing, or DNA sequencing, to determine which part of a DNA molecule contains genes and which part contains regulatory information. Sequencing allows them to identify differences between people with certain traits and those without them.

**4- Next Generation Sequencing (NGS):** Instead of sequencing a person's entire genetic code, this type of technique sequences fragments of a person's DNA at a time and then compares the results to a reference set of genetic data. Any differences or mutations can be identified during the process.

**5- CRISPR:** CRISPR consists of repeated sequences of genetic code that are interrupted by spacer sequences, likely remnants of the genetic code of past invading viruses. CRISPR is a powerful gene-editing technology that allows researchers to target specific parts of the genetic code, even in living cells, and change the DNA within them. This futuristic capability could allow scientists to repair damaging mutations or disease susceptibility in living organisms without the side effects of traditional drug treatments, and even correct genetic diseases for which there are no drug options [23].

**6- Pharmacogenetics:** Pharmacogenetics is the study of how genetic differences affect drug metabolism pathways or how individuals respond to specific drug interventions based on their unique genetic makeup. This science forms the basis of many targeted medicine efforts, such as selecting individual drug combinations to attack a specific type of cancer.

**7- Biomarkers:** Biomarkers are widely used in all clinical settings, to indicate that a disease, infection, toxicity, or other process is occurring in an organism.

**8- Biobank:** In many ways, genomic research is most beneficial when conducted on a large scale. In order to identify patterns in populations in a reliable and reproducible way, researchers must have access to large volumes of patient data. Biobanks are collections of this information [24].

## Individualized Medicine Approaches to Cancer Treatment

In the role of individualized medicine, cancer treatment is considered for each patient individually and in combination with other methods (Figure 3). The approaches that should be considered in this treatment method are:

- ✓ Considering the unique biochemical and biological characteristics of each person.
- ✓ Paying attention to the patient's values and perspectives.
- ✓ Considering the decisions of the patient's family in choosing the treatment method [25].

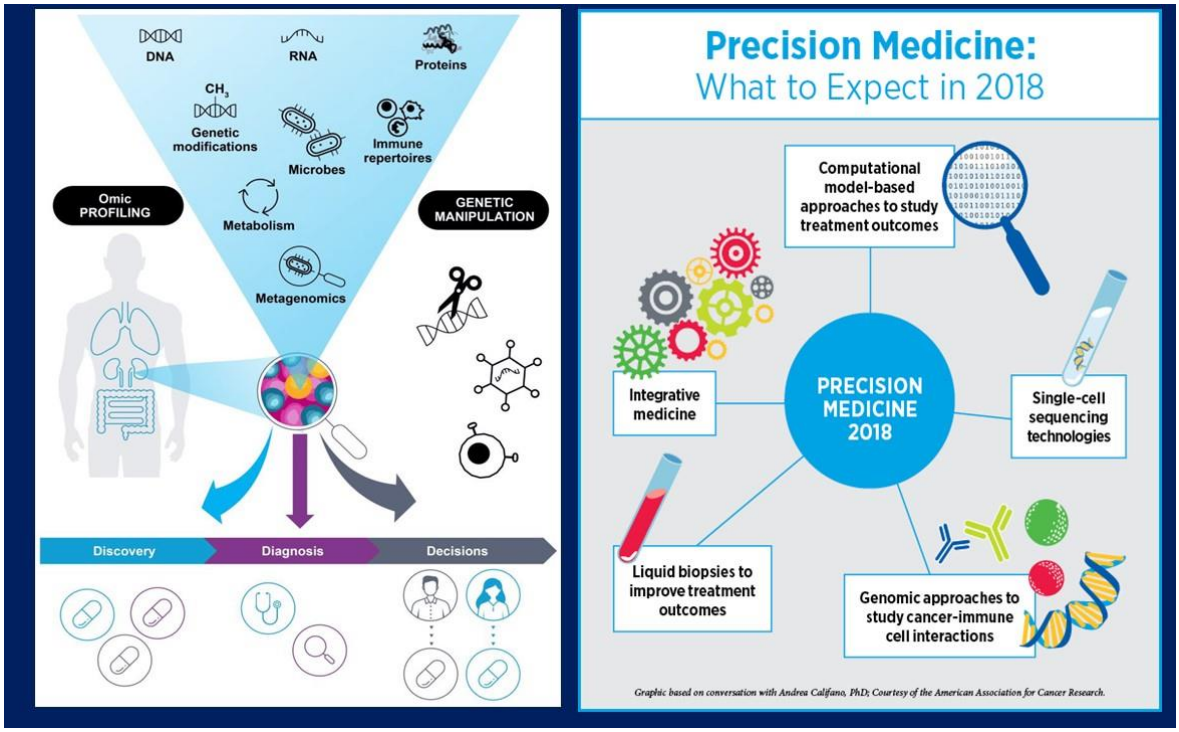


**Figure 3.** Individualized Medicine Approaches to Cancer Treatment

## The impact of individualized medicine in cancer treatment

In choosing a treatment method, individualized attention is paid to the patient's individual needs based on the patient's demographics, biology, tumor type, and individual preferences. In individualized treatment, the doctor does not use precise and predetermined criteria, but rather involves the patient in decision-making and pre-treatment preparations by consulting and providing the necessary guidance [26].

The different measures used to assess the effectiveness of personalized medicine in cancer treatment are based on new measures, such as days of survival and quality of life at home, rather than on previous measures that

measured patient mortality or years of survival after cancer.

## Targeted drugs in personalized medicine for cancer treatment

The FDA has approved more than a dozen drugs that target one of these mutations. These drugs currently include imatinib (Gleevec), a drug used for chronic xylogenous leukemia, and the breast cancer drug trastuzumab (Herceptin). Studying tumor genetics can tell doctors which drugs are effective and which are ineffective [27].

For example, if a colon cancer has a genetic mutation, two common colon cancer drugs may not be effective because the mutation changes the course of treatment. Many cancer clinics use a personalized medicine approach to look at and study the genes in a person's tumor. If the patient's cancer is found to have certain mutations, they can start treatment with a specific drug designed to target the genetic mutation in the cancer cells.

For example, if it's breast cancer, a genetic test can determine whether the patient will benefit from Herceptin, a breast cancer drug. If other treatment options, such as chemotherapy, haven't worked for the patient, studying the tumor's genes can still help.

A genetic mutation might lead the medical team to an unexpected drug, such as one originally designed for a different type of cancer. Personalized medicine works better than traditional treatments to shrink and treat tumors and save lives, but sometimes not all treatments are needed [28].

Tumors can contain cells with different gene mutations. So a targeted therapy designed to eliminate cells with a mutation may only work on a portion of the tumor. The remaining cells may continue to grow. What treatment plan will be effective for each individual cancer depends entirely on the doctor's findings and discretion.

## Benefits of Personalized Medicine

**1- Increased effectiveness of treatments:** One of the most important benefits of personalized medicine is increased effectiveness of treatments. For example, drugs that are effective for one person may not be suitable for another, or may even cause side effects. In personalized medicine, treatments are designed exactly to the needs of the individual, leading to better outcomes.

**2- Reduced side effects:** Since drugs are prescribed based on individual characteristics, the likelihood of side effects seen in general treatments is reduced. This helps improve the treatment experience and reduce patient problems [29].

**3- Disease prevention:** Personalized medicine is not only focused on treating diseases, but also helps prevent them. Using genetic information and personal data, doctors are able to identify the risk of developing specific diseases and consider preventive measures for each individual.

**4- Chronic disease management:** In chronic diseases such as diabetes, heart disease and cancer, personalized medicine can help provide more precise and effective treatments. For example, a study conducted by hematologist Philipp Stauber at the Medical University of Vienna investigated an innovative treatment strategy in which drugs were tested on the patient's own cancer cells, which were cultured outside the body.

In February 2022, researchers tested 130 compounds on cancer cells to identify the best treatment. The study found that a type of kinase inhibitor that is approved for thyroid

cancer but rarely used for lymphoma was effective. Doctors prescribed a special treatment regimen for the patient that included the drug. The results showed that the cancer cells shrank and the patient was able to undergo a stem cell transplant. The trial is an example of personalized medicine in action, which has been shown to increase the effectiveness of treatment [30].

## What is being studied in personalized medicine?

In personalized medicine, instead of relying on pre-existing genetic data, scientists specifically study each patient's genome. The goal is to use different methods to monitor the course of the disease and ultimately provide a personalized treatment for each patient. This approach allows doctors to design unique treatments for each person, tailored to that person's genetic characteristics and health status.

## How are personalized medicine tests performed?

In the personalized medicine process, when extracting a sample of a cancerous lymph node, surgeons typically immerse the tissue in formaldehyde to prepare it for standard pathology analyses. However, this method kills the cells, making them useless for functional tests. For this reason, the researchers convinced the surgeons to keep the tissue alive and send it to the lab for processing immediately [31].

In the lab, the researchers use tools like a knife, forceps and a nylon strainer to break up the cells and prepare a solution that is distributed in a 386-well plate. Each well contains a different combination of drugs, including chemotherapy agents, enzyme-targeted drugs and immune-modulating therapies. After an overnight incubation, the data will determine which drugs are effective in treating this type of cancer and which are not. This method helps doctors determine the best and most effective type of treatment for each patient [32].

For example, in a trial, researchers found that 17 of 29 patients with refractory acute myeloid leukemia (AML) responded to drug-screening-based treatments and entered remission. Also, research from the University of Mississippi found that patients with aggressive brain tumors had better outcomes when their chemotherapy treatments were guided by precision medicine than conventional treatments. This method, which was invented in the late 20th century, was initially not welcomed due to limitations in cancer treatment methods, but today, with the advancement of science and technology, this precise method can be used to treat cancer individually.

## What are the challenges of personalized medicine?

Although the concept of screening a group of drugs to treat patients seems simple, its implementation in practice faces several challenges. One of the main problems is the complex and technical methods used to culture cancer cells outside the body, which are not only time-consuming but also expensive [33].

Another major challenge is the difficulty in simulating the environment inside the human body. For example, a solid tumor may respond positively to one drug in vitro, but in the body and under different physiological conditions, it may have a different outcome. These factors highlight the need for further advances in technology and laboratory methods, if

personalized medicine is to fully realize its potential in precisely treating patients. Personalized medicine represents a revolution in the field of healthcare and, by combining genetic knowledge, advanced technology and data analysis, has a promising future.

This new approach focuses on providing precise treatments tailored to the individual characteristics of each patient, rather than the same treatments for all patients. As scientific and technological advances continue, personalized medicine is expected to become an integral part of healthcare systems. In the future, individuals will be able to benefit from treatments that are not only more effective, but also safer and tailored to their unique circumstances, with access to digitized genetic and health information. This development promises to improve patients' quality of life and reduce healthcare costs globally [34].

## The Role of Genomics in Precision Medicine

Genomics, the study of an individual's complete set of genes, plays an important role in precision medicine. By analyzing an individual's genetic information, scientists can identify genetic changes that may contribute to the development of diseases or affect the response to certain drugs. This information can then be used to guide treatment decisions and develop personalized treatments.

Advances in genomic technologies such as next-generation sequencing have made it possible to sequence an individual's entire genome at a relatively affordable cost and in a reasonable timeframe. This has opened up new opportunities to understand the genetic basis of diseases and tailor treatments accordingly. Genomic information can be used to identify genetic mutations that are associated with specific diseases, such as cancer or rare genetic disorders.

By identifying these mutations, healthcare professionals can determine the most appropriate treatment options, including targeted therapies or clinical trials that specifically target the underlying genetic abnormality. In addition, genomics can also help predict an individual's response to certain medications.

Pharmacogenomics, a branch of precision medicine, focuses on how an individual's genetic makeup affects their response to medications. By analyzing genetic variations that affect drug metabolism or drug targets, healthcare professionals can optimize drug selection and dosing to maximize effectiveness and minimize adverse effects [35].

## Integrating environmental and lifestyle factors

In addition to genetic information, precision medicine also considers environmental and lifestyle factors that can influence a person's health and response to treatments. These factors include diet, exercise, exposure to toxins, stress levels, and socioeconomic status.

By taking these factors into account, healthcare professionals can develop a more comprehensive understanding of a person's health and provide personalized recommendations for lifestyle modifications or interventions. For example, if a person has a genetic predisposition to a particular disease, such as heart disease, but leads a healthy lifestyle, their risk of developing the disease may be significantly reduced [36].

On the other hand, if a person has a genetic susceptibility to a disease and also engages in unhealthy behaviors, their risk may be further increased. Integrating environmental and lifestyle factors into precision medicine allows for a more holistic approach to healthcare.

It recognizes that genetic information alone is not sufficient to fully understand an individual's health, and that external factors play an important role in disease development and treatment outcomes [37].

## Precision Medicine Benefits

Precision medicine offers several advantages over traditional healthcare approaches. By tailoring treatments to each individual's unique characteristics, precision medicine has the potential to improve treatment outcomes and reduce adverse effects. This personalized approach can lead to more effective treatments, faster recovery times, and improved quality of life for patients. In addition, precision medicine has the potential to revolutionize drug development.

By identifying specific genetic targets or biomarkers associated with diseases, researchers can develop targeted therapies that are more likely to be effective. This can streamline the drug development process, reduce costs, and increase the success rate of clinical trials [38].

In addition, precision medicine has the potential to improve healthcare efficiency and reduce healthcare costs. By identifying individuals who are at higher risk for developing specific diseases, preventive measures can be taken to reduce the likelihood of developing the disease. This proactive approach can lead to early diagnosis, early intervention, and potentially lower healthcare costs in the long run.

## Challenges of Precision Medicine

While precision medicine holds promise, it also faces several challenges that need to be addressed. One of the main challenges is the availability and accessibility of genetic and health data. In order to develop personalized treatment plans, healthcare professionals need access to comprehensive and accurate genetic and health information [39].

However, there are still barriers to data sharing and privacy concerns that need to be addressed. Another challenge is the integration of precision medicine into routine clinical practice. Adopting new technologies and implementing personalized treatment strategies requires changes in healthcare infrastructure, healthcare professional training, and reimbursement models. These changes can be complex and time-consuming, and require collaboration between multiple stakeholders, including healthcare providers, researchers, policymakers, and patients.

In addition, there are ethical considerations that need to be addressed in precision medicine. These include issues of informed consent, privacy, and the potential for discrimination based on genetic information. It is important to ensure that individuals have a clear understanding of the implications of genetic testing and that their privacy is protected. Despite these challenges, precision medicine has the potential to revolutionize healthcare by providing personalized and targeted treatments. As advances in technology and data analytics continue to accelerate, precision medicine is expected to play a significant role in improving patient

outcomes and changing the healthcare landscape [40].

## What cancers can be treated with precision medicine?

We offer genomic sequencing for most solid and liquid cancers that have not responded to treatment. Some examples include:

- ✓ Abdominal cancers such as pancreatic cancer, appendix cancer, and stomach cancer.
- ✓ Esophageal cancer.
- ✓ Head and neck cancer.
- ✓ Leukemia.
- ✓ Lung cancer that has not been successfully removed by surgery.
- ✓ Melanoma.
- ✓ Metastatic breast cancer.
- ✓ Metastatic colon cancer.
- ✓ Metastatic prostate cancer.
- ✓ Ovarian cancer.

Genomic sequencing is not available for cancers that are responding to current treatment. Please note that precision medicine is an effective alternative to standard chemotherapy for many patients, but it is not necessarily a cure.

Our goal is to choose the most appropriate treatment for your individual cancer, so that you can enjoy better health and a longer, better life. Cancer may be a cruel disease, but precision oncology is here to revolutionize the way cancer is diagnosed, monitored, and treated. Unlike traditional methods, precision oncology diagnoses cancer at the genetic level.

This makes the diagnosis much more accurate and comprehensive. Different elements of precision oncology are applied to different tumors. Your doctor is the best person to decide on the course of treatment.

## Discussion

In February 2022, researchers tested 130 compounds on cells grown from Sander's cancer. They basically tried everything they had to see what might work. One option looked promising. It was a type of kinase inhibitor that is approved to treat thyroid cancer but is rarely or never used for a rare subtype of lymphoma [41].

Doctors prescribed him a treatment regimen that included the drug, and it worked. The cancer shrank, enabling him to undergo a stem cell transplant. He has been in remission ever since. "I'm a little freer now," says Sander, a 38-year-old procurement manager who lives in Austria. "I'm not afraid of death anymore," he adds. "I try to enjoy life." His story is a testament to this kind of intensive, highly personalized approach to drug screening, known as "functional precision medicine." It aims to tailor treatments to patients, but it differs from the genomic-guided paradigm that has dominated the field.

Instead of relying on genetic data and the best available understanding of tumor biology to choose treatments, doctors test everything they have on cancer cells in the lab to see what works. What it sometimes lacks in sophistication can make up for in results. In pilot studies, Stauber and his colleagues found that more than half of people with leukemia whose treatment was guided by a functional drug trial enjoyed longer remissions than those who received traditional treatments. Large-scale testing of genomic approaches has shown that these approaches are very effective against some cancers [42].

Overall, however, they benefit only about 10 percent of patients. Stauber and his team's latest trial is the first to compare functional and genomic approaches with treatments

guided by standard pathology and physician intuition. “This will be a very powerful study and will likely validate the utility of these functional assays,” says Anthony Letai, a hematologist at Dana-Farber Cancer Institute in Boston, Massachusetts, and president of the Functional Precision Medicine Society. Companies around the world are already offering this type of personalized drug testing service, but proponents of the strategy still have a lot to prove [43].

While the concept of screening a batch of drugs seems simple, the methods used to grow cancer cells outside the body can be technically difficult, time-consuming, and expensive. The challenges are particularly difficult for solid tumors, which live in complex environments inside the body. Simulating that environment is no easy task. Researchers are trying out a variety of approaches, from growing tumor samples in mice and chicken embryos to cultivating precisely engineered organoids and even delivering an infinite number of different drugs to a tumor while it’s still in a patient’s body. “It won’t be easy to figure out what works in terms of cost and scale and what’s practical,” says Christopher Kemp, a cancer biologist at the Fred Hutchinson Cancer Center in Seattle, Washington. “But this is revolutionary. Patients are demanding this approach.” Down a long hallway, beyond a set of orange doors, is the Vivi-Bank at the Medical University of Vienna [44].

The term stands for “Viable Biobank,” and it’s a room filled with barrels of liquid nitrogen, each containing frozen lymphoma samples. When surgeons extract samples of cancerous lymph nodes, they usually immerse the tissue in formaldehyde to prepare it for standard pathology analysis. However, this kills the cells and makes them useless for functional testing. So to make the drug screening process possible, Stauber and Ingrid Simonitsch-Klupp, a hematopathologist who co-supervises the VV Bank, had to convince their fellow surgeons to change their method, keeping the tissue alive and sending it quickly for processing and storage. “The fresh tissue is the most important thing,” Simonitsch says. A portion of the tissue arrives at Stauber’s lab, where researchers use a knife, forceps and a nylon strainer to break up the cells, creating a watery substance to distribute in a 384-well dish [45]. In each well, they test a different drug combination, including chemotherapy agents, enzyme-targeted drugs, immune-modulating therapies, and more. After an overnight incubation or exposure to the right environmental conditions of humidity and temperature, the tests show which drugs are active against the cancer and which are not. A multiwall plate is a laboratory dish with small holes that are evenly spaced.

A team of doctors uses this information to determine the most appropriate course of treatment for each patient. Several groups have reported success with this general approach. For example, in a trial from the University of Helsinki, researchers found that drug screening of leukemia cells provided informative results significantly faster than genomic profiling and also led to significant clinical responses [46].

Of 29 people with refractory acute myeloid leukemia (AML), 17 responded to drug screening-based treatments and went into remission. Similarly, Candace Howard, a radiologist at the University of Mississippi Medical Center in Jackson, and her colleagues published a study last year showing that

people with aggressive brain tumors lived longer and spent less on health care each year when their chemotherapy regimens were guided by tests than when their treatment was guided by a doctor's intuition alone.

Jagan Valluri, a cell biologist at Marshall University in Huntington, West Virginia, who founded a Huntington-based company called Cordgenics to commercialize the method used in Howard's trial, says it's cheaper and more effective. Drug-function testing is not a new idea. It was embraced by cancer researchers in the late 20th century, but it quickly fell out of favor. That was due to the limitations of the assay at the time and the limited set of anticancer drugs. Technological advances and an expanded drug repertoire have changed that. However, like most lab-based testing systems, the equipment required can be expensive and requires trained personnel to set up [47].

This is a major limitation, says Joan Montero, a biochemist at the University of Barcelona in Spain. It prevents the widespread implementation of accurate drug testing, especially in low-resource settings. To address these challenges, Montero and her colleagues are developing inexpensive, portable microfluidic devices for rapid, in-situ testing of cancer cells. However, their microfluidic platform is years away from practical use and may only guide treatment for certain types of cancer. That's because protocols developed for targeted therapies against leukemia don't always work for solid tumors of the breast, lung, liver, and other organ systems.

Biopsies from solid tumors often provide fewer cells, requiring more steps to culture the cells before drug screening. In addition, solid tumors have complex interactions with the healthy cells around them, meaning the models need to be more sophisticated [48].

## Growing Pains

The first challenge is growing enough tumor tissue for testing. David Ziegler, a pediatric neurologist at the Children's Hospital of Sydney in Australia, had decided to conduct separate drug screenings for about 1,000 children with high-risk cancers as part of a childhood cancer program. But in experiments, he and his team found that after a few days in the lab, more than a fifth of the patient samples either had no cancer cells at all or were outnumbered by healthy, normal cells. Researchers quickly learned to screen cultures for tumor cells, using imaging, cellular analysis, or genetic profiling before testing them against drugs. Cell cultures from solid tumors can in principle be subjected to the same type of testing used for leukemia, but a growing number of research groups are building complex structures known as organoids to test these patient-derived 3D tissue models, which are created by growing tumor samples on specialized scaffolds over a period of weeks to simulate the complex tissue architecture of a tumor and thus more accurately represent the cancer that doctors are trying to treat.

"We want to put tumor cells in an environment that is as close as possible to how they grow in the body," says Alice Soragni, a cancer biologist at the University of California, Los Angeles.

"This process can add weeks to our timeline for getting drug sensitivity data," says Carla Grandori, co-founder of Precision Medicine, "but the extra effort and investment in time is worth it." In clinical validation studies, Grandori and her colleagues found that drug

screening results using organoids matched patient results with about 80 percent accuracy. The findings have not yet been published, but case reports have been published in the past year describing people with difficult-to-treat cancers who, after exhausting treatment options, found unexpectedly effective treatments by testing drugs on organoid samples [49].

"Her response was definitely one of the best I've seen," says Heidi Gray, a gynecologic oncologist at the University of Washington Medical Center in Seattle who treated one of the patients, a woman with ovarian cancer. The drug they tried is typically used to treat leukemia, but it helped the woman's ovarian tumor beat back for more than a year, allowing her to travel and enjoy precious time with loved ones before finally giving up. "We've profoundly improved her quality of life, and that wouldn't have happened without the knowledge provided by this trial," Gray says.

## The Efficiency Model

In the hope of testing drugs against more realistic cancer systems, some researchers have chosen to study them in mice implanted with tumor samples. These personalized "avatars" were once heralded as the next big step in cancer care, but it wasn't long before it became clear that many tumors don't grow in mice. Screening drugs in bone marrow transplants is too time-consuming to make timely recommendations, and the cost of the approach, often more than $50,000, is beyond what patients and health care systems can afford [46].

"It was too slow, too expensive, and not robust enough," says David Sidransky, an oncologist at the Johns Hopkins University School of Medicine in Baltimore, Maryland, and a co-founder of the bone marrow model development. Although some drug companies continue to use bone marrow transplants for research, and some oncologists think there are specific situations where the method could help with patient care, for the most part, researchers do not use mice for functional testing in the clinic, and some have turned to other living systems.

One such alternative was proposed by Hon Leong, a cancer biologist at Sunnybrook Hospital in Toronto, Canada, and his colleagues, who developed a system for screening drugs on tumor biopsy samples grown on developing chicken embryos. The approach is both rapid and inexpensive, Leong says, and allows researchers to evaluate different drug options in a matter of weeks rather than months.

The ongoing trials focused on advanced breast and kidney cancers that had spread to other parts of the body. Leong and his team have successfully used chicken embryos to identify people who would benefit from immunotherapies. Another approach is from Ross Cagan, a developmental biologist at the University of Glasgow, England, who is using genome sequencing and genetic engineering to recreate the unique characteristics of a patient's tumor in fruit flies. This involves introducing mutated forms of cancer-promoting genes or combining sequences that limit cancer-suppressing genes [47].

Feeding flies diets containing different drugs could identify treatment regimens that suppress cancer growth, either by directly affecting tumor cells or indirectly affecting the animal's biology. Using the same approach, Keegan and colleagues identified a new three-drug combination that included a lymphoma treatment, a blood pressure drug,

and a arthritis treatment that, when tested in a man with a rare salivary gland tumor, helped prevent the cancer from progressing for a year.

In another case, a man with aggressive colon cancer, using fly avatars guided researchers to administer a melanoma drug along with a bone-strengthening agent, which resulted in significant tumor shrinkage and a clinical response lasting nearly a year [48].

A London-based biotech startup called Vivan Therapeutics now offers this custom fly-based drug screening service for $15,000 per patient. However, every model has biological limitations. So some researchers have decided to forgo animal models or cell clones altogether. Instead, researchers have developed implantable devices that allow doctors to test drugs directly on patients' tumors, and to do so while the cancer is still in the body [49].

Last year, Oliver Jonas, a bioengineer at Brigham and Women's Hospital in Boston, and his colleagues demonstrated the feasibility of this strategy in people with lung and brain cancers. In small trials, surgeons inserted tiny drug-delivery devices, each loaded with nanodoses of up to 12 drugs, into the tumors while the people underwent surgery to remove the cancerous tumor. During surgery, drugs flowed from separate reservoirs in a device the size of a grain of rice into the surrounding tissue.

Those tissues, along with the device itself, are then removed at the end of the procedure and subsequently analyzed for molecular markers of drug efficacy. So far, the data collected has not been used to guide treatments, but the analysis suggests potential benefits. Two companies with Jonas's involvement are now developing these kinds of on-site drug-testing platforms. Predictions of treatment outcomes are only as good as a patient's ability to access the recommended drugs, and if those drugs are expensive or unapproved, costs and insurance reimbursement can be a barrier for patients. Pamela Becker, a hematologist at City of Hope Cancer Center in Duarte, California, has faced some of these challenges when trying to prescribe drugs identified during guided treatment trials for people with multiple myeloma and other blood cancers. "I couldn't get my best choice," she says [50].

Becker had to narrow down the list of recommendations and eventually find drugs that would be covered by insurance. Fighting such policies depends on the availability of compelling clinical data, but collecting such data can be challenging. Functional testing strategies may even work for conditions outside of cancer.

In cystic fibrosis, for example, organoid models made from rectal or intestinal tissue are starting to help doctors find effective drug regimens for people with rare disease-causing mutations who don't qualify for any approved treatments. Many cancer researchers feel the same way, and now they just need to prove it to the broader medical community. So all eyes are on Stauber and his trial, which researchers predict will go a long way toward convincing doctors that genomics is not the end of personalized care [51].

Precision medicine is a model of care that proposes personalizing healthcare by tailoring medical decisions, practices, or pharmaceutical products to each patient. In this model, diagnostic tests are often used to find optimal treatments based on a person's genetic makeup. Tools used in precision medicine include molecular diagnostics and imaging. In this new study, researchers at

Rutgers University are applying precision and personalized medicine to cancer treatment. Their analysis covers the entire process of capturing PPM data, creating PPM products, and the social and economic consequences of using PPM. In the study, which is the result of work by several researchers at the university, the researchers report that PPM has the potential to transform cancer treatments. Conventional approaches involve diagnosing a tumor and then using general treatment approaches such as surgery, chemotherapy, and radiation therapy (Figure 3).

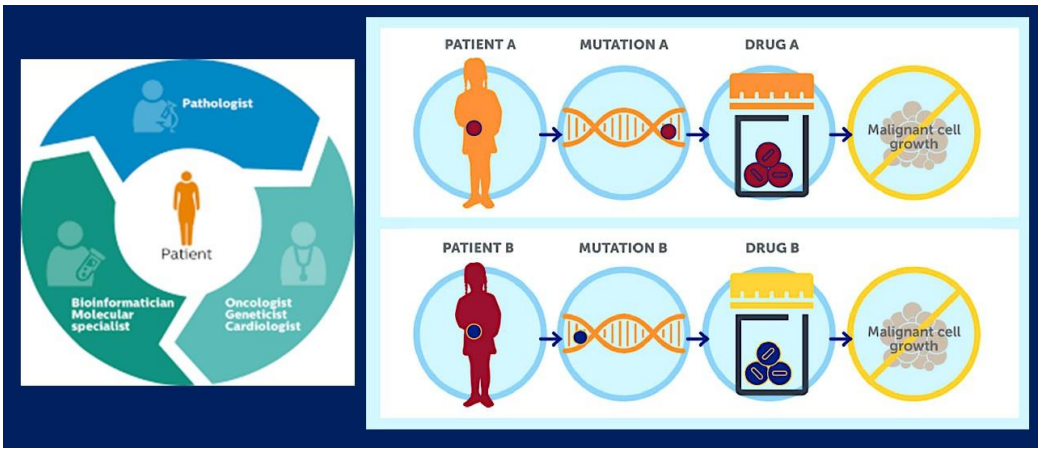


**Figure 3.** Westchester Medical Launches Precision Medicine Initiative

In contrast, in PPM, researchers use targeted treatment approaches that are more effective and have fewer unwanted side effects. These treatments are identified by analyzing specific tissues, gene mutations, and personal factors specific to each unique case of cancer. Examples of these emerging therapies include immunotherapy and cancer vaccines. In addition, these researchers have raised social issues related to precision and personalized medicine in health care and wellness. According to the researchers, some challenges need to be resolved before precision and personalized medicine becomes a part of standard cancer care [52].

These challenges include legal challenges, economic concerns, and the feasibility of using precision and personalized medicine, which is associated with socio-economic and individual problems. Today, precision and personalized medicine is becoming an effective and satisfactory approach, and the aforementioned challenges must be overcome before this therapeutic approach can be introduced into the fight against cancer [53].

## Conclusion

Personalized medicine, targeted medicine or precision medicine are new concepts in the world of health. This field of medicine tries to take a comprehensive interdisciplinary approach, that is, by simultaneously taking advantage of the capacity of different sciences such as genetics, basic medical sciences, laboratory sciences, medical engineering, and computer sciences, to benefit from the practical integration of their achievements in order to improve medical diagnostic and therapeutic knowledge and provide services that best match the medical needs of patients. In this way, by considering the unique genetic and family conditions of each person, the

occurrence of a specific disease in the future is predicted and by providing appropriate health advice and making lifestyle changes, efforts are made to reduce the likelihood of its occurrence. Finally, in the event of a disease, treatment is taken by pursuing one or more treatment methods that are likely to be more effective for the individual. Personalized medicine is one of the most promising approaches to dealing with diseases that have not responded to existing treatments so far. Cancer, neurological diseases, and rare genetic diseases are among the most important of these diseases. Many cancers can be prevented to some extent by lifestyle changes such as quitting smoking and alcohol, managing weight, and changing diet, but most cancers are caused by a genetic predisposition to the disease. Many major neurological diseases, such as Alzheimer's disease, have a similar situation regarding the basis of heredity. The financial, clinical, and social imperatives of finding treatments for these diseases have led to a growing interest in targeted medicine. With the availability of abundant digital data and the computational and analytical power of statistics and computer science, researchers are discovering the relationships between disease-causing genes, drugs, and human populations. Traditionally, medical treatments have been developed based on population averages and general guidelines. However, it is increasingly recognized that individuals respond differently to diseases and treatments due to genetic variations, environmental factors, and lifestyle choices. Precision medicine seeks to fill this gap by using advanced technologies and data analysis to identify the specific characteristics of each patient and develop personalized treatment plans. At the core of precision medicine is the understanding that each individual's genetic makeup is unique. The human genome, the complete set of genetic information in an individual, contains approximately 20,000-25,000 genes that determine various traits and susceptibility to diseases. By analyzing an individual's genetic information, scientists and healthcare professionals can gain insights into the underlying causes of diseases and identify targeted treatments that are more likely to be effective. Precision medicine encompasses a wide range of medical fields, including genomics, pharmacogenomics, digital health technologies, and big data analytics. These fields work together to provide a comprehensive understanding of an individual's health and develop personalized treatment strategies.

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