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EMERGING ROLE OF PRECISION MEDICINE IN CANCER TREATMENT

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ABSTRACT

Background: Cancer remains a serious threat with high risk of mortality. Cancer begins when genetic changes interfere with the orderly process of cell growth. The changes that occur in one person's cancer may not occur in others who have the same type of cancer. And, the same cancer-causing changes may be found in different types of cancer. Precision cancer medicine comes from studies of human genes and the genes involved in different cancers. **Methods:** Previously published articles regarding the role of precision medicine in cancer treatment have been collected and reviewed. **Observations:** Precision medicine refers to the tailoring of medical treatment to the individual characteristics of each patient. Cancer is a major focus of the precision medicine initiative. Precision cancer medicine focuses on matching the most accurate and effective treatment to each individual cancer patient based on the genetic profile of the cancer and the individual. Genetic testing may help determine if a patient was born with a higher risk of developing cancer due to an inherited gene mutation. There exists a growing category of precision products called companion diagnostics (CDx), which are molecular assays that measure levels of proteins, genes, or specific mutations to reveal a specific, efficacious therapy for an individual's condition. Advanced genomic testing is designed to help identify the DNA alterations that may be driving the growth of a specific tumor. Information about genomic mutations that are unique to individual cancer may help doctors identify treatments designed to target those mutations**.** Experts believe precision medicine could help lower health care costs in some ways. Precision medicine can help guide doctors in choosing the right tests,

which can then help them choose the treatments that will work best and hopefully have the fewest side effects**.**

KEYWORDS: Precision medicine, Personalised medicine, Genes, Cancer treatment.

INTRODUCTION

Genes play a fundamental role in cancer - that is, cancer is caused by certain changes to genes that control the way human cells function. These can be inherited but can also be introduced during a person's lifetime through external agents (e.g. carcinogenic chemicals or radiation). Each person's cancer has a unique combination of genetic alterations. Some of these changes may be the result of cancer, rather than the cause. As the cancer continues to grow, additional changes will occur. Even within the same tumor, cancer cells may have different genetic changes.

The mapping of the human genome has accelerated discovery of driver genetic alterations in cancer and the development of drugs to target or otherwise exploit these events. The identification of pathways involved in the pathophysiology of carcinogenesis, metastasis, and drug resistance, as well as the emergence of technologies enabling tumor molecular analysis and the discovery of targeted therapies, have stimulated research focusing on the optimal use of targeted agents.

One of the major discoveries of the last decade has been the identification of some specific alterations that are able to change the signal in the tumour cell and create a phenomenon called "addiction". This phenomenon means that the tumour can survive and reproduce itself mainly because this alteration is present. These alterations may be of different types. The majority of them are gene mutations, translocations and amplifications. It is therefore intuitive that giving a drug that targets these specific alterations is fundamental in fighting the war against cancer. This is the biological basis of personalised medicine. Precision cancer medicine comes from studies of human genes and the genes in different cancers. It is a way health care providers plan specific care for their patients based on person's genes in cancer cells.

The overall goal is to match therapies to individuals to ensure that they receive effective treatment with minimal toxicity.

Precision or Personalised

There is a lot of overlap between precision and personalised medicine. According to National Research Council, personalised medicine is an older term with meaning similar to precision medicine. The scientific community changed to precision medicine out of concern that personalised would imply treatments and preventive measures developed uniquely for the individual. In precision medicine, the focus is on identifying approaches which will be effective for patients based on genetic, environmental and lifestyle factors.

Genomics play a vital role in both precision and personalised medicine. However, even highly personalised information may or may not lead to improved health outcome and the individualised therapy may not be practical due to cost and complexity. Moreover, precision medicine approaches may lead to non-personalised interventions that can be used population wide.

Precision medicine

Precision medicine refers to the tailoring of medical treatment to the individual characteristics of each patient.[1] It does not literally mean the creation of drugs or medical devices that are unique to a patient, but rather the ability to classify individuals into subpopulations that differ in their susceptibility to a particular disease or in their response to a particular treatment.

It looks at how a specific mutation in gene affects a person's risk of getting a cancer or in case of cancer patients, how genes in cancer cells affect cancer treatment. The approach uses.[2] information from genetic tests to help doctors to make a plan for treatment that usually involves very specific recommendations.

Precision cancer medicine utilizes molecular diagnostic testing, including DNA sequencing, to identify cancer-driving abnormalities in the tumor's genome. In certain cases, precision medicine can help make a more accurate diagnosis and improve treatment and in other cases it can help make decisions on earlier screening tests and other steps towards prevention if a person is at risk for a particular cancer. It is an approach to care that allows doctors.[3] to select treatments based on genetic understanding of a person's disease. This genetic understanding is done by testing blood, tumor tissue or saliva to get a molecular analysis of cancer cells.

Precision as a single word means to hit a target on the same place over and over again. Likewise, precision medicine aims to create medicine models that target a similar feature of a disease that appears in multiple cancers/diseases. All the data generated by a precision medicine approach would be used to[4] replace or complement the current diagnostic criteria and to identify patient subgroups with similar genetic, phenotypic and lifestyle parameters contributing to disease (Fig 1).

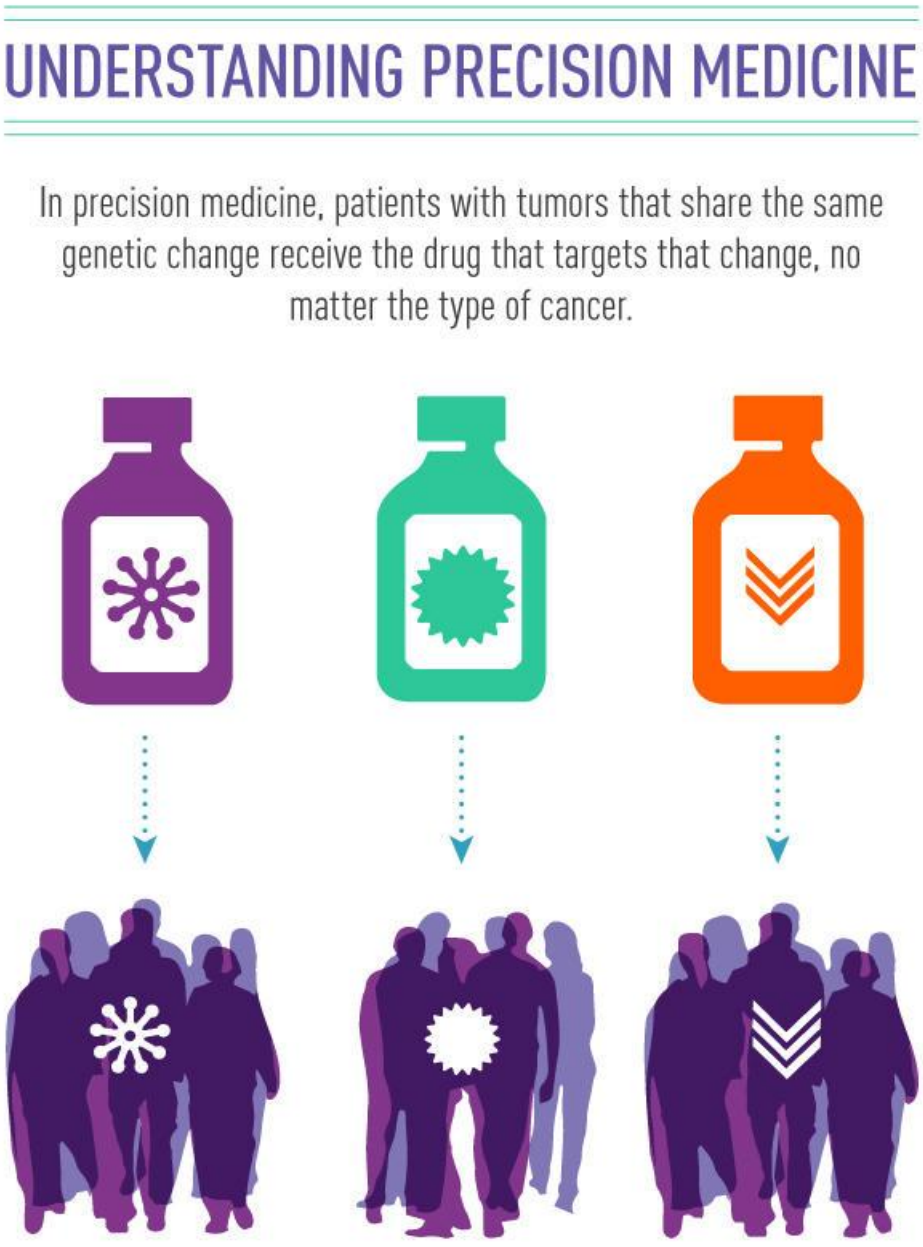

Fig. 1: In precision medicine, patients with tumors that share the same genetic change receive the drug that targets the change irrespective of the type of cancer.

Precision medicine in cancer

Cancer is a major focus of the precision medicine initiative and developments in precise and effective treatments could benefit many other chronic diseases. Precision oncology or precision medicine of cancer focuses on matching the most accurate and effective treatment to each individual cancer patient based on the genetic profile of the cancer and the individual. Because every single cancer patient exhibits a different genetic profile and the profile can change over time, more patients will benefit if therapeutic options can be tailored to that individual.

Currently, a cancer patient is required to undergo extensive testing to identify the stage and grade of cancer. The treatment that a patient receives will depend on the type of cancer, its size, and whether it has spread to other regions. Based on the reports, a team of oncologists decides the course of treatment. There are four main types of standard cancer treatments: surgery, radiation therapy, chemotherapy, and immunotherapy. Some individuals will only require one treatment, but most often,[5,6] a combination of treatments is used to tackle the resistant nature of cancer. The effectiveness of these treatments depends on many individual factors, such as the type, stage, and location of the cancer as well as the patient's age and overall health.

With precision medicine, information about genetic changes in tumor can help decide which treatment will work best. This suggests that several personal factors should be considered before selecting a cancer treatment. Traditional model for cancer therapy is overly simplified; it results in ineffective, expensive treatments and causes patients to suffer from unnecessary side effects. A more effective model, poised to change this "one size fits all" approach, is based on precision medicine (Fig 2). This perspective promotes the development of specialized treatments for each specific subtype of cancer, based on the measurement and manipulation of key patient genetic and omic data (transcriptomics, metabolomics, proteomics, etc.).

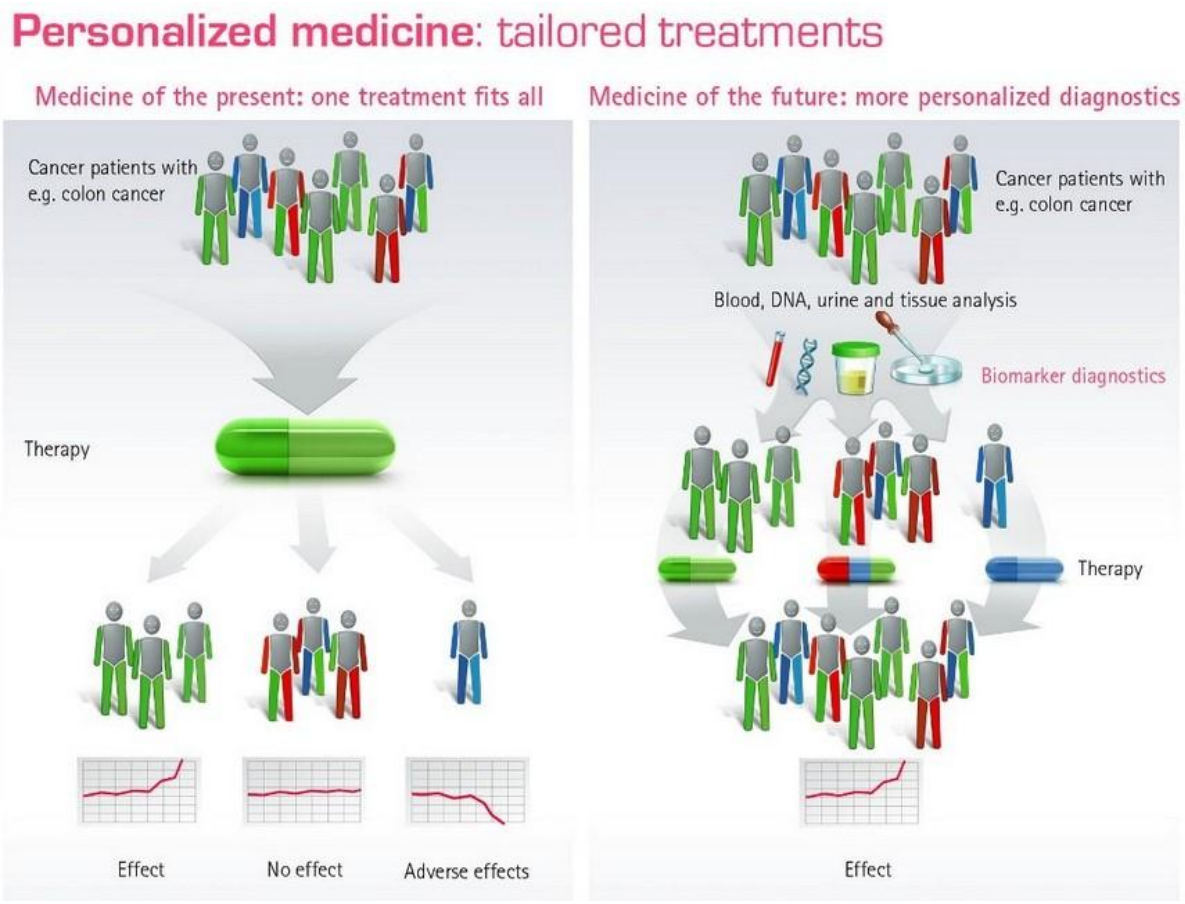

Fig. 2: Traditional medicine follows a one-size-fits-all approach. Drugs and other therapies are designed to treat large groups of people with the same disease. Whereas precision medicine, create medicine models that target a similar feature of a disease that appears in multiple cancers.

Precision medicine in cancer prevention

Sometimes precision medicine is[6] used for people with certain cancers or who are at higher risk for developing certain cancers. For example, a person might realize cancer runs in their family, or their doctor might notice a pattern of cancer in their family. In these cases, the patient might meet with a certified genetic counselor and consider having genetic testing. The testing can show if they have a gene change or mutation that puts them at a higher risk for certain types of cancer. If so, the doctor might recommend screening and other tests (often at a younger age than usual) to help find cancer early and prescribe medicines or suggest healthy habits that might help lower cancer risk.

Genetic testing

Genetic testing may help determine if a patient was born with a higher risk of developing cancer due to an inherited gene mutation. Being diagnosed with a hereditary condition may empower patients to make more informed decisions about how to manage their cancer risks.

Genetic testing may be useful in making informed decisions about how to manage future risks of cancer. For example, if it is determined that a person is at greater risk than the "average" patient for breast cancer recurrence, it may recommend adding breast MRIs to the routine screenings. A genetic test requires a DNA sample that can be obtained from blood, saliva or a mouthwash sample.

The test results provide information on the role of genes and hereditary in the development of cancer and which of the family members may be affected. The test results may also help the doctor to develop a individualized care plan

Precision medicine in cancer diagnosis

For people with a cancer diagnosis, their tumor might be tested for certain types of gene changes or proteins made from those gene changes. This testing can provide information about how their cancer grows and spreads. These tests might be called biomarker tests, chromosome tests, gene tests, or biochemical tests. It might be done using a blood or saliva sample, biopsy tissue, or body fluids.

There exists a growing category of precision products called[7] companion diagnostics (CDx), which are molecular assays that measure levels of proteins, genes, or specific mutations to reveal a specific, efficacious therapy for an individual's condition. Some examples include Dako Denmark's HERCEPTEST and HER2 FISH PharmDx Kit, which determine HER2 protein and gene overexpression in fixed breast, metastatic gastric, or gastroesophageal junction adenocarcinoma tissues. Another example, Myriad Genetic Labs' BRACAnalysis CDx, detects and classifies DNA variants in the protein coding region of the BRCA1/2 genes using patient whole blood samples. These CDx allow for the selection of a treatment that is more likely to be effective for each individual based on the specific characteristics that their cancer possesses.

Precision medicine in cancer treatment

In some cancers, the gene testing done on a tumor can affect treatment choices. This is because certain gene changes can affect how a tumor responds to certain treatments. And some tumors have gene changes that are different from other tumors of the same type. For example, not every melanoma skin cancer will have the exact same gene mutations. This means these tumors might not respond to a treatment the same way. The goal is to give a treatment that can target a gene mutation, without causing too many side effects, and to avoid giving treatments that might not work.

Types of cancer where precision medicine is used

It's important to understand that precision medicine is not used for every cancer. However, the hope is that one day, treatments will be[8] customized to the specific gene changes in each person's cancer. Much research is being done in this area.

Some of the more common cancers where precision medicine is being used to help with treatment decisions include:

- Colorectal cancer
- Breast cancer
- Lung cancer
- Certain types of leukemia
- Certain types of lymphoma
- Melanoma
- Esophageal cancer
- Stomach cancer
- Ovarian cancer
- Thyroid cancer

Advanced genomic testing

Advanced genomic testing is designed to help identify the DNA alterations that may be driving the growth of a specific tumor. Information about genomic mutations that are unique to an individual cancer may help doctors identify treatments designed to target those mutations. These targeted assessments study the DNA profile of the patient's tumor, searching for genetic abnormalities that can be matched to drug therapies that may not have otherwise been considered**.**

A biopsy will be taken of tumor. Cancer cells will be isolated and extracted from the biopsy, then their DNA will be sequenced in the lab. Highly sophisticated equipment will be used to scan the sequenced genetic profile for abnormalities that dictate how the tumor functions. The abnormalities will be[9] analyzed in a lab to determine whether they match known mutations that may have responded to therapies or where evidence suggests there may be a potential treatment option not previously considered. If there's a match oncologist may be able to use the results to suggest treatments that have been used in the past to target the same mutations.

Cost of precision medicine in cancer

Experts believe precision medicine could help lower health care costs in some ways. This is because precision medicine can help guide doctors in choosing the right tests, which can then help them choose the treatments that will work best and (10) hopefully have the fewest side effects. This means a patient might avoid getting treatments that are not likely to work well, along with unnecessary side effects.

But precision medicine can also increase some costs

- Tests for gene mutations can be expensive, and insurance might not cover all genetic testing costs.
- For people who are at high risk for cancer because of a gene mutation, there might be increased costs from getting recommended[11] screenings and other preventive care. (On the other hand, they are doing what's needed to help prevent a cancer diagnosis or to find it early when it's often easier to treat, which can prevent higher costs in the future.)
- For people who need a specific targeted therapy or immunotherapy treatment because of a tumor's genetic makeup, the drug might be very expensive.

Benefits of precision medicine in cancer

- The wider ability of the doctors to use[12] patient's genetic and other molecular information as a part of routine medical care.
- Chance to incorporate patient's personal preferences to specialize a treatment plan.
- Extended survival rate, especially in the case of cancer patients.
- Figuring out effective treatment for the cancer patient
- Design of new tools for building and analyzing treatment data.
- A better understanding of the underlying mechanism causing the disease.
- Reduction in the total cost of treatment.
- Fewer side effects and avoidance of unnecessary treatment.

Limitations of precision medicine in cancer

- Access to the latest precision medicine research might be limited.
- A lot still needs to be learned about how precision medicine can be used in cancer.
- Many clinical trials are done with patients who have specific types and stages of cancer. But to be part of a precision medicine clinical trial, a person must have a certain genetic change that can be targeted by a medicine that is being tested.
- Precision medicine[13] clinical trials are often available only at larger cancer centres. This means sometimes the chances to be part of a clinical trial can be limited.
- Even when precision medicine is available outside of a clinical trial, it might not always be used as well as it could be.
- A patient's family history of cancer might not be well known or evaluated. Or, genetic testing might not have been done, its results might not be adequate, or its results are not used to make decisions about health.
- Even if a person is diagnosed with a type of cancer where gene tests are available, the tumor might not be tested to find out if there is a gene mutation that might change treatment choices.
- The cost of gene testing and the tests and medicines that might be recommended as a result of gene testing can be a concern.

Future of precision medicine

There are many critics of medical innovations around the world that have constantly argued that such technologies are over-hyped and medical professionals must stay careful with the extent and use of such tools. The same is true about precision medicine as well.

Precision medicine has been downgraded a number of times in the past. The[14] prospects of precision medicine are vast and should not be underestimated. There are software and algorithms that can actually be used to map mutations and associated them with treatments that are most likely to work faster for patients. The cost of genome sequencing has reduced from millions to thousands, and now it is possible to derive cancer cells from the blood of the patient for analysis than to take a tissue sample for biopsy Technology is, therefore, expected to bring a lot of positive changes in how treatment is delivered to cancer patients. The same is the case of precision medicine, which is all set to become a part of the mainstream medical practice in the near future.

Scope of review

This review aims in summarizing and providing the recent developments of our understanding on the emerging role of gene based precision medicine in cancer treatment.

CONCLUSION

Cancer is a major focus of the precision medicine initiative and developments in precise and effective treatments could benefit many other chronic diseases. Precision oncology focuses on matching the most accurate and effective treatment to each individual cancer patient based on the genetic profile of the cancer and the individual.

Precision based therapy is widely used in the diagnosis, treatment as well as prevention of many cancers. Gene testing, genomic testing, companion diagnosis etc are the various application of precision therapy in the field of oncology. Experts believe precision medicine could help lower health care costs, although the initial costs of performing genetic analysis for every patient ahead of first line therapies is currently unrealistic.

The prospect of precision medicine is vast and is, therefore, expected to bring a lot of positive changes in how treatment is delivered to cancer patients and become a part of the mainstream medical practice in the near future.

Conflict of interest

The author (s) declared no conflict of interest with respect to the authorship, research or publication of the article.

REFERENCES

1. Apostolia-Maria Tsimberidou, Nancy G. Iskander, David S. Hong et al. Personalized Medicine in a Phase I Clinical Trials Program: The MD Anderson Cancer Center Initiative; Clinical Cancer Research, 2012; 18: 6373-83.
2. Andrea Garofalo, Lynette Sholl, Brendan Reardon et al. The impact of tumor profiling approaches and genomic data strategies for cancer precision medicine; Genome Medicine, 2016; 8: 79-89.
3. Kyaw L. Aung, Sandra E. Fischer, Robert E. Denroche et al. Genomics-Driven Precision Medicine for Advanced Pancreatic Cancer: Early Results from the COMPASS Trial; Clinical Cancer Research, 2018; 24(6): 1344-54.

4. Barbara C. Worst, Cornelis M. van Tilburg, Gnana Prakash Balasubramanian, et al. Next-generation personalised medicine for high-risk paediatric cancer patients -The INFORM pilot study; European Journal of Cancer, 2016; 61: 91-101.
5. Lorraine A. Chantrill, Adnan M. Nagrial, Clare Watson, Amber L. Johns et al. Precision Medicine for Advanced Pancreas Cancer: The Individualized Molecular Pancreatic Cancer Therapy (IMPaCT) Trial; Clinical Cancer Research, 2015; 21: 2029-37.
6. Katerina Politi and Roy S. Herbst; Lung Cancer in the Era of Precision Medicine; Clinical Cancer Research, 2015; 21: 2213-20.
7. Andrew J. Aguirre, Jonathan A. Nowak, Nicholas D. Camarda et al. Real-time Genomic Characterization of Advanced Pancreatic Cancer to Enable Precision Medicine; Cancer Discovery, 1096-111.
8. Burney IA & Lakhtakia R Precision medicine: Where have we reached and where are we headed? Sultan Qaboos Univ. Med. J, 2017; 255–58.
9. Li SZ, Todor A & Luo RY, Blood transcriptomics and metabolomics for personalized medicine. Comput. Struct. Biotechnol. J, 2016; 14: 1–7.
10. Masayuki Nagahashi, Toshifumi Wakai, Yoshifumi Shimada et al. Genomic landscape of colorectal cancer in Japan: clinical implications of comprehensive genomic sequencing for precision medicine; Genomic Medicine, 2016; 8: 136-148.
11. Linda Huang, Helen Fernandes, Hamid Zia et al. The cancer precision medicine knowledge base for structured clinical-grade mutations and interpretations; Journal of the American Medical Informatics Association, 2017; 24(3): 513–19.
12. Hiroshi Ichikawa, Masayuki Nagahashi, Yoshifumi Shimada et al. Actionable gene-based classification toward precision medicine in gastric cancer; Genome Medicine, 2017; 9: 93-105.
13. Chantal Pauli, Benjamin D. Hopkins, Davide Prandi et al. Personalized In Vitro and In Vivo Cancer Models to Guide Precision Medicine; Cancer Discovery, 2017; 7(5): 462–77.
14. Elena Garralda, Keren Paz, Pedro P. Lopez-Casas et al Integrated Next Generation Sequencing and Avatar Mouse Models for Personalized Cancer Treatment; Clinical Cancer Research, 2014; 20: 2476-84.