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Personalized Medicine in Cancer Chemotherapy

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Abstract : Personalized medicine is used to learn about a person's genetic makeup and how their tumor grows. Personalized medicine simply means the prescription of specific therapeutics best suited for an individual. Personalization of cancer therapies is based on a better understanding of the disease at the molecular level. The field of cytopathology has evolved from basic Pap staining of tumors to the use of immune cytochemistry and complementary ancillary molecular diagnostics to aid in specifying the disease. This "personalized" approach to diagnosis allows the clinician to provide therapy based on specific genetic mutations of the tumors from their patients. The FDA has dramatically increased the number of approved in vitro assays for patients with genetic mutations that respond to drugs that prevent the expression of the mutations, such as tyrosine kinase inhibitors. These alternative forms of therapy have dramatically increased the survival rate in patients with stage four and metastatic cancer.

Introduction:

Every day, millions of people are taking medications that will not help them¹. The top ten highest grossing drugs in the United States and India help between 1 in 25 and 1 in 4 of the people who take them. For some drugs, such as Statins -routinely used to lower cholesterol –as few as 1 in 50 may benefit⁴. Classical clinical trials harvest a handful of measurements from thousands of people. Personalized medicine requires different ways of testing interventions. Researchers need to probe the myriad factors genetic and environmental, among others that shape a person's response to a particular treatment^{2,3}.

Personalized medicine also called individualized or precision medicine is a medicinal model that uses patient's genetic profile to customize decision made to choose the proper medication, therapy and dose in regards to the prevention, diagnosis and treatment of the disease. Under a personalized medicine scheme, drug prescribing and dosing no longer would be "one size fits all" but would be carefully tailored to a patient's individual genetic variants. Knowledge of a patient's genetic profile can help doctors select the proper medication or therapy and administer it using the proper dose or regimen⁵. They also want to find treatments

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that cause fewer side effects than the standard options. By performing genetic tests on the cancer cells and on normal cells, doctors may be able to customize treatment to each patient's needs. This term is usually described as providing "the right patient with the right drug at the right dose at the right time."⁶

In the application of personalized medicine to cancer it is very important to distinguish somatic from germ-line variation. The report of the Royal Society in 2005 on the future of personalized medicine focused almost entirely on the personalization of the efficacy and safety of drugs based on genetic studies^{7,9}. Every person has a unique variation of the human genome. Although most of the variation between individuals has no effect on health, an individual's health stems from genetic variation with behaviors and influences from the environment⁸. The advancement of personalized medicine mostly depends on technology that confirms patient's fundamental biology such as DNA, RNA, or protein, which ultimately leads to confirming disease⁹. For example, techniques such as genome sequencing can reveal mutations in DNA that influence diseases ranging from cystic fibrosis to cancer. Another method, called RNA-seq, can show which RNA molecules are involved with specific diseases¹⁰.

The concepts of personalized medicine can be applied to new and transformative approaches to health care. They also want to find treatments that cause fewer side effects than the standard options²⁹. By performing genetic tests on the cancer cells and on normal cells, doctors may be able to customize treatment to each patient's needs¹¹.

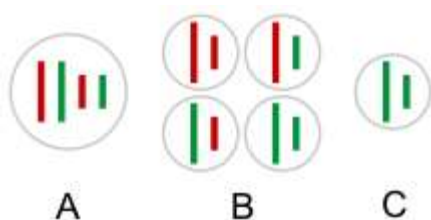


Fig. No: 1 – Gametes of a hybridogenetic hybrid contain the genome of one parental species (C), instead of all possible combinations of both parental (red and green) chromosomes (B). A - somatic cell¹².

Personalized vs. Precision Medicine:

The terms personalized medicine and precision medicine are often used interchangeably. While experts are not in agreement as to whether the two terms mean the same thing, the definitions of personalized medicine and precision medicine seem to be merging¹³. Even President Obama, in his remarks about the Precision Medicine Initiative, commingled the two: "Precision medicine – in some cases, people call it personalized medicine – gives us one of the greatest opportunities for new medical breakthroughs that we have ever seen."³⁰

Examples of personalized medicine:

Some examples of personalized medicine strategies for cancer include the following:

A **targeted treatment** targets a cancer's specific genes and proteins that allow the cancer cells to grow and survive. Researchers are finding new targets each year and creating and testing new drugs for these targets¹⁴. This is a few, but not all of the cancers where targeted treatments are used.

- Breast cancer
- Colorectal cancer
- Gastrointestinal stromal tumor
- Kidney cancer¹⁶
- Lung cancer
- Melanoma
- Multiple myeloma
- Some types of leukemia and lymphoma
- Some types of childhood cancers^{14,15}

Pharmacogenomics:

Pharmacogenomics is one of the part of personalized medicine. Pharmacogenomics looks at how a person's genes affect the way the body processes and responds to drugs¹⁷. These changes influence how effective and safe a drug is for a person. For example, some people's bodies may process a medicine more quickly than others. This means that the person would require a higher dose of that drug for it to be effective. However, someone else's body may not process a drug as quickly¹⁸. The drug would then stay in the bloodstream for a longer time and may cause more severe side effects. Pharmacogenetic testing presupposes the availability of validated genetic tests, i.e., tests for which there are data linking the presence or absence of specific variants with a specific outcome, such as improved therapeutic response or reduction in adverse events. People with colorectal cancer sometimes have a specific altered gene. These patients may have serious side effects when treated with the drug, Irinotecan (Camptosar)¹⁹. This gene makes it harder for the body to break down the drug. In these patients, doctors prescribe lower amounts of the medicine so patients will have fewer side effects²⁸.

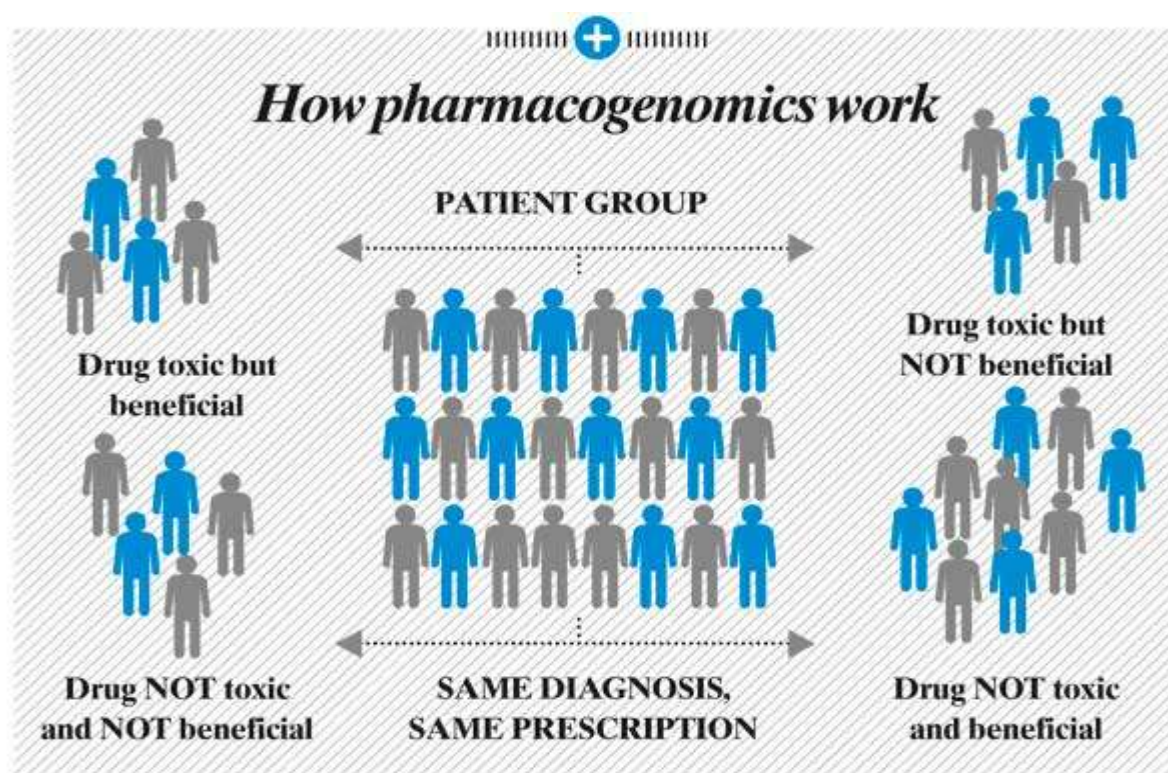


Fig. No: 2 – How Pharmacogenomics Work?²⁷

Why personalized medicine is important?

People with the 'same' cancer can have different forms of the disease so responses to treatment can vary. Cancers growing in different parts of the body may also share the same genetic faults so respond to similar treatments. Personalized medicine is important because of the following reasons

- Personalized Medicine is a Multi-Faceted Approach to Patient Care.
- Personalized Medicine Promises Improved Patient Outcomes.²⁰
- Personalized Medicine Can Improve Efficiencies within the Health Care System.
- A New Treatment Paradigm i.e., The molecular profile of an individual patient and their disease influences the effect of a medicine; biomarker diagnostics help to target the right medicine to the right patient.²⁶
- Personalized Medicines Are Benefitting Patients Across Many Different Diseases.
- Oncology is on the Leading Edge of Personalized Medicine.²¹
- Advances in Personalized Medicine Improve Outlook for Patients with Blood Cancers.
- Advances in Personalized Medicine Improve Outlook for Patients with Blood Cancers.

- Personalized Medicine Yields Treatment Breakthroughs: Metastatic Melanoma.
- Personalized Medicine Helps Predict Treatment Response: Metastatic Colorectal Cancer.
- Personalized Medicine Enables Targeting of the Underlying Cause of Disease: Cystic Fibrosis.²²
- Personalized Medicine Can Create Efficiencies in the Health Care System.



Fig. No: 3 – Personalized medicine programme

Who benefits from personalized medicine?²³

When treatment gets personal everyone will benefit:

- **Patients** will receive access to a range of new more effective, targeted treatments.
- **Scientists** will be able to develop new drug treatments that target specific genetic faults and design more efficient clinical trials.
- **Doctors** will be given access to high-quality genetic tests that enable them to tailor treatment for each patient.
- **The NHS** will benefit from time and cost savings so doctors can treat patients more effectively.

Taking Steps towards Personalized Medicine:

A lot of work has already been done to make cancer care more personalized, because cancer is so complex where we are unable to know the cause of it also. Decades of advances in basic science, technology, therapeutics, and the understanding of the genetic causes of cancer have coalesced, it is learned that cancer can arise from any number of genetic malfunctions, and often is due to a combination of errors, that ultimately lead to the out-of-control cell growth that causes tumors to grow and spread²⁴.

Targeted therapy took off in the late 1990s and early 2000s, with the advent of drugs that interfere with the essential functions of cancer cells in order to get them to die off – such as by stopping cancer cells from dividing or keeping tumors from making the new blood vessels they need to grow.

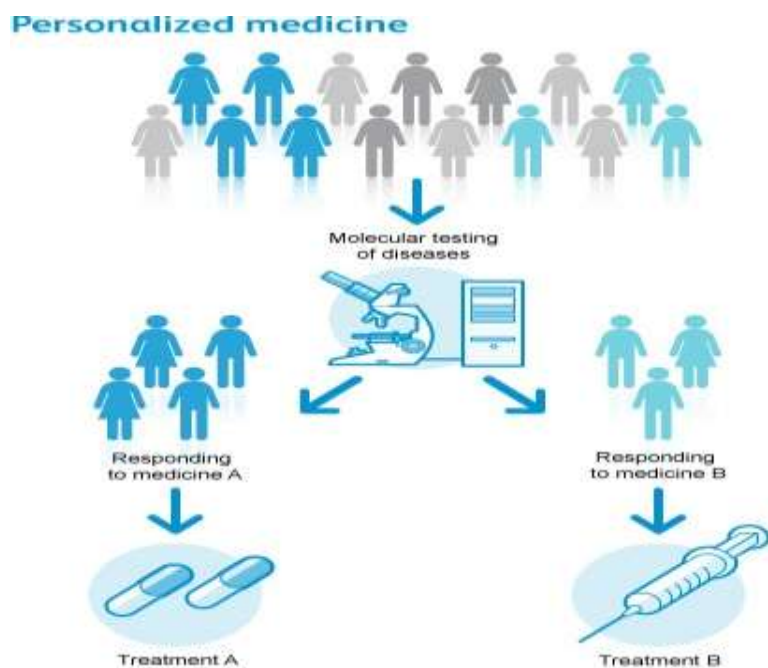


Fig. No: 4 – Personalized Medicine

Better Treatments, Fewer Side Effects:

When it comes to cancer, personalization can take several different forms currently. It might mean: testing a person's cancer to find out if a certain type of treatment will work on it, looking at a person's genetics to decide whether he or she can handle a specific medicine, or conducting a genetic test to determine if a person has certain genetic mutations that could put them at a higher risk for developing cancer.²⁵

Conclusions:

Overall, there is no doubt that considerable progress has been made in the field of personalised medicine. At least in part this has resulted from the extraordinary developments in the speed and accuracy of genome sequencing combined with equally remarkable progress in the disciplines related to genomics, notably transcriptomics and proteomics. The ability to look at the genetic makeup of a person's tumor in a relatively quick and low-cost manner has been one of the most important contributors to progress in personalized cancer care.

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