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Precision and personalized medicine: new way for cancer management

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Abstract

Precision and personalized medicine (PPM) introduce to the tailoring of medical treatment to the individual characteristics of each patient. Cancer is one amongst the leading causes of death in India. Maximum chemotherapeutic agents are used for cancer patients, but lack of long-time effectiveness and severe side effects from these agents, to improve therapeutic outcome to developed new tool called PPM as follow. Better understanding of pharmacogenomics has been help to developed and the potential for customizing health care for cancers patients.

Recently, PPM has mainly involved the systematic use of genetic or other information about an individual patient to select or optimize that patient's preventative and therapeutic care. Information a couple of patient's proteinaceous, genetic, and metabolic profile may be accustomed tailor treatment to it individual's needs. A key attribute of this medical model is that the development of companion diagnostics, where by molecular assays that measure levels of proteins, genes, or specific mutations are wont to provide a specific therapy for an individual's condition by stratifying disease status, selecting the right medication, and tailoring dosages there to cancer patient's specific needs. In light of this, there is growing interest in the role of health care system or department of oncology to try to enhance a precision and personalized approach, underlining some recent successes.

This review will focus on the existing and future technologies that could speed the development of PPM products for Treatment of resistant cancer in individual patients. Specifically, it will concentrate on reviewing the phenotypic (activity based) rather than genotypic (mechanism based) approach to develop PPM useful for cancers patient. This article is perspective, during which attention is targeted on the particular alterations of the tumor, has opened the door to precision and personalized treatment.

Keywords: Personalized medicine, cancer, tumor, therapeutic outcome

1. Introduction

Precision medicine refers to the tailoring of medical treatment to the individual characteristics of every patient. The concept of personalized medicine recognizes this heterogeneity and considers each patient as having a novel tumor. A personalized medicine usually refers to a medical approach that put forward the customization of healthcare system — with medical decisions, practices, and/or products being tailored to the individual patient. Thus personalized medicine is often synonymous with precision medicine[12].

Since precision medicine relies on the comprehensive comprehension of individual molecular profiles using an early detection of markers like genomic, proteomic, metabolomics, as well as bioinformatics approaches to procure a thorough understanding of the correlation between the regulation of gene(s) (functional protein) and disease status, it depends largely on microarray and next generation sequencing (NGS) in obtaining the genetic information[3,4] .

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The Precision and Personalized medicine (PPM) approach is characterized by individualized treatments tailored to specific tissues, gene mutations and personal factors relevant to each unique case of cancer.

Adoption of immunotherapy has steered the sector of cancer treatment toward the concept of precision and personalized medicine, during which therapy selection is customized to every individual[5]. and it's a more effective model, poised to change this "one size fits all" approach, is based on PPM[6].

It is a perspective encourage the development of specialized treatments for each specific subtype of cancer, based on the quantification and manipulation of key patient heredity characteristics and omics data (transcriptomics, metabolomics, proteomics, etc.) as an example, Soda et al. identified a mutation in the anaplastic lymphoma kinase (ALK) that drives tumor formation in about 5% of non-small-cell lung cancers [8] Other chemotherapeutical and modern chemotherapeutical agent are failed due to either severe side effects or loss of effectiveness. And main reason for the loss of effectiveness is the development of chemo resistance[7].

To repress such problem, a new approach called precision medicine or personalized medicine has been recommend and initiated by the National Institutes of Health. There also exists a growing category of PPM 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[8]. 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 gastro esophageal Junction adenocarcinoma tissues[8,9].

These CDx provide the choice of a treatment that's more likely to be effective for every individual supported the particular characteristics that their cancer possesses. The FDA has shown support within the PPM approach with their approval of those and other technologies since 1998, when the drug trastuzumab was approved for the treatment of HER2 receptor positive breast cancer[9]. Moreover, the ratifying of the Precision Medicine enterprise in 2015 has also pushed the PPM field forward, by requiring the FDA to develop new platforms to evaluate PPM diagnostics and therapies.

Personalized medicine provides new tools to physicians that are more precise to probe not just the visually obvious, like a tumor on a mammogram or the looks of cells under a microscope, but the very molecular makeup of every patient.

A profile of a patient's genetic variation can guide the choice of medication or treatment protocols that minimize harmful side effects or ensure a more successful outcome. It may also indicate susceptibility to certain diseases before they become manifest, allowing the physician and patient to line out a concept for monitoring and prevention. The ability to profile the activity of genes, proteins, and metabolites is redefining how we classify diseases and choose treatments, allowing physicians to travel beyond the "one size fits all" model of medicine to make the most effective clinical decisions for each patient can mention above. Hence PPM more effective beneficial tool for cancer patient t for its managements.

Cancer is one of the leading causes of death in the India. In 2020 alone, there will be an estimated 1324 413 new diagnoses and 851678 cancer-related deaths[10]. Much work is ongoing to higher understand and treat this group of diseases. The general defining feature of cancer is accumulated cell mutation, which manifests as tumors with uncontrolled growth. However, cancer is a complex, extremely heterogeneous condition. There are over 100 types of cancers, located in different organs and sub tissues and originating from different cell types[5,8,10]. In population the Number of new cancer cases of male patient are found 646 030 and female patient are 678 383. Number of cancer male patient death are 438 297 and female patient 413 381 per year(5,8,10).

In the process of Development of a new drug is a costly and lengthy process. Theoretically, the use of pharmacogenomics data, or information about how patients' genes affect their drug responses, could reduce the time and cost of drug. Using genetic tests, researchers could preselect patients for studies, using those possibly to retort or least likely to suffer side effects. "Enriching" the run pool, as this approach is named, could reduce the scale, time, and expense of clinical trials. Hence it is very costly and more time consuming. Moreover, use of pharmacogenomics early within the drug development process could reduce product failures by focusing resources on drug candidates. And hence most likely to be safe and effective treatment for cancer patients. The goal of personalized medicine is to use the proper drug at the correct dose, with minimal or no toxicity, for the correct patient at the correct time. This article discusses the state of the art of this is very impotent management strategy of using the example of cancer[11,12].

2. History of PPM

The origins of precision medicine don't seem to be precisely known. That sway confusion about what is precision and personalized medicine. In upcoming year to know the mean by PPM. What's the link of precision medicine to personalized medicine? If any, is being made with evidence-based medicine. Hasn't health care professional always wandered to provide error free counsel? The phrase has come to refer to the way personal data and biomarkers surprisingly genetic biomarkers might be used to tailor treatments for individual patients of cancer. To well understanding of genetic information and other patient data have long been used to proceed, has meant over time might we understand what's actually new about the age-old aim to move from individual and pretendedly idiosyncratic patient outcomes to generalizable knowledge about management and disease, and the crucial role statisticians have historically played in that process[13–16].

Despite the palpable breadth of the term, precision medicine's modish proponents effectively have two visions in mind. The first is basically an advancement of pharmacogenetics—the development of pharmaceuticals on the premise of genetic information. Pharmacogenetics itself isn't new, and therefore the broader desire to use genetic data to boost health outcomes has its own long history.

Nineteenth-century pioneers in biometry and statistics—including Karl Pearson and Francis Galton—were deeply engrossed in the relationship of genetics and disease and in particular in promoting eugenical reforms to avoid the manifestation of 'degeneration' in diseases starting from psychological state to cataracts, it is emphasis on individual variation, to reveal and measure the interaction of "constitutional" and environmental factors in the distributions of disease. Pharmacogenetics had already begun the program of linking therapeutic response to both the biochemistry of drug agents and to the role of genetics and evolution in shaping individual differences. Precision medicine's proponents essentially coopted pharmacogenetics after the successful conclusion of the Human Genome Project round the turn of the century. Subsequent investments of the National Institutes of Health (NIH) under Francis S. Collins attempted to capitalize on this new knowledge to transform genetic medicine far beyond the study of well-known mutations and chromosomal anomalies[13,14].

Indeed, some of the new discoveries have been profound; a handful of successful high-profile drugs based on the genetics of cancer cells—for example, Herceptin (trastuzumab), Erbitux (cetuximab). Have given hope that over time our understanding of more diseases will be transformed.). Just as the 19th-century bacteriologist Robert Koch's postulation of all disease– one-organic-cause paradigm fit diseases like tuberculosis perfectly et al not in any respect, however, some diseases will likely be amenable to genetic approaches et al. not most.

A second vision proponents of precision medicine espouse is an increased ability to harness and aggregate new data sources concerning the manifestation and treatment of disease. The idea is that by identifying specific genes, biomarkers, or other factors that alter the probability of acquiring or alleviating disease, researchers are able to design more precise interventions[15,16].

This conception of PPM also draws on a long history of using biomedical data to tailor therapies to individual patients to compare treatment outcomes numerically, and to develop statistical tools. Physicians have, of course, long portrayed their job as tailoring therapeutic recommendations to patients' specific characteristics and particular management of disease.

This was true for pre modern medical knowledge across most of the India from traditional medicine which asserted that every person encompasses a natural balance of humors or cardinal substances. With disease occurring as a result of imbalance. Though ideas about etiology and treatment may are grounded in theoretical understandings. The contrast that contemporary precision medicine advocates often make is instead with empirical studies of therapeutics, namely, the determination of which treatments lead to measurably better outcomes. The idea of testing (trying) therapies on groups of patients and comparing outcomes also encompasses a long history[13,14,16].

3. Why Do We Need It?

However, DNA from different cells is the same, genes coding in one organ behaves differently than genes in other organs. In cancer, different tumors may have identical DNA, but the organic phenomenon pattern is different in numerous tumor types. Technologies such as gene-expression microarray allow us to inspect the gene expression profile of hundreds of genes at a time and to discriminate a cancer-associated gene expression profile from normal profiling. For decades, standard treatment has been guided by cohort-based epidemiological studies within which the genetic variability of

people isn't accounted for and most of the conclusions are based at the population level. Precision and personalized medicine takes into account an individual's genetic makeup and disease history before a treatment regimen is generated. This is in contrast to traditional personalized medicine, within which care relies on a patient's case history, social circumstances, environment, and lifestyle. This is the following parameter to use of PPM[12,17].

3.1. Reduce Time, Cost, and Failure Rate of Clinical Trials

Developing a brand-new drug could be a costly and lengthy process. Theoretically, the use of pharmacogenomics data, or information about how patients' genes affect their drug retaliation, could reduce the time and cost of drug development. Using genetic tests, researchers could preselect patients for studies, using those presumably to retort or least likely to suffer side effects. "Enriching" the trial pool, as this approach is termed, could reduce the scale, time, and expense of clinical trials. Moreover, use of pharmacogenomics early in the drug development process could reduce product failures by focusing assets on drug candidates most likely to be safe and effective[18].

3.2. Reduce the Cost of Health Care

Assimilate the precision and personalized medicine into the fabric of the health care system can help resolve many embedded inefficiencies, such as trial-and-error dosing, hospitalization of patients who have severe reactions to a drug, late diagnoses, and reactive treatment. Economists have estimated that the use of a genetic test to properly dose the blood thinner, warfarin, could prevent 17,000 strokes and 85,000 "serious bleeding events" each year and avoid the maximum amount as 43,000 visits to the hospital room. Overall cost savings to the health care system would be billion of amount annually[8,11]. An economic analysis of the Oncotype Dx gene expression test looked at the real costs of treating women with breast cancer in a of more member health plan[19]. Were limited to those patients with metastatic colorectal cancer whose KRAS gene is not mutated, because those are the only patients who benefit from the drugs[11]. Personalized medicine—prescribing the correct treatment to the correct patient at the correct time to extend efficacy and reduce side effects—can result in both improved clinical results and reduced costs. Along with increased access, these should be the goals of intelligent health care reform.

3.3. Make Drugs Safer

Many numbers of hospital admissions are associated with adverse drug reactions (ADRs). Many ADRs are the result of variations in genes coding for the cytochrome P450 family of enzymes[20,21]. These variants may cause a drug to be metabolized either faster or slower than within the general population. As a result, some individuals may have trouble inactivating a drug and eliminating it from their body, leading, effectively, to an "overdose" because it accumulates, while others eliminate the drug before it has a chance to work. The consequences of not considering variation in these genes when dosing can be anything from unpleasant to lethal. Administration of the drug, warfarin, won't to prevent blood clots, is complicated by genetic variations during a drug metabolizing enzyme (CYP2C9) and a vitamin K metabolizing enzyme (VKORC1). Dosing is usually adjusted for the individual patient through multiple rounds of trial and error throughout the primary year of treatment, during which the patient could also be in danger of excessive bleeding or further blood clots. The need to get warfarin dosing right the first time to avoid adverse effects led the Food and Drug Administration to recommend genotyping for all patients receiving warfarin[22]. Hence well understanding done by approaching a PPM.

3.4. Increase Patient Compliance to Treatment

Patient noncompliance to treatment ends up in adverse health effects and increased costs. When personalized therapies prove more effective or present fewer side effects, it can be presumed that patients will more likely comply with their treatments. The impact could be greatest for the treatment of diseases such as asthma, diabetes and cancer in which noncompliance commonly exacerbates the condition. At least one study supports this point [30]. Inherited sorts of hypercholesterolemia (high cholesterol) can increase the chance of infarction before the age of 40 by over 50-fold in men and 125-fold in women. Conventional monitoring of cholesterol levels can catch the condition early, but genetic testing offers additional benefits. In addition to detecting the condition before there are observable signs of disease, knowledge of a genetic predisposition for hypercholesterolemia provides patients with a robust incentive to create lifestyle changes and to treat their condition seriously. Patients with a genetic diagnosis have shown more than 86% adherence to their treatment program after 2 years compared to 38% prior to testing[11].

4. Use of PPM model over traditional treatment strategies

Before a PPM treatment can be developed and used in patients, a specific gene or mutation must be corresponded with a clinical outcome. This is a major convenant; it can take years of research performed by many scientists to uncover a phenotype or polymorphism that is clinically meaningful. Besides, understanding which polymorphism leads to a

positive versus negative treatment response in patients requires additional analysis. The first step in this process toward understanding the genetic code is to sequence DNA from many individuals by using Human Genome Project (HGP). With the extension of sequencing technologies, this step is becoming easier. The major challenges lie in interpretation of these enormous data sets, which is where bioinformatics plays a major role.

Another class of cancer treatments that have paved the way to more specific and effective therapies is immunotherapy, which harnesses a patients' own immune system to fight cancer. Immunotherapy treatments include monoclonal antibodies (mAbs), checkpoint inhibitors, cytokines, vaccines, and adoptive cell transfer, most prominently within the type of hematopoietic somatic cell transplants (HSCTs) and chimeric antigen receptor (CAR) T-cell therapies[1823]. Adoption of immunotherapy has steered the sphere of cancer treatment toward the concept of precision and personalized medicine (PPM), within which therapy selection is customized to every individual. Over the past decade it's become increasingly clear that no two patients' cancers are precisely the same, and hence, may have variable responses to generic treatments like chemotherapy and radiation[24]. This is 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 PPM. The field of PPM is based on data that captures current and past physical health and environmental exposure. Based on these data, patients are categorized into groups for different, clinically relevant purposes. A few samples of the uses of PPM include determining genetic predisposition to a disease, identifying patient groups for clinical trials, and identifying individuals that are more likely to respond well to a specific therapy[25].

The completion of the Human Genome Project (HGP) gave scientists the flexibility to read and interpret an individual's order and to spot genetic predispositions to certain diseases. This milestone event changed the attitude on health from reactive to preventative. Today, scientists are working toward obtaining a close understanding of the function of the body from multiple omics levels and characterizing how genetic predispositions are tormented by environmental exposures.

Together, all of this information will ultimately allow scientists and doctors to better predict how patients will respond to a certain treatment. As highly valuable tools that assist personalized therapies, CDx assay patients for genetic traits that identify whether the patient would reply to a selected treatment. This approach can have a significant impact on the care of the patient. The revolution lies in the change from a clinician selecting a generic therapy that is more or less experimental for the patient, to one that effectively targets the disease with PPM[12,15,24].

This review comments on the fields of personalized medicine and precision medicine, taken together as PPM. Although today the terms are often interchanged —they both refer to the use of unique characteristics from patients to select the best treatment — the field was originally referred to as personalized medicine[265]. However, because it gained popularity and also the term became more widely employed in science, media, and society, it began to hold a misconception. Many people incorrectly assumed that thanks to the "personalized" nature, unique treatments were being developed for every individual. In order to clarify the particular goal of the sphere, the scientific community, specifically the National Research Council, has pushed for the utilization of precision and personalized medicine. Still, PPM continues to be more widely recognized by the general public[27].

In this review, the present state of the sector of PPM with reference to cancer is presented in three categories. We begin by describing the methods of

- Acquiring PPM Data. - Here, the multiple omics techniques (genomics, transcriptomics, proteomics, and metabolomics) accustomed characterize an individual's disease state are discussed. The understanding and application of these data as tools in clinical trial design and treatment selection are discussed in.
- Developing a PPM Therapy. - Emerging cancer products, like organoids, mAbs, cancer vaccines, and CAR T-cells are presented from a PPM perspective. Also addressed are the evolving federal regulations for PPM products, so as to confirm their safety and efficacy.
- Broader Consequences of PPM. -The economic and ethical concerns of PPM are considered. Establishing PPM is complicated from an economic point-of-view, likely requiring alterations to the contemporary insurance payer system.

The nature of the sector also can be daunting from an ethical perspective, requiring the establishment of sufficient protections to the Privacy and health of targeted patients. It is the opinion of this review that the sphere of PPM is helpful to the patient and therefore the scientific community, by stretching collaborations and expanding understanding of the biological complexity of cancer and its treatments.

This, however, doesn't come without the broad challenges and adaptations that are related to newly emerging fields, particularly from the standpoint of biotechnology companies and Society as a full. A comparison of the key differences within the traditional model of cancer treatment and therefore the emerging precision and personalized medicine (PPM) model. Traditionally, cancer has been treated using general, "one size fits all" approaches such as chemotherapy, radiation, and surgical excision of tumors.

These treatments vary widely in efficacy across individuals and also often cause harm to healthy, noncancerous organs and tissues. The PPM approach is characterized by individualized treatments tailored to specific tissues, gene mutations, and private factors relevant to every unique case of cancer[2816,17].

Companion diagnostics (CDx) help identify which treatments are simplest for a particular patient's tumor, and novel cell therapies are accustomed target the cancer with minimal damage to healthy tissues, making the PP M model more effective and safer given in figure 1.

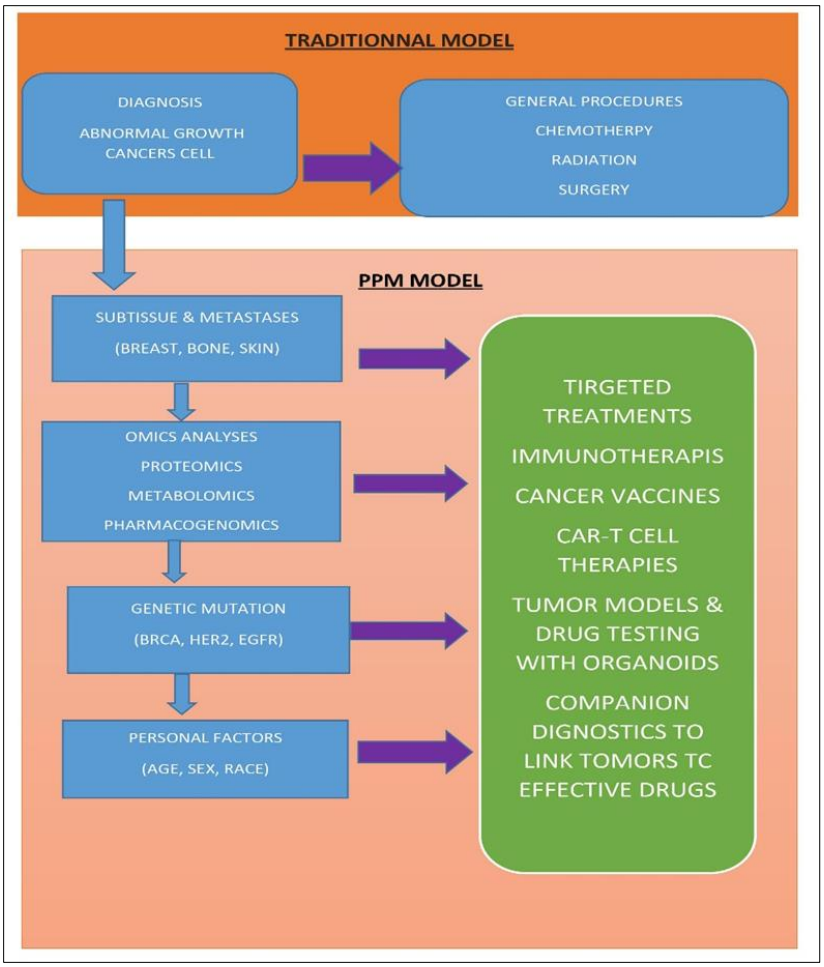

Figure 1 Traditional versus PPM model for cancer treatment[5,6,20]

5. Role of Clinical Pharmacist in Precision & Personalized Medicine

Doctor of pharmacy professionals are well trained in medication usage, dose adjustment and are involved in promotion of appropriate medication usage and concept of Personalized medicine is well suited from the professional's therefore clinical pharmacist (CP) from PharmD background can practice more effectively on Personalized medicines in cancer management.

Still there is need of awareness and more studies required on topic but from current scenario we can say that in future clinical pharmacist or pharmacologist acquire the large part of Personalized medicines in cancer management[10–12,24,29].

6. Conclusion

The PPM field has grown and matured tremendously since the milestone achievement of sequencing a whole human genome in 2003. PPM for patients diagnosed with solid tumors has resulted in several advance development in recent in decade. To obtain a relevant and real change which could improve all clinical outcome, a higher understanding of biology is required. To improve, a multi-omic approach able to integrate DNA and RNA alterations, proteomics, and metabolomics are necessary.

Personalized medicine involves not only tailoring the correct treatment/drug for the correct person but also evaluating predisposition to disease, sometimes several years before a disease is fully developed. It is timely and important to ask: Are we at the purpose of having the ability to treat each patient uniquely supported the whole DNA structure of their cancer? The answer is not any, we aren't there yet. However, the sphere is evolving, and personalized medicine has much to supply toward improving cancer treatment for today and tomorrow.

This article has moved beyond sequencing more accurately to linking this information to individual patient outcomes and treatment responses. Cancer treatment in particular stands to highly benefit from PPM therapies, since extensive variability between tumors presents a need to target each case in a personalized manner. Recent work has focused on the event of more accurate tumor models (organoids) and harnessing the specificity of the system to develop effective cancer vaccines or mAbs. The precision and personalized treatment approach has resulted in improved patient outcomes in terms of response rate and progression-free survival in Phase I clinical trials that selected patients using a specific biomarker. Additionally, generation of PPM therapies must be carried out with careful regards to evolving regulations.

As researchers acquire PPM data and companies develop PPM therapies, regulators, clinicians, patients, and the public must consider the broader consequences of PPM. A major collaborative effort between all associated groups — scientists, biopharmaceutical companies, insurers, clinicians, regulators, and patients — are going to be necessary to stay driving PPM forward and make it a viable field that benefits all.

Compliance with ethical standards

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Disclosure of conflict of interest

All Authors contributed equally and declared that they have no conflict of interest.

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