
REVIEW ARTICLE

Personalized Medicine: an Emerging Revolution in Health care

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ABSTRACT

Personalized medicine is an extension of traditional approaches to understanding and treating disease. Personalized medicine is a rapidly emerging multi-faceted therapeutic approach that uses an individual's genetic and epigenetic information to tailor drug therapy or preventive care. Personalized medicine aims at providing better diagnosis with earlier intervention, and more efficient drug development and therapies. Impact of personalized medicine in the treatment of various disease processes, its applications and future perspectives in health care are reviewed in the present study.

Keywords: Personalized medicine, genetic, epigenetic, drug therapy

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INTRODUCTION

With the completion of human genome project in the year 2003, personalized medicine started emerging as the crucial field in health care. Rapid developments in genomics, computational biology, medical imaging, regenerative medicine and the invention of the microarray biochip technology have further enhanced the development of personalized medicine. Personalized medicine or individualized medicine or precision medicine is a therapeutic approach that involves the use of an individual's genetic and epigenetic information to tailor drug therapy or preventive care. Personalized medicine aims at making the treatment as individualized as the disease. It involves identifying genetic, genomic, and clinical information that allows accurate predictions to be made about a person's susceptibility of developing disease, the course of disease, and its response to treatment. The traditional standard "one-dose-fits-all" approach to drug development and clinical therapy has been ineffective, as it incurs all risks of subsequent drug toxicities and treatment failures. Personalized medicine aims to develop rational means to optimize drug therapy, with respect to the patient's genotype, to ensure maximum efficacy with minimal **adverse effects**. Personalized medicine can assist clinicians in determining ideal drug dosing for their patients thereby preventing adverse reactions. The ultimate goal of personalized medicine is to furnish the proper treatment to the right person at the right time.

PERSONALIZED MEDICINE IN THE TREATMENT OF HIV

Abacavir, a nucleotide reverse transcriptase inhibitor used to treat patients with human immunodeficiency virus (HIV), is known to cause a life threatening hypersensitivity syndrome in some patients within six weeks of the onset of therapy. Before the advent of personalized medicine, this hypersensitivity reaction was made by clinical diagnosis. In 2002, two independent studies demonstrated a possible genetic link between the hypersensitivity reaction and the major histocompatibility complex class I allele HLA-B*5701 [3, 5]. Mallal *et al.*, conducted a follow up study in which they gave abacavir only to patients who were negative for the HLA-B*57:01 gene, and there was no hypersensitivity reaction in that patient population. The results demonstrated that patients who carry the HLA-B*5701 gene have a 60% chance of developing a hypersensitivity reaction when treated with abacavir, while patients who do not carry the gene do not develop the drug reaction at all [2,4, 6]. These studies clearly demonstrate that a patient's genome can predict response to a specific drug therapy.

PERSONALIZED MEDICINE IN THE TREATMENT OF CANCER

Personalized medicine can be used to predict a person's likelihood of developing certain types of cancer. It also helps doctors to learn about a person's genetic makeup and how their tumor grows. With this information, doctors hope to find prevention, screening, and treatment strategies that may be more effective. Physicians can also find treatments that cause fewer side effects than the standard options. One of the earliest and most common examples is breast cancer, the first cause of death by cancer in women worldwide. Mutations of the *BRCA1* and *BRCA2* genes that have been implicated in familial breast cancers and the loss of *APC* gene function in familial adenomatous polyposis. These genetic analyses would help predict a patient's likelihood of developing the disease and select screening strategies to lower the risk [8].

Researchers identify specific genes and proteins that allow the cancer cells to grow and survive, find new targets and test new drugs for these targets. Targeted treatment is used in various cancer treatments including breast cancer, colorectal cancer, gastrointestinal stromal tumor, kidney cancer, lung cancer, melanoma, multiple myeloma, some types of leukemia and lymphoma and some types of childhood cancers.

PERSONALIZED DRUG DOSAGE

Pharmacogenomics, the study of how genes affect a person's response to drugs is an important area of personalized medicine. For example, the processing time of a medicine may vary with individuals. Based on this variation, appropriate drug dosage can be prescribed which in turn helps in avoiding adverse effects of medications. Millions of genetic variations may exist among individuals and identifying all these variations may be time consuming. However certain genetic tests are carried out to predict a patient's likely responses or poor reactions to certain medications.

Ideal drug dosage can be determined for the widely used anticoagulant drug warfarin based on genetic test. Supratherapeutic dosage of warfarin leads to an increased risk for adverse bleeding, while subtherapeutic levels leave the patient prone to clotting. Studies have shown that variations in three genes namely, *CYP2C9*, a gene encoding the enzyme responsible for warfarin metabolism; *VKORC1*, a gene encoding the enzyme that recycles vitamin K (the drug's primary target); and *CYP4F2*, a gene encoding the enzyme responsible for vitamin K metabolism are responsible for the inter-individual variability of this drug [7]. Based on the genetic profile, patient's age and weight, the ideal drug dosage can be determined.

A group of enzymes known as CYP 450 is responsible for metabolizing more than 30 types of medications. CYP 450 genotyping test can determine how quickly and effectively these agents are eliminated from the body. Depending on an individual's genetic makeup, the body might not break down the medication fast enough, instead allowing drug levels to accumulate, resulting in severe side effects. Conversely, a patient might have a genetic variation that causes the body to break down the medications too quickly before they have a chance to work. The CYP 450 test can be used to determine dosing and effects of specific antidepressant medications, anticoagulants such as warfarin, proton pump inhibitors, and a number of other agents [9].

Thiopurine methyltransferase is an enzyme responsible for the breakdown of chemotherapy drug thiopurine, used in the treatment of some leukemias and autoimmune disorders. Some people with genetic variation do not produce this enzyme which results in the accumulation of thiopurine in the body thereby leading to severe toxic reactions. Thiopurine methyltransferase test prior to the treatment would aid in better dosing guidelines for clinicians [9].

UGT1A1 is an enzyme that determines how the body breaks down irinotecan (Camptosar, Pfizer), a chemotherapy drug used in the treatment of colorectal cancer. Variation in the gene encoding for *UGT1A1* results in deficiency of this enzyme. These patients may have serious side effects when treated with the drug irinotecan (Camptosar). The medication can build up to toxic levels, possibly causing suppression of the bone marrow, infection, and even death. Doctors can carry out *UGT1A1* TA repeat genotype test to detect this genetic variation prior to the treatment and then customize the dosage to prevent a toxic buildup of the drug. Alternatively, if a patient has normal levels of the *UGT1A1* enzyme, the test may help to ensure that the dosage of irinotecan won't be lower than necessary [9].

The medication 5-fluorouracil (5-FU), along with its related compounds, is one of the most commonly used chemotherapy agents. Some people have a genetic variation that results in a decrease in the dihydropyrimidine dehydrogenase enzyme, which is responsible for breaking down 5-FU. As a result of this deficiency, some people may experience severe or even fatal reactions to 5-FU. Dihydropyrimidine dehydrogenase test can be used to detect patients with this enzyme deficiency which in turn would help doctors to determine the dosage thereby preventing a dangerous adverse reaction [9].

FUTURE PERSPECTIVES

Enormous revolutions made in the field of personalized medicine would aid in the development of safer and more effective treatment methods. Personalized medicine can be used to analyze a patient's genome to predict his/her likelihood of developing a specific illness, and can direct decision making about preemptive intervention. As a screening tool, personalized medicine can identify protein markers of disease long before clinical manifestations, and thus allow for earlier treatment and decreased morbidity and mortality [1]. It is anticipated that once fully developed, personalized medicine would revolutionize the practice of medicine and alter the paradigm of diagnosis-based medical practice. Further developments have to be made in the field of personalized medicine to make it cost-effective in order to benefit the man kind as a whole.

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