

The Promising Prospects of Precision Medicine

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Abstract

The emerging concept of personalized Medicine or precision medicine has recently become more popular both among the health-care providers and patients. The focus of personalized medicine is to target prevention and treatment strategies based on patients' variability in genotype, environment and lifestyle. Since precision medicine will make the clinical guidelines much more conditional and branched, It is expected that physicians would increasingly require informatics and algorithms supports to assist them with information management and evidence-based decision-making in medical contexts.

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Introduction

In recent years, the term "Precision Medicine" and its synonyms Personalized Medicine and Individualized Medicine have become much more popular among health-care providers and patients (1,2). Precision medicine denotes targeting prevention and treatment strategies based on individual variability of patients which include variation in genotype, environment and lifestyle (3). The goal of precision medicine is to increase the clinical outcomes and decrease untoward side effects through selecting the appropriate therapeutic intervention for each individual patient. The history of precision medicine could be referred to the earliest efforts of Splitter physicians (vs lumpers) who tend to apply accurate definition of diseases and describe more discrete entities (1). Historically, blood typing before blood transfusion and antibiogram determination before prescribing antibiotic in infectious diseases are considered two well-known application of precision medicine.

Another advanced example is the replacement therapy in patients with hemophilia by recombinant factors VIII and IX according to their deficiency. However, the major progress in precision medicine has coincided with recent developments of high throughput methods in characterizing patients especially in different molecular levels (e.g. genomics, transcriptomics, proteomics and metabolomics). These techniques provide large scale biological data which help us to have a better understanding about various diseases and their mechanisms and therefore, put a great momentum in improving precision medicine. Of note, recent developments in sequencing technologies have made a major effect on the acceleration of precision medicine. S such, the whole genome sequencing could cost 2.7 billion US\$ and took 13 years for human genome project while nowadays, by Next Generation Sequencing (NGS) it takes 3 days and costs less than 1000 US\$.

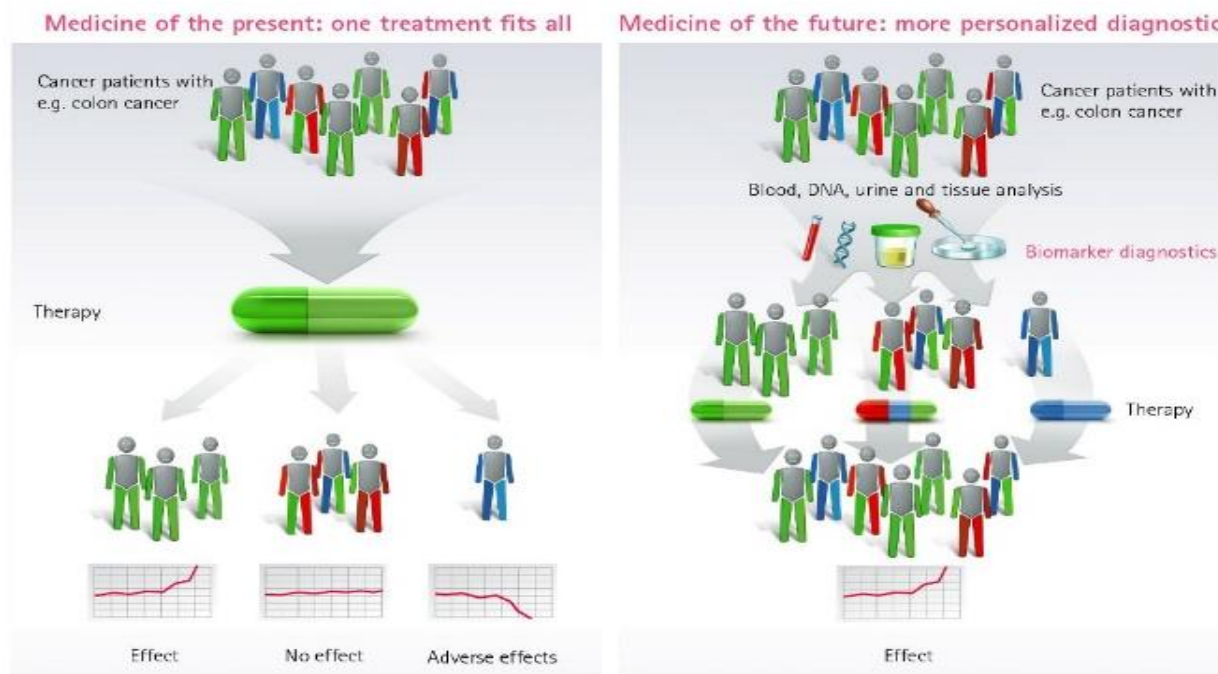
Therefore, it is now possible to consider the genome and the transcriptome of patients in the process of selecting appropriate interventions.

The genotype of patients has influence on both pharmacokinetics and pharmacodynamics of a drug. Pharmacogenomics is a part of precision medicine in which the role of genetic variation in drug absorption, distribution, metabolism and elimination are investigated as well as drug receptor target effects. On the other hand, pharmacogenomics tries to optimize drug therapy according to the patients' genotype, to ensure maximum efficacy with minimal adverse effects.

The costs of whole genome sequencing have dramatically decreased over recent years, however it is not reasonably cost-effective yet to be used in minor diseases. Therefore, development of affordable biomarkers is needed to increase the application of precision medicine.

but also in discovery and development of new personalized drugs.

The advent of medications for diseases with heterogeneous nature is one of the most outstanding applications of precision medicine. Based on the advances in molecular characterization, the etiology of such disease can be investigated with higher resolution for each individual patient. Indeed, cancer is the most famous example of a multifactorial disease and development of discriminating biomarkers for classification of them could have a great effect on selecting appropriate intervention. For instance, herceptin is an effective drug for women with breast cancer whose tumors overexpress HER2(4). In some diseases, predicting the prognoses of a therapeutic intervention is in fact an up-hill task. Bioinformatics and computational approaches are useful in finding simple as well as sophisticated



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A feature which is objectively measured and evaluated as an indicator of normal biologic processes, pathogenic processes, or pharmacologic responses to a therapeutic intervention is defined as a biomarker(4). Biomarkers are not only beneficial in personalizing the use of existing drugs,

discriminating patterns and development of new biomarkers. The necessity of improving precision medicine becomes more tangible, owing to the fact that the top ten highest-grossing drugs in the United State are considered helpful for only 25 percent of individuals who take them and in some other drugs

this ratio is as few as 2 percent or less (e.g. Statins). This is generally referred to as the number needed to treat (NNT).

For example, Nexium which is used to treat symptoms of gastroesophageal reflux disease (GERD) and other conditions involving excessive gastric acid, only helps one out of 25 patients treated with (i.e. NNT Of 25). As well, for Crestor (rosuvastatin) which is used to treat high cholesterol and high triglycerides in the blood, for every person who touches its benefits, 19 patients fails to improve (NNT of 20) (3). Moreover, since the composition of participants in many classical clinical trials is biased toward white Western, even FDA-approved drugs may have harmful effects in a particular ethnic group. Another promising aspect of precision medicine is the application of autologous tissue and cell transplants in the treatment of diseases. Autologous tissue and cells are obtained from the same individual in whom they will be re-implanted.

Autologous transplantation has the fewest complications in terms of immune rejection and pathogen transmission. The patient's own cells are the least expensive to harvest and their use avoids legal and ethical concerns. The combination of these features with the notable potential of advanced genomic techniques such as CRISPR/Cas9, facilitates future developments of new therapeutic approaches.

Furthermore, personalized medicine is hopeful in the field of preventive medicine. In predictive medicine, the risk of disease in an individual is estimated and personalized management is applied accordingly (4). The concept of predictive medicine is expanded further to predict the clinical response of a disease to a particular therapeutic option. A significant decrease in disease-related mortality as well as a reduction in costs can be expected if the prevention and screening are pursued in individuals at risk(4).

The promising prospect of precision medicine in improving the efficacy of medical treatments attracts large investments to accelerate its development. In January 2015, the U.S. government spent 215-million US\$ for national Precision Medicine Initiative(3) and it seems sooner or later, other countries will start such plans for their own ethnic populations.

Additionally, it appears that in line with the investments on research for improving precision medicine, a critical revision on medical schools curricula should be pursued aiming to familiarize physicians with such an emerging practical concept.

Since precision medicine will make the clinical guidelines much more conditional and branched, memorization would no longer play a key role and physicians would require informatics and algorithms supports to assist them with information management and evidence-based decision-making in medical contexts.

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