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Review Article

Genomics in Personalized Medicine

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ABSTRACT

Background: Genomics is the study of the complete genetic material of an organism. Personalized medicine is a type of medicine that uses data and information about an individual's genes to prevent, diagnose, and treat a disease. The main goal of this paper was to review the applications and roles of genomics in personalized medicine.
Materials and Methods: A literature search was conducted on Pub Med and Google scholar electronic databases.
Results: One of the most important areas that involve the application of genomics is pharmacogenomics, which is the leading technology for personalized medicine. Genomics plays significant roles in personalized medicine by making genomic data and information available, which eventually guides decision-making to choose the most appropriate and most effective treatments, thereby reducing drug adverse reactions. Genomics also plays a vital role in personalized medicine by reducing risk associated with multiple medications (polypharmacy).
Conclusion: Genomics makes personalized medicine a reality. Personalized medicine is dependent on scientific advances in understanding of how an individual's unique genetic and molecular profile place one at risk of some kind of diseases. More importantly, scientific discoveries increase our ability to predict which medications will be effective and safe for individual patients, and which medications will not be.

Keywords: genomics; personalized medicine; pharmacogenomics; pharmacogenetics; precision medicine.

INTRODUCTION

Individual variation to drug response has been one of the ongoing difficulties to the optimum use of medications. [1] Inability to predict individual differences to drug response often result in serious drug reactions in a number of patients and loss of drug efficacy in others. [1] Additionally, unpredicted loss of efficacy and drug toxicity could result in large financial expenses in term of the general cost of healthcare; some authors have shown that annually, it costs more to treat the effects of adverse reactions to drugs than the medical treatments themselves. [1] Personalized medicine is an evolving field with an aim of applying data and information obtained from genomics to predict the risk of having a certain disease and to individualize medical treatments. [1] According to the National Cancer Institute, Dictionary of Cancer Terms, Personalized Medicine is defined as "A form of medicine that uses information about a person's genes, proteins, and environment to prevent, diagnose, and treat diseases". [2] More recently, personalized medicine is being referred to as precision medicine or individualized medicine. Precision medicine recognizes the idea that not all patients requiring drug therapy are going to react to that drug in the same way, because of

individual variation in genetic composition coupled with the influences of environmental and dietary factors. [1] In the past decade, there has been a significant progress in linking genetic variation in genes associated with drug disposition to predict response to drugs and adverse drug reaction. [1] The four main goals of precision medicine have been: "(1) to identify therapeutic agents for which inter individual variability is a key issue for effective treatment; (2) to address/identify factors leading to inter individual variability of these agents; (3) to treat each patient with the right drug and right dose on an individualized basis by considering all these factors; and (4) to aid in the prevention of adverse reactions and thereby more effectively cure or ameliorate disease progression." [1] By making genomic data available, the four main of goals of precision medicine become achievable.

Genomics is the study of the complete genetic material, including genes and their functions, of an organism. [2] It focuses on obtaining and analyzing genome data, that is, data at the level of DNA by trying to discover specific patterns of gene expressions or biological molecules the so-called biomarkers (signature molecule and molecular marker) which differentiate the disease state from the normal state and also determine variability in patients' response to drugs. [1,3] Genomics is transforming medical practice by individualizing medical treatment through the provision of patient genetic data. [4] Medicine is individual; we are not all the same and our genetics variations determine how an individual will respond to therapy. [3,4] These variations in the sequence of a gene can result in differences in enzymes that metabolize drugs. This explains why enzymes appear in different forms in individuals. This is also why different people process one or the same drug differently. [3,4] Why does one drug work effectively for some people, but not for others? Why does somebody require twice the regular prescribed quantity of drug to work effectively? Why do some people experience side-effects of drugs, but others do not? Why do some people get cancer/any diseases, but others do not get. [3,4] These are reasons why personalized or individualized medicine is important for all.

The primary reason that the present medical practice has to bank on the one-size-fits-all way of treatment is because of inadequate availability of individual genetic information. Precision medicine is an effort to remove this practice by using genetic data and information which defines individual circumstances rather than just one of most common patients. Personalized medicine depends on scientific advances in understanding of how an individual's unique genetic and molecular profile place one at risk of some kind of diseases.

More importantly, scientific discoveries increase our ability to predict which medications will be effective and safe for individual patients, and which medications will not be. [1,3]

The main goal of this paper is to review the applications and roles of genomics in personalized medicine.

MATERIALS AND METHODS

A literature search was conducted on the Pub Med electronic database. The Google scholar search engine was also utilized. In order to facilitate the search the following keywords: genomics, pharmacogenomics, personalized medicine, and precision medicine were adopted. Only original papers, review articles, and articles available in full text and published in English were included. Organizational websites such as the Food and Drug Administration (FDA), National Cancer Institute (NCI) were also utilized. Forty-seven papers were initially retrieved. Although 47 papers were initially retrieved, only 10 met the inclusion criteria and were finally reviewed. Of these ten, five were review articles and five were research papers.

RESULTS

Applications and Roles of Genomics in Personalized Medicine

Based on the reviewed papers, the main identified application of genomics in personalized medicine is pharmacogenomics. Pharmacogenomics, the study of genetic differences that affect an individual's response to therapies, is an important application of genomics in personalized medicine. This application helps to improve the effectiveness of various drugs, as well reducing adverse drug reaction and the risk factors associated with polypharmacy thereby ensuring patient safety and in the long run reduce health care cost.

Applications of Genomics in Personalized Medicine

Pharmacogenomics

Pharmacogenomics, one of the most important areas that involve the application of genomics, is the leading technology for personalized medicine. Twenty to ninety-five percent of the variation in patient's response to drugs has been shown to be caused by genetic differences**.** [1] Many studies have outlined that the knowledge of an individual's genetic difference might reduce the possibility of developing adverse drug reactions and enhance the efficacy of the drug which, in the long run, will result in a higher chance of positive influences on the patient. [1,4,5 -10] In the past decades, there has been noteworthy progress in linking genetic difference in genes associated with drug disposition to predict response to drugs and the development of adverse reaction to drugs. [1]

For instance, in the treatment of cancer of the breast, one of the most common and earliest genomic applications in precision medicine came in trastuzumab. Approximately thirty percent of breast cancer patients have a type that over-expresses a protein called HER2, which does not respond to standard/routine treatment. Trastuzumab was approved for breast cancer patients who have HER2 positive tumor and additional studies also indicated that trastuzumab decreased relapse of the cancer by fifty-two percent when use in combination chemotherapy. [11]

Another important example of genomic applications in precision medicine is seen in the treatment of melanoma, cancer of the skin. BRAF is the human gene that controls the synthesis of a protein called B-RAF, which is involved in sending signals inside cells to direct cell growth, and shown to be mutated in cancers. As a result, a drug known as vemurafenib, a B-RAF protein inhibitor, and the companion BRAF V600E Mutation Test were approved for the treatment melanoma in advance stage. Vemurafenib is only effective in patients who test positive for the V600E BRAF mutation. About sixty percent of melanoma cases have a BRAF mutation, and roughly ninety percent of those are BRAF V600E mutation positive. [11]

The above stated examples show how the genomic application in personalized medicine is transforming the treatment of many diseases, thereby ensuring individualization of treatment

Roles of Genomics in Personalized Medicine

Improved Drug Effectiveness

Genomics plays significant roles in personalized medicine by making genomic data and information available, which eventually guides decision-making. [1,4] For instance, knowledge of a patient's genetic make-up can assist in selecting an effective and suitable therapy for the patient. Besides, this knowledge can aid in reducing adverse outcomes by instituting more effective treatment and avoiding adverse reactions of marginally effective medications. From the patient's genomic data, it is possible to recognize persons who metabolize drugs fast and people who are poor drug metabolizers. These inconsistencies in drug metabolism can influence both the effectiveness of a treatment plan and the possibility of occurrence of drug toxicity. [1]

Improved Patient Safety and Cost Reduction

Generally speaking, the knowledge gained from the individual's genetic make-up is very crucial in determining patients who will benefit from certain drugs or individuals who will not benefit or individuals who will be more prone to drug toxicity or patients who will not prone to the development of severe drug reactions. [1] According to the Institute of Medicine (IOM), approximately 1.5 million patients may have developed adverse reactions to drugs yearly and that this has resulted in a high hospitalization rate, high health care costs and an increase in death numbers. [1] Thus, knowledge of patients' genomic profile has the potential to increase the efficacy of therapeutic agents and reduce the risk of developing serious drug toxicity as well as decreasing healthcare costs. Genomics also plays a vital role in personalized medicine by reducing risk associated with multiple medications. Isidoro-García et al. pointed out that knowledge of a patient's pharmacogenomics or genomic profile offers new approaches to the old problem of multiple medications the so-called polypharmacy. [7] This is especially important, as increasing the number of drugs prescribed can increase the likelihood of adverse drug reactions. [7]

It is very obvious that for personalized medicine to become a reality or clinically meaningful, genomics as well as clinical and environmental influences must be considered together. [1] Genomics has great potential to shape the approach use to think about, identify, and manage medical challenges. Genomics has started to positively impact patient care and research and this influence will increase as genomic understandings and technologies expand.

DISCUSSION

Pharmacogenomics is a well-recognized area of application of genomics in personalized medicine and it has been very useful in individualizing patient treatment such as in treatment of breast cancer and melanoma. The knowledge gained from the individual's genetic make-up through genomics has been shown to play crucial roles in improving the effectiveness of drugs, as well reducing adverse drug reaction and the risk factors associated with polypharmacy thereby ensuring patient safety.

However, the application of genomic data in personalized medicine does not come without challenges. Some of the identified major barriers to complete and routine use of genomic data in clinical practices are as follows: High cost of genomic testing-which is a huge problem, but some authors have pointed out that as the cost of genomic testing decreases, many people will have access to it and it will become more readily available. [11,12]

Moreover, Ormond et al. stated that in order to interpret a whole-genomic sequence one must have excellent information regarding all known genetic diseases and pharmacological risks. [11] But, this information is not only difficult to acquire, but very hard to keep current. [11] The researchers mentioned further that the fast growth of genetic knowledge increases concerns. A genome is interpreted in view of present knowledge. By tomorrow that knowledge will be different and as a result, certain "old" potential risks will have disappeared and novel risks will have surfaced and be reported. As the knowledge of the interaction of individual genomic risk with other genomic variations and with the environment change the magnitude of the individual risk will also change. [11-13] The question now arises as to how the patient's genome will be reevaluated in view of the new information, and when and how the changes in information will be passed across to the patients.

CONCLUSION

What makes personalized medicine possible is one of the areas of application of genomics, which is called pharmacogenomics, the study of genetic differences that affect the response of patients to drugs, and it helps in individualizing medical treatments.

Genomics has a great potential to shape the approach use to think about, identify, and manage medical challenges. Genomics has started to positively impact patient care and research, and this influence will increase as genomic understandings and technologies expand.

Personalized medicine, the idea that we can tailor healthcare diagnoses, prevention, and treatment based on a person's genetic composition, is becoming more of a reality. Therefore, it should be embraced by all.

Contribution of Author

I declare that this work was done by the author named in this paper and all liabilities pertaining to claims relating to the content of this article will be borne by the author.

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