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Advances in Personalized Medicine: Pharmacogenomics and Its Impact on Drug Response

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ABSTRACT:

Personalized medicine is to be administered to the proper patient within the right dose. Prediction of drug response of an individual helps to increase the success of therapies and decrease the incidence of adverse side effect. Pharmacogenomics investigates the genetic basis of inter-individual differences in drug responses, such as efficacy, dose requirements and adverse events. It is a trending clinical practice that provides decisions to the prediction, prevention, diagnosis and treatment of disease. Personalized medicines are used to maximize the likelihood of therapeutic efficacy and to minimize the risk of drug toxicity for an individual. It has an immense contribution in cancer therapy. There are certain limitations of personalized medicine as well as pharmacogenomics. Personalized medicines are used to prevent adverse drug reactions caused by several drugs and its contraindications.

Keywords: Personalized Medicine, Pharmacogenomics, Drug Response, Drug Discovery, Patient Compliance

Introduction:

The principle objective of personalized medicine is that the proper drug should be administered to the proper patient for the right period of time.[1] The definition for personalized medicine is appropriately referred to as the management of a patient's disease or disposition by utilizing the best molecular knowledge to accomplish the best medical result for that individual.[2] The base of global health is personalized medicine. Since the discovery of penicillin, the steady rise in life hopes worldwide owes it to a succession of innovative medicines.[3] The ability of restricting the gap between what is planned from clinical trials and what really happens in custom is accredited to personalized medicine.[4] Huge progress in genomics containing the view of resequencing of total genomes at the population stage for a modest fee has been boosted by the international interest with personalized medicine.[5] The tyrosine phosphatase inhibitors in the therapy of chronic myelogenous leukemia and the monoclonal antibody trastuzumab against HER-2, the human epidermal growth factor receptor that is overexpressed in individual breast cancer cells are the examples of earlier path.[6] The genetic polymorphisms of the cytochrome C drug metabolizing enzymes such as CYP3A4, CYP2D6 P-glycoprotein and multidrug resistance protein are the examples of the last path.[7] The value and position of pharmaceutical industries, FDA,NIH, etc. need not be forgotten in the development and production of the drug, in order to reach personalized medicine objectives.[8] The area of research that addresses the genetically determined variation in how individuals respond to specific drugs, in terms of differences in dose requirement, efficacy and the risk of adverse drug reactions is named as pharmacogenetics.[9] Pharmacogenetics and pharmacogenomics have been used interchangeably in line with the increasing use of functional genomics.[10] The field with greatest clinical potential to radically improve patient care through the implementation of personalized medicine is pharmacogenomics , since the completion of the Human Genome Project. To maximize therapeutic benefit and avoid ADRs, the terms personalized medicine and pharmacogenomics are often used together.[11] A generic term used in numerous different meanings that often disagree about its real meaning is Personalized medicine. Thus, it should be analyzed from the highest positions in Europe and USA.[12] It is referred to as an emerging – evolving approach to medicine that uses scientific insights into the genetic and molecular basis of health and disease brought on by the sequencing of the human genome, to guide decisions in regard to the prediction, prevention, diagnosis and treatment if disease according to the European Parliamentary Research Service.[13] A report suggested that personalized medicine does not literally mean the creation of drugs or medical devices that are unique to a patient, but rather the ability to classify individuals into subpopulations that differ in their susceptibility to a particular disease or their response to a specific treatment. Preventive or therapeutic interventions can then be concentrated on to=hose who will benefit, sparing expense and side effects for those who will not according to the President's council of Advisors on Science and Technology – Executive Office of the President of the United States.[14] Identification of candidate genes and polymorphisms, correlation of polymorphisms with therapies, prediction of drug response and clinical outcomes, reduction in adverse events, and selection and dosing of drugs based on genotype is included in pharmacogenomics.[15] For better management of the disorders, the associated genotypes need to be known by the clinicians and health

professionals. These are important for individual responses to medications, a major part of personalized medicine.[16] an outstanding opportunity for safety and efficacy of drug usage is provided by prescribing a drug based on individual's genetic variations.[17]

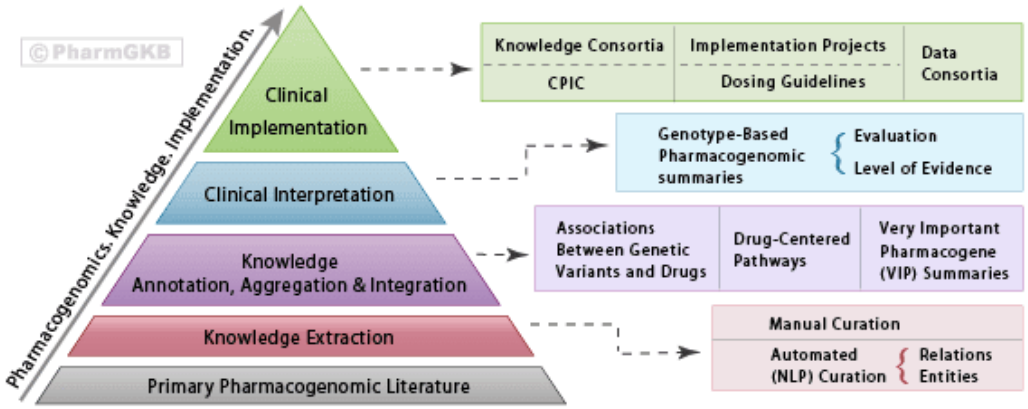

Figure 1. The Pharm GKB Knowledge Pyramid[18]

Drug prescribing decisions can be improved by testing the genes in the current situation also could lead both providers and patients to lose trust.[19] Disease determinants, environmental exposure, genetic and micro biome factors included in the multiple factors are responsible for hundreds of thousands of people die every year due to adverse drug reactions.[20]

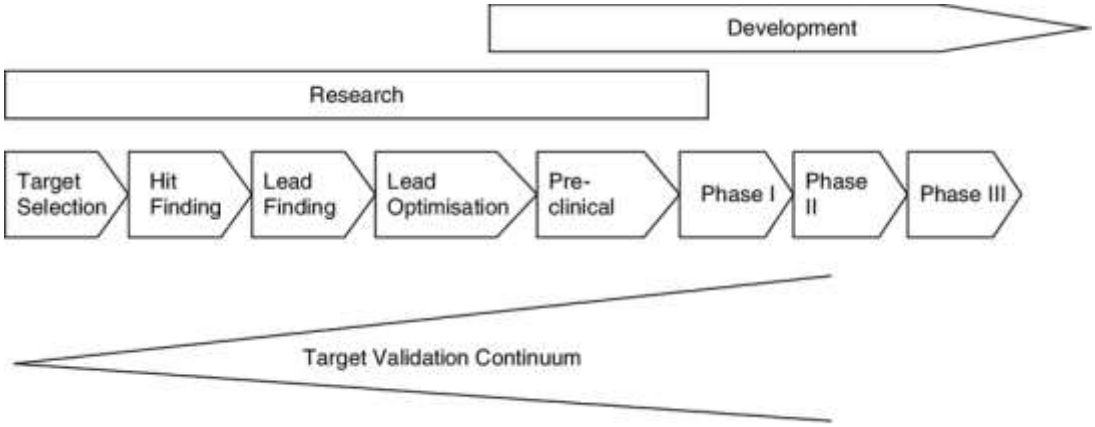

Figure 2. Traditional drug discovery – a linear process[21]

Precision Medicine vs. Personalized Medicine:

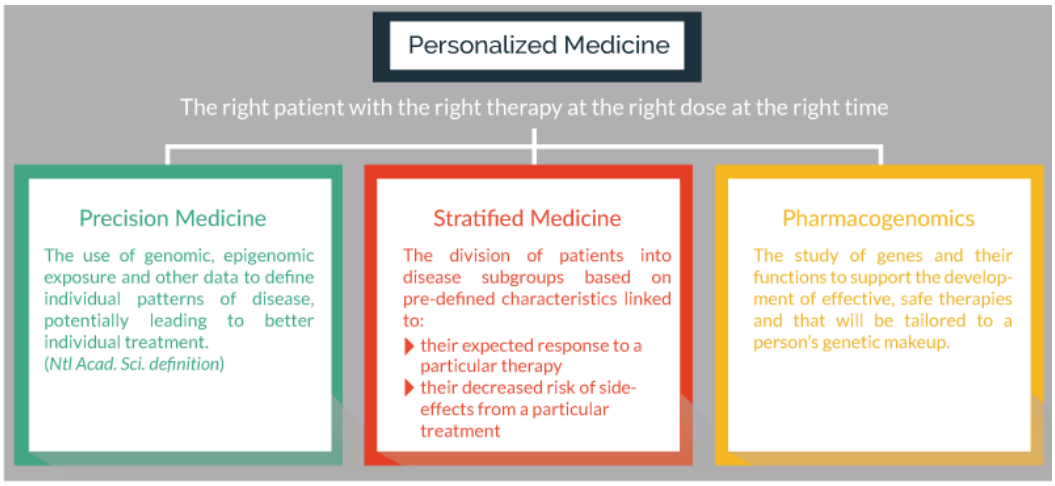

Figure 3. Difference between precision medicines versus personalized medicine[22]

Development of Personalized Medicine:

Those enzymes that are largely liable for drug metabolism and have steered making use of a person genetic variant at these loci to prefer patients for clinical trials would shrink ADRs by means of 10-20% have been suggested by contemporary reports of human genetic version within the cytochrome P450 (CYP).[23] The opportunity to seize sufferer medical data, imaging and in vitro molecular response knowledge simultaneously is afforded by the clinical phases of drug progress.[24] A different response as compared to a patient with lower or no expression level of the same protein is produced in patients with the higher expression level of a protein.[33] The factors affecting response of drug are genetic polymorphism, epigenetic and other factors, etc.[34]

Clinical Applications and Future Perspectives of Personalized Medicine:

It is widely used in oncology, psychiatry and P5 medicine system, neurology, cardiovascular diseases, chronic conditions, metabolomics profile and personalized lifestyle medicine.[25] The revolution in scientific research particularly in the area of drug discovery is associated with the completion of the human genome and the human micro biome projects.[26] To identify drug targets and potential drug candidates through various drug discovery approaches is applied by an interplay between genomics, transcriptomics, proteomics and pharmacomicrobiomics.[27] Particularly in relation to inflammatory and auto immune diseases, micro biomes have proved to be a spot on drug discovery.[28] Inter-individual genetic variations that has significant impact on the human variome has been served as a warehouse by the human microbiomes.[29] A rich source of millions of potential unmined drug targets is described to be the human micro biome community.[30] The center on the effect of multiple human genes on drug response is complemented by the interplay between pharmacogenetics and pharmacogenomics.[31] The suffering from the scarce presentation of cultural understanding and diversified environmental factors in the research is due to the continued development of meticulous medication.[32] Using information such as age, sex, genetic profile, expressions related to disease, medical tests, and history of the disease are helpful in estimating the risk of disease and possible outcomes of treatment.[35] The impact of pharmacogenomics on personalized medicine are cancer, neurodegenerative diseases, thrombosis, cardiovascular diseases, anesthesia, type 2 diabetes, depression, psychiatry, hypertension, etc.[36] The application of pharmacogenomics tests into health care is delayed due to the lack of clinical utility of a drug.[37] The drugs that have potential for personalization are thiopurines, oral anticoagulants, phenytoin and carbamazepine, codeine, targeted cancer therapy(tyrosine kinase inhibitors), trastuzumab and cetuximab, imatinib, other drugs.[38] Personalized medicine can prevent more than 100 000 deaths per year due to adverse drug reactions.[39] The clinical applications are shift emphasis in medicine from reaction to prevention, select optimal therapy, make drugs safer, increase patient compliance to treatment, reduce time, cost, and failure rate of clinical trials, rescue drugs failing clinical trials and reduce the cost of health care.[40] Imatinib is the most often cited example of personalized medicine.[41] Another example of personalized medicine involves cancer treatments such as immunotherapies.[42] An app is designed to treat and bring relief to an individual affected by a medical or psychological condition, leading to the concept of digital therapeutic.[43] Paying for personalized medicine practices may be complicated and prove to be expensive in the future.[44]

Conclusion:

The most powerful therapy that goals of sickness, keeping off toxicity for sufferers and for payers it's attractive as a mechanism to make the application of steeply-priced drugs, and preclude useless highly-priced on treatments which can be useless has been promised to be benefitted by personalized medicine. It is largely believed to present satisfactory healing and therapy for patients with critical illnesses despite the challenges. Pharmacogenomics plays a central role in personalized medicine due to more efficient, cheaper and safer new drugs with genomic data. Thus, personalized medicines are important to avoid several ADRs caused due to the drugs and the contraindications.

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