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Editorial

Personalized Medicine : An Overview

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"The power in tailored therapeutics is for us to say more clearly to payers, providers and patients; "this drug is not for everyone, but it is for you'. That is exceedingly powerful".

John C. Lechlieter Former Chairman,
President and CEO, Eli Lilly and Company
U.S.A.

The advancements in Science and Technology are paving way to reconsider the manner in which we define disease, drug development, diagnosis and treatment. The analytical capabilities of biological specimens have seen an explosion and have contributed tremendously to the diagnosis of diseases in general and genetic diseases in particular. There is a transformation of description of diseases from simple anatomical location and clinical symptoms which failed to take into consideration the unique biological profile of the patient, which could determine the therapeutic efficacy of the drugs being administered.

Hippocrates in the medical school started in 400 BC focused on combined assessment of four humors, blood, phlegm, yellow bile and black bile to determine the appropriate course of treatment for each patient. With a greater understanding of human physiology and pathophysiology, it is evident now that each patient responds to treatment distinctly with regard to the safety and efficacy of the therapeutic agents and this is greatly dependent upon the molecular architecture of the patient. The approach of a treating physician should therefore be, to provide the best treatment to the patients with right doses which would benefit them.

The human genome project, which enabled the systematic exploration of entire genes, has laid foundation for genetic variations, defining diseases at molecular levels and the concepts of genomic or personalized medicine. The advances in genotyping and sequence technologies, bioinformatics and computational biology all have led to important discourses in defining the molecular aspects of diseases which has resulted in improvements in patient care approaches.

Though, there are challenges the future of genomic medicine appears to be promising and meaningful. Major outcome of extensive DNA sequencing effort has resulted in identification of disease biomarkers, drug targets and molecular diagnostics. NGS Technology allows the direct measurement of not only the common variants but also all variations in a genome. The line of knowledge is that the population frequency of germ line variants could be about 1 in 1000 of the 3.2 billion nucleotide position, giving rise to about 3 million variants in the human genome. The effect genetic variations within 1% of the genome that comprise the active genes is predictable to certain extent. However, the real challenge is the analysis of the variants in the non-coding regions of the genome.

The National Human Genome Research institute initiated the project ENCODE, the encyclopedia of DNA elements with a goal to functionally annotate non coding regions of genome. This, would certainly give insights in to the organization and regulation of genes enhancing the ability to interpret genetic variants, hitherto known without any significance. Today, GWAS and NGS are integral tools in the basic genomic research with a profound role in clinical diagnosis of rare genetic disorders, treatment based on molecular targeting and real time out breaks of infectious diseases.

Based on the extensive genomic data available and the tremendous scope for genetic

variations in the genome, it is not surprising that patient population is not going to present a stereotype of signs or symptoms for a particular disease, but shall be presenting subtle or serious body responses and effectiveness to drugs. Research across the globe has come out with convincing data that reiterates the concept "one size does not fit all" and needs a tailored approach to deal with same disease to ensure the right medicine to the right patient. This approach has culminated in the concept of precision medicine or personalized medicine one of the applied aspects of genomic medicine. Targeted therapies for cancer have been remarkable and have made convincing impact in the prevention and treatment of cancers. There are now more personalized medicinal products for patients than before available and it's worth noticing that 1 in 5 FDA approvals in the USA have been for targeted therapies.

With the advent of systems Biology, computation biology genomic profiling precision medicine could be a more meaningful approach to diseases. The advantages of it in a nutshell could be viewed, prevention of diseases viz., life style modification, treatment, risk assessment or genetic predisposition, targeted therapy to avoid trial and error approaches, detection of diseases early, reduction in adverse drug reaction and active monitoring of the treatment response.

Circumventing cumbersome interventional procedures is one of the commendable achievements of precision / genomic medicine. Molecular tests in majority of occasions require blood samples and could replace invasive procedures like biopsies. A classical example, Allomap a multi-gene expression test, detects whether the immune system of heart transplant recipient is rejecting the new organ. One in four heart transplant patients experience rejection and to monitor for the rejection, biopsies are performed as frequently as once in a week, every few months and even for years. It is shown that patients who are monitored with Allomap have shown comparable outcomes as those who have undergone heart tissue biopsies.

It took $ 1billion and 13 years to sequence the first draft of the human genome. However the cost to sequence a human genome today is approximately $1000 and in many ways it is not a staggering amount in comparison to the cost of treatment for some diseases. "Between 2012 and 2016, we have invented technologies that allow us to change human genomes intentionally and permanently. We can now 'read' human genomes, and we can 'write' human genomes in a manner inconceivable just three or four years ago".

Gene editing is also generating interest in personalized medicine. The discovery of CRISPR (clustered regularly interspaced short palindromic repeats) and CRISPR-associated (Cas) genes has allowed for the development of efficient and reliable means to make accurate and predictable changes to the genomes of living cells. Gene editing by using the CRISPR/ Cas9 technology may allow for the correction of disease-causing mutations in humans. The potential application of this technology for personalized treatment strategies spans a wide spectrum of health conditions, from congenital blindness to cancer.

For integrating personalized medicine into health care system, Health care providers, policymakers, patients and their families, need to have a better understanding of personalized medicine concepts, technologies, policies, practices related to patient engagement, privacy, data protections, and other ethical, legal, and societal issues regarding the use of individual molecular information.

While research continues on the development, validation and relevance of personalized medicine, the attention is also predominantly drifting to address the impediments in the implementation and utility of the personalized medicine. All the stakeholders recognize that personalized medicine offers an extraordinary opportunity to improve the lives of patients. Genomic medicine, a dream two decades ago is now beginning to materialize as a reality in the healthcare system for risk assessment as well as to guide the treatment of complex diseases. Technology continues to assist this ad-

vancement but translating the outcomes into practice is highly complex requiring awareness on the intricacies including ethical issues and therefore this gap has to be filled up to achieve the expected goal.

Today, we are on progressive path towards the practice of personalized medicine. However, the path is marred with several impediments and it could be unsafe as well. Thus, it remains to be seen whether personalized medicine will actually improve health when simpler clinical and preventive strategies have been unsuccessful. These strategies toward improving disease diagnosis and treatment with the information derived from genomics are there to continue and there are all reasons for humanity to be optimistic in this endeavor of healthcare approach.

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