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PERSONALIZED MEDICINE PAVE THE WAY TO A MODERN MEDICINE ERA

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ABSTRACT

Background: The traditional medical treatment model is generalized for all patients. Resulting into a treatment successful for a few patients and not for others. This creates a need to replace the ancient method with an innovative approach in treatment and cure, Personalized medicine which has become increasingly important in the future of healthcare. The review article focuses on a modern approach of treatment strategy based on individual biological makeup. **Summary:** Personalized medicine is used to classify, understand, treat, prevent disease based on the data of individual biological and environmental differences. It applies a data-driven approach seeking knowledge about the genetic factors and enzyme mechanism of each individual making healthcare more effective.

KEYWORDS: Pharmacogenomics, theranostics, precision medicine, next-generation sequencing.

INTRODUCTION

The advances in the field of human genetics began post completion of the Human Genome Project. This gave an insight to the unique variations and differences in individual human genome. These slight differences in genetic makeup of every individual leads to the individual responses to a drug treatment or causing drug toxicity in some. In modern medicine, using genomic information (RNA, proteins) paves a path for treatment decision making. Genomic medicine that is a part of Pharmacogenomics is a major component of Personalized medicine. At the base-pair level human genome is 99.9% but 0.1% variation makes each individual unique. Pharmacogenomics studies how genomic variation affects a patient's response to a particular medication. Scientists assess gene variants affecting an

individual's drug response by identifying the genetic loci associated with known drug responses and then testing individuals whose response is unknown.

Personalized medicine can be broadly described as customisation of healthcare that accommodates differences in all stages from prevention through diagnosis and treatment to post-treatment follow up. Consequently, a long-term vision of a true system-based approach to healthcare would be hindered by personalized medicine using individual genome sequencing.

History

A study over a few decades resulted that variation in drug responses has been administered. This individual response can be genetically determined with various factors like age, epigenetic factors, nutrition, niche. In order to obtain an individual patient drug therapy, there is a need for accounting different drug response patterns with a drug toxicity to drug benign ratio of a population geographically.

Scientists observed a greater ratio and a highly variable drug responses that led to the discovery of a new treatment methodology bound to different disciplines of genetics, biochemistry, molecular medicine and pharmacogenomics. Commercialization of this research application now emerged as personalized medicine. PM is considered to be an extension of the traditional treatment with greater precision.

Landscape

A patient's genetic profile through sequencing can help select drugs or treatment methodology that would minimize the side-effects and ensure successful outcomes. Medical professionals can not go beyond a generalized treatment for a disease to an individual treatment in order to achieve effective results. PM provides a structural model with a network of electronic health records and a record of genome sequencing of every patient linking the molecular and clinical information. This would assist physicians in making appropriate treatment decisions for individual patients.

Next-generation sequencing

In genetics and biochemistry, sequencing means to determine the primary structure or primary sequence of an unbranched biopolymer. By understanding the sequence of DNA, researchers have been able to elucidate the structure and function of proteins. Next

Generation Sequencing (NGS) is a powerful platform that has enabled the sequencing of thousands to millions of DNA molecules simultaneously. This powerful tool is revolutionizing fields such as personalized medicine, genetic diseases and clinical diagnostics by offering a high throughput option with the capability to sequence multiple individuals at the same time. The advent of capillary instrumentation and the use of fluorescent-based detection methods accompanied by automated analysis, has moved traditional DNA Sequencing into 'Next Generation' Sequencing (NGS).

Next generation sequencing (NGS) data is extremely high throughput, allowing for exponentially higher amounts of data to be generated than the traditional Sanger Sequencing. When performing whole genome sequencing or exome sequencing, it is expected that the result will be highly uniform (as there should be a 1:1 ratio in the starting material).

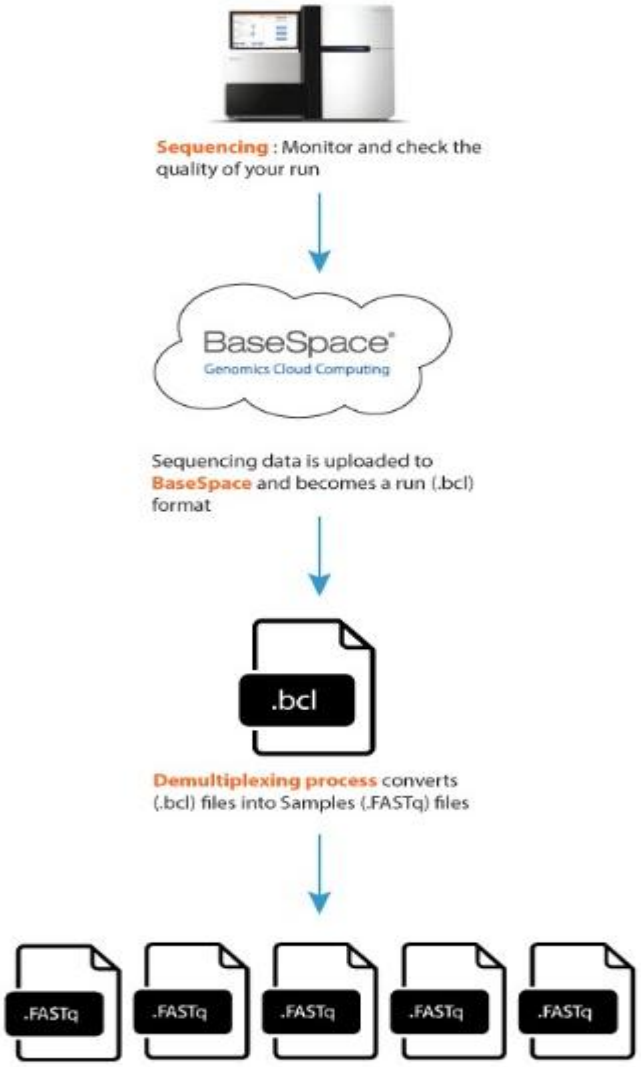

Figure 2: Flowchart of an NGS workflow.

Application boosted by NGS technology was the study of protein binding sites in genomic DNA especially that of transcription factor binding sites based on Chromatin ImmunoPrecipitation (ChIP). The application of next-generation sequencing (NGS) to ChIP has revealed insights into gene regulation events that play a role in various diseases and biological pathways. A combination of genome-wide association studies (GWAS) and specific targeting by sequence. capture of the genomic regions detected is now used extensively trying to identify the variants that functionally link the DNA with the phenotype. Similarly, genome sequencing can be used as a tool to characterize genetic variation in a specific population. Thus far studies have been mostly performed on the level of cell cultures, whole tissues or sorted cell populations. Although the yield per cell, 30%–70% of all RNA or DNA present, can still be improved recent NGS developments have now made genome-wide single cell analysis feasible. Individual cells turn out to be quite different showing extensive genomic and transcriptomic heterogeneity in both normal development and disease.

Pharmacogenomics

Pharmacogenomics is the branch of pharmacology which deals with the influence of genetic variation on drug response in patients by correlating gene expression or single-nucleotide polymorphisms with a drug's efficacy or toxicity. It aims to develop rational means to optimize drug therapy, with respect to the patient's genotype. Such approaches promise the advent of personalized medicine. Pharmacogenomics is the whole genome application of pharmacogenetics, which examines the single gene interactions with drugs. The term comes from the words pharmacology and genomics and is thus the intersection of pharmaceuticals and genetics. Pharmacogenomics combines traditional pharmaceutical sciences such as biochemistry with annotated knowledge of genes, proteins, and single nucleotide polymorphisms. The most common variations in the human genome are called single nucleotide polymorphisms (SNPs). Today, clinical trials researchers use genetic tests for variations in cytochrome P450 genes to screen and monitor patients. In addition, many pharmaceutical companies screen their chemical compounds to see how well they are broken down by variant forms of CYP enzymes. Another enzyme called TPMT (thiopurine methyltransferase) plays an important role in the chemotherapy treatment of common childhood leukemia by breaking down thiopurines. Knowing one's genetic code will allow a person to make adequate lifestyle and environmental changes at an early age so as to avoid or lessen the severity of a genetic disease. The main aims of it are; personalized therapy, improvement in efficacy and reduction in adverse drug reactions correlation of genotype with

clinical genotype, identification of novel targets for new drugs and pharmacogenetic profiling of patients to predict disease susceptibility and drug response.

Theranostics

Theranostics commonly known as Pharmacodiagnostics is a term derived from a combination of the words therapeutics and diagnostics. New materials and technologies are revolutionizing therapeutic treatments in various domains, such as preventive and diagnostic medicine, management of diseases and implants. The field applying theranostics approach promises to allow the medical professionals to use detailed genotypic information of a patient and simultaneously monitor the individual's therapeutic regimen and track the therapeutic response.

The Application of Theranostics in Cancer

Cancer is a tricky entity, because it is not just one disease, but a heterogenous group of diseases that is characterized by uncontrolled and rapid cell growth. This is usually due to genetic and/or epigenetic changes in affected patients. Current therapies for cancer include chemotherapy, radiotherapy, immunotherapy and surgery.

Chemotherapy in particular has limited usefulness owing to the reduced concentration of drug molecules that reach the tumors which they are intended to treat. Further limitations of chemotherapy include the development of resistance to treatment during therapy, and of course the many side effects associated with the drugs used.

Here nanomedicine with the help of nanoparticles shows great potential in addressing the limitations of conventional treatment. These particles allow molecular targeting to ensure higher concentrations of drug molecules at the tumor site. This has been the focus of extensive studies on drug delivery systems which incorporate nanotechnology, in recent years. These studies investigate the use of nanomedicines in an active or passive manner to trigger site-specific release of drugs. This ensures that the drug bypasses tissues that are off-target, and in doing so improves the therapeutic precision.

Artificial Intelligence in Personalized Medicine

Artificial Intelligence is now been used for years in the field of healthcare and biomedicine. In Computer Science, Artificial intelligence (AI) sometimes called machine intelligence mimics cognitive functions that human associates. Personalized medicine is considered to be

incomplete without some add-ons like machine learning algorithms. Machine learning is a subfield Artificial Intelligence that provides the ability to automatically improve from experience without being explicitly programmed. ML specializes in the development of computer programs which can retrieve data and use it to learn for themselves. Most commonly used ML algorithms in medicine includes SVM, deep learning, logistic regression, DA, decision tree, random forest, linear regression, Naïve Bayes, K-nearest neighbor (KNN) and hidden Markov model (HMM). Three types of machine learning algorithms:

1. Unsupervised (ability to find patterns)
2. Supervised (classification and prediction algorithms based on previous examples)

Reinforcement learning (use of sequences of rewards and punishments to form a strategy for operation in a specific problem space) For a few years now, AI has been used in various medical treatments like neurodevelopmental disorders that includes autism spectrum disorder, intellectual disorder. AI can help identify the casual genes and locus using Bioinformatics tools. Along with this it even assist in Phenotypic and genetic heterogeneity identification, gene to gene interactions, and also in computer aided drug discovery.

One of the promising advances of AI in the field of medicine is the development of Biomarkers. Biomarkers are objective medical signs (as opposed to symptoms reported by the patient) used to measure the presence or progress of disease, or the effects of treatment. Biomarkers can have molecular, histologic, radiographic, or physiological characteristics.

Benefits of Personalized Medicine

The development of PM could bring benefits to patients in a number of ways;

Improved efficacy: patient more likely to receive a medicine delivering a clinical benefit, and treatment targeted at patients who will respond

- Improvements in overall survival
- Reduced adverse events: PM could be targeted at patients who are less likely to have an adverse reaction, reducing safety concerns.

The use of genetic and other forms of molecular screening could help predict the best dosing schedule or combination of medicines for a particular patient. This offers the potential to improve healthcare provision by better matching patient needs and therapeutic benefits, and through a more informed choice of therapy. Genetic information can distinguish between patients who are likely to respond strongly to pharmacologic treatment and those who will receive no benefit. Genetic testing is becoming widely used to evaluate which medicines may

work best for cancer treatment.

Type of impact	Key findings
Targeted and personalised intervention that identifies patients most likely to respond	• Tumour profiling in metastatic colon cancer has shown that approximately 40% of patients are unlikely to respond to cetuximab and panitumumab because their tumours have a mutated form of the KRAS gene.[57] • A meta-analysis of phase II clinical trials (570 studies; 32,149 patients) showed that oncology PM therapies had higher response rates than cytotoxic therapies.[58]
Better outcomes – improvement in overall survival	• Adjuvant treatment was shown to result in an approximately 50% reduction in recurrence of the disease after a median follow-up of 1–2.4 years' treatment in patients with HER2+ breast cancer.[59] • With the introduction of new personalised treatments for stage 4 melanoma, one-year survival rates in women with stage 4 melanoma have increased from 36.1% 2012 to 59.6% in 2014. • In NSCLC, new anti-PD-1 immunotherapy in addition to a standard chemotherapy regimen has makes it only half as likely that a previously untreated patient will die.[60]
Better outcomes – reduced adverse events	• In advanced urothelial carcinoma, pemprolizumab with chemotherapy has reduced the frequency of adverse events from 49.4% to 15.0%.[61] • In a HIV treatment, a genetic test can avoid adverse events by indicating the need for alternative therapeutic options.[62]

Figure 3: Impact of PM on delivering better treatments for patients.

CONCLUSION

Technology improves and so does the healthcare system. The blooming field of modern medicine has the potential to bring out the improved health results with assistance of precise drug development. Unlike PM, conventional drug therapy typically considers large patient populations to be relatively homogeneous. Any given drug can be therapeutic in some individuals but ineffective in others, and some individuals experience adverse drug effects whereas others are unaffected. PM also offers an opportunity to enhance the value of currently approved drugs with limited market share because of significant toxicity or limited efficacy, enabling prescribers to identify patients for whom they can be both effective and safe. Such recognition of interindividual differences in drug response is an essential step toward optimizing therapy. Many times we have already seen that the marriage of drug-related diagnostics can provide better utilization parameters for new products as well as

improve safety profiles or efficacy of older chemically based medications. In this second decade of the 21st century, health care will be reframed and designed for at least the next decade. PM provides a kinetic energy to foster change in the health care system.

REFERENCES

1. https://www.researchgate.net/publication/312250815_Personalized_Medicine_The_Future_of_Health_Care
2. https://www.sciencedirect.com/science/article/pii/S1098301513018615
3. https://www.spandidos-publications.com/10.3892/br.2017.922
4. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC2957753/
5. https://hms.harvard.edu/news/next-gen-medicine
6. https://translational-medicine.biomedcentral.com/articles/10.1186/s12967-020-02316-w
7. https://pubmed.ncbi.nlm.nih.gov/28240172/
8. https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7580505/