Precision Medicine: A Personalized Treatment from Your Gene

P. K. Balasubramani[1(✉)], K. Preetha[1], and M. Aswanth Harish[2]

[1] Innov4Sight Health Care and Biomedical Systems Private Limited, Bengaluru, KA, India
balasubramanipk@gmail.com
[2] Department of Biotechnology, Sri Venkateswara College of Engineering, Chennai, TN, India

Abstract. Poor healthcare linked to 5 million annual death worldwide. Health is increasingly shaped by ageing populations, urbanization and globalization of unhealthy lifestyles, resulting in a transition in the burden of health care towards non communicable diseases, mental health and injuries. Many of these conditions are chronic, requiring long-term care, with patients commonly suffering from multi-morbidities, all of which adds to escalating health care costs. Precision medicine (PM) is a new approach to health care that matches individual patients with targeted treatments that work best for each them. PM is still in its infancy, but holds so much promise for the healthcare industry which considers genetic variations, environment and lifestyle. There would be global shift in the treatment modalities where people are moving towards pharmacogenomics which takes into consideration of the individual drug response to how body metabolize it helping in catering the patients with minimal Adverse Drug Reaction (ADR). Another field which is showing promise in the healthcare industry is wearable bio-services for better health and disease management. PM has roadblocks to clear before it hits the market clinician acceptability, pharma industry to cater drug to small population, developing diagnostic tests with sufficient sensitivity and specificity and having string regulatory mechanism to ensure clinical validity to the tests.

Keywords: Biomarker · Gene · Genome · Metabolome · Microbiome · Pharmacogenomics · Phenotype · Polymorphism

1 Introduction

Precision medicine (PM) is the emerging disease treatment approach in the last couple of decade moving towards personalization and evidence-based medicine. The tailor made treatment strategy in the future would not only take in to consideration of the genomic variations but also other contributing factors like gender, age, geography, race, family history, immune profile, metabolic profile, microbiome, environment vulnerability and set of circumstances [1]. The benefit of the PM on the patient's perspective is immense establishing personalized health plan and drastically saving the healthcare cost incurred and significantly reducing any adverse reaction from the drug. The approach of treating patients in PM is completely based on the variation in the

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genomic read out towards susceptibility for illness and also for the ability of the patient responding to drug metabolism [2]. An personalized approach of this sort would help to cut down to medical cost treating the patient and to provide better care with increased efficacy. Through sequencing of many patient who can be grouped into similar category which in turn would reduce the cost, duration for carrying out clinical trial and early release of the drug to the market [3].

Through omics based approaches (Genomics, Proteomics, Transcriptomics, metabolomics, Epigenomics) data are initially segregated through patient's biopsy and integrated to create a unique molecular profiles corresponding to an individual. Sequenced DNA is reserved in cloud computing Block chain Technology where AI play a vital role by integrating the sequence with large number of reference sequences and seek for polymorphism and Biomarker. These profiles are then challenged with previously defined disease profiles to seek biomarkers, omics signatures or network/pathway signatures that can guide the selection of treatment [4]. Based on those assays and data analysis drug is prescribed, to improve the chance of successful treatment and reduce the probability of side effects. Being an emerging field in healthcare which promises to make treatment modalities cost effective has been well supported by key technologies making it possible for its remarkable rapid growth [5]. The Nano pore based sequencing (fourth generation DNA sequencing technology) are accurate, fast and reliable and the entire genome can be sequenced for less than $1000 with timeline less than a day. High-performance computer systems too have played in key role in analyzing massive genomic data ($\sim$1.5 GB) which fosters early genome drug discovery. Modern bench top sequencers allow independent researchers run in small laboratories; allowing rapid and efficient sequencing solutions. Many global players are setting up large scale genomic repositories across various countries to analyze genetic polymorphism for various diseases and well the accepted by general population by active a participation in the genomic projects. At clinics the Clinical Decision Support System (CDSS) also been playing key role helping physicians to make quick concrete decision towards the treatment with relevant information. Cloud computing services has been providing the valuable boost by offering cloud based bioinformatics suites and genomic processing services. Machine learning and big data analytics have come handy to see beyond traditional data sets, gives a more specific picture of an individual's health reducing individuals. And newer technologies like Blockchain also functions as a good auditing tool by securing patient genomic data. Mobile apps/wearables are bridging the gap in providing real time follow-up data from the patients.

The new horizons of the Precision medicine have lot of wide potential benefits helping the medical professionals and the patients by preventing, diagnosing, managing and treating a wide range of diseases. The new approaches of PM reduce the adverse side effects of drug by the traditional methods. The drugs can be improvised by designing them specifically to the patients [6]. Hence, time consuming for the trials and treatment is reduced. Moreover, the patients with rare undiagnosed diseases are cured to a certain extent by PM. The respective treatments for those conditions can be predicted. Also, the understanding of the roots of certain diseases can be traced out well. The patients will be provided with individualized patient care. There will be less practice of trial and error prescribing, because patient safety plays a pivotal role. The

efficacy of the treatment modality is improved by targeting the response rate and in the overall survival The Electronic Health records of the patients can be easily accessed by the doctors and patients. PM uses the health care resources wisely by reducing expensive costs and more efficient clinical trials in Research and Development. The informed decisions will be made properly with the help of PM. Due to the better targeted therapies for the patients, the probability of desired outcomes is very high. The onset of any diseases can be traced back.

PM being an emerging field is also presented with unique set of challenges where in interpretation genetic polymorphism/variation remains a challenge across the study population. Any drug in the body is metabolized is determined by multiple set of genes interacting with each other. Analyzing and interpretation of the variation SNPS is time consuming and tedious process. The translation of PM from research to clinical adoption lacks awareness among the patients towards personalized therapies and even many healthcare organizations do not yet have formal plans to use genomics or advanced data for personalized patient care has been huge drawback in translating PM at the clinical level. The regulatory pathway for personalized medicine is still in its infancy as there is no clear roadmap for laboratory-developed tests (LDTs) [7].

2 The Role of Artificial Intelligence in Precision Medicine

The very foundation of precision medicine is strongly supported by various AI based algorithm such as deep learning, natural language processing, and machine learning to deal with the high dimensional data to make clinically viable decisions [8]. Current treatment modalities by physicians across the globe still rely on their experience, judgement, and problem-solving skills while using rudimentary tools and limited resources during treatment. Artificial Intelligence [AI] would assist in analyzing large & complex data set in real-time; wherein support coming from the high end computational power to draw meaningful conclusion supporting the physician community for effective treatment and lowering the risk of adverse drug reaction. The main objective of Precision medicine is based on the grouping of patients based on their disease susceptibility, diagnostic/prognostic information, and treatment response [9]. Complex algorithms, digital health applications and 'Omics'-based tests are the three types of precision medicine to be emerged in clinical practice. The influence of biomarkers, artificial intelligence-based technologies maintain the investment in health care. AI-based technologies will be converting the images to develop algorithms that incorporate scan results into more accurate information. Some of the key benefits to the diseases community is the ability of the AL based deep learning models to achieve higher accuracy of disease risk prediction. It a valuable tool in the detection of cancerous tumor growth from the scanned images in a very period of time interval [10]. Storage if omics data over the cloud and integration of records have tremendously benefited the patients. AI approach towards PM has revolutionized cancer screening and real-time monitoring, and improve the reduction of adverse events and improved patient outcomes. Other areas of application of AI include are drug discovery and gene-editing using CRISPR–Cas9 technology. Recent mobile health markets are flooded with wearables and the internet of things (IoT). Deep learning algorithms have been

shown to make diagnoses at least as well as physicians in cardiology, dermatology, and oncology. The Potential of AI immense where-in back then in 2016 Atomwise able to identify effective drugs for Ebola infectivity in matter of day time [11]. Other specific application of AI in PM include variant calling, interpretation and reporting. In Variant calling the genomic variants coming from the NGS data are analyzed by aligning the read-out sequence with the reference genome. In the process of interpretation any novel variants observed in the read-outs are used a crucial biomarker in the clinical care of the patients and treatment planning. In future the AI can independently analyze the data and draw meaningful conclusion as well disease correlation and actively support the physician community.

3 Global Initiatives

The countries which have initiated precision medicine are United States, United Kingdom, France and Japan. "All of us" a PM initiative started at US in the year 2016. The primary objective is to improve health research and medical breakthroughs, enabling individualized prevention of diseases and its treatment, and care for all the Americans. This goal will be met by nurturing relationships with 1 million participants, developing a large and rich biomedical dataset, and improve the ecosystem of researchers and funders to use and support the system. $130 million was allocated to NIH to develop a cohort-National extensive research contributor group and $70 million was allocated to the National Cancer Institute to lead efforts in cancer genomics as part of PMI for Oncology. In UK, "100,000 Genomes" established in December 2012. The main aim is to benefit the people in health care system of UK. The second goal is to initiate the development of a UK genomics industry by creating the space, potential, and bequest of precision medicine in the United Kingdom. Genomics England will pay £78 million for Illumina to carry out the genetic sequencing, and the company will invest £162 million in the country over the next 4 years. In France "The French plan for genomic medicine" was started in April 2015. The sequencing should be implemented in every clinical practice. The French patients who suffer from rare or common diseases, cancer etc. should be getting easy access to the genomic medicine along with the people who are concerned to the patients by 2025. The second objective is to develop a national genomic sector in which France should be placed among all the leading countries in the field of genomic medicine within next 10 years. The budget is 670 million euro. "Initiative on rare and undiagnosed diseases" is an initiative from Japan started in June 2015 works on the patients who have rare diseases, which was not be diagnosed because of paucity of proficiency and capital. They aim for the better life for those patients and the budget is 6 million USD. "World Economic forum" took precision medicine initiative in March 2017 at San Francisco. This project is aimed at developing protocols that improves the benefits of emerging technologies by minimizing the risks to societies. The project has nine programs; they are Artificial Intelligence and Machine Learning, Blockchain, Future of Drones and Tomorrow's Airspace, Future of Urban and Autonomous Mobility, Internet of Things and Connected Devices, Digital Trade and Cross-Border Data Flows, Environment and the Fourth Industrial Revolution, Future of Production and Precision Medicine [12].

4 Future of Precision Medicine

Future treatment for any disease would take into consideration of complete genome sequence and in-the future would be default test for the patients. The lack of early treatment for most of the hereditary diseases would be addressed in the future by PM [13]. The role played many genetic determinants towards a disease can be ascertained. There has been an ever increase in the interest in the general population to use wearable to monitor health in real time [14]. In precision medicine arena it has been flourished with implantable biosensors. Advances in the fields of electronics and micro fabrication techniques have caused increased interest in the use of implant-able medical devices in precision medicine. These devices have uncanny ability to provide real-time and continuous data points based on the analyte of interest with the need for intervention of the physicians and patients community. Few of the commonly used wearables are insulin pump for Type I diabetes; BioScarf an air filtration device for to reduce the risk of respiratory disorder; Body guardian heart to monitor cardiac arrhythmias etc. [15]. A better antibiotics of choice for treatment for during serious illness like sepsis; medication with fewer drug side effects as PM would eliminate to make any guess work towards the treatment. Drug metabolism is based not only on our genetic makeup; it is also affected by many factors, such as epigenetics, exposure, body size, and age. Pharmacogenomics procedure can improve patient safety, health outcomes, and decrease overall health care costs so that the right drugs will be given to the right patients [16]. This strategy may also provide an opportunity to advance the field of pharmacogenomics by collecting data on genetic testing results and drug effectiveness, including costs of therapy and avoiding adverse events. Specific diagnosis for cancer are already been undertaken only post accessing the gene expression level of the key protein (HER2 in breast cancer). The future of PM towards healthcare looks very promising and would be highly impactful on the patient community [13].

5 Challenges of Precision Medicine

The medical fraternity is been challenging to deliver the best available treatment benefiting the patients but the same advancement in technology like PM is not easy to adapt straightaway replacing the tradition knowledge based medicine [14]. The identification of each disease must be linked to highly specific biomarker to make a strong genetic predisposition in the identification of disease using the modern sequencing platform. Association of biomarker(s) to a disease is daunting task for which genomic sequence across large population has to be sequenced and global key players are playing a major role in setting up large genome project. We still lack robust genomic sequence analytical tools and supplementary tools like that assist in accurate determination of drug stability, bio-distribution and immune response post administration of the drug of interest. The field of precision medicine since being very naive has ever more hurdles to cross [17]. For PM to be outreach solutions for any treatment modality has to have a novel strategy and solution to make in more meaningful and useful to global patient community. The Precision Medicine Initiative is found to raise ethical, social, and legal issues because of its consequences. The sequencing of the several

patients would be an expensive affair and also make a use full interpretation would be a tedious task for the health care initiatives. The data of the patients has to be protected to safe guarded is also can crucial task [18]. Currently there is no standardized format in analyzing the genomic data coming from the various sequencing machines available in the market. A clear-cut data-processing software for diseases marker are still not applied in practical use. The conversion of these basic medical research findings into clinical practice is an obstacle for precision medicine. The public must also play a key role in the due participation to providing biological samples which would be beneficial for the generations to follow. Evaluation of the disease solely through genetic testing parallely raised many ethical hurdles and there is also a need to establish specific guidelines [16]. Genomic data analysis has been the key missing link in the chain in the PM approach for curing the patients because of the challenges faced in data acquisition and its meaningful interpretation. A strong support system coming in from the government agency would drastically improve the early stage innovations by sharing the clinical findings.

6 Conclusion

Precision medicine are already been in the limelight being publicly available at a time where patient satisfaction on disease treatment with reduced incidence of adverse effects is considered primed important to ensure better quality of life. With the support coming in the way from sequencing technology platform, data analysis, supercomputing facility, regulatory body. PM is nicely shaping up be the go-to future disease treatment methodology taking over the conventional medicine.

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