Personalised Medicine/Drugs

Ridwan Abiodun LAWAL
University of Lagos

Introduction

Personalized medicine is a unique approach referring to a tailoring or modifying of medical treatment to the individual features of each patient. Personalized medicine is also known as precision medicine. Every individual has his/her own unique variation in the human genome, due to combination of genetic variations and environment influence. Not all of those genome variations affect their state of health, but could manifest in different individual drug responses during treatment.

In order for physicians to know if a mutation is connected to a certain disease, researchers often do a study called a "genome-wide association study" (GWAS). In genomic medicine, information from genomes and their derivatives (RNA, proteins, and metabolites) is used to guide medical decision making. According to Schilsky (2010), genomic medicine is an important component of personalized medicine, which has been described as a rapidly advancing field of health care based on each person's unique clinical, genetic, genomic, and environmental information.

Along the continuum from health to disease, genome information can provide DNA-based assessment for common complex disease, molecular indication for cancer diagnosis and prognosis, genome-guided therapy, dose selection, and much more for personal health care. This is moving fast in technological development, social and information revolution which will affect the way of thinking in healthcare solutions (Schilsky, 2010). In simple words, genomic medicine is using information from genomes, either human or other organisms, and their derivatives to guide decision making in medicine.

Furthermore, it is now possible to examine a person's entire genome (or a fraction of it as you need) to assess individualized risk prediction and treatment decisions. Many patterns of gene expression across the entire genome are also now readily assayed. Thus, health and disease states can now be characterized by their molecular fingerprints to develop meaningful stratifies for patient populations and to elucidate mechanistic pathways based on genome-wide data.

Personalized medicine is a broad and rapidly advancing field of health care that is informed by each person's unique clinical, genetic, genomic, and environmental information. Health care with personal medicine encircled could integrate and coordinate the evidence-based approach for patient care individually from health to disease.

Personalized medicine needs multidisciplinary health care teams to reach its goal in promoting health and wellness, patients education and satisfaction, also disease prevention, diagnose and treatment. By genomic medicine, personalized medicine could understand molecular pathways of disease, therefore optimal health care strategies could be established in the earliest stage and optimal medical care could be reach for better outcomes for each individual, to include treatments, medication types and dosages, and/or prevention strategies may differ from person to person, resulting in an unprecedented customization of patient care (Schilsky, 2010).

Development of Concept

Diagnostic testing is often employed in personalized medicine for selecting appropriate and optimal therapies based on the context of a patient's genetic content or other molecular or cellular analysis. The use of genetic information has played a major role in certain aspect of personalized medicine (e.g pharmacogenomics), and the term was first coined in the context of genetics, though it has since broadened to encompass all sorts of personalization measures, including the use of proteomics (Priyadharshini et al., 2020) imaging analysis, nanoparticles-based theranostics, among others (Xie et al., 2010).

Background to Personalized Medicine

Every person has a unique variation of the human genome (Dudley & Karczewski, 2014). Although most of the variation between individuals has no effect on health, an individual's health stems from genetic variation with behaviors and influences from the environment (Lu et al., 2014).

Modern advances in personalized medicine rely on technology that confirms a patient's fundamental biology, DNA, RNA, or protein, which ultimately leads to confirming disease. For example, personalized techniques such as genome sequencing can reveal mutations in DNA that influence diseases ranging from cystic fibrosis to cancer. Another method called RNA-seq, can show which RNA molecules are involved with specific diseases. Unlike DNA, levels of RNA can change in response to the environment. Therefore, sequencing RNA can provide a broader understanding of a person's state health. Recent studies have linked genetic differences between individuals to RNA expression (Battle et al., 2014) translation (Cenik et al., 2015) and protein levels (Wu et al., 2013).

The concept of personalized medicine can be applied to new and transformative approaches to health care. Personalized health care is based on the dynamics of systems biology and uses predictive tools to evaluate health risk and to design personalized health plans to help patients mitigate risks, prevent disease and to treat it with precision when it occurs. The concept of personalized health care is receiving increasing acceptance with

veterans' administration committing to personalized, proactive patient driven care of all veterans (Snyderman, 2012).

In some instances personalized health care can be tailored to the markup of the disease-causing agent instead of the patient's genetic markup; examples are drug resistant bacteria or viruses (Altmann et al., 2007).

Genome-Wide Association Study

Genome-wide association study (GWAS) is used by physicians to know if a mutation is connected to a certain disease. In a GWAS study, the researcher will look at one disease, and then sequence the genome of many patients with that particular disease to look for shared mutations in the genome. Mutations that are determined to be related to a disease by a GWAS study can then be used to diagnose that disease in future patients, by looking at their genome sequence to find that same mutation. The first GWAS, conducted in 2005, studied patients with age-related macular degeneration (ARMD). It found two different mutations, each containing only a variation in only one nucleotide (called single nucleotide polymorphisms, or SNPs), which were associated with ARMD. GWAS studies like this have been very successful in identifying common genetic variations associated with diseases. As of early 2014, over 1,300 GWAS studies have been completed.

Disease Risk Assessment

Multiple genes collectively influence the likelihood of developing many common and complex diseases. Personalized medicine can also be used to predict a person's risk for a particular disease, based on one or even several genes. This approach uses the same sequencing technology to focus on the evaluation of disease risk, allowing the physician to initiate preventive treatment before the disease present itself in their patient. For example, if it is found that a DNA mutation increases a person's risk of developing Type 2 Diabetes, this individual can be asked to begin lifestyle changes that will limit the chances of developing Type 2 Diabetes later in life.

Applications of Personalized Medicine

Diagnosis and Intervention

Having the ability to look at a patient on an individual basis will allow for a more accurate diagnosis and specific treatment plan. Genotyping is the process of obtaining an individual's DNA sequence by using biological assays. By having a detailed account of an individual's DNA sequence, their genome can then be compared to a reference genome, like that of the Human Genome Project, to assess the existing genetic variations that can account for possible diseases. A number of private companies, such as 23andMe, Navigenics, and illumine, have created Direct-to-Consumer genome sequencing accessible to the public (Dudley & Karczewski, 2014).

Having this information from individuals can then be applied to effectively treat them. An individual's genetic make-up also plays a large role in how well they respond to a certain treatment, and therefore, knowing their genetic content can change the type of treatment they receive.

An aspect of this is pharmacogenomics, which uses an individual's genome to provide a more informed and tailored drug prescription. Often, drugs are prescribed with the ideas that it will work relatively the same for everyone, but in the application of drugs, there are a number of factors that must be considered.

The detailed account of genetic information from the individual will help prevent adverse events, allow for appropriate dosages, and create maximum efficacy with drug prescriptions. For instance, warfarin is the FDA approved oral anticoagulant commonly prescribed to patients with blood clots. Due to warfarin's significant inter-individual variability in pharmacokinetics and pharmacodynamics, its rate of adverse events is among the highest of all commonly prescribed drugs. However, with the discovery of polymorphic variants in CYP2C9 and VKORC1 genotypes, two genes that encodes the individual anticoagulant response, (Breckenridge, et al., 1974; Rieder et al., 2005). Physicians can use patients' gene profile to prescribe optimum doses of warfarin to prevent side effects such as major bleeding and to allow sooner and better therapeutic efficacy. The pharmacogenomics process for discovery of genetic variants that predict adverse events to a specific drug has been termed toxgnostics (Church et al., 2014).

An aspect of a theranostic platform applied to personalized medicine can be the use of diagnostic test to guide therapy. The test may involve medical imaging such as MRI contrast agents (T1 and T2 agents), fluorescent markers (organic dyes and inorganic quantum dots), and nuclear imaging agents (PET radiotracers or SPECT agents) (Xie, et al., 2010; Kelkar and Reineke, 2011).

In addition to specific treatment, personalized medicine can greatly aid the advancements of preventive care. For instance, many women are already being genotyped for certain mutation in the BRCA1 and BRCA2 gene if they are predisposed because of a family history of breast cancer or ovarian cancer.

As more causes of diseases are mapped out according to mutations that exist within a genome, the easier they can be identified in an individual. Measures can then be taken to prevent a disease from developing. Even if a mutation were found within a genome, having the details of their DNA can reduce the impact or delay the onset of certain diseases. Having the genetic content of an individual will allow better guided decisions and thus treating it or preventing its progression. This will be extremely useful for disease like Alzheimer's or cancers that are thought to be linked to certain mutations in our DNA.

Companion Diagnostics

This is another tool that is being used now to test efficacy and safety of a drug specific to a targeted patient group/subgroup. This technology is an assay that is developed during or after a drug is made available on the market and is helpful in enhancing the therapeutic treatment available based on the individual (Amgen, 2014).

These companion diagnostics have incorporated the pharmacogenomics information related to the drug into their prescription label in an effort to assist in making the most optimal treatment decision possible for the patient (Amgen, 2014).

Drug Developent and Usage

Assessing the genomic information of an individual can be significant in the process of developing drugs as they await approval from the FDA prior to public usage. Today in medicine, physicians commonly employ a trial and error method until they find the most effective treatment therapy for their patient. According to Dudley and Karczeweski (2014), personalized medicine allows these treatments to be more specifically tailored to an individual and hence give insight into how their body will respond to the drug and if that drug will work based on their genome.

The personal genotype can allow physicians to have more detailed information that will guide them in their decision in treatment prescriptions, which will be more cost-effective and accurate. As quoted from the article *Pharmacogenomics*: *The Promise of Personalized Medicine*, "therapy with the right drug at the right dose in the right patient" is a description of how personalized medicine will affect the future of treatment (Mancinelli et al., 2000). For instance, Tamoxifen used to be a drug commonly prescribed for women with ER+ breast cancer, but 65% of women initially taking it developed resistance. After some research work by David Flockhart, it was discovered that women with certain mutation in their CYP2D6 gene, a gene that encodes the metabolizing enzyme, were not able to able to efficiently break down Tamoxifen, making it ineffective treatment for their cancer (Ellsworth et al., 2010). Since then, women are now genotyped for those specific mutations, so that immediately these women can have the most effective treatment therapy.

Screening for these mutations is carried out via high-throughput screening or phenotypic screening. Several drug discovery and pharmaceutical companies are currently utilizing these technologies to not only advance the study of personalized medicine, but also to amplify genetic research; these companies include Alacris Theranostics, Persomics, Flatiron Health, Novartis, among others.

Pharmacy Compounding

Pharmacy compounding is another application of personalized medicine. Though not necessarily utilizing genetic information, the customized production of a drug whose various properties (e.g. dose level, ingredient selection, routes of administration, etc.) are selected and crafted for an individual patient is accepted as an area of personalized medicine.

Theranostics

Theranostics is a personalized approach in treating cancer, using similar molecules for both imaging (diagnosis) and therapy. The word theranostics is derived from the words therapeutics and diagnosis. It is now commonly applied to the field of nuclear medicine where radioactive molecules are attached to gamma or positron emitters for SPECT or PET imaging, and to beta, alpha or Auger electrons for therapy. An earlier use of these methods includes the use of radioactive iodine for treatment patients with thyroid cancer.

Cancer Genomics

The genetic variety of types of cancer has been enumerated in cancer research over the past few decades. There has also been increasing awareness of heterogeneity of tumors and/or genetic diversity within a single tumor. Hence, we consider personalized onco-genomics as the application of personalized medicine to cancer genomics. High throughput sequencing methods are used to characterize genes associated with cancer to better understand disease pathology and improve drug development. Currently, onco-genomics is an emerging field of genomics, particularly because of its implications in drug therapy. An example is tyrosine kinase inhibitors such as imatinib (marketed as Gleeve) have been developed to treat chronic myeloid leukemia (CML), in which the BCR-ABL fusion gene is present in more than 95 per cent of cases and produces hyper activated abl-driven protein signaling. These medications specifically inhibit the Ableson tyrosine kinase (ABL) protein and are thus a prime example of “rational drug design” based on knowledge of disease pathophysiology.

Conclusion

In the fast advancing era of Genomic and Molecular medicine, stakeholders are inevitably inclining to specificity in the practice of medicine. Patient satisfaction on disease management is centered on the demand for drug therapies to be more effective with reduced incident of adverse effects to ensure improved quality of life. Physicians are also welcoming therapies which will result in definite cure and minimize trial-and-error diagnosis and treatment. In addition, medical practice is accepting the molecular and genetic basis of assessing disease risk factors and preventive mechanisms.

Pharmaceutical and biotechnology companies are also advancing in drug development pathways, which are quicker with much predictive outcomes in order to save time and money. Regulatory authorities are also being pressured to approve drug therapies with minimum adverse reactions and increase efficacy. Government agencies and healthcare agencies have also developed an interest in more precise treatments in order to prevent expenditure on ineffective dugs which will lengthen patients' morbidity span and incur more health bills. In conclusion, although conventional medicine cannot be totally ruled out, it is evident that Personalized drugs are shaping the future of medicine and stands a promising chance of overtaking conventional drugs in the future.

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About Author

Ridwan Abiodun LAWAL was awarded a Ph.D. degree in Biochemistry from the University of Lagos, Lagos, Nigeria in 2015. He works as a Senior Lecturer in Biochemistry in the Department of Biochemistry, College of Medicine of the University of Lagos. His area of research interest includes Development of anti-cancer agents from Medicinal plants, Medicinal chemistry and Cancer Biology. He is a member of several scientific societies like the European Association for Cancer Research and has published in local and international peer-reviewed journals

E-mail: rilwan_y2k@yahoo.com, ORCID: 0000-0002-4029-1864

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