A Comprehensive Review: Personalized Medicine for Rare Disease Cancer Treatment

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Abstract   In the United States, cancer is one of the major causes of death. In 2010 alone, over 1.5 million fresh instances were recorded and over 0.5 billion died. After the completion of human genome sequence, significant progress in characterizing human epigenomes, proteomes and metabolomes has been made; a stronger knowledge of pharmacogenomics has been established and the capacity for individual personalization of health care has grown considerably. Personalized medicine has recently been primarily used to systematically select or optimize the prevention and therapeutic care of the patient through genetic or other data about the particular patient. Molecular profiling in healthy samples and cancer patients can allow for more personalized medications than is currently available. Patient protein, genetic and metabolic information may be used for adapting medical attention to the needs of that individual. The development of complementary diagnostics is a key attribute of this medicinal model. Molecular tests measuring the level of proteins, genes or specific mutations are used to provide a specific treatment for a particular individual by stratify the status of a disease, selecting the right drugs and tailoring dosages to the particular needs of the patient. These methods are also available for assessing risk factors for a patient for a number of conditions and for tailoring individual preventive therapies. Recent advances of personalized cancer medicine, challenges and futures perspectives are discussed.

Keywords   Personalized medicine, Type, Cancer treatment

1. Introduction: Personalized Medicine and Cancer

The incidence and prevalence of cancer are growing alarmingly, but there has been slow progression in treatment and treatment advantages are measured over weeks to months. Patient care is traditionally provided by physicians, which is supported by pathology, disease symptoms and medication history. A number of types of cancer can be detected before pathological symptoms develop, following advances in diagnostic science or early detection markers. These are biochemistry, genetic, imagery, metabolomic, and proteomic markers. These markers with an option of multiplexing may be detected by technologies in clinical samples. In general,

the application of over one marker in the same sample increases cancer detection sensitivity and specificity and enables a doctor to diagnose early and accurately. This information is very important because individual special treatment regimes can be developed on the basis of the cancer presence and stage as concluded from the profiles of the above markers. In clinical practice, pathological diagnostics continue to be a gold standards; however, molecular diagnosis may be different from the pathological one with additional information. Somatic or hereditary genetic aberrations could lead to cancer. The following cancer genetics can be understood for hereditary cancers, which are a large proportion of medical genetics. Family cancers only comprise 10-15 per cent of total cancers, and the remaining cancers have environmental, infectious and lifestyle influences. These data help scientists determine the risk of developing cancer in the lifetime of an individual[1]. Nevertheless, there are only a few cancer-disposing syndromes where the autosomal segregation of an allel contributes to the high risk of development of cancer. Moreover, NGFs contribute to mutations or other genetic modifications. In people without family history of cancer, cancer has also been found to develop. In addition to genetic variations of tumors per se, inherited genetic variants of genes which metabolize and process drugs also influence treatment response. These variants can increase the toxicity of certain medicines. This knowledge has helped to develop a' pharmacogenomics' science which identifies individuals who will respond to a specific therapy based on their genotype information [2]. The goal of personalized medication is to use the right medicine for the right patient at the right time at the right dose, with minimal or no toxicity. This article discusses, with the cancer example, the state of the art of this science.

2. Why Personalized Medicine Is Needed

Every gene that is coded in an organ (and its cells) has a different behavior than genes, though DNA from different cells is the same thing. Different tumors can have the same DNA in cancer, but in different tumor types the pattern of gene expression varies. Technologies like the micro-array expression of the gene are suitable to examine the profile of gene expression of hundreds of genes and to distinguish between the profile of cancer-related gene expression and normal. The standard medical treatment was guided over decades by the epidemiological research of cohorts that does not take into account individual genetic variability and most of the findings are population-based[3]. Before the treatment regimen is created, modern personalized health takes account of the genetic make-up and history of an individual's diseases. This contrasts with traditional personalized medicine, in which care is based on the history, social conditions and lifestyles of patients ' families. Targeted therapy is based on the modern personalized medicine. It is important that information about the modified route and the components of cancer is provided in targeted therapy. In women with breast cancer, for example, Herceptin is used to show higher levels of HER-2. In chronic myleloid leukemia, Gleevec is prescribed for tyrosine kinase inhibition. Reciprocal translocation between chromosome 9 and chromosome 20 occurs in these patients, causing the abl-driven protein signal to be hyperactivated. This is described in detail below.

3. The Contribution of "Omics" to Personalized Medicine in Cancer

A "reactive" approach has been a traditional way of treating individual medicine, where a doctor examines a patient, diagnoses a disease based on symptoms and then prescribes medicine. The physician, in contrast, evaluates the genetic history and family history of the patient in modern treatment first and then prescribes therapy. We know more about the genomic changes (changes in copy number, deletions, mutations, single nucleotide polymorphisms) as well as their association with various cancers. These association studies help to identify those at high risk for cancer development. Cancer genomics is understandable and is hoped for a further development of personalized medicine through DNA sequencing and cancer cell analyzes in patients to detect new genetic changes related to specific cancers. Building a full catalog of major genomic changes of many major cancer types and subtypes will help to develop more effective ways of diagnosing, treating, and preventing cancer. The disease of the genome is cancer. More information on specific types of tumors reinforces the conclusion that each tumor has its own set of genetic changes. The understanding of genetic changes and gene expression profiles in cancer cells will lead to more effective therapy strategies tailored to each patient's genetic profile. The Cancer Genome Atlas (TCGA) project is at the National Institutes of Health and is exploring information and resources to better understand the importance of cancer genomics.

Proteomic data also adds to customized medicine in relation to genomic data. A profile of all the peptides and proteins in a clinically healthy person was determined in the Human Proteome Project and compared to a patient's peptide and protein profile. The human proteome project has created a map of the protein-based molecular architecture of the human organism by characterizing all 21,000 genes of the known genome, making it a resource to elucidate biological and molecular functions and advance disease diagnosis and treatment. Although function capabilities are coded into genes, proteins perform the real function. Most drugs authorized in the United States Administration of Food and Drugs (FDA) is targeted at proteins. Indeed, in the early phases of testing for cancer detection J endorsed by FDA. Person. Pers. Protein-based diagnoses (immunohistochemistry) were 2 4 and Med. 2012. MAP kinase pathways, apoptosis, EGFR pathways, tyrosine kinase pathways, Notch pathways and their interactions (signal transductions) are based on protein interactions. Their interactions are the main ways of developing carcinoidal disease. Although a mutation initiates the cancer process, the expression of this process is mediated via the translation of proteins and enzyme-mediated signals. In the context of important health-related and disease cellular states including cancer, the IHEC coordinates the development of reference maps for human epigenomas.

The IHEC set the ambition to decipher at least 1,000 epigenomes in the next 7–10 years in order to achieve a substantial coverage of the human epigenome. The goal is to create high resolution historical modification maps, high-resolution DNA methylation maps and landmarks for all protein coding genes and the entire catalogue.and Non-coding and tiny RNAs expression patenting and comparative analysis of epigenome maps of models for human health and disease-related organisms. The connection between genetic and epigenetic variability globally can be determined using surveys of people, pedigrees and genetically identical twins. NIH Roadmap Epigenomics is another program which offers reference requirements for epigenomic maps. The research of low molecular weight molecules or metabolites discovered in cells and biological systems is a fresh addition to the fields of customized medicine. The metabolome is a determination of the performance of biological processes. As such, its functionality is often regarded as more representative than other "omics" measures, e.g. genomics or proteomics. An instance is a metabolic profiling of the urine and blood of patients treated with acetoamide (paracetamol). Before therapy, elevated p-cresol sulfate and little acetoamide sulphate before therapy demonstrates up to acetylaminoglucuronide after therapy. Mass spectrometry (MS) and atomic magnetic resonance (NMR) spectroscopy, hundreds to thousands of single chemical entities, are common technologies for metabolome measurement. Although promised early, difficulties stay before metabolomics ' complete potential is realized. Existing metabolomics facilities are capable of providing comparatively few researchers with extensive metabolomics knowledge and lack of training possibilities. Some businesses provide the facilities and restricted norms of metabolomics; However, cost problems, intellectual property rights and incentives to restricted profit reduce their use in fundamental, clinical and translation studies to a minimum.

4. Samples of customized drugs in several Cancers

The concept of personalized healthcare is based in connection with present cancer understanding on prevention or therapeutic methods[4]. Although personalized medicines have been used in several cancers, we have chosen only a handful of cancers below, with elevated cancer incidence and prevalence in the US and more information than others. In addition, I have selected breasts, colons, lungs, prostate, myeloid neoplasm, leuchemia and lymphoma from below, so all the type of cancers cannot be covered in one article.

4.1. Breast Cancer
The leading cancer of women's breasts is based on the rate of mortality. Genetic, environmental and behavioral (diatomy, practice and lifestyle) variables contribute to breast cancer. A broad population has embraced preventive methods such as mammogram screening. BRCA1 and BRCA2 screening is also prevalent practice in women's age hospitals and parity status. Current and future personalized approaches to medicine in people with breast cancer were discussed by Song et al.[5]. Interventions do not always succeed because of variations in people's genetics and the sensitivity of persons to environmental variables and modifiable variables. More proof promotes the susceptibility of the personal genome as an important factor in response to action and avoidance. This strategy comprises changes to the conduct of those with high risks (main preventative behaviour), early detection and thorough tracking of the genetically prone topics, and non-invasive therapy of early

phase cancer instances (secondary prevention). In accordance with the molecular characterization of breast cancer, individualized preventative strategies can be designed and implemented for personalized health care although there are also some disputes I discussed at the end of this section. The significance of personalized medication in patients ' treatments is demonstrated by the genotyping of CYP2D6 (cytochrome P450, family 2, subfamily D, polypeptide 6), and its impact on breast cancer therapy through tamoxifen.[6]. For patients with favorable breast cancer steroid receptors, tamoxifen is a standardized (endocrine therapy). Cytochrome P450 activates4-hydroxytamoxifen and endoxifen metabolites[7]. These metabolos have an affinity of two magnitudes in comparison with tamoxifen with the steroid receptor. This inhibits cell proliferation. CYP2D6 has distinct varieties and is suspected to be associated with elevated recurrence of breast cancer with poor metabolizers and CYP2D6 significantly impaired[8]. Thus, before therapy, genotyping of CYP2D6 can predict therapy reaction. The possibility of selecting powerful CYP2D6 inhibitors that might inactivate active metabolites may be created intelligent clinical decisions.

Since CYP2D6 is a genotype used in pharmacogenomic methods with an idea of a phänotype of private metabolizers, moral problems need to be resolved in advance. The therapy policies of patients and their caregivers should be well informed[9]. In bad CYP2D6 patients with metabolism, raloxifen becomes an alternative therapy choice[9]. Recommendations have been produced by Schroth et al.[10] for widescreen CYP2D6 allle coverage and high throughput, MALDI-TOF MS / CAN, in order to decrease phenotype error classifications (MALDI-TOF MS / CAN). Erb-B2-based breast cancer expression therapy has shown promising results in the field of personalized medicine[11,12]. Nevertheless, the recent report suggests that the routine evaluation for tamoxifen therapy CYP2D6 should not be considered as a guide for treating tamoxifen. These researchers have suggested that aromatase inhibitors should not be given to pre-or permenopausal patients.

Fleeman et al.[16] have suggested further investigation into all other than CYP2D6 and the identification of patients that respond to tamoxifen treatment. The metabolite of tamoxifen, norendoxifen, is seen as a prospective therapeutic lead compound owing to its aromatase inhibition properties[17].

4.2. Colon Cancer

Colon cancer is well distinguished by its genetics and epigenetics and is renowned for its biomarkers for early detection of colon cancer. There are a number of popular therapies (chemotherapy, radiation and surgery) to treat colon cancer[21,22]. Colonoscopy screening also assisted detect this cancer when polyps begin to form. A correlation is being finished in the tumor correlation between mutations, microsatellite instability and hypermethylation in each patient. The data from such studies assist to define subgroups that may and may not react to a specific therapy regime[4]. This enables patients who will most probably receive ideal treatment and will prevent unnecessary toxicity and expenses for those who are not likely to benefit. Generally, many patients survive at least five years following diagnosis when colon cancer is early treated. The disease is regarded to be cured when colon cancer does not repeat within 5 years. Cancers in stages I, II and III are considered to be curable. In most instances, stage IV cancer is not regarded to be curable, even if exceptions exist. One researcher is of different opinion and, according to the researcher, five years of survival should not be considered curable, because there are known recurrences of colon cancer and other tumor entities and a 5-year survival rate decreased at a higher stage in cancer (also in stages I –III).

Certain therapies in colorectal cancer also have been shown to not work. For instance, mutations of KRAS which include approximately 40% of colorectal tumors do not react with cetuximab or panitumumab to anti-epidermal growth factor receptor treatment[23-25]. Sarasqueta et al.[26] lately assessed the pharmacogenomics and the correlation of polymorphism with prevision of illness for colon cancer in GSTP1, ERCC1, and ERCC2 (genes engaged in metabolism of oxaliplatin). Maxico has also reported a response to the lack or presence of polymorphism in the methylenetetrahydrofolate reductase (MTHFR) gene in a different research in 5-flurouracil / folinic acid treated patients[28].

4.3. Respiratory organ Cancer

Lung cancer is two primary kinds: non-small-cell cancer of the lung (NSCLC) and small-cell cancer of the lungs (SCLC). Approximately 20% of all instances of pulmonary cancer occur with small cells. Cancer is known as mixed tiny cell / wide cell cancer, consisting of both kinds. If cancer has begun and spread to the lungs somewhere else in the body, it is called metastatic lung cancer. Due to cell heterogeneity, the treatment of pulmonary cancer is highly hard. Regular methods for treating lungen cancer have been used,

especially surgical techniques and chemotherapy. Recent information are being used as therapeutic objectives based on knowing the genetic foundations of lung cancer and EGFR, K-ras, ALK, MET, CBL, and COX2[29]. The use of crizotinib for NSCLC therapy has been lately proved by curran[30]. Anaplastic Lymphoma Kinase (ALK) inhibitor Crizotinib is shown to have promising outcomes. Other Persian. Other Persian. The advantages of the use of crizotinib for lung cancer therapy were also noted by Med. 2012, 2 7 researchers[31.22].

Also important clinical findings were given by Erlotinib and EGFR lung mutation cancer[33]. Also promising outcomes were shown in the FLEX trial[34]. In assessing the state and its aggression, data from histopathological examination and patient history are also taken into consideration. In Japanese populations undergoing gefitinib therapy, Nyberg and al.[35] studied association of the SNPs with acute interstitial lung illness. This study was the foundation of additional studies. In the Chinese population, the susceptibility to lung cancer in patients receiving chemotherapy was correlated with polymorphism ABCC1[36]. In small cell lung cancer patients also the genomic differences in EGFR and ERCC1 have linked to medication reaction[37,38].

4.4. Prostate Cancer

The second major cause of cancer death for males is prostate cancer. In elderly individuals, the rate of this cancer is high. The digital rectal examination and prostate particular antigen (PSA) tests are the primary screening methods used to identify prostate cancer. Due to the absence of pain, and the need to evolve over a number of years, doctors and patients are challenged to determine ideal therapy approaches for localized prostate cancer, biochemically recurrent prostate cancer and later stage cancer. Thirdly, chemotherapy, hormone therapy, surgery, and radiation are the prevalent therapy. Changes in age related to the treatments may affect all of these treatments, including metastatic diseases; and the risk-benefit ratio of these treatments will change[39]. New instruments are being created, such as the Comprehensive Geriatric Assessment, to better predict who can react to treatment. This can also contribute to the estimate of a certain prostate cancer patient's remaining life expectancy. As autonomous predictors for a recurrancy after radical prostatectomy in Caucasian and Asian countries, Audet-Walsh et al.[40] showed the connection between various SRD5A1 variants (steroid5-alpha reductase) and SRD5A2. In another study, BCL2 polymorphism was found to be associated with adverse outcome in prostate carcinoma patients [41].

4.5. Myeloid pathologic process

The growth of Myeloid neoplasm is supported by abnormal genetic and epigenetic occurrences. Most of these changes were localized in the pathways of hematopoietic differentiation and proliferation[42]. There have been several therapeutic agents developed to treat myeloid dysplasia. There have been attempts to include genomic data in the pathological data in order to explore the future direction of custom genomics[43]. Lymphomas are strongly linked to lymphoid leukemias, which are also found in lymphocytes but typically consist of only circulating blood and bone marrow (where hematopoiesis is a source of blood cells) and do not generate static tumors. The lymphoma is of many kinds, and the lymphoma is in turn component of a large group of illnesses known as hematological neoplasms. The CYP3A5 polymorphism of imatinib traugh concentration and clinical responsiveness among chronic myeloid leukemia patients was proved by Takahashi et al. [44].

5. Challenges, Future Perspectives, and Conclusions

When personalized medicine becomes commonplace, those who pay for treatment become more common. For insurance companies it is costlier to provide medical care if additional tests are carried out to diagnose a disease and if custom treatment is used. In the long run, personalized medicine is useful because it will help to develop strategies to disease prevention through data on a person's condition and reaction to specific therapies and treatments. Genetic testing covers only 5% of all private health insurers. It raises the question of how the current health care system could effectively incorporate personalized medicine in the United States. In insurance companies, the costs for personalized medicine for far fewer persons are calculated on basis of costs in large population groups. To be successful, large-scale models of medicine must be revised. If a specific diagnostics are made in order to prevent unnecessary or wasteful procedures, to prevent adverse events, and to provide more reliable, oriented services, it will cost the payer less over the long term. The "quality pay" theory is further encouraged and the costs of healthcare are minimized. Healthcare providers need to develop instruments to keep patients ' information up to date

and sophisticated tools to support decision-making. Doctors and primary care physicians should do more in their research, obtain training and practical experience in and understanding genomic and proteomic testing, improve policy resources, and build health and well-being programs that offset incomes lost by traditional medical practice. For diagnosis, an oncologist must not only be able to weigh cancer genes and genetics, but also their gender, health status, lifestyle and goals. By authorizing personal medicine tests quickly, government must play an active role and provide opportunities for their use. Initiated in the United States was the Genomics and Personalized Medicine Act. This includes research barriers, consumer adverse conditions and regulatory barriers. The general public should also be involved in public education and consultation on personalized medicine. Consumers should also be shielded from potential damage arising from the imminent translation of scientific findings, and innovations enhancing personal health knowledge must be promoted innovatively and economically.

In the coming years, an approach based on epidemiological studies will be followed. Such experiments were intended to test the newly found pre-clinical intervention in initial clinical trials. Over the period, population and clinical trials are intended to assess genetic and non-genetic factors in their prevalence, associations, interactions, sensitivity, specificity and predictive value.

Conflicts of interest

The authors declare that there is no conflict of interest.

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