Genomic/ Personalized Medicine: A Strategy To Revolutionize HealthCare System

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INTRODUCTION
Healthcare system is the organization of people, institutions, and resources to deliver health care services to meet the health needs of target populations. A health system consists of all organizations, people and actions whose primary intent is to promote, restore or maintain health. This includes efforts to influence determinants of health as well as more direct health-improving activities. The use of health information lies at the root of evidence-based policy and evidence-based management in health care. Increasingly, information and communication technologies are being utilized to improve health systems in developing countries through the standardization of health information, computer-aided diagnosis and treatment monitoring, informing population groups on health and treatment [1,2].

Genomic/ Personalized Medicine
Personalized medicine is a medical model that proposes the customization of healthcare with medical decisions, practices and products being tailored to the individual patient [3]. It involves identifying genetic, genomic and clinical information that allows accurate predictions to be made about a person's susceptibility of developing disease, the course of disease, and its response to treatment. Personalized medicine can allow screening, early intervention and treatment to be concentrated on those who will benefit, reducing expense and side effects for those who are not likely to benefit [4]. It is important to note that the application of personalized medicine goes beyond genetic disease and can optimize treatment for many diseases including HIV and epilepsy.

Need for Genomic Studies in Treatment
People may vary from one another in many ways based on their DNA, environmental factors which play a role in health and disease. For example, the natural variations found in the genes could influence the risk of developing a certain disease, and the degree to which it progresses. Disease diagnosis is often based on symptoms that might be indicative of several diseases. It is, however, now possible for

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the diagnosis of some diseases to be made more easily and in a more timely manner as genetic tests for disease-specific mutations become increasingly available. Genome studies are revealing a large number of molecular biomarkers relating to specific gene variations. These may confirm the clinical diagnosis in the presence of overt disease. They may also indicate an asymptomatic person’s susceptibility to a specific disease and more reliably predict a person’s differential response to treatment. Such biomarkers can serve as the basis of new genomics-based predictive and diagnostic tests, the results of which may be used by a trained health professional in several ways [5].

Clinical Significance
Genomic medicine helps in the determination of risk of developing several specific medical conditions.

Cancer
Genomics provides a “snapshot” of gene activity within a cell. With the advancements in technology, there has been a shift away from viewing cancer in terms of the organ where a tumor forms, and toward a concern with the genetic instructions that govern both the growth and division of individual tumor cells and the interaction of the tumor with the person who serves as its unwilling host [6, 7].

Cardiovascular disease
The application of genomic medicine to the prevention and treatment of Cardiovascular diseases will ultimately lessen the burden. Given the complex nature of Cardiovascular disease, information derived from newer evolving fields, such as transcriptomics, proteomics and metabolomics will allow to fully interrogate features of the human genome to better understand disease pathogenesis and to identify new drug targets [8].

Neurodegenerative disease
The recent development of induced pluripotent stem cells provides a method to create live, patient-specific models of Alzheimer’s disease and to investigate disease phenotypes in vitro. The genetics of AD patients and the potential for induced pluripotent stem cells to capture the genomes of the individuals and generate relevant cell types can make them to model neurodegenerative diseases [9].

Advantages of Genomic Medicine
- Ability to make better medical decisions
- Higher probability of desired outcomes to better-targeted therapies
- Reduced probability of negative side effects
- Detect disease at an earlier stage, when it is easier and less expensive to treat effectively
- Stratify patients into groups that enable the selection of optimal therapy
- Reduce adverse drug reactions by more effective early assessment of individual drug responses
- Improve the selection of new biochemical targets for drug discovery
- Reduce the time, cost, and failure rate of clinical trials for new therapies
- Shift the emphasis in medicine from reaction to prevention and from disease to wellness

Diabetes
Failure to understand the pathophysiology of diseases such as type 2 diabetes frustrates efforts to develop improved therapeutic and preventive strategies. The identification of DNA variants influencing disease predisposition will, it is hoped, deliver clues to the processes involved in disease pathogenesis. This would not only spur translational innovation but also provide opportunities for personalized medicine through stratification according to an individual person’s risk and more precise classification of the disease subtype [10, 11].

Hepatitis C
Hepatitis C is a viral disease transmitted principally by blood, which affects millions of people worldwide. A significant proportion of those affected develop severe liver disease as a result. Only a fraction of patients are responsive to interferon treatment, highlighting the need for further research into genetic factors involved in response to therapy in order to optimize treatment. The only current approach for end-stage disease is liver transplant, which ironically does not cure the condition [12, 13].

Impact on Health Care
Advances in genomics have already found clinical application in the development of new, targeted drugs to treat some cancers and genetic tests that can predict whether individuals would benefit from particular interventions [14]. As advancements and discoveries in genomics continue at an ever increasing rate, the clinical ability to accurately
predict disease risk and drug response will continue to improve. It is through the use of such tests that the promise of personalized medicine may be realized [15, 16].

In addition to the promise of improved patient care and disease prevention, there is potential for personalized medicine to impact on the cost of health care. Health care costs may be lowered by individual genetic test results or by analysis of an individual’s full genome sequence allowing for screening, and the tailoring of drugs and treatments to minimize side effects and improve outcomes. Testing can also rule out individual disease susceptibility where there is an increased risk in the family, reducing the need for costly and sometimes invasive screening and preventative therapy. These functions all play a role in ensuring more targeted and cost-effective health-care into the future [17-19].

Role of genetic differences in disease
Gene–environment interactions refer to the fact that the same environmental exposures can have different effects on disease risk in people because of genetic differences. Our increased ability to study genomic variation is now making it possible to pinpoint the genetic factors that can lead to higher levels of risk.

One example of this is recent research into multiple sclerosis. While the cause of multiple sclerosis is still unclear, it has long been believed that there is a link between multiple sclerosis and vitamin D deficiency. A new study has found a very clear link between a particular genetic variant, which causes reduced levels of vitamin D and multiple sclerosis. When people inherit two copies of the variant in gene CYP27B1, they develop a genetic form of rickets, a disease caused by vitamin D deficiency. When they inherit just one copy, a particular enzyme is affected which leads to lower levels of vitamin D [20-22].

Applications of Personalized Medicine
Personalized medicine can provide medical practitioners with an additional biological basis with which to categorize some diseases. This will influence genomic based improvements in screening, diagnosis and prognosis. It will also allow for greater optimization of preventative and therapeutic care [23].

Personalized medicine can facilitate disease prediction, prevention and treatment strategies by:
- Determining if someone is at increased risk of developing a disease, followed by promotion of and support for compliance with available prevention strategies;
- Diagnosing disease earlier in development using optimal surveillance, thereby allowing more effective interventions or treatment options;
- Enhancing therapeutic efficacy by ensuring the most appropriate drug is used and that the dosing regimen takes into consideration any genetic variants, which may influence metabolism of the drug;
- Avoiding preventable drug related complications and side effects resulting from generic “one size fits all” drug prescribing [24, 25].

Scope
The main aim of the genomic medicine is to tackle more complex diseases, which was believed to be influenced primarily by environmental factors. The role of genomics in personalized medicine and its potential to improve health care highlights the clinical utility of various genetic and genomic tests as it is this often overlooked aspect of testing that determines the likelihood of an improved outcome for the individual.

Fig 1. Patient group responding differently with same prescription

<table>
<thead>
<tr>
<th>Personalized Medicine</th>
<th>Genomic Medicine</th>
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<tbody>
<tr>
<td>Pharmacogenomic studies</td>
<td>Drug X-AA</td>
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<tr>
<td>AA genotype</td>
<td>Drug X-AT</td>
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<td>AT genotype</td>
<td>Drug X-TT</td>
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<tr>
<td>TT genotype</td>
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Patients treated with a specific drug

Adverse effects
Poor responders
Good responders
Fig 2. Work flow chart underlying personalized medicine

Symptomatic or asymptomatic patient

Patient enters diagnostic & therapeutic efficacy processes

Medical Imaging procedures → Molecular lab testing

Determination of variations in genes, gene expression, proteins & metabolites of patient, diseased tissue or tumour

Lab methods to determine optimal drug therapy

Mandated lab companion testing to assess efficacy

Additional genomic testing for efficacy

Appropriate drug therapy initiated

Continuing medical imaging during therapy to assess efficacy

Continuing molecular lab testing to assess efficacy

Therapeutic drug monitoring to determine adequacy of dosing

Fig 3. Personalized medicine with new molecular and diagnostic technologies to match selected groups of patients to give effective treatment
Table 1. Improvement in cancer treatment using personalized treatment

<table>
<thead>
<tr>
<th>S. No</th>
<th>Cancer disease</th>
<th>Old model</th>
<th>Old survival</th>
<th>Personalized model</th>
<th>Personalized survival</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Acute promyelocytic leukemia</td>
<td>Chemotherapy</td>
<td>19 months</td>
<td>All-trans retinoic acid</td>
<td>&gt; 58 months</td>
</tr>
<tr>
<td>2</td>
<td>Chronic myeloid leukemia</td>
<td>Chemotherapy</td>
<td>6 years</td>
<td>Imatinib</td>
<td>&gt; 22 years</td>
</tr>
<tr>
<td>3</td>
<td>Melanoma</td>
<td>Decarbazine</td>
<td>&lt; 10 months</td>
<td>Vemurafenib</td>
<td>16 months</td>
</tr>
<tr>
<td>4</td>
<td>Medullary thyroid cancer</td>
<td>Chemotherapy</td>
<td>36 months</td>
<td>Imatinib</td>
<td>Not reached</td>
</tr>
<tr>
<td>5</td>
<td>Gastrointestinal stromal tumour</td>
<td>Chemotherapy</td>
<td>12-18 months</td>
<td>Imatinib</td>
<td>5 years</td>
</tr>
<tr>
<td>6</td>
<td>Released Hodgkin lymphoma</td>
<td>Chemotherapy</td>
<td>1.2 years</td>
<td>Brentuximab vedotin</td>
<td>22.4 months</td>
</tr>
</tbody>
</table>

CONCLUSION
Personalized medicine research attempts to identify individual solutions based on the susceptibility profile of each individual. Robust evaluation and sensible regulation of genetic tests are necessary to realize the promise of personalized medicine. This includes consideration of a drug and treatment’s efficacy, and genetic test’s analytical and clinical validity, in order to ensure that the test is safe, and performs as intended. It incorporates Clinical Genetics and molecular pathology, and is as valuable in frontline care as in public health. For this to flourish and deliver the best patient outcomes possible, all specialties and fields need to work together in a strategic way. Recent advances in the genetic etiologies of common diseases will surely improve pharmaceutical development. Raising awareness of the genetic factors as part of public health programmes will therefore help individuals make more informed decisions about health and wellbeing.

REFERENCES


