Genomics and Future of Medicine

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Photo: Vivan Mehra

If all the promises that medical science and technology advancements have to offer, advances in our understanding of the human genome and genomic medicine are poised to have a profound impact on the delivery of healthcare. The opportunity is enormous and will help shift the focus of care from intervention to prevention.

V.L. Ramprasad, the COO of genomics-based diagnostics firm, MedGenome, draws from his years of experience as a researcher in molecular genetics, to throw light on how genomic medicine could revolutionise healthcare by fairly accurately predicting disease risk and providing personalised treatment.

The Human Genome Project, which took 13 years to complete, has led to the discovery of more than 1,800 disease genes and helped identify the genetic causes of rare diseases. It has greatly contributed in revealing the many genetic variations that increase the risk of specific diseases, such as Alzheimer's, and has helped researchers observe and detect genetic mutations that are often seen in cancerous cells.

With over four million Indians suffering from some form of dementia and Alzheimers, and 1.4 million cancer patients in 2016 - an estimated 1.73 million cancer patients by 2020 - genomic medicine could do wonders for the Indian population. Besides, the country has come a long way since the first study to chart the complete genome sequence of a woman from Kerala was done in 2012. Now, researchers are better equipped in understanding India's genetic diversity and assessing its disease burden.

In fact, we are in a position to characterise health and disease states by their molecular fingerprints and develop meaningful, individualised risk predictions and treatment decisions based on genome-wide data through diagnostic and therapeutic strategies.

At the Core

Genomics is the study of understanding the structure of the genome, which contains all genetic instructions for developing and directing the activities within an organism in the form of DNA. The genomic information of every individual is unique as the structure, sequence of gene, or genome, varies between individuals. These variations in a gene may affect the function of its encoded protein products and sometimes may cause a disease. Hence, Genomics has many implications in medicine and health, often referred to as Genomic medicine, as it examines the molecular mechanisms and the interplay of genetic and environmental factors of a disease.

By sequencing individual genomes, researchers can uncover large amounts of information concerning all aspects of an individualâ€™s physiology. [Photo: Jyoti Kapoor]

Variations in a Gene

The Human Genome Project sequenced DNA pooled from a range of individuals, to create an average or 'reference' genome. Therefore, it is a "representative" or generic sequence, providing the essential reference map for the human genome. It also stimulated the development of technology and analytic tools to process massive quantities of genomic data. The human genome is made up of more than three billion genetic letters and, hence, sequencing the genome is a pre-requisite to understanding it in its entirety. With the advancements of DNA sequencing technologies, it is also becoming practical and affordable for individuals to get their genomes sequenced. An individual's genomic sequence is compared with the 'reference' genome to identify the variations across genome, with the help of bioinformatics tools. These genomic variations are correlated with the individual's physiological state to confirm whether such genomic variation is pathogenic or not.

Personal Genomics

By sequencing individual genomes, researchers can uncover large amounts of information concerning all aspects of an individual's physiology, from their susceptibility to certain diseases to the way they respond to specific drugs.

The first individuals to have their personal genomes sequenced were Craig Venter, founder of Celera Genomics, and James Watson, co-discoverer of the DNA double helix. Steve Jobs, co-founder of Apple Inc., was one of the first 20 people in the world to have his DNA sequenced, for which he paid $100,000. He also had the DNA of his cancer sequenced, in the hope that it would provide information about more appropriate treatments for him and for other people with the same cancer.

Personal genomics can also be used to predict a genetic disease by looking at an individual's genome. These kinds of tests are often called lifestyle testing. For example, it can be used to tell a woman if she carries the BRCA1 breast cancer gene and, if so, how much it increases the probability of her having breast cancer. Furthermore, an individual's genomic information helps to predict a person's response to drugs or genes that are affected by a drug. Therefore, regulatory requirement for clinical trials, procedural streamlining and enhanced clinical and economic effectiveness will be the biggest challenges that would be overcome. Issues related to adverse drug reaction and staggering cost of manufacturing ineffective drugs could also drive the change in pharmacogenomic research.

Precision Medicine

Precision medicine or 'specific treatment' will also help researchers and doctors understand the exact treatment they need to offer to patients. The advent of precision medicine is moving us closer to more precise, predictable and powerful healthcare customised for the individual patient.

Certain individuals have specific variations in their drug metabolising genes, and their drug metabolising activity changes accordingly. Thus, pharmacogenetics helps to tailoring a drug treatment to match a person's genetic makeup. For example, if a person is categorised as Ultra-rapid metaboliser (UM) based on his or her genetic changes in drug metabolism and transporter genes, he or she can be prescribed a higher dose than the normal. Likewise, poor metabolisers (PM) may need lower dose because the drug will not easily be removed from blood stream than normal. This kind of personalised medicine will be highly helpful to avoid side effects during chemotherapy.

Pharmacogenomics has proved to be very useful in many clinical practices; the prescription of drugs like analgesics, antidepressants, and anticoagulants. It resorts to population genetic information to carry on research, design and develop new drugs, and understands the uses and dosage of these drugs in clinical practice. Intense research is being carried out and it may assist in paving the path for customised drugs for patients.

Medical research has proved the presence of almost 4,000 inherited diseases that are caused by one single gene. It has also revealed how diseases are a result of a large number of combined genes. A person may have inherited a genetic predisposition to an illness like diabetes but the correct medical counseling which would include right diets, exercises and more, could prevent the person from becoming diabetic.

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Future of Personalised Genomics

Though it is at a nascent stage, precision medicine is evolving at a fast pace. Moving from a traditional medical model of treating pathologies to an individualised predictive and preventive model of personalised medicine promises to reduce healthcare costs. The increasing number of catalogues of causative and risk genes will provide a foundation for personalised medicine and pharmacogenomics. The advent of next generation sequencing has helped in bringing down the cost of genome sequencing to less than $1,000. However, there are many other new technologies on development that will make the sequencing even faster and more economical, such as the Oxford Nanopore technologies (GridION‚„¢ System based on nanopore-based sensing). The future perspective of this advanced technology may reduce the cost of screening diseases to $100. Research is proving that the therapies that are intended for one type of cancer could, in the future, be used to treat other types of cancers, on the premise of changes occurring in a person's DNA. Discovery of mutations via sequencing and optional treatments may offer much hope towards better customised treatments for individuals. People can now take distinct medical advice, follow prescribed regimens and a course of medication to avoid getting affected by the same.

Genomics continue to bring about far-reaching and impactful changes in the manner of diagnosis, and treatment of infectious diseases. Consistent research is being made particularly in diseases like cancer, congenital diseases and acute infections. In the case of those carrying a gene mutation-assisted reproduction (IVF) with pre-implantation testing of embryos is adopted so that only unaffected embryos are used. For those affected with tuberculosis, the sequencing of a genome will showcase the antimicrobials which would influence positively. Public health will also be impacted positively through genomics. The information acquired through genome sequencing will help initiate strategies to fight and prevent epidemics like Zika and the swine flu.

Information technology and biology together may revolutionise the world of genomics and unfold many new discoveries of the enigmatic DNA of organisms in the future. This will make genome sequencing economically more viable to the less privileged sections of the society and will enhance the techniques of testing. ~