

## Making way for self-reliance in genome-based medicines

28 April 2022 | Views | By Dr V. Gupta, Asst. Prof, UPES School of Health Sciences and Technology

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The current pandemic has shown us the power of biotechnology to transform healthcare. Be it the fast turnaround time to develop vaccines based on mRNA or the indigenous development of RT-PCR kits by various Indian institutions for diagnosis of COVID-19; Biotechnology has played a vital role in mitigating COVID-19 and provides a glimpse of the future of healthcare.

Remarkably, the use of modern genomics tools to track a quickly evolving infection such as COVID-19 which is in its fifth lineage of variants of concern, Xe. These tools allow us to quickly sequence (or read the DNA of) the infective pathogen isolated from the body fluids of current patients to determine the lineage (or variant) of the pathogen and quickly associate the potential prognosis of the infection associated with the identified variant.

This has been made possible through large scale data-sharing efforts across the world, such as GISAID or NextStrain (represented by INSACOG from India), whereby researchers in close collaboration with medical practitioners maintain a catalogue of sequences of various variants, a list of symptoms, and potential prognosis or how the disease may progress in the patients. This allows us to make retrospective statements that the second wave caused due to the Delta variant was associated with a much more severe prognosis than the third wave caused by the Omicron variant of COVID-19.

It has been evident to researchers for a while now how such catalogues of genome-based information can help in identifying the infective agents that led to the sequencing of the *Epstein-Barr-virus* causing mononucleosis in the early 1980s to sequencing and identification of the Influenza-causing bacteria *Haemophilus influenzae*, the first organism to be fully sequenced in 1995. One of the key motivations behind the Human genome project, established in 1988, that aimed to genome sequencing of human DNA was also to “Find genes, Establish function and disease mechanism, to find a cure”. This has spurred a host of large-scale gene and mutation finding global projects that first identified the causative genes and mutations commonly found in various familial or inherited diseases, such as the BRCA1 gene in Breast cancer or APOE gene in Alzheimer’s disease.

Given the continually diminishing cost of sequencing powered by next-generation sequencing technologies that can read an entire human in a day for less than Rs 35,000, researchers have catalogued many more disease-causing mutations from both rare inherited and common complex diseases.

Researchers have gone even a step further to find associations between various drugs and mutations in genes that are either metabolise these drugs or are their direct targets. These associations are known as Pharmacogenomics studies and directly affect healthcare whereby a person's genetic makeup (described by various mutations in her genes) can directly determine the kind of drug type and its dosage for various diseases. This has been particularly useful in cancer therapy; for example, the widely available genetic test for the DYPD gene, encoding the enzyme dihydropyridine dehydrogenase, determines patients at high risk for toxicity to a common chemotherapeutic agent- 5FU.

This has led to a whole industry of gene-based predictive healthcare companies such as 23&me in the US, that claim to read your genetic makeup and suggest potential drug susceptibility profiles based on a catalogue of such data collected from published articles and their in-house datasets. Soon clones of 23&me also emerged in India, of particular note being MapMyGenome with Indianized version of the predictive genetic test called Genomepatri™.

However, the adoption of such tests remains relatively low mainly due to the lack of data representation from India in most genome projects. Even though India is a large milieu of people with very different genetic backgrounds, only a few populations that have been selected abroad ever feature in such genome-based catalogues. However, post-2018 and especially post the second COVID-19 wave, this situation is rapidly evolving as the Indian government through INSACOG and other such initiatives establishing sequencing facilities, has empowered various institutions to develop such catalogues that will deliver state-of-the-art genomics-based medicine to Indians and may seed genomics start-ups that will bring down the cost.

Such efforts will allow access to genome-based precise healthcare across socio-economic groups in India, making gene-based predictive healthcare a reality in India.

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