Completing the Human Genome Project: Filling in the gaps

Editorial

The Human Genome Project was declared to have been completed in 2003. Since then, we geneticists are using the data on a regular basis for genetic diagnosis. High throughput technology has made the diagnosis of monogenic disorders very easy, and the scope of exome sequencing and genome sequencing is becoming broader andmore universal. Now, the challenge is the roughly fifty percent of cases where exome sequencing and even genome sequencing do not provide the answers. The important reasons are causative variants in the region not covered and the sequence variants of types which cannot be detected by current analyzing techniques. As the technology for sequencing improves, the patient sequencing data and analysis pipelines are giving better results. Better reference genome and annotation of each nucleotide in the human genome needs more work.

Though the Human Genome Project was declared complete, about 10% of the genome was not sequenced. This includes telomeric regions, pericentromeric regions and centromeres. The work of filling the gaps of the genome is going on. The GenExpress in this issue talks about the 'Telomere to Telomere' consortium and completion of X chromosome sequencing. The long-read sequencing technologies are making this possible. The other aspect is representation of all populations in the reference genome so that the variants in normal populations are documented. Only 0.1% of our genome varies from individual to individual, but even 0.1% of 3 billion nucleotides amounts to a lot. The current human reference genome does not have representation of many populations. The Human PanGenome Consortium aims at removing the racial and ethnic biases in the human reference genome.It is working towards thedevelopment of a next-generation genome reference representation that can capture all human genome variation and support research on the full diversity of populations. With a complete pangenome reference sequence along with information of structural variants and epigenetic marks, novel genetic mechanisms for diseases may get identified and improve the diagnostic yield. As these gaps in the genome sequence are getting filled, the Society forIndian Academy of Medical Genetics (SIAMG) continues to fill the gap in your knowledge as we gain some. Also, there as gaps in our knowledge, gaps in communication with patients, gaps with contacts with referring physician, etc. There is a lot of work for 2022.

Wish you all a happy and healthy, corona-free new year.

Dr. Shubha Phadke
1st January 2022