Human Genome Project: A Milestone in the History of Humankind

Editorial

The ambitious Human Genome Project was successfully completed in 2003 and the information about the sequences on all chromosomes became available to researchers and for patient care. This issue has an article briefly describing the methodologies and issues involved in the Human Genome Project. This is an important and exciting milestone in the history of humankind and medicine. What was achieved by spending 3 billion or more US dollars can now be achieved by a few lacs of Indian rupees. Whole genome sequencing and sequencing of all coding regions of genes (exome) is being used widely in the clinic and research laboratories. The diagnostics of monogenic disorders has already shown a paradigm shift through the use of massively parallel sequencing (also known as next generation sequencing or NGS) either in the form of a multi-gene panel test or through exome sequencing for phenotypes where predicting the causative gene on a clinical basis is difficult or not possible. NGS based techniques have also made possible the diagnosis of aneuploidies and monogenic disorders in the fetus by using free fetal DNA (ffDNA) in the maternal plasma. Sequencing of the whole genome (WGS) prenatally or immediately after birth is now feasible and has already been done for more for than 1500 neonates! WGS can be a useful tool for the diagnosis of sick neonates. Use of WGS for newborn screening (NBS) is also being explored by many centres. The National Institutes of Health (NIH) has already started 4 projects of WGS of newborns to explore various aspects like its use for screening for disorders routinely included in NBS as well as additional genetic disorders, utility of WES data to paediatricians and parents during infancy and childhood for healthcare, and the ethical, legal and social implications of such huge predictive data available immediately after birth. Preliminary research shows that parents are also interested in using WGS of newborns. Though practically and technically feasible, WGS of newborns is likely to have many more ethical and social repercussions and there is a strong need to look into various issues to make informed decisions about how and when to use such powerful technology. Counseling for NGS is complex and demanding but it also involves a lot of understanding on the part of patient families and could be emotionally taxing as illustrated in the 'HearToHearTalk' of this issue.

Identification of a number of loss-of-function mutations in everyone and in many without a phenotype has come out as a great surprise as a result of NGS technology. Thus, non-penetrance may be much more common than we currently know. Prediction of pathogenicity and explanation of non-penetrance are big challenges ahead. Johnston et al. (2015) have developed a new approach of iterative phenotyping which is likely to be useful in clinical research. This landmark article is included in the 'Genexpress' of this issue. Other articles related to the use of NGS in prenatal diagnosis and newborn screening are equally revolutionary. One more article included in the Genexpress needs special mention. This is an article depicting a novel form of maternal inheritance where mutation in the mother and the fetus are essential to express the phenotype. 'Genetic Clinics' is happy to bring these latest exciting developments in molecular genomics to you.

Enjoy the new year of this molecular era!

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