JSTMU Journal of Shifa Tameer-e-Millat University

https://j.stmu.edu.pk

Open Access

SHORT COMMMUNICATON

Impact of the human genome assignment on biology and generation

Sumreena Mansoor[1], Almas Ashraf [2]

[1] Associate professor, Department of Biochemistry, Shifa College of Medicine, Shifa Tameer-e-Millat University, Islamabad, Pakistan

[2] Instructor, Department of Biochemistry, Shifa College of Medicine, Shifa Tameer-e-Millat University, Islamabad, Pakistan

Author`s Contribution

[1] Data collection

[2] Manuscript proof reading

Article Info.

Conflict of interest: Nil

Funding Sources: Nil

Correspondence

Sumreena Mansoor

sumreena.scm@stmu.edu.pk

Cite this article as: *Mansoor S, Ashraf A. Impact of the human genome assignment on biology and generation. JSTMU. 2020; 3(1):58-61.*

A B S T R A C T

The Human Genome Project has revolutionized biology by deciphering a reference human genome sequence along with many other organisms' complete sequences. The project reflects a great example of integrated inter-disciplinary approach to develop sophisticated technology and brought engineers, computer scientists and mathematicians at one platform with biologists. Further improvements have made from projects ENCODE, to find functional elements of genome; and Human Proteome Project, to map human proteins through the genetic map. Moving one step ahead, the gaps that were present to study evolution of many species are now decreasing due to better understanding of the genome. There has been an open approach to data sharing and open-source software, thereby data is publicly accessible for more breakthroughs from data banks such as GenBank. Physicians approach to practice medicine is changing and becoming more personalized as a result of this project. There has been development in treatments of many diseases for example through genome-wide association studies. Diseases prognosis and risk can be now more accurately predicted through the advancements in HGP. However, we are still in initial stages and in the process of understanding the huge data generated by HGP and its implications. Moreover, the ethical, social and political issues that arise due to this genetic research needs to be addressed alongside.

Keywords: *Human genome project, proteomes, genome-wide association study, gene mapping.*

Introduction

Human Genome Project:

The Human Genome Project (HGP) has played a key role in transforming the fields of biology and medicine. Initially, most of the biologists were against the idea of human genetic mapping and it was favored more by the US congress and the US Department of Energy (DOE) than scientific community.[1,2] The project started in 1990 and its data was published in 2004.[3] It all started with first generation sequencing which was slow and cumbersome.[4] For improvement, Craig Venter created 'Celera' to decipher the sequence using bacterial artificial chromosome (BAC) vectors which expedited the project.[5] For more accuracy, smaller genomes such as yeast were mapped before mapping human genome. HGP fostered the advancement in mathematics, computers and statistics for handling the analysis of large amount of data generated by this research project. Scientists produced accurate genome data for each chromosome with very small gaps.[3] These reference sequences paved the way for further studies involving gene transcription and regulation.[6]

Influence on Biology:

The Human Genome Project was released with the intention to map the parts of complex biological system at molecular level in order to understand their connections, dynamics and functions.[7] For instance in 2003, the project by NIH called ENCODE (Encyclopedia of DNA elements) was initiated, that aim at finding the functional elements of

the genome. Various techniques including the second-generation sequencing were used to yield massive data linked to regulatory networks that control gene expression.[8] This played a pivotal part in the emergence of "Systems Biology".

Furthermore, the HGP also paved the way for the proteomics.[9] Human Proteome Project (HPP) is mapping human proteins through a genetic map.[10] However, it is challenging project to accomplish due to cell type specific, spatial and temporal nature of protein expression and its functions.[11,12] The completion of HPP and greater understanding of proteins, will lead to precise diagnostic, prognostic, therapeutic, and preventive medical applications.[13]

Through human genome project initiation, approximately 4000 sequences have been identified, of humans and other species mostly of bacteria.[14] It has given an insight of how microbes and humans are connected, about their lineage and trace steps of evolution.[15] Moreover in future, it will help in understanding of how new genes are formed, reorganized, homology of sequences among species; the list goes on. One of the most interesting discovery was the collection of the Neanderthal genome. A minor percentage of common genetic-code between Neanderthal man and humans suggests crossbreeding between the two species during their evolution.[16]

Influence on Technology:

The HGP led to the advancement in technology especially in computation and mathematics that created a common platform for biologists, physicists, engineers, mathematicians and software experts.[17] HGP also focused on the idea to make the availability of this knowledge accessible to the public by user friendly data banks for example GenBank at the UCSC (University of California Santa Cruz) Genome Browser.[18,19] In addition, the HGP also promoted open-source software, that provides the source code of programs which can then be edited according to the needs of researchers and scientists.[20] Physicians can access this data cloud and use it for personalized medicine in future that will change the practice of medicine and greatly contribute to the next generation of health systems.

In 2010, Human Proteome Project introduced a gene-centric approach to map protein expression from every gene locus.[21] HGP has facilitated quantitative mass spectrometry for reference sequences and value of masses of peptides in human proteome. Mass spectrometry-based proteomics technology has given platform to new applications like targeted proteomics.[22] HGP also requires precise computational resources, like Peptide Atlas and Trans Proteomic Pipeline.[11,12]

Influence on Medicine:

Human Genome Project has led to several advancements in medicine. For instance, many common single nucleotide polymorphisms (SNPs) have been identified in various human communities.[23,24] Furthermore, new SNPs, both common and rare, are being discovered every day that provide a high-resolution map of genetic variation among humans.[25]

Information has also been generated through genome-wide association studies (GWAS), which associate targeted genetic variants to risk of a disease through case control studies and statistics.[26] This GWAS approach has modified the prognosis and treatment of various diseases such as multiple sclerosis, age related macular degeneration and Parkinsons.[27] Since 2005, over 1,350 GWAS have been published.[26]

With thousands of exomes and whole-genomes sequenced, it will be easy to identify disease causing variants and we will be able to establish strong relationships between structural differences and precise phenotypes. The perfect case is of using large scale data for analysis of different cancer types.[28] As expertise grows with information and techniques, it will be possible to clearly pinpoint the underlying mechanism of diseases as well as to identify and quantify the risks of different diseases. Patients and healthy adults will be able to see the pattern to predict the occurrence of disease or to track its prognosis. They will be able to modify and improve their own healthcare through prevention or personalized therapeutic strategies which have been based on their genome sequence.[29]

Influence on Society:

HGP has forced scientists to think about its ethical consideration almost at every step with social implications from the initiation of the project to the succeeding projects

in genetics. Around 5% of their budget was allocated for the social, ethical and legal aspects of human genome sequence research.[30] This process will continue as bioethics is an integral part of research. Ironically, biologists are unable to identify any race or cast related genes in humans but based merely on ancestors interbreeding and migration.[31]

The concerns of this research and its implications are valid for one as the impact can be huge. Firstly, it includes privacy and fairness in the use and interpretation of genetic information such as questions of ownership and control of genetic information. Secondly, fair use of this information for insurance, employment, criminal justice, education, adoption, and the military will be necessary. Moreover, reliance of genetic technology to make right decisions by individuals on issues of their health will influence them for rest of their lives and maybe even their off springs. So, to question the effectiveness and reliability of genetic research is importance as that; do we even have enough evidence to make certain decision or not. This further highlight and question how knowledgeable the health professionals are, because they have a huge influence on the decision that patient make. Then, the use of genetic research by the third party for commercialization of the products from human genetic research. Examples are questions of the ownership of tissue and tissue derived products, patents, copyrights, and accessibility of data and materials. It can be further disturbing, if using this facility to tweak human genomes without knowing the consequences, for instance to enhance intelligence or strength.

How far we have come?

Despite innumerable opportunities in research and huge application of human genome project, basic question of how to respond to this nebulous information remains a challenge.[32] We are still in the learning phase of many processes. The quality of testing may be unreliable and the level of quality control of different genetic laboratories might vary. Many therapies based on genetic discoveries are still in process of clinical trials and their results might not correlate as predicted.[33]

However, the advances made by human genome project cannot be ignored. There have been advancements in approach to medicine. Clinical practice has been shifted to precise, predictive and personalized medicine.[29] Each individual can predict their risk linked to certain diseases. As each individual genome can be mapped, the treatment and progress of each individual can be personalized according to his/her requirements.

Few decades ago, there were many challenging questions which can be answered now. For instance, determination of three dimensional structures of proteins or link regulatory mechanisms at molecular level; or discovering gene products like RNA and proteins that are essential for life, and whether these ingredients be used to synthesize organisms from scratch or how components of a cell interact or can we develop our own computer model of a cell, a life? And most importantly, will we be able to accurately reconstruct the history of human populations and evolution of life on Earth?

References

1. Mapping and Sequencing the Human Genome. Washington, D.C.: National Academies Press; 1988
2. Report on the Human Genome Initiative for the Office of Health and Environmental Research. (cited 2019 Oct 7).
3. Lander E. Finishing the euchromatic sequence of the human genome International Human Genome Sequencing Consortium. Nature. 2004; 431:931-45.
DOI: https://doi.org/10.1038/nature03001
4. Smith LM, Sanders JZ, Kaiser RJ, Hughes P, Dodd C, Connell CR, et al. Fluorescence detection in automated DNA sequence analysis. Nature. 1986; 321(6071):674-9.
DOI: https://doi.org/10.1038/321674a0
5. Venter JC, Adams MD, Sutton GG, Kerlavage AR, Smith HO, Hunkapiller M. Shotgun sequencing of the human genome. Science. 1998 Jun 5.
6. Shendure J, Aiden EL. The expanding scope of DNA sequencing. Nature Biotec. 2012; 30(11):1084.
DOI: https://doi.org/10.1038/nbt.2421
7. Hood L. A personal journey of discovery: developing technology and changing biology. Annu Rev Anal Chem (Palo Alto Calif). 2008
8. ENCODE: Encyclopedia of DNA Elements – ENCODE. (cited 2019 Oct 7).
9. Hood L, Rowen L. The human genome project: big science transforms biology and medicine. Genome Med. 2013; 5(9):79.
DOI: https://doi.org/10.1186/gm483
10. Omenn GS. The HUPO Human Proteome Project (HPP), a Global Health Research Collaboration. Cent Asian J Glob Hea. 2012; 1(1).
DOI: https://doi.org/10.5195/cajgh.2012.37
11. Desiere F, Deutsch EW, King NL, Nesvizhskii AI, Mallick P, Eng J, et al. The PeptideAtlas project. Nucleic Acids Res. 2006
12. Deutsch EW, Mendoza L, Shteynberg D, Farrah T, Lam H, Tasman N, et al. A guided tour of the Trans-Proteomic Pipeline. Proteomics. 2010 Mar.

13. González-Gomariz J, Guruceaga E, López-Sánchez M, Segura V. Proteogenomics in the context of the Human Proteome Project (HPP). Expert Rev Proteomics. 2019 Mar.
14. Theobald DL. A formal test of the theory of universal common ancestry. Nature. 2010 May 13.
15. Stoneking M, Krause J. Learning about human population history from ancient and modern genomes. Nat Rev Genet. 2011 Aug 18 (cited 2019 Oct 7);12(9):603-14.
16. Schatz MC. Computational thinking in the era of big data biology. Genome Biol. 2012 Nov 29 (cited 2019 Oct 7);13(11):177.
17. Mizrachi I. Chapter 1: GenBank: The Nuckeotide Sequence Database. The NCBI Handbook. 2002:1-4.
18. Kent WJ, Sugnet CW, Furey TS, Roskin KM, Pringle TH, Zahler AM, et al. The human genome browser at UCSC. Genome Res. 2002 Jun.
19. Bioconductor - Home. (cited 2019 Oct 7).
20. Rabilloud T, Hochstrasser D, Simpson RJ. A gene-centric human proteome project: HUPO--the Human Proteome organization. Mol Cell Proteomics. 2010 Feb (cited 2019 Oct 7); 9(2):427-9.
21. Aebersold R, Mann M. Mass spectrometry-based proteomics. Nature. 2003; 422(6928):198.
DOI: https://doi.org/10.1038/nature01511
22. Belmont JW, Boudreau A, Leal SM, Hardenbol P, Pasternak S, Wheeler DA, et al. A haplotype map of the human genome. Nature. 2005; 437(7063):1299–320.
DOI: https://doi.org/10.1038/nature04226
23. Altshuler DM, Gibbs RA, Peltonen L, Schaffner SF, Yu F, Dermitzakis E, et al. Integrating common and rare genetic variation in diverse human populations. Nature. 2010; 467(7311):52–8.
DOI: https://doi.org/10.1038/nature09298
24. 1000 Genomes Project Consortium. An integrated map of genetic variation from 1,092 human genomes. Nature. 2012;4 91(7422):56.
DOI: https://doi.org/10.1038/nature11632
25. GWAS Catalog. (cited 2019 Oct 7).
26. Simón-Sánchez J, Singleton A. Genome-wide association studies in neurological disorders. Lancet Neurol. 2008 Nov (cited 2019 Oct 7);7(11):1067-72.
27. The Cancer Genome Atlas Program - National Cancer Institute. (cited 2019 Oct 7).
28. Hood L, Flores M. A personal view on systems medicine and the emergence of proactive medicine: predictive, preventive, personalized and participatory. N Biotechnol. 2012 Sep 15 (cited 2019 Oct 7); 29(6):613-24.
29. Knoppers BM, Thorogood A, Chadwick R. The Human Genome Organisation: towards next-generation ethics. Genome Med. 2013; 5(4):38.
DOI: https://doi.org/10.1186/gm442
30. Foster MW, Sharp RR. Beyond race: towards a whole-genome perspective on human populations and genetic variation. Nat Rev Genet. 2004 Oct (cited 2019 Oct 7);5(10):790-6.
31. Horton RH, Lucassen AM. Recent developments in genetic/genomic medicine. Clinical Science. 2019; 133(5):697-708.
DOI: https://doi.org/10.1042/CS20180436
32. Amendola LM, Jarvik GP, Leo MC, McLaughlin HM, Akkari Y, Amaral MD, et al. Performance of ACMG-AMP variant-interpretation guidelines among nine laboratories in the Clinical Sequencing Exploratory Research Consortium. Ame J of Human Gen. 2016; 98(6):1067-76.
DOI: https://doi.org/10.1016/j.ajhg.2016.03.024