A review of human genome project (HGP) from ethical perspectives

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A B S T R A C T

The human genome is the collection of DNA in the nucleus of human cells. It contains twenty-three pairs of chromosomes and serves as identification marks or blueprints. These distinct structures differentiate humans from other living organisms such as microorganisms, flora, and fauna. Despite this groundbreaking increase in human genetics knowledge, it has led to the emergence of complex ethical, legal and social issues particularly related to the Human Genome Project (HGP). Therefore, this paper intends to provide much deeper insights into the study of concepts, applications of modern genetics and human genetics issues that may arise in contemporary society and the Human Genome Project from ethical perspective in science. Apparently, this study employed descriptive literature review and the results show that the Human Genome Project has significantly increased the level of understanding of the basic damage or genetic defects, the structure of DNA, the identification of the position of all genes and human genome databases as well as HGP major contributions in the field of biology specifically in developmental biology and neurobiology. This indicates that the Human Genome Project has opened up a new era in modern biotechnology that may improve life quality of mankind. Nevertheless, the newfound genetic knowledge or any HGM-related research should be based on ethics known as ELSI (Ethical, Legal and Social Implications) so that it does not damage the population and the descendants of the human beings.

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membrane containing numerous genes. By contrast, unlike prokaryotes, eukaryotic organisms generally possess large linear; single or two chromosomes in the form of thin, coiled, elastic and contractile, thread like stainable structures, the chromatin threads similar to that in human cell which have 23 pairs of homologous chromosomes (2n=46) (Thieman and Palladino, 2012) formerly known as chromatin (Brooker, 2015). Chromatin consists of many genes which responsible in controlling the phenotype of an organism. Upon gene expression, it would influences on organism's physical appearance or individual behaviour which then transmitted to the next generation (Klug et al., 2014). In addition, a series of research has discovered that DNA is believed to be the medium for encoded genetic information storage for most of living organism. Even so, most tiny viruses encode their genetic information in RNA. Generally, genetic information has its own function towards genotype (replication), phenotype (gene expression) as well as mutation. Conversely, by definition, DNA is a long molecule that consists of our unique genetic code and encodes genetic information. It comprises of chains of subunits known as nucleotides (also called "bases") consists of and a phosphate molecule, a sugar molecule (5-carbon) and a nitrogen base. Each strand is composed of a long sequence of the four basic building blocks or 'bases'. DNA is a type of his information in DNA is stored as a code made up of four chemical bases namely; adenine (A), cytosine (C), thymine (T) and guanine (G) (Brown, 2011). More precisely, these nucleotides are paired together to form units called base pairs in a very specific manner. An "A: on one strand will always pair with a "T" on the other strand. Whereas a "C" nucleotide on one strand will always pair with a "G" on the other strand. Each pair is joined together by hydrogen bonds and the strands are separated during DNA replication. James Watson and Francis Crick were credited for their 1953 new discovery of the DNA structure. The discovery that the nucleotides are arranged in two long DNA strands called a double helix model. Thus, DNA has a unique 'double helix' shape like a twisted ladder with the base pairs forming the ladder's rungs while the sugar and phosphate molecules forming the vertical sidepieces of the ladder. Following this, for a creation of protein, DNA would firstly undergo the process of DNA transcription and RNA translation, which formerly known as a central dogma of molecular biology (Hartl and Ruvolo, 2011). This central dogma depicts the two step process, transcription and translation by which the information in genes produces proteins: DNA-RNA-protein. RNA is an essential molecule with long chains of nucleotides. It contains nitrogenous base, a ribose sugar and a phosphate. Also, RNA has the bases Adenine (A), Uracil (U) (instead of thymine in DNA), Cytosine (C) and Guanine (G). RNA is central to protein synthesis comprising of three types; Messenger RNA (mRNA), ribosomal RNA (rRNA) and transfer RNA (tRNA). On the other hand, a cell will go through a series of stages collectively known as the cell cycle. This is another essential stage and process in all living organism. During the cell cycle, the cells will go through a cell growth, reproduction and division in a coordinated way leading to nuclear division. This process occurs using the process of mitosis that usually restricted and could only be seen in the (diploid somatic cells) resulting in the production of two daughter cells and meiosis (mature sex cell or gametes) which produces haploid cell (Hartl, 2012). It will then followed by the final step of nuclear division which occurs concurrently namely cytokinesis process (cytoplasm division of a parental cell into two daughter cells). Each parental cell giving rise to two daughter cells, each time they divide via fusion process and this new cell population is known as clone (Snustad and Simmons, 2012). In short, three processes should respectively involve during cell division. These include; DNA duplication, DNA replication (parental cell and daughter cell) and cell division (Pierce, 2010). Additionally, it also appears that prokaryotic cell and eukaryotic cell carries different process of cell division. As such, for eukaryote cell, mitosis process is very crucial as it will not merely lead to the growth of multicellular organism, but also contributes to cell repair where certain cells are being constantly replaced. Mitosis is divided into the following five stages namely; Interphase, Prophase, metaphase, Telophase and Anaphase (Plopper et al., 2013; Snustad and Simmons, 2012). On the other hand, Meiosis involves two sequential cycles of nuclear and cell division called meiosis I known as reduction division involving homologous chromosome. In reduction division, the chromosome number is reduced from diploid to haploid. The following process would be equation division which also known Meiosis II. During this phase, the sister chromatids within the two daughter cells separate (Pierce, 2010). Both processes seem to be essential to form haploid from diploid in gamete to genesis leading to produce sperm via spermatogenesis and ovum through oogenesis which generates genetic variation.

As mentioned earlier, the process by which the instructions in the DNA are converted into a protein is called gene expression. Nonetheless, considering that the DNA would not be able to directly produce protein, the basic process of central dogma thus involved in producing RNA. It involves several distinguish steps through which DNA is converted to an RNA which in turn is converted into a protein. The stages are DNA transcription and DNA translation. The first process of DNA transcription is when the DNA in a gene is copied to produce RNA transcript namely messenger RNA (mRNA) by which this is carried out by an enzyme RNA. Transcription binds to specific nucleotide sequences in the promoter region and assists in the binding of RNA polymerases (Dale et al., 2011). Transcription involves four steps. These include amongst others; Initiation, Processing, Elongation and Termination. Further, the subsequent process will be DNA...
In this dedicated process, messenger RNA (mRNA) molecule is decoded by a ribosome and the mRNA sequence is thus used as a template to assemble and produce a series of specific chain of amino acids. As transcription, DNA translation also involves four steps namely Translation, Initiation, Elongation and Termination. In view of the above, this signifies that the correct process with fairly high fidelity of transcription and translation are thus required to produce a chain of amino acids that finally leads to the formation of a unique protein. Nevertheless, in certain cases, mistakes do happen in which an error occurred during DNA replication/DNA transcription will cause mutation. Two significant situations which amounting to mutation; DNA replication errors/ DNA transcription error and chemical or physical influences causes by various factors leading to mutation (Brown, 2011) or spontaneous mutation.

Likewise, numerous literatures could be found when discussing on modern genetics. Thus, it is imperative to further note that in principal, modern genetic covers a wide range of areas which include DNA Forensic, genomic and medical, epigenetic and stem cell as in (Klug et al., 2014), whereas Brooker (2015) gives special attention to DNA recombinant, biotechnology, genomic and bioinformatics as well as genetic engineering (Hartl, 2012). Dale et al. (2011) on the other hand concentrates on modern genetics for transgenes is and animals and plants cloning. Preventive diseases and its treatment for example, vaccine production and gene therapy are amongst his interest of research too. Modern genetic with special reference to agriculture, medical and societies have been discussed by Snustad and Simmons (2012) whereas Khan (2011) further claims that the evolution of modern genetic begun from the double helix DNA structure as originally discovered by James Watson and Francis Crick. Similarly, a study conducted by Lewis (2012, 2007) has further explores the common uses of DNA (DNA evolution and progression, DNA controlling and DNA recombinant), genetics (testing and counseling), reproductive technology. Principally, recombinant DNA technology is used extensively in gene manipulation. In practice, the process often involves combining the DNA from different organism with the goal to identify, map and sequence genes. Over the years, the application of DNA recombinant techniques is also the cornerstone of biotechnology industry and thus involves genetic engineering (Russell, 2006). Apart from that, DNA cloning has also been widely used among researchers in producing recombinant DNA molecule. This generates a large quantity of DNA fragment that could be used which include; DNA mapping, DNA sequencing, DNA mutating and cell transforming. This technique has formerly known as gene cloning. Essentially, gene cloning is a molecular biology technique that makes many identical copies of a piece of DNA. In a typical cloning experiment, a fragment of DNA (target DNA) is inserted into a circular DNA molecule via vector which acts as a vehicle to produce a recombinant DNA molecule. The vector transported and inserted the gene into the host cell then allowing the recombinant molecule to be replicated many times. It will then transform into the progeny thus producing many identical copies of the same recombinant molecule. This process is called transformation (Rastogi and Pathak, 2009). It is notable that in many occasions and experiments, one important vector used in recombinant DNA bacteria is Escherichia coli (E. coli) and bacteriophage which have become the most popular expression platform (Roy, 2010; Rastogi and Pathak, 2009). Further to that, the term genetic engineering initially referred to the direct manipulation and modification of DNA molecules. It is used to describe the process by which one or new DNA is manually added to an organism in order to modify and alter an organism or population in the organism (Sanderson, 2007). Genetic engineering has broad applications in agriculture and industry, medicine and also can and can be used on a wide range of plants, animals and microorganisms including human (Engdahl, 2006). According to Roy (2010), the advantages outcome from this genetic engineering application in crops plants are enormous; increase photosynthesis, enhance crop yields productivity, maximize the crops production and improve nitrogen use efficiency leading to boost transgenic crops. Engdahl (2006) further adds a wide range of genetic engineering application has currently developed in agriculture, which include amongst others; Genetically modified crops (GM crops), genetically modified food (GM food) and genetically modified organism (GMOs). Initially, genetically modified organisms (GMOs) refer broadly to organisms (i.e., plants, animals or microorganisms) in which the genetic material (DNA) has been altered or modified either by mating and/or natural recombination through a process called as genetic engineering. GMOs offer potential benefits in agriculture and medical (Sanderson, 2007). In particular, genetic engineering has accrued numerous benefits and provides excellent tools in GMO medicine, GMO biological medicines and gene therapy. Gene therapy on the other hand is an experimental technique that uses genes to treat or prevent disease by inserting a gene into a patient’s cells instead of using drugs or surgery via genetic engineering which normally conducted towards mammalian especially human. Gene therapy is designed with the main goal to inactivate the enzyme and protein that are functional improperly and replacing mutated gene that causes disease by introducing a new gene to treat disease. Typically, there are two types of gene therapy treatment: Somatic gene therapy and germ line therapy using adenovirus vector; in vivo gene therapy and ex vivo. In view of the above, in line with the advancement of modern genetics, in biotechnology, Bacteria E.coli has been widely employed as a promoter in most research and experiments associates with prokaryote organism pacifically in synthesis biology and metabolic engineering (Pawel and Wong, 2015). Also, Bacteria
E. coli offers useful tools for genetic research due to several grounds; relatively has small size, widely used in genetic research and experiments. As a result, these outstanding findings have become a bacterial model in gene system (Oliphant and Struhl, 1988; Harley and Reynolds, 1987; Hawley and McClure, 1983). Another concern is that, in order to increase the production soluble protein, it is imperative to choose the most suitable promoter and host vector since the promoter strength is pertinent in genetic engineering and synthetic biology (Rosano and Ceccarelli, 2014; Liu et al., 2013; Gopal and Kumar, 2013) which eventually leads to the development of Bioinformatics, enhancement of database and introduction of a new technology (Pawel and Wong, 2015). As elucidates above, it clearly signifies that benefits of DNA recombinant and genetic engineering are experienced in a whole array of fields which include; medical and medicine, agriculture, food production, environment and many more.

2. Human genetics issues: A closer look

Although remarkable accomplishment has been denoted to human genetics revolution, its potential for enhancing public health and excitement has been tempered by many ethical issues.

These ethical concerns stem from the fear that human subjects are being discriminated due to various popular issues associated with human genetics, human cloning and human genome project (Majeed, 2002). Meanwhile, Ignacimuthu (2009) further describes four main issues namely (i) Human reproduction, human life and death, (ii) Health and biomedical innovation, (iii) Genetic engineering, biosafety and experiments and (iv) Biodiversity, Intellectual Property Rights (IPR) and environment. Of these, special attention has been paid to the human genome project, gene manipulation, cloning, gene therapy and genetic modification organism (Smith, 1988; 2009; Rajasekaran et al., 2002; Majeed, 2002; Purohit, 2005). Admittedly, his new scientific discoveries served as a platform molecular biology and genetic engineering. Nevertheless, it has been found that this new evolvement has been surrounded with controversial issues ranging from legal, ethical and social implications (Saifuldeen et al., 2005). Similarly, human cloning technique has also raised and creates extremely complex ethical questions and become debatable issues amongst scientist and societies at large. There are few good reasons to develop the technology and many reasons not to develop it. In particular, given that the cloning process is not sexual reproduction but is more akin to asexual replication of organisms that simply split into two, the question remains unresolved as to how to justify the radical impact of this technique towards our society. Other than that, ethically and legally, human cloning disrespects human lineage and being irreconcilable. On the same vein, over a period of time, Islam recognizes the general idea of the development of human creation in stages and thus human beings are considered as a special act of Allah's creation. The starting point in human reproduction is sexual intercourse between legitimate legal marriage between male and female based on the natural inclination (fitrah). Through this legal process, the legitimacy of the offspring and progeny are thus certain and protected. Unfortunately, this by far might not been happened in the human cloning. The ethical objection asserts from human cloning include; it is contrary to human dignity as it would lead to ambiguity in legitimate parentage (nasab) leading to the identity crisis. As a result, there is a significant likelihood that human cloning would change the shape of the family structure and institution. Due to these reasons, Muslim jurists across the world have unanimously agreed to object and prohibit human cloning from being invented (Sekaleshfar, 2010). This Islamic verdict has received full support various Islamic Association worldwide, for example; Jama'ah Kibar al-Ulama from Egypt, Al- Azhar Islamic Research Academy, European Council For Fatwa and Research, Majma’ Fiqh Islami, legislative Council of the Islamic Organization of Islamic Countries Jeddah, Islamic Medical Association of North America (IMANA) and Islamic Organization for Medical Sciences Kuwait (IOMS). As vehemently as reproductive cloning is judged by Muslim Jurists, therapeutic cloning, by contrast, is viewed as permissible provided that the procedures and requirements contain therein are adhered to the Islamic principles (Al-Hayani, 2008), whereas Islam et al. (2012) elucidates a comparative study of Western Secular and Islamic Bioethics Perspective with special reference to an ethical consideration of human cloning. This implies that Muslim scholars have looked into reproductive cloning in great detail and have elaborated on the legal arguments for and against it which lead to the prohibition while favor the therapeutic cloning subject to certain pre requisites thereto. This global consensus on allowing room for research in therapeutic cloning has been derived from the Scientific Legal Conference which took place in Jordan. Conducting Human genetics in medical research for to cure disease and improve health are thus permitted. It was observed that the proponents of human cloning particularly in western countries are bombarded with various social implications. Deprivation of the marriage institution, ambiguities in human progeny, illegal sexual intercourse, lesbian and homosexual are amongst the critical implication due to human cloning (Sekaleshfar, 2010). Hence, these are among the biggest challenges and obstacles hinders from biotechnology evolvement facing by Theologiest, Muslim scholars and as well as the medical experts (Brockopp, 2008). Taking into account this serious impact, the consensus discussion, opinion and views should be unanimously conducted amongst Muslim scholars, scientist and relevant authoritative bodies to find the best solution.
3. An insight towards human genome project (HGP)

In essence, the Human Genome Project (hereinafter referred to as HGP) is an international research effort with the main goal is to analyze the structure of human DNA and to identify all genes in the human genomes. From the outset, one of the defining goals of HGP is also to determine the DNA sequence of the entire human genome and store sequence information thus contributing to biology, particularly biological and neurobiological development (Khan, 2011). A series of preliminary research on HGP has allowed researchers to begin to understand the blueprint for building a person. This knowledge about the functions of genes and proteins has also successfully contributed to improve human health by enabling a better understanding of the genetic defects and molecular basis of other diseases, which in turn has led to the development of new therapies and diagnostic methods as a preventive measures in cure such traits (Smith, 2009). Hence, maneuvering towards HGP is obviously due to the fact that it profound a major impact in the fields of medicine, biotechnology, and the life sciences. Historically, the HGP has its ideological origins in early 1985 and was pioneered by James D. Watson. James D. Watson was appointed to lead the National Institute of Health (hereinafter referred to as “NIH”) United States of America in 1988. He resigned in 1992 and the following year i.e., in 1993, Francis S. Collins was named director and NIH has evolved into the National Human Genome Research Institute (hereinafter referred to as “NHGRI”). Generally speaking, the first working draft sequences of the human genome has been completed in 2000. This project involved an international collaboration amongst geneticist from various developing countries for example U. S.A, United Kingdom, France, German Japan, China and India (Khan, 2011). Craig Venter and Francis Collins have further announced the complete draft on the human genome sequence in 2001 and finishing the project by 2003 in which 98% human genome has been sequenced with an accuracy of over 99.9% (Marcus, 2010). Initially, the formation of the HGP is an initiative joint effort by USA and Department of Energy (hereinafter referred to as “DOE”) which begun in 1990 with the purpose is to assemble data on the structure of DNA in human chromosomes and those of other organisms (estimated contains 800000 – 100,000) and its sequence (approximately 3 billion DNA base pairs that creates the human DNA) contains in human chromosomes (Thieman and Palladino, 2012). On the other hand, a study released in 2014 shows that HGP has begun earlier around mid-1970. The accomplishment of the rough draft of human genome sequence has taken place in 2002 based on joint collaboration between the DOE and NIH and is expected to be completed within 15 years (Khan, 2011). Earlier, the HGP was very ambitious and had several aims including: to construct human genetics mapping, to determine the identity of the three billion nucleotides comprising the human genome and characterize the full repertoire of genes encoded in 24 chromosomes therein by 2005 (Snustad and Simmons, 2012). Also, HGP is enable to analyse human genetic variation, Mapping and sequencing of the DNA of model organisms, develop new technology and tools for analyzing sequence data, disseminates new information on the genome to scientist and societies at large and to address relevant ethical, legal, and social issues associated with HGP (Thieman and Palladino, 2012). On top of that, the detailed knowledge of the human genome is an initial step to help us to understand and eventually treat many of the more than 3000 human genetic diseases that afflict human kinds as well as multifactorial diseases thereby enhancing human health (Strachan and Read, 2010). Moreover, the United of America (USA) has proposed seven (7) primary aims of HGP starting from 1998 to 2003 (Collins et al., 1998). This includes; (i) DNA Sequence of Human Genome (ii) Sequence Technology (iii) Human Genomic Variation Sequence, (iv) Technology for Genomics Function, (v), Ethical, Legal and Social Implication (ELSI), (vi) Bioinformatics and Computational Biology and (vii) Research Training.

Meanwhile, several target and achievement of HGP in 1990-1995 were to have greater knowledge and detail information on the genetic linkage map, construction of complete physical map and DNA sequencing technology (Lee, 2013), which in turns providing new knowledge such as biomedical through the Combined DNA Index System (hereinafter referred to as” CODIS”). This CODIS system is very useful in the forensic fields. The emergence of this field has led to ability to identify the individuals through fine samples such as saliva, hair sheets, dry blood springs or semen thus capable of solving current criminal cases (Croce, 2016). Apart from that, a new space in the field of anthropology has been introduced to identify the origins of humans, including their race, demography, genetic diseases and so on (Slatkin and Racimo, 2016; Parrington, 2015; Schiffels and Durbin, 2014; Richards and Hawley, 2010) and research on structure and function of human brain circuits (Green et al., 2015) for example the application of innovative technologies and tools to identify the brain cell types, its interconnected between different region and neurons in the brain by circuits and processing the brain signals and sensor in which has been conducted by The United States’s Brain Research through Advancing Innovative Neurotechnologies (hereinafter referred to as “BRAIN”). Croce (2016) has listed five (5) advanced research on HGP namely International HAPMA Project, 1000 Genomes Project, DNA Fingerprinting, Forensic Analysis and Applied Genetic whereas Vihinen et al. (2016) highlights on Human Variome Project with the defining goal is to collect all information on genetic variation that impedes human health. Similarly, 1000 Genomes Project is to produce an extensive and comprehensive catalog of
human genetic variation that will support future medical research studies. Another primary concern is to also provide a resource of almost all human genetic variants that exist in regions by applying whole-genome sequencing to a diverse set of individuals from multiple population and distribution of genetic variation across the global sample and implications for common disease studies. (Telenti et al., 2016; Auton et al., 2015). Interestingly, Panofsky (2015) and Wilson and Nicholls (2015) further emphasize on the potential treatment for certain multifactorial disease for example some of the cancers that most often affect women and human population health. Following this, the article entitled “Twenty-five years of big biology” by Green et al. (2015) has further outlined six (6) lesson embraced from the HGP; embrace partnership, maximize data sharing, plan for data analysis, prioritize technology development, addresses the societal implications of advances and be audacious yet flexible. Meager and Lee (2016) gives full support towards this lesson insight from HGP by developing research program namely ELSI (Ethical, Legal and Social Issues) which act as an integral part of HGP. The above endeavor indicates that the modern technology advancement embedded within HGP should in line with the ethical, legal and social implication profound from HGP. To further protect the well-being of societies and environment, greater attention should be paid off towards this issue. Notably, the scientific advancement of genetic research the last 21st century has apparently make substantial contusion to a number of human diseases. Rather, complex relationship between human genetics and various diseases have successfully discovered. Consequently, these ongoing efforts has increased the medical diagnosis and accessed to more effective medicines and designed precise treatment to alleviate such disease (Whitmarsh and Jones, 2010). Rather, its goal is to cultivate interest and awareness of the complex relationship between human genetics and various disease states. A series of subsequent discoveries have led to the knowledge enhancement on human’s life (Whitmarsh and Jones, 2010). Roberts (2010) further adds that in recent years, genome research is relatively an advanced research which allow to generate profitable income. Genetic and genomic information is the kind of valuable medical data that companies are eager to. To improve personal health, these elements shall be given at paramount consideration especially by DNA profile. Obviously, this suggests that human genome research in the genetic field leads to a new landmarks in modern biotechnology. In short genetics research would dramatically improve the quality of human life. Even so, in achieving this aspiration, these advantages offered have been followed by various challenges and difficulties that need to be pursued by biotechnologist and societies since the human genome’s research is closely related and interconnected with ethical, legal and social implications (Ethical, Legal and Social Implications-ELSI) beliefs and religions (Gilbert, 2008; Amin, 2013).

In addition, human genomics research occupies a central role in bioinformatics where this field has emerged as a new branch of modern biotechnology (Thieman and Palladino, 2012). Common uses of bioinformatics include: the application of computational techniques and information technology to develop computer database and to analyses the information associated with biomolecules on a large-scale and to accelerate statistical method in identifying and analyzing biological data (Purohit, 2005). Often, this method would expedite research and information delivery and increase the effectiveness of biological data storage. With the completion of HGP, the defective genes responsible for more than 4,000 genetic diseases could be detected. These defective genes would later be replaced by a new fictional gene. This technique is formerly known as gene therapy. Gene therapy as discussed earlier involves the insertion of genes into an individual’s cells and tissues to treat a disease, and hereditary diseases in which a defective mutant allele is replaced with a functional one using genetic engineering technique (Roy, 2010).

4. Conclusion

Having discussed above, it is further submitted that HGP tenders great benefits in medical sciences in which it is capable to improve human’s standard of living. Nonetheless, in conducting this outstanding human genomics research, it is pertinent to main its benefits and advantages offered to. Thus, this study further concludes that ELSI (Ethical, Legal and Social Implications) model is indispensable important to be complied with by all scientists, genetics and HGP-related researches in conducting their research and experiments. Failure to diligently adhere to such approach will obviously violate human values and dignities which eventually will cause destruction to human population worldwide.

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