International Journal of Management, Sciences, Innovation, and Technology IJMSIT

Review Paper

Vol.3, Issue.1, pp.34-43, Jan (2022) **ISSN:** 0000-0000

Human Genomics: the Unknown Future

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Available online at: https://ijmsit.com/volume-3-issue-1/

Received: 26 Dec, 2021 Revised: 27 Jan, 2022 Accepted: 29 Jan, 2022

***Abstract*—** Genomics is a branch of genetics concerned with the study of the genetic material in the bodies of living organisms. The field includes extensive efforts to fully sequence DNA and micro-mapping the genome. This specialization also includes the study of a number of phenomena that occur within the genome such as heterosis, heterotic and other interactions between different loci and alleles within the genome. In contrast, when a limited number of genes (not all genes) are studied it is called molecular biology or genetics, and it is a topic that is usually popular in biomedical research. Research on a single gene (or a limited number of genes) It does not fall within the definition of genomics unless the aim of this research is to study the effect of a gene on the entire networks within the entire genome. The genome is the sum of the genes of an individual as a whole. Therefore, genomics is the study of genes in a cell, or tissue, at the level of DNA.

***Keywords*—** Genomics – Genome – Human Genome – DNA – RNA.

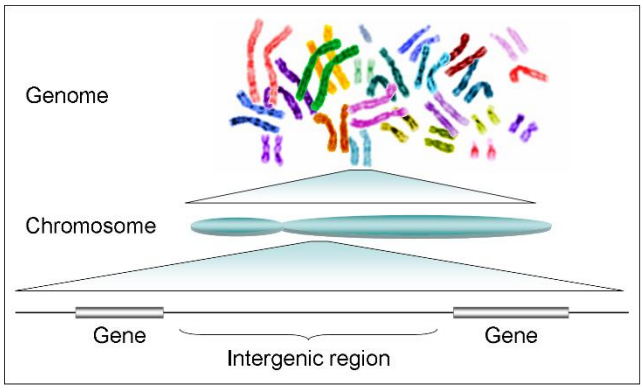
I. INTRODUCTION

The human genome is the complete set of more than 100,000 genes found in the cell nucleus of most human cells. The female nuclear genome is divided into twenty-three pairs of structurally similar chromosomes, but the X chromosome in males is paired with the non-homologous Y chromosome, so there are 24 different types of human chromosomes. In other words, we can say that the genome is the complete deoxyribonucleic acid (or DNA for short) in a particular organism, including its genes. These genes carry all the proteins needed by all living things. These proteins determine, among other things, what an organism looks like, how its body metabolizes food or fights infection, and sometimes even determines how it behaves

II. HUMAN GENETICS

The DNA molecule in humans and primates consists of two strands wrapped around the other so that they resemble a twisted ladder whose two sides, consisting of sugar and phosphate molecules, are connected by rungs of nitrogen-containing chemicals called bases and symbolized by abbreviation A, T and C and G. These bases are repeated millions or billions of times in all parts of the genome. The

human genome, for example, contains three billion pairs of these bases, while the human body contains about 100 trillion (100,000,000,000, 000,000,000) cells!



The specific arrangement of the letters A, T, C and G is very important, as this arrangement determines all aspects of biodiversity, in this arrangement lies the genetic code, just as the arrangement of the letters that make up the words is what makes them meaningful, the arrangement of these letters It determines whether this organism is a human being or belongs to another living species such as yeast or fruit flies for example, which each have its own genome and on which several special genetic research has focused.

And since all living things are related in common through the similarity of certain DNA sequences, the insights we gain from non-human organisms enable us to achieve greater understanding and knowledge of human biology.

Each combination of three of the four letters represents a specific amino acid, and there are 20 different building blocks - amino acids - that are used in a huge variety of combinations to produce our proteins. Different combinations are in turn different proteins in our bodies.

The information contained in the human genome is enough to fill paper books of a height of 61 meters, which is equivalent to the information contained in 200 phonebooks, each containing 500 pages!

Among us humans, DNA differs from one individual to another by only 5.2%, or 1 in 50 letters, bearing in mind that human cells each contain two copies of the genome.

If we were to read the human genome at a rate of one letter per second for 24 hours a day, it would take a century to finish reading the Book of Life!

If two different people started reading their respective Books of Life at a speed of one letter per second, it would take about eight and a half minutes (500 seconds) before they reached their first letter order difference!

A typist who writes at a speed of 60 words per minute (about 360 characters) and for eight hours a day, needs half a century to finish printing the Book of Life!

The DNA of humans is 98% similar to that of chimpanzees.

The estimated number of genes in mice and humans is 60,000-100,000, in roundworms it is 19,000, in yeast it is about 6,000, while the number of genes in the pathogen that causes tuberculosis is 4,000.

The function of the vast majority (97%) of the DNA in the human genome remains unknown to us until now.

The first fully decoded human chromosome was chromosome number 22, and this was done in the United Kingdom in December 1999, specifically at the Sanger Centre, Cambridge.

The DNA in each of our cells is 1.8 meters long, stacked in a 0.0001 centimeter block (which could easily fit into a space the size of a pinhead).

If all the DNA in the human body is singled out end to end, the resulting strand can reach from the Earth to the sun and back 600 times [100 trillion x 1.8 meters divided by 148,800,000 kilometers = 1200].

Researchers at the Human Genome Project decode 12,000 letters of human DNA per second.

If all the letters (3 billion) that make up the human genome were spread out so that they were 1 millimeter apart, they would stretch 3,000 kilometers — or about 700 times the height of the Empire State Building, the famous skyscraper in New York City.

In 1984, at a joint meeting between the US Department of Energy and the International Committee for the Prevention of Environmental Mutagens and Carcinogens, for the first time seriously asked the question: (Can, or should we, do the sequencing of the human genome? In other words: Should we develop a technology that will enable us to obtain an exact copy (word for word) of the entire genetic code of a (normal) human being?

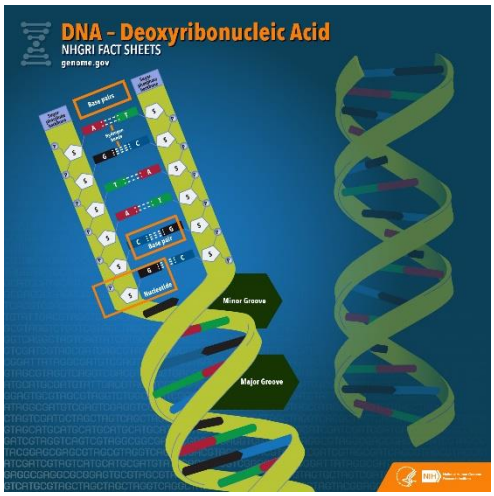
The answer to this question was not easy, so several working sessions were held during 1985 and 1986, and the whole topic was studied by the Advisory Group of the Department of Energy, the Office of Technology Assessment of Congress, and the National Academy of Sciences, in addition to the controversy that raged at the time among scientists themselves at both the public and private levels. In any case, the consensus eventually settled that we should move in this direction.

In 1988, the Human Genome Organization (HUGO) was established in the United States. The goal of this international organization was to decode the entire human genome.

On June 29, 2021, the Human Genome Project and biotech company Celera Genomics announced that the sequencing of the human genome, about two decades ago, was not actually a complete genome; About 15% of the genome's composition was still unknown. Given the limitations of technology, scientists have been unable to understand how certain stretches of DNA relate to each other, particularly those with a large number of repeating letters (i.e., base pairs). Over time, scientists were able to decipher this mystery; however, the most recent human genome, which has been referenced by geneticists since 2013, is still 8% short of complete sequencing."

On June 28, 2021, Nature published a scientific paper in which it stated that researchers participating in the Telomere-to-Telomere Consortium, referred to for short as the T2T Consortium, and whose membership includes 30 institutions, were able to fill in the genome gaps. Adding that a research draft was issued on the 27th of May 2021 entitled: "The complete sequencing of the human genome," Karen Mega, a genetics researcher at the University of California, Santa Cruz, and her colleagues reported that they had been able to complete the sequence of the remaining

part of the genome, by discovering about 115 new genes, and that these genes are responsible for coding for a total of 19,969 proteins.



"It's exciting to find solutions to some aspects of the problem," says Kim Pruitt, a bioinformatics specialist at the US National Center for Biotechnology Information in Bethesda, Maryland, adding that their finding is a "huge achievement."

This newly sequenced genome, called T2T-CHM13, adds nearly 200 million base pairs to the human genome sequence identified in 2013. Instead of taking DNA from a living person, this time the scientists relied on a cell line taken From a complete hydatidiform molar, a type of tissue that forms in the human body when a sperm fertilizes an egg without a nucleus, resulting in a cell containing chromosomes from the father alone, which saves scientists the hassle of differentiating between two sets of chromosomes from two different people.

Mega says that this achievement would not have been possible without modern DNA sequencing technology, pioneered by Pacific Biosciences of Menlo Bart, Calif.; It is a technique that uses lasers to scan long stretches of DNA extracted from cells, at a rate of about 20,000 base pairs at a time. Conventional methods of genomic sequencing are based on reading DNA sequences in fragments of only a few hundred base pairs at a time. Researchers liken these extensions to pieces of a puzzle. Larger pieces are easier to assemble, as they often contain overlapping sequences.

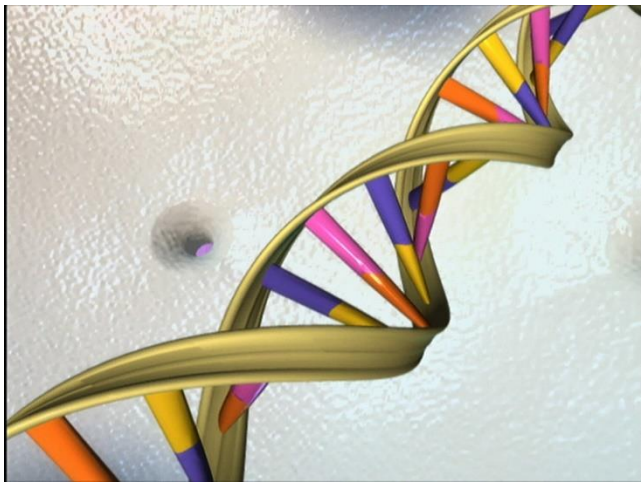
The source quoted the researchers as saying that the T2T-CHM13 genome is not the ultimate in human genome studies. Scientists have struggled with some regions, and the team notes that there may be errors in about 0.3% of the genome. It's true that we have a genome free of gaps, but Mega says that quality control processes in these genomic regions have been extremely difficult. The sperm cell that made up the "molar tissue" contained the X chromosome, which means that scientists have not yet determined the genomic sequence of the Y chromosome, which is responsible for the formation of males.

Megan expects genetic researchers to find out quickly whether the newly sequenced genomic regions, and their potential genes, are relevant to human disease. ". Now, we should be getting information about the functions of newly discovered genes much faster than in the past. Considering the “massive amount of resources we have at our disposal,” Mega said.

III. VITAL CHAIN

The sequencing of human DNA begins with blood samples from volunteers, which are extracted using routine chemical methods, pooled, cooled to zero degrees Fahrenheit, and cut

into superimposed sequences each about 150,000 characters long. Despite this, there is not enough DNA in these original samples for analysis, so the next step is to cloning each fragment in the bacteria, which makes several copies of it as it multiplies.



Robots are used to transfer these bacterial colonies to a machine that Amplify makes even more.

The technology used by this machine is called Polymerase Chain Reaction - PCR, and its discoverer earned the American chemist Cary Mullis a Nobel Prize in 1993.

Then, the sequence of each fragment is decoded using a machine called a Sequencer, which carries out a set of chemical reactions developed by Nobel Prize-winning British scientist Fred Sanger. To simplify, we say that these interactions involve marking each letter in any particular fragment with a colored molecule that can be read by laser beams. A computer analyzes the result of the laser scan to produce a sequence for this fragment, then combines all the sequences of the overlapping fragments to form the genome of the original sample.

The Human Genome Project will offer many benefits to humanity, some of which we can expect while others will be surprised. The expected benefits of gene therapy are enormous, and can be summarized in several areas as follows:

Developing new medicines and treatments: In addition to creating new medicines, the Human Genome Project can be seen as the beginning of a new era of personalized medicine. People tend to respond very differently to the medications they prescribe - up to 50% of people who take a particular drug will either find it doesn't work, or they will experience unwanted side effects. The "hit and lose" method is a terrifying waste of time and money, and may even endanger life itself.

In addition, we all differ in our susceptibility to various diseases. Whereas a man may lead a relatively healthy lifestyle before falling victim to a heart attack in middle age, his friend who smokes twenty cigarettes a day and eats a fried breakfast every day may remain strong until the age of ninety-three. But why? An important part of the answer lies in the human genome.

It turns out that 99.9% of the DNA sequences are the same in all humans (and therefore we all belong to the same species), but this difference of just 0.1% may explain our individual responses to drugs and our susceptibility to disease.

IV. FORESEEABLE RISKS AND ETHICAL ISSUES

When genetic manipulation becomes a delicate procedure, prospective parents will be faced with a wide range of possibilities. They will, of course, want to make sure that during the genetic stage of their offspring, gene therapists

correct any problems that may arise due to faulty genes, and parents may also ask those therapists to raise their children's IQs, add a few inches to their height, or give them Super athletic abilities, curly hair, blue eyes, and up-to-date skin.

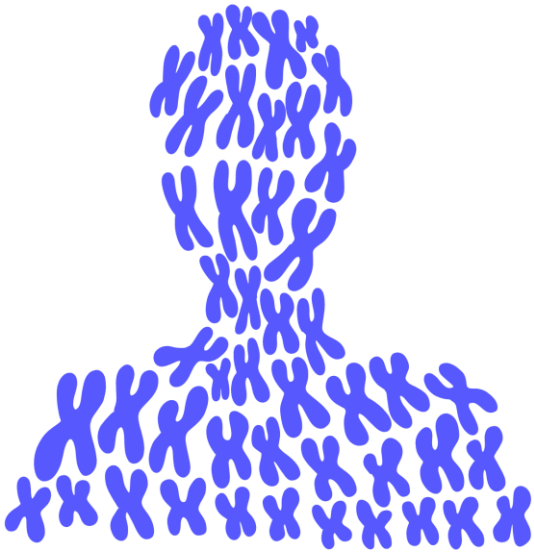
The possibilities for genetic transformation are likely to be wide, but that would be available only to rich parents, and having (children on demand, It is assumed, from birth, that they are (superior), serious social problems.

Gene therapy could gain wider public acceptance if it could be prevented as a treatment advantageous to the wealthy, and Philip Kitcher, author of Lives To Come: The Genetic Revolution and Human Possibilities, predicts that such complaints about gene therapy will be rare. "If a future society ensures equal access for all its citizens (and) if it takes care first of urgent health needs before creating opportunities to improve capabilities," he says.

We must also bear in mind the effects of genetic engineering in the social and political spheres. Given that the agricultural and medical benefits of genetic engineering are prohibitively expensive, neither poor individuals nor poor nations will be able to afford them—at least for the next few years. As a result, the economic gap between the rich and the poor is likely to widen. In addition, third world leaders are trying to protect unusual plants and animal species from Western exploitation. Western companies want these species for genetic engineering projects, and they hope to obtain them at the lowest possible cost. .

Science in itself is neither good nor bad, but the uses for which it is used raise ethical questions. Genetic engineering is only a technique. We must decide if, when and how we want to use it, and these decisions must be everyone's responsibility.

The concerns that people display in relation to genetic engineering can signal the beginning of effective citizen action on global environmental issues, and the longer we act, the less likely we will be to save ecosystems and their biodiversity.



Several examples of the strong association between genetic variation and drug response are available in the scientific literature. It was possible to describe the molecular bases for some of them, including examples of the variation of genes responsible for drug absorption and metabolism, and the nineties of the twentieth century witnessed a great revolution in life sciences (biology), and it is expected that the technologies developed and the discoveries made in this project will lead to Changing both the future of the pharmaceutical industry and current medical practices; The knowledge of doctors and pharmacists about the relationship between a patient’s genotype and the efficacy of the drug he is taking will increase, and classifying

patients according to their genotypes will lead to the selection of drugs that increase the efficiency of their therapeutic effects and at the same time decrease their side effects.

Genomic therapy, or genomic drugs, is a new science that did not exist before the mid-nineties of the twentieth century, and it combines traditional pharmaceutical sciences, such as biochemistry and pharmaceutical sciences, with modern information available about the human genome project, the forms of genes, mutations, proteins and the effects of environmental factors, And all that is associated with science and knowledge, and this science includes pharmacogenetics, which is concerned with studying the differences between individuals in terms of drug response due to differences in their genetic structures, and it explores ways to use these differences to predict a patient's response to a drug: Is it a good, poor, or no response?

The response to medication is not only determined by genes, but is also influenced by the environmental conditions surrounding patients. Although a large number of environmental factors can be identified, identifying the genes responsible for that response is not easy. Therefore, studies of genomic treatments tend to identify genetic variations that determine the quality of drug response, and in many cases some doctors may prescribe a specific drug, so the patient discovers that it has poor side effects, or that it has not achieved any benefit, and the doctor is forced to use other drugs with the intention of finding appropriate treatment of the disease. It is expected that genomic therapy will provide alternative methods of diagnosis and treatment that are better than those currently in place, and it is hoped that in the not-too-distant future, the patient will go to his doctor's office, where he will diagnose his disease, analyze a DNA sample from him, or study it from an electronic chip that the patient carries with him, showing all the information about his genome. And then prescribe the appropriate treatment for him.

V. GENOMIC THERAPY

Medicines are currently manufactured on a collective basis, but the patient is the one who should be taken care of, for example: up to 35% of patients do not respond to beta-blockers, and up to 50% of them do not respond to tricyclic antidepressants, which makes these patients no benefit from them, or they It may lead to harmful results. A certain amount of pain-relieving drugs, such as codeine, may produce the desired effect in some individuals, but may be without effect in others, and may even produce bad effects, and may threaten the lives of some. In some diseases, the patient may wait a long time before discovering whether the treatment he is using is acceptable or not, and may have to repeat this by trying other treatments, and it is hoped that genomic therapies will provide the necessary means for the doctor to tell the patient: "This is the medicine for your disease." And these are the appropriate doses of it."

Testing genetic variations in humans is neither easy nor cheap, but it will become so as research advances and technology and capabilities advance. This will lead in the future to achieving great savings, based on economic aspects such as: the high costs as a result of the failure of a

drug that does not achieve any therapeutic benefit, even if it is for a small number of patients, or as a drug that causes an increase in health care costs, or the costs of treating patients who have developed toxicity medication or other bad side effects, or the costs of their frequent visits to doctors' offices or hospitals.

The researchers keep in mind that the efficiency of the drug depends on its acceptance of absorption, that its metabolism is correct, that it is linked to its goal, and not with other components in the patient's body, and that the remnants of its metabolism are removed so that they do not accumulate in the body. Genetic differences in any of these functions may result in large or small differences in drug response. One of the best examples of this is the genes that encode the production of enzymes that metabolize pharmaceutical drugs, such as the cytochrome P450 group of enzymes (cytochrome P450 CYP450) responsible for the metabolism of a large group of human drugs, and individuals differ in the speed of drug metabolism according to the type of enzymes they possess, as people who have the metabolism of Slower exposure to the drug's active substances is longer, and they are exposed to less metabolites than those with metabolites. The enzyme CYP2D6 is responsible for the metabolism of a large number of cardiac drugs, including beta-blockers. Individuals with slow metabolisms are characterized by a drug concentration in their serums of two or three times, which causes dizziness and may lead to harmful side effects. A number of other such tests are also being prepared.

A test is currently available to measure an individual's ability to produce the enzyme thiopurine S-methyltransferase (TPMT), which is necessary to metabolize thiopurine drugs used to treat acute lymphoblastic leukemia (ALL), the most common childhood cancer. The test provides an opportunity for clinicians to classify patients according to their genotypes of this enzyme production, and helps them determine the appropriate drug dose for each of them, for example if the patient is found to be poor in the ability to produce the enzyme (and thus less tolerant of thiopurine drugs); The drug dose is greatly reduced.

On the other hand, many questions related to the legal, ethical and regulatory frameworks for these studies are still waiting to be answered. There is no doubt that it is necessary to carry out extensive educational campaigns for patients, physicians and pharmacists accompanying the expansion of the implementation and application of these new studies.

VI. FUTURE PROSPECTS

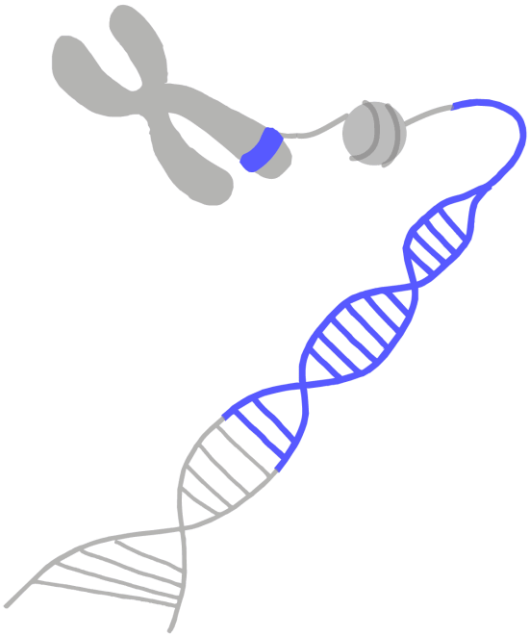
A scientific study in 1998 published in the Journal of the American Medical Association JAMA showed that drug

interactions led to the occurrence of more than 2.2 million serious injuries, as well as the death of more than one hundred thousand patients in American hospitals, and this makes these interactions one of the main causes of death in those countries. . At present, there are no easy ways to predict whether good or no drug responses will occur, or no response. Pharmaceutical companies still use a "one-size-fits-all" system today, depending on the average response of patients to the drug, even though this can cause severe illness or death. Genomic therapy studies will provide a viable solution to these problems. It will have important practical benefits, including the following:

The detection of many new genetic mutations, important information regarding the interactions between heredity and the environment, and the identification of genetic patterns and chromosomal abnormalities associated with various diseases.

Adding the genomic diagnosis of diseases to other medical diagnoses, in order to detect them at an early stage.

Enabling pharmaceutical companies to make pharmaceuticals based on proteins, enzymes, and RNA molecules associated with genes and diseases. Producing treatments geared toward specific diseases with precision. This will achieve significant increases in the drug's therapeutic effects and reduce damage to healthy cells.



Production of vaccines made from genetic material (DNA or RNA) capable of activating the immune system, and they will be safer, cheaper and easier to store, in addition to the possibility of genetically engineering them to affect several strains of the pathogen at the same time.

Reducing the length of time needed to manufacture a new drug, leading to its introduction on the pharmaceutical market, (for example, in America: from 15 years now to about two years), and greatly reducing its production costs.

VII. CONCLUSION

In April 2003, studies of the Human Genome Project were completed, and invaluable information was available about the sequence of bases in the deoxyribonucleic acid (DNA) of human chromosomes that make up about 35,000 genes in its cells. This project showed that about 99.9% of the information available in the genes is the same in all people, and that the remaining small differences are the key distinguishing human personality and body functions.

Although these differences do not usually cause problems with an individual's growth and development, or their biological functions, they may affect their predisposition to certain health problems, and may determine how the body reacts to various parameters, including how the metabolism of different drugs is used. Among the benefits of this project has been the development of studies of genomic therapy, which are looking to determine the interactions between genes and drugs. It is hoped that in a few years, accurate identification of patients' genotypes will provide the opportunity for them to be treated with drugs of high efficacy and safety. In other words, a doctor can prescribe the right dose of the right drug for the patient, an investigation of so-called "personalized" medicine.

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