

## Human Genome Project

### **Introduction**

The Human Genome Project (HGP) is an internationally collaborative venture to identify and mark all the locations of every gene of the human species. The HGP in the United States was started in 1990 and was expected to be a fifteen year effort to map the human genome. There have been a number of technological advances since 1990 that have accelerated the progress of the project to a completion date sometime during the year 2003. The U.S. HGP is composed of the Department of Energy (DOE) and the National Institute of Health (NIH) which hopes to discover 50,000 to 100,000 human genes and make them available for further biological study. There are a number of other countries that are involved in the project, including Australia, Brazil, Canada, France, Germany, Japan, and the United Kingdom. Besides numerous countries involved in the project there is also a number of commercial companies that are involved in sequencing. The collaborative 3 billion dollar price tag will be used to sequence the possible 3 billion DNA base pairs of human DNA.

The possibilities from the information that will be obtained from the project are virtually endless. It will most likely change many biological and medical research techniques and many of the practices used by our medical professionals today. The knowledge that will be obtained will help lead to new ways of diagnosing, treating, and possibly preventing diseases. Through the discovery of the human genome, the possibilities are endless for agriculture, health services, and new energy sources also. The end result of the HGP will be information about the structure, function and organization of DNA, as we know it today.

Since the beginning of time, people have yearned to explore the unknown, chart where they have been, and contemplate what they have found. The maps we make of these treks enable the next explorers to push ever farther the boundaries of our knowledge - about the earth, the sea, the sky, and indeed, ourselves. On a new quest to chart the innermost reaches of the human cell, scientists have now set out on biology's most important mapping expedition: the Human Genome Project. Its mission is to identify the full set of genetic instructions contained inside our cells and to read the complete text written in the language of the hereditary chemical DNA (deoxyribonucleic acid). As part of this international project, biologists, chemists, engineers, computer scientists, mathematicians, and other scientists will work together to plot out several types of biological maps that will enable researchers to find their way through the labyrinth of molecules that define the physical traits of a human being.

Packed tightly into nearly every one of the several trillion body cells is a complete copy of the human "genome" - all the genes that make up the master blueprint for building a man or woman. One hundred thousand or so genes sequestered inside the nucleus of each cell are parceled among the 46 sausage-shaped genetic structures known as chromosomes.

New maps developed through the Human Genome Project will enable researchers to pinpoint specific genes on our chromosomes. The most detailed map will allow scientists to decipher the genetic instructions encoded in the estimated 3 billion base pairs of nucleotide bases that make up human DNA. Analysis of this information, likely to continue throughout much of the 21st century, will revolutionize our understanding of how genes control the functions of the human body. This knowledge will provide new strategies to diagnose, treat, and possibly prevent human diseases. It will help explain the mysteries of embryonic development and give us important insights into our evolutionary past.

The development of gene-splicing techniques over the past 20 years has given scientists remarkable opportunities to understand the molecular basis of how a cell functions, not only in disease, but in everyday activities as well. Using these techniques, scientists have mapped out the genetic molecules, or genes, that control many life processes in common microorganisms. Continued improvement of these biotechniques has allowed researchers to begin to develop maps of human chromosomes, which

contain many more times the amount of genetic information than those of microorganisms. Though still somewhat crude, these maps have led to the discovery of some important genes.

By the mid-1980s, rapid advances in chromosome mapping and other DNA techniques led many scientists to consider mapping all 46 chromosomes in the very large human genome. Detailed, standardized maps of all human chromosomes and knowledge about the nucleotide sequence of human DNA will enable scientists to find and study the genes involved in human diseases much more efficiently and rapidly than has ever been possible. This new effort - the Human Genome Project - is expected to take 15 years to complete and consists of two major components. The first - creating maps of the 23 pairs of chromosomes - should be completed in the first 5 to 10 years. The second component - sequencing the DNA contained in all the chromosomes - will probably require the full 15 years.

Although DNA sequencing technology has advanced rapidly over the past few years, it is still too slow and costly to use for sequencing even the amount of DNA contained in a single human chromosome. So while some genome project scientists are developing chromosome maps, others will be working to improve the efficiency and lower the cost of sequencing technology. Large-scale sequencing of the human genome will not begin until those new machines have been invented.

### **Technical Aspects of HGP**

There are a number of goals that have been set forth by the HGP that they hope to have finished by their completion date in 2003. One of the first goals of the project is to identify the 50,000 to 100,000 genes that are found in DNA (2,3,4). The second goal of the HGP is to sequence the 3 billion chemical bases that make up human DNA. DNA sequencing is the process of determining the order of the chemical building blocks "bases" that make up the DNA of the human chromosome. This information will then be stored into a large database so that information can be used by other individuals'. The HGP hopes to then be able to develop tools for the analysis of this data. Finally, the HGP would like to address the ethical, legal, and social issues that will no doubt arise from the project. As of 10/8/99, the working draft sequence's goal of 90% by the summer of 2000 is at 13.6% of its goal (453,968,000 bases). The finished high quality sequence's goal of 100% by 2003 is at 13.8% (466,883,000 bases) of their goal(1).

The DNA that is being used in the project is from four individuals (5). This can be done because humans differ in their genetic makeup by 0.1% of their DNA. This 0.1% accounts for all of the genetic variability that we see and recognize in our society today.

There are a number of different techniques that are used in the genome project to determine the sequence of DNA. One is the use of a new high resolution mass spectrophotometer equipped with vacuum ultraviolet photoionizer to sequence ferrocene-tagged DNA(1). This new technology could eliminate the need for both gel electrophoresis and radioactive tagging while sequencing DNA segments. This method is accomplished by a primer being labeled with organometallic compound such as ferrocene. The new DNA segments that terminate at each occurrence of a particular DNA base are built up on the primer using the original DNA template. Later, the primer is read in a high resolution time of flight mass spectrophotometer where masses and sequences are determined.

Another technique is automated DNA sequencing. This process is used to speed up the task of DNA sequencing. There are a number of dyes that attach specifically to the bases of the DNA (2). The fragments of DNA are then sent through a glass tube that is filled with a transport gel. The fragments are then excited by the use of a laser and each dye will give off a certain color. These colors are then read by a computer, which will give the DNA sequence.

### **Benefits of the HGP**

The benefits of the Human Genome Project will more than likely be felt throughout the world. The expenditures on genomics research in U.S. industry is projected to be 45 billion dollars by 2009. This projected dollar amount is through the sales of DNA based products and technologies in the biotechnology industry.

One of the potential benefits is in the field of molecular medicine. The benefits in this field could include better diagnosis of disease, early detection of certain diseases, and gene therapy and control systems for drugs (1). In the future there should be new treatments in molecular medicine that don't treat the symptoms but look at the causes of the problem at hand.

Another field that may reap the benefits of the HGP is the field of microbial genomics. This field may be able to find new energy sources, through the sequencing of a bacterial genome. This could lead to discoveries that are useful in energy production, toxic waste reduction, and industrial processing (2).

The HGP can also be very useful for the understanding of human evolution and human migration. It may help lead scientists to find out how humans have evolved and how humans are evolving today. It will also help to understand the common biology that we share with all life on earth. Comparing our genome with others may help to lead to associations of diseases with certain traits.

One last field that will undoubtedly receive monumental benefits from the HGP is the field of agriculture and livestock breeding. This technology could help to develop disease, insect, and drought resistant crops thus being able to produce more for the world. It would also help to produce healthier, more productive, and possibly disease resistant animals to be sent to market.

Most inherited diseases are rare but taken together the more than 3,000 disorders known to result from single altered genes rob millions of healthy and productive lives. Today, little can be done to treat, let alone cure, most of these diseases. But having a gene in hand allows scientists to study its structure and characterize the molecular alterations or mutations that result in disease. Progress in understanding the causes of cancer, for example, has taken a leap forward by the recent discovery of cancer genes. The goal of the Human Genome Project is to provide scientists with powerful new tools to help them clear the research hurdles that now keep them from understanding the molecular essence of other tragic and devastating illnesses, such as schizophrenia, alcoholism, Alzheimer's disease, and manic depression.

Gene mutations probably play a role in many of today's most common diseases, such as heart disease, diabetes, immune system disorders, and birth defects. These diseases are believed to result from complex interactions between genes and environmental factors. When genes for diseases have been identified, scientists can study how specific environmental factors, such as food, drugs, or pollutants interact with those genes.

Once a gene is located on a chromosome and its DNA sequence worked out, scientists can then determine which protein the gene is responsible for making and find out what it does in the body. This is the first step in understanding the mechanism of a genetic disease and eventually conquering it. One day, it may be possible to treat genetic diseases by correcting errors in the gene itself, replacing its abnormal protein with a normal one, or by switching the faulty gene off.

Finally, Human Genome Project research will help solve one of the greatest mysteries of life: How does one fertilized egg "know" to give rise to so many different specialized cells, such as those making up muscles, brain, heart, eyes, skin, blood, and so on? For a human being or any organism to develop normally, a specific gene or sets of genes must be switched on in the right place in the body at exactly the right moment in development. Information generated by the Human Genome Project will shed light on how this intimate dance of gene activity is choreographed into the wide variety of organs and tissues that make up a human being.

## **Ethics issues of the HGP**

The general public and people in the HGP have shown a lot of concern over the ethical issues involved with the Human Genome Project. Because of this concern the Department of Energy and the National Institutes of Health have put 3 to 5% of their annual budget for the HGP to studying the ethical, legal, and social issues (ELSI) involved in the project (1,3). The use of sequencing will make a profound impact on genetic screening of individuals. Medical professionals will be able to look at a person's genome and be able to tell many things about a person just by looking at the person's genes. This new technology will bring a number of issues such as the fairness in the use of genetic information. This issue is targeted mainly at who should have access to genetic records and how can they be used. Some of those targeted are insurers, employers, courts, schools, and the military. If this information is used by some of these agencies there could be discrimination based on genetic disorders. This discrimination could be from diseases that run in a family to mental disorders that a person cannot help.

The privacy and confidentiality of genetic information could also lead to problems. For certain reasons, many people would want for no one to see what their genetic makeup is. There would also be concerns of psychological problems associated with knowing your own genetic makeup. If someone were to find out they have a good chance of developing a rare disease it would most likely drastically change their thinking on life. For reproduction, there could be compatibility problems of two individuals to have normal children. This would cause stress in a large number of people's lives.

Another issue that has risen is the use of gene therapy to treat disease. The use of a person's genome to tell if a person carries a genetic disease will help in the treatment of these diseases. In gene therapy a faulty or infected gene is replaced with a normal gene, so the individual does not display the trait that they were naturally born with. Many people feel that this is wrong because we are more or less taking over the course of nature, and they feel that this is not the natural way.

There are also clinical issues that need to be overseen with the HGP. When the project is finished, many new techniques will need to be taught to our health service people. There will also be a need to educate patients and the general public as to what is happening in these procedures. There will need to be genetic counselling for people undergoing genetic testing. Health care providers will need to know how to tell people the ramifications that go along with the testing that they will be undergoing.

The HGP will also cause concerns over commercialization of the technology if there are only a few agencies that are working on the project who will get the rights to the technology. The major concerns will most likely be over the patents and copyrights of the technology.

There are also critics of the HGP that contend that the high cost of the project is not justified. Some critics also say that the ability to diagnose a genetic disorder before any treatment is available causes more harm than good, because it will create anxiety and frustration among individuals. There is also the very big question of what is "normal". When and where will the use of genetic material be able to be used in society after the HGP is finished.