DNA
An Overview

Introduction

In the early 1950's two scientists, James Watson and Francis Crick, discovered what we know today as Deoxyribonucleic acid (DNA). Little was known about DNA then except for the fact that it was found in our bodies. Since then, we have made great advancements in our knowledge of DNA and the chemistry behind its synthesis. Today, we know that the color of our eyes, hair, and height are determined by our genes. Genes are part of our DNA, and the way they are linked together, or synthesized determines our physical traits. When our DNA is synthesized problems can occur if the DNA does not align properly and can result in certain diseases or birth defects. These misalignments are known as mutations. By learning more about DNA and the chemistry behind it, doctors and chemists are able to help many people. The chemistry of DNA synthesis has come a long way since its discovery with scientists constantly learning new ways to apply this knowledge with the hope that continual breakthroughs will lead to improved ways of helping people.

What is DNA?

Discovery

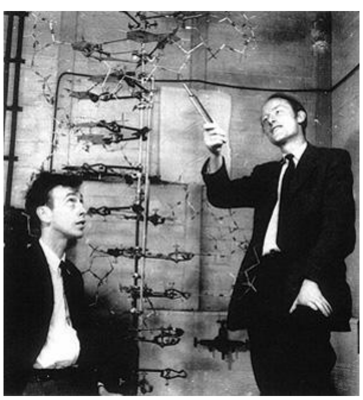

Figure 1: Watson and Crick explain the Double Helix.

In 1868, the Swiss scientist Friedrich Miescher was conducting studies in the nuclei of cells from samples obtained from discarded patient bandages. His research was the beginning of the discovery of what we know as Deoxyribonucleic acid (DNA). In 1943 a group of scientists led by Oswald Avery were the first to determine that there was genetic information in DNA. Rosalind Franklin, a chemist by training, was able to photograph DNA by using X-Ray diffraction, in 1951. Then in 1953 the duo of James Watson, an American geneticist, and Francis Crick, an English physicist, produced a work that overshadowed their predecessors. By incorporating research from a number of other scientists, Watson and Crick were able to link the various pieces of information together to produce a model structure for DNA which they termed to be a double helix (See Figure 1).

Structure

The model devised by Watson and Crick leaned heavily on the photos produced by Franklin but was three-dimensional. The structure began with two strands of a sugar-phosphate backbone that were twisted around the same axis and connected by rungs known as nucleotide bases. After deducing this form, Watson and Crick next turned their attention to the bonding of the bases with strands. They already knew there were four bases, Adenine (A), Guanine (G), Thymine (T), and Cytosine (C). Adenine and Guanine were purines meaning they had two carbon-nitrogen rings in their structures. Thymine and Cytosine were pyrimidines, composed of one carbon-nitrogen rings. Upon observing the pairing of Adenine and Thymine and of Guanine and Cytosine, the partners noted that the base pairs bonded to the strands by hydrogen bonding which formed DNA's distinctive double helix shape (See Figure 2).

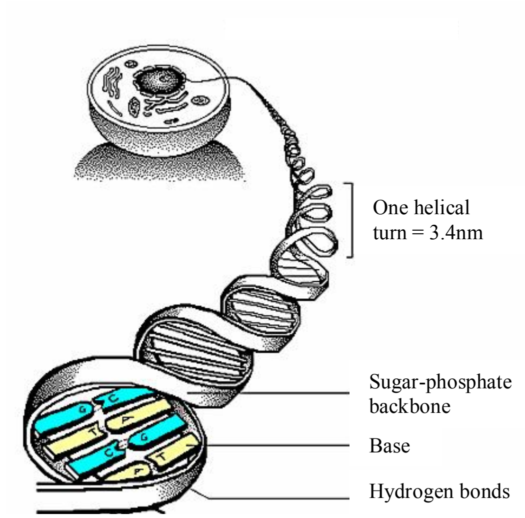

Figure 2: Structure of DNA showing the double helix form which is located in the nucleus of a cell.

Roadmap to Life

As mentioned earlier, DNA plays a vital role in determining one's physical characteristics. Each DNA molecule contains many genes which function as the basic building blocks of hereditary. Defects or abnormalities in DNA caused by several sources such as sunlight, cigarettes smoke and radiation, can lead to mutations. DNA molecules are some of the largest molecules known and hold many genes (See Figure 3). "A gene is a specific sequence of nucleotide bases, whose sequences carry the information required for constructing proteins, which provide the structural components of cells and tissues as well as enzymes for essential biochemical reactions" ("Life", Science Master). The total group of genes for a particular organism makes up its genome. The genome provides a detailed roadmap with all the instructions for the cellular structure required during an organism's lifetime. Some estimates set the number of genes in the human genome to be as high as 100,000. The gene

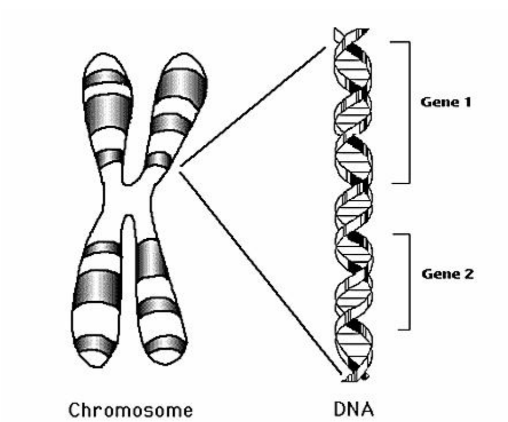

Figure 3: DNA sequences form Genes which in turn form Chromosomes.

sequences formed by the DNA strands are contained in chromosomes. A chromosome is a large macromolecule found inside the cell nucleus. Multiple chromosomes are known to exist inside each cell's nucleus. Humans have twenty-four distinct chromosomes, and the chromosomes in the cell are divided into two separate sets, one from each parent. Each of these sets is made up of 46 chromosomes, one of which will be either the female X chromosome or the male Y chromosome. The center of the chromosome is known as the centromere where the p-arm and q-arm intersect. Having the incorrect number of chromosomes can cause genetic problems like birth defects.

<u>Properties of DNA</u>

Formation

DNA, like most substances, has many extensive properties that range from how it looks to its complex way of bonding and replicating. DNA is a linear structure, which consists of two strands that wrap around each other to form what we now call a double helix. Repeated subunits called nucleotides make up DNA's structure. A nucleotide consists of three main parts, a five carbon sugar, a phosphate, and a nitrogenous base. There are four nitrogenous bases that pair with each other, adenine pairs with thymine, A-T or T-A and guanine with cytosine, G-C or C-G (See Figure 4). The way these bases join up is known as base paring. Nucleotides covalently link up with each other to form DNA strands by phosphodiester bonds (a form of hydrogen bonding). The backbone of a DNA strand is made up of alternating sugar and phosphate groups, connected by the nitrogenous bases. The two DNA backbones run in opposite directions, one strand starts with the 5 prime (5`) and ends with the 3 prime (3`), and the other starts with 3` and ends with 5`. The 3` and 5` derive their names from the carbon that ends them, a 3` ends with a third carbon in its sugar ring, and a 5` ends with a five carbon (See Figure 5). The A-T or T-A and G-C or C-G pairs alternate with the adenine and thymine pairs linked together by two hydrogen bonds while the cytosine and guanine pairs coupled together with three hydrogen bonds.

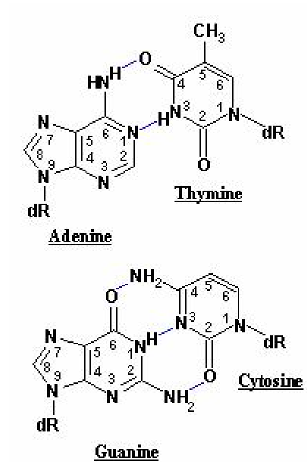

Figure 4: Base pairs are formed by Adenine/Thymine and Guanine/Cytosine.

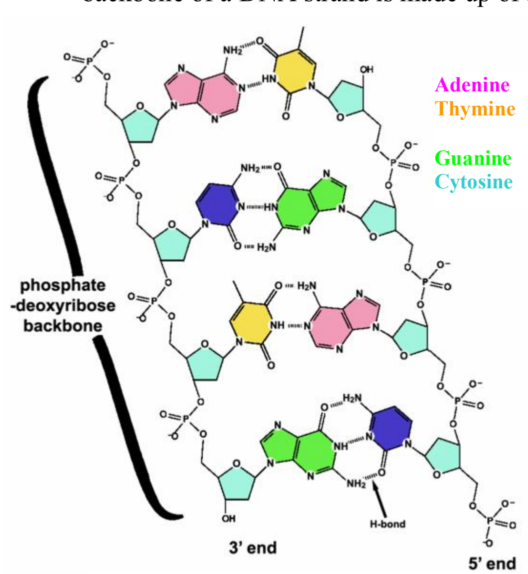

Figure 5: The bases form the DNA Backbone and are linked by hydrogen bonds.

Replication

To allow information in DNA to be passed on, the DNA must be copied by a process known as DNA replication. Initiation, elongation, and termination are the three steps that make DNA replication. To begin the initiation step of replication, the twisted DNA helix must be unwound through the breaking of the hydrogen bonds that hold it together. This action is carried out by an enzyme called helicase.

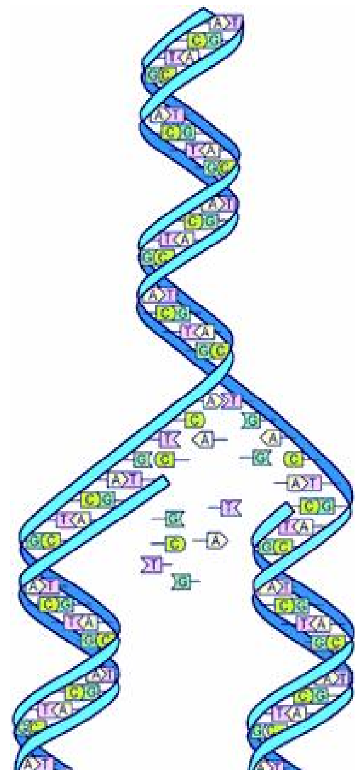

Figure 6: The y-shaped replication fork formed by the leading and lagging edges of the DNA strands.

The origin of replication is a specific site where synthesis of new DNA will begin by using the existing strands as guidelines. After the DNA helix has been “flattened out”, the two strands form a *y*-shaped pattern called the replication fork (See Figure 6). During the process of replicating, the DNA strands tend to twist and rotate, so in order to prevent tangling, the enzymes topoisomerases hold the strands in place. The adding on of nucleotides to an existing DNA strand is the major function of the elongation phase and the enzyme polymerase performs these additions. DNA polymerase is able to consistently add nucleotides to the leading strand of DNA when synthesis is in the 5` to 3` direction. The lagging strand is made discontinuously. Instead of being made up of long strands of nucleotides, the lagging strand consists of pieces of nucleotides called Okazaki fragments. Since the lagging strand is being synthesized from the 3` to the 5`end, instead of the normal way, 5` to 3`, the DNA polymerase can not work; thus another enzyme is needed to bond the fragments together. Scientists call this enzyme DNA ligase. Termination provides the last step in the replication of a new DNA strand and completes the process by adding hydrogen bonds to form the new base pairs. After the formation of the base pairs has been completed, an identical copy of the original DNA molecule will have been formed.

<u>The Uses of DNA</u>

Medical

In today’s world, physicians understand that DNA plays a vital role in the health of the human anatomy. Mutations in our bodies that cause disorders and birth defects are very rare but when they do occur, it is because something went wrong during DNA replication. If one of the DNA’s nucleotides did not pair up correctly with its partner, then that newly replicated strand is going to code for a totally different amino acid and in the end will cause a mutation. Mutations can be heritable, permanent mistakes in the base pairing of DNA. There are other types of mutations, such as silent mutations which do not have any phenotypic effects, missense and nonsense mutations which completely change the amino acid sequence of the encoded protein, and point mutations which occur when there is a single base change. Mutations are known to cause disorders such as cancer, sickle-cell anemia, and cystic fibrosis.

Forensics

Criminal investigators have found that DNA can be a major part of solving crimes by helping identify the persons who committed the offense. Human DNA can be found in samples of hair, saliva, blood, semen, or skin that may be left at the scene of a crime (See Figure 7). To find out whom exactly the DNA belongs to is a process called genetic fingerprinting, or DNA profiling. "DNA profiling was developed in 1984 by British geneticist Sir Alec Jeffreys of the University of Leicester, and was first used to convict Colin Pitchfork in 1988 in the Enderby murders case in Leicestershire, United Kingdom" ("DNA", Wikipedia). Even though this method of genetic fingerprinting is one of the most reliable sorces for fighting crimes, it is not always prefect, as in the case when no DNA can be retrived, or when the DNA of many different suspects confuse the crime scene.

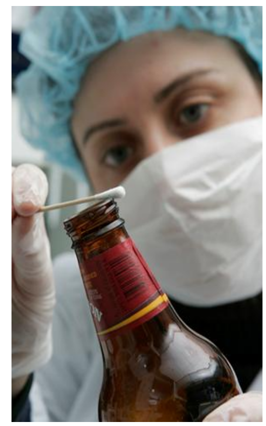

Figure 7: Crime lab technician gathering DNA samples.

Genetic History

Since mutations in DNA are passed down over time from generation to generation, a record of what has occurred can be obsevered in DNA samples over time. Geneticists have used these different DNA sequences in an attempt to piece together the history of various life forms. Different DNA sequences can also be used in developing family trees. Similarly, DNA sequences are valuable in the study of particular populations and have also been used in establishing familial relationships between descendants. This is known as phylogeny and is a valuable tool in gathering information on the history of particular populations.

Conclusion

In the more than fifty years since Watson and Crick made a breakthrough with their model of Deoxyribonucleic Acid, scientists have expanded the research base in this crucial substance. It is now known that DNA holds the key that controls physical traits. Since DNA determines hereditary, scientists better understand why offspring resemble their parents. The chemistry associated with how DNA forms, replicates and mutates is very complex. Ironically, this process is extremely repetitive, but when the process breaks down, major defects can occur called mutations. New technologies like forensics have given rise to new ways of applying the science of DNA. Still, there is much more to be understood about DNA, especially when dealing with mutations that have negative effects. With ongoing research, the future of applications for DNA to help people seems to be unlimited.

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Figure 1: Department of Psychology, University of Plymouth . 2 Mar. 2006. University of Plymouth. 11 Nov. 2006; <http://salmon.psy.plym.ac.uk/year3/PSY339EvolutionaryPsychologyroots/watson-crick-dna.jpg>.

Figure 2: "Structure of DNA." Access Excellence Resource Center. National Health Museum. 11 Nov. 2006; <http://www.accessexcellence.org/RC/VL/GG/ structure.html>.

Figure 3: "Structure of DNA." Access Excellence Resource Center. National Health Museum. 11 Nov. 2006; <http://www.accessexcellence.org/RC/VL/GG/ genes.html>.

Figure 4: "DNA Pairing Image." Wikipedia. 1 Nov. 2006. 11 Nov. 2006; <http://en.wikipedia.org/wiki/Image:Dna_pairing_aa.gif>.

Figure 5: "DNA Chemical Structure Image." Wikipedia. 1 Nov. 2006. 11 Nov. 2006; <http://en.wikipedia.org/wiki/Image: DNA_chemical_structure_aa.gif>.

Figure 6: "DNA Splitting Image." Wikipedia. 1 Nov. 2006. 11 Nov. 2006; <http://en.wikipedia.org/wiki/Image: Dna-split_aa.gif>.

Figure 7: "Forensic Biology ." Human DNA Testing. 2006. Genetic Technologies Limited . 4 Dec. 2006; <http://esvc001057.wic005u.server-web.com/image_attachments/2/Forensics.jpg>.