The Structure of the DNA Molecule

Background

Although scientists as far back in history as Aristotle recognized that the features of one generation are passed on to the next (...like begets like...) it was not until the 1860's that the fundamental principles of genetic inheritance were described by Gregor Mendel. Mendel's work with common garden peas, pisum sativum, led him to hypothesize that phenotypic traits (physical characteristics) are the result of the interaction of discrete particles, which we now call genes, and that both parents provide particles which make up the characteristics of the offspring. His theories were, however, widely disregarded by scientists of the time.

As the 20th century began many scientists noticed similarities in the theoretical behavior of Mendel's particles, and the visible behavior of the newly discovered chromosomes. It wasn't long before most scientists were convinced that the hereditary material responsible for giving living things their characteristic traits, and chromosomes must be one in the same. Yet, questions still remained. Chemical analysis of chromosomes showed them to be composed of both protein and DNA. Which substance carried the hereditary information? For many years most scientists favored the hypothesis that protein was the responsible molecule because of its comparative complexity when compared with DNA. After all, DNA is composed of a mere 4 subunits while protein is composed of 20, and DNA molecules are linear while proteins range from linear to multiply branched to globular. It appeared clear that the relatively simple structure of a DNA molecule could not carry all of the genetic information needed to account for the richly varied life in the world around us!

It was not until the late 1940's and early 1950's that most biologists accepted the evidence showing that DNA must be the chromosomal component that carries hereditary information.

Watson and Crick

In 1951, the then 23-year old biologist James Watson traveled from the United States to work with Francis Crick, an English physicist at the University of Cambridge. Crick was already using the process of X-ray crystallography to study the structure of protein molecules. Together, Watson and Crick used X-ray crystallography data, produced by Rosalind Franklin and Maurice Wilkins at King's College in London, to decipher DNA's structure.

This is what they already knew from the work of many scientists, about the DNA molecule:

1. DNA is made up of subunits which scientists called nucleotides.
2. Each nucleotide is made up of a sugar, a phosphate and a base.
3. There are 4 different bases in a DNA molecule: adenine, cytosine, guanine and thymine
4. The number of purine bases equals the number of pyrimidine bases
5. The number of adenine bases equals the number of thymine bases
6. The number of guanine bases equals the number of cytosine bases
7. The basic structure of the DNA molecule is helical, with the bases being stacked on top of each other

Working with nucleotide models made of wire, Watson and Crick attempted to put together the puzzle of DNA structure in such a way that their model would account for the variety of facts that they knew described the molecule. Once satisfied with their model, they published their hypothesis, entitled "Molecular Structure of Nucleic Acids: A Structure for Deoxyribose Nucleic Acid" in the British journal Nature (April 25, 1953. volume 171:737-738.) It is interesting to note that this paper has been cited over 800 times since its first appearance!

Here are their words:

"...This (DNA) structure has two helical chains each coiled round the same axis...Both chains follow right handed helices...the two chains run in opposite directions. ..The bases are on the inside of the helix and the phosphates on the outside..."

"The novel feature of the structure is the manner in which the two chains are held together by the purine and pyrimidine bases... The (bases) are joined together in pairs, a single base from one chain being hydrogen-bonded to a single base from the other chain, so that the two lie side by side...One of the pair must be a purine and the other a pyrimidine for bonding to occur. ...Only specific pairs of bases can bond together. These pairs are: adenine (purine) with thymine (pyrimidine), and guanine (purine) with cytosine (pyrimidine)."

Source: Pamela Peters, Ph.D., Access Excellence, Genentech, Inc.