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Medicine for Managers

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DNA

For many of us, DNA was not in the lexicon when we were children. It is now the most famous molecule in the world. DNA is DEOXYRIBONUCLEIC ACID (dee-ox-ee-rye-bow-new-clay-ic acid). It is our genetic code, present in almost every cell in the body and amazingly, carries the instructions for our development, growth, maturation, reproduction, body function and even for our ageing and death.

One of those coffee morning pieces of information that makes everyone go 'wow' is that if all the DNA in the human body was straightened out, it would reach to the sun and back, more than three hundred times!

The foundation of modern genetics was laid in 1866 by ***Gregor Mendel,*** who discovered that traits (characteristics) were inherited and could be passed through generations.

The DNA molecule was identified by Johann Miescher in 1869. However, it was in the late 1940s that ***Francis Crick***, at the University of Cambridge began to use X-rays to study crystals and their structures, a process called ***X-ray crystallography***.

He later started working with ***James Watson*** at Cambridge. The two of them, who shared an interest in genetics and how the body proteins controlled the replication of cellular activity, identified the importance of the DNA molecule.

At the same time, at King's College in London, Rosalind Franklin and Maurice Wilkins were undertaking similar research and obtained X-ray photographs of DNA fibres. Franklin's work established unequivocally the structure of DNA.

Wilkins shared her findings with Watson and Crick. They also became aware of research by ***Linus Pauling*** in the United States who had discovered that the protein filament had a helical form

Watson and Crick, working with Franklin, established that DNA was a double helix. Having established its form, the next major discovery was how the two individual strands forming the helix were actually joined together.

They identified four ***nucleotides*** (more commonly known as ***bases***). They are called adenine, thymine, guanine and cytosine.

When they realised that the amount of adenine and thymine was equal and that the amount of guanine and cytosine was equal, they recognised that the base-pairings (the way in which the two strands of the helix were joined) was by links either of ***adenine-thymine*** or ***guanine-cytosine***.

There was no other form of linkage between the four nucleotides.

On February 28th 1953, they made the definitive discovery of the double helix nature and structure of DNA, which was published in the journal *Nature* two months later.

This is the now very famous picture of Watson and Crick with their helical model (Watson on the left, Crick on the right)

The DNA double helix as illustrated, has the two key components.

1. The two strands which effectively form the backbone of the molecule and which are composed of a sugar molecule, called ***deoxyribose***, a phosphate molecule and a nitrogen-containing component
2. The four nitrogen-containing bases or nucleotides which are:
    a. Adenine
    b. Thymine
    c. Guanine
    d. Cytosine

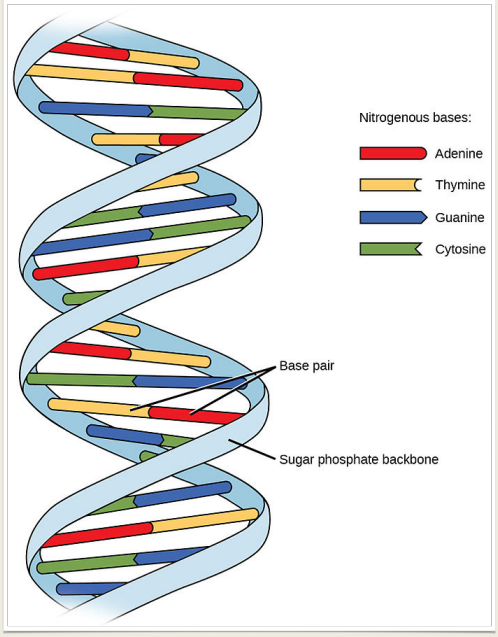
The complete structure is described as having the form of a ladder.

Each individual has a unique DNA genetic code.

Within it are all the instructions for every element of bodily form and function. The instructions contained in each individual's DNA molecule are passed from parent to child. Because of the nature of sexual reproduction, roughly half of each child's DNA originates from the father and half from the mother.

Most of our DNA is located in the cell ***nuclei***. Some of it is also found in the ***mitochondria*** which are scattered through the cells and are the powerhouse of cellular function. Each cell contains a two-metre length of DNA. In order to accommodate the DNA, the strands are coiled around proteins called ***histones*** and the resulting structure is called ***chromatin***.

Each chromosome contains ***one DNA molecule***. Humans have twenty-three pairs of chromosomes (23 from each parent), making a total of forty-six. The shared acquisition by the



individual of genetic material from each parent explains why, for example, a child may inherit (say) the brown hair of one parent and the blue eyes of the other.

Not all creatures have the same number of chromosomes and, for example, a fruit fly has eight chromosomes and a pigeon has eighty.

Each length of DNA has codes for the formation of specific proteins and these are called ***genes.***

Each gene carries specific information for specific characteristics such as eye colour or the shape of the ear.

Humans are thought to have somewhere between between 20,000 and 30,000 genes, which comprise about three percent of the DNA molecules. The function of the remainder of the DNA molecule is less clear but is believed to have a range of functions, important amongst which is the transcription of the molecule.

Chromosomes vary in complexity. Chromosome 1 is the largest with about 8,000 genes. Chromosome 21 is the smallest with about 3,000 genes.

At the end of each chromosome, are ***telomeres***, which are regions of repeated nucleotides (bases). They protect the chromosomes from being damaged or fusing with other chromosomes. During the normal ageing process, these protective regions become progressively smaller.

Each time a cell divides and DNA is replicated, the telomere becomes shorter.

For the genes to create a protein there are two principal stages. Firstly, the DNA code is ***transcribed*** to create ***messenger RNA*** (mRNA). The RNA copy differs from the original DNA in that it is normally ***single-stranded*** and also that the base thymine is replaced by ***uracil***.

The mRNA is then ***translated*** into amino acids. Each of the many parts of the RNA enable the creation of amino acids, which are the component parts of proteins. In this way, complete and exact copies can be made of body protein.

The results of these and subsequent discoveries have been revolutionary in the development of understanding and research in medicine. Crick and Watson received the ***Nobel Prize*** in Physiology or Medicine in 1962.

The understanding of DNA, its application and its testing, have had ramifications, not only through medicine, but in forensic science, genealogy, agriculture and many other areas.

DNA is simply necessary for the inception and reproduction of life. In medicine it has led to discoveries about a host of diseases such as Alzheimer's disease which occur because of DNA damage. In time, cures will be able to be created and customised to repair the DNA damage.

It has become possible to identify individual rogue genes which result in hereditary diseases. Pre-natal testing can be used to discover incurable or complex disease. This will lead to treatments to prevent those damaging diseases in future generations.

In genealogy, DNA can be used to trace ancestors or lost relatives. Paternity testing is also able to be used to identify parents and resolve issues with missing children.

DNA developments will allow medical research to identify the nucleotides in pathogens. The Eschericia coli bacterium, for example, has a DNA molecule with 4,000,000 nucleotides. It may well be that influencing the DNA will be the route to treatment of the diseases it causes.

Such testing has also come to the fore in Covid-19 with the identification of the nature and structure of virus variants which has facilitated their treatment and the development of new vaccines.

DNA testing is already proving useful in agriculture.

DNA is being used to change crop varieties to, for example, improve resistance to disease or increase yield. Not only plants but some animal breeds have been modified with the help of genetic engineering techniques.

DNA in forensic science has been instrumental in solving many criminal cases. DNA from crime scenes is used to verify a person's identity. The police and the judiciary have come to rely on DNA techniques to catch criminals.

DNA has proved to be a powerful endorsement of Darwin's theory of evolution because it can be shown how DNA is passed from organism to organism and provide evidence of development and origin from a common ancestor.

All these developments, many beyond the imagination of man, have occurred during the lifetime of many of us. Yet discoveries in this area are perhaps only just beginning and, in another sixty years, who knows what DNA may have made possible.

The world has a great deal for which to thank John Watson and Francis Crick.

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