

DECIPHERING THE STRUCTURE OF THE HEREDITARY MATERIAL.

By

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People have wondered since ancient times how the characteristics of parents are passed on to children. The puzzle was finally solved in detail in the 1950s in probably the greatest scientific advance of the twentieth century. This breakthrough gave birth to genetic engineering, molecular genetics and modern biotechnology. These developments touch all our lives - and we are only at the beginning. Mere mention of the terms DNA and the genetic code conjures up images of Francis Crick and James Watson, who solved the structure of DNA in 1953. But, as is the nature of science, their breakthrough was only possible because of previous discoveries made by many other scientists.

In the fourth century BC Aristotle proposed that semen contains plans that direct the unformed maternal blood to shape offspring. In the Middle Ages, Thomas Aquinas 'explained' that vigorous seed develops into males and weak seed produces females. Later, sperm cells were examined in the light microscope. It was 'observed' that each contains a tiny pre-formed child, termed the homunculus [*homunculus* in italics]. The mother was considered to merely incubate the homunculus, who emerged as a baby 9 months later.

Modern genetics began with Gregor Mendel's brilliant experiments on heritability in pea plants. Mendel showed that discrete hereditary elements (genes) are responsible for hereditary traits. These genes are passed on by both parents and the genes can independently sort and segregate between offspring. (See previous article on the work of Gregor Mendel).

The scientific world was not ready for Mendel's results, published in 1865. His concept of the sorting and segregation of discrete hereditary units could not be accommodated by the crude understanding of the cell than available. He also used a statistical approach, which was foreign to the current biological thinking.

Mendel's work was re-discovered at the turn of the century, by which time the rest of science was 'up to speed'. In the meantime chromosomes (the structures in the cell nucleus that contain the hereditary material) had been discovered. Mitosis (the process whereby chromosomes duplicate and are shared equally between two daughter cells when the parent cell divides) was understood, as also was meiosis (the process whereby a parent cell divides twice to produce 4 sex cells (egg or sperm)). The chromosomes duplicate only once during meiosis and consequently each germ cell receives half the chromosome number of the parent. Chromosome number is restored when a sperm combines with (fertilises) an egg to form an embryo). Mendel's theory could now be projected onto structures visible in the microscope. Also, by now the use of statistics was now common in biology.

An explosion of developments in genetics now began. It became clear that genes are arranged linearly along chromosomes and that they can undergo sudden permanent changes (mutation) resulting in changed traits in the organism. Genetics could also explain the mechanism of evolution. Mutations are the main source of novelty in evolution and natural selection chooses organisms bearing novel genes that make them better suited to survive in the environment.

Genetic understanding made it possible to design breeding programmes to improve animal and plant varieties and in medicine it opened the way to design interventions for prevention and cure

of disease.

But the molecular mechanism whereby the gene exerts its effect remained a mystery. However, interesting speculation was in the air. In 1945, Erwin Schrodinger, [two dots over o] published a book 'What is Life'. He suggested that the gene is a one-dimensional aperiodic crystal of a few repeating elements whose pattern of succession represents the hereditary information.

In 1944 O.T. Avery and co-workers showed that genes must be embodied in Deoxyribonucleic Acid (DNA), known since 1920 to be a major component of chromosomes. However, structurally it was thought that DNA was made of identical repeat units and therefore incapable of bearing information.

In 1952, A.D. Hershey and M. Chase again demonstrated that genes are made of DNA. By now much more was known about the structure of DNA. In 1950 Edwin Chargaff had shown that DNA from different biological sources showed distinct differences and could carry information.

Four kinds of chemical structures are linked together in DNA - Deoxyribose, Phosphoric Acid, Purine Bases (Adenine - A and Guanine - G), and Pyrimidine Bases - (Thymine - T and Cytosine - C). Chargaff showed that DNA from different sources had different relative amounts of A, T, G and C, and that, regardless of source, A and T were always present in equal proportions, and G and C were always present in equal proportions.

In the late 1940s/early 1950s, W.T. Astbury, Maurice Wilkins and Rosalind Franklin produced vital X-ray diffraction pictures of DNA showing it was probably a 2-stranded helical structure. Francis Crick and James Watson, using X-ray diffraction and model-building, and drawing on all the available evidence, solved the structure of DNA in 1953.

The DNA molecule is a double helix in which two strands wind around each other. A repeating combination of sugar and phosphoric acid (deoxyribose-phosphate) make up the backbone of each stand and the bases protrude from these backbones into the heart of the double helix. A always pairs with T on the other strand, and G always pairs with C. Information in DNA resides in the base sequences. One unit of information is represented by a sequence of 3 bases. The 4 letters of the genetic alphabet (A,T,G,C) can therefore form 64 words, or units of information (4x4x4).

The structure of the genetic material is, like all great truths, elegantly simple, and simply beautiful. Watson and Crick made their breakthrough as young men. They have since been feted as heroes. And indeed they are great scientists. But they enjoy their fame because science was ready to hear what they had to say. Their results were not premature, like those of poor Gregor Mendel, who died a lonely death with his great work unappreciated.

(This article first appeared in The Irish Times, December 22, 1997.)