

Half a Century of DNA

Dicle GÜÇ

Department of Basic Oncology, Oncology Institute, Hacettepe University, 06100 Sıhhiye, Ankara - Turkey

Received: December 18, 2003

Fifty years have passed since the discovery of the structure of DNA by James Watson and Francis Crick, but in fact the DNA story actually started in 1869 with the discovery of an acidic substance "nuclein" in the nuclei of pus cells by Fritz Miescher (1). Fifty years later, in 1919, Phoebus Aaron Levene proposed that the structure of DNA was "tetranucleotide", whereby the 4 bases of DNA were arranged one after another in a set of 4. Later, in 1928, the "transformation" phenomenon was defined by Frederick Griffith, and this was followed 10 years later by Rudolf Singer, Torbjorn Caspersson and Einer Hammarsten, who estimated the molecular weight for DNA to be between 500,000 and 1,000,000 daltons (1). Griffith's transformation phenomenon was clarified by Oswald Avery, Colin MacLeod and Maclyn McCarty in 1944 and they suggested that DNA may function as a genetic material capable of altering the heredity of bacteria. Their findings received little acceptance for a variety of reasons, the most significant being the work on the composition of DNA. This dated back to its first identification 75 years earlier and at that time scientists concluded that DNA was too limited in its diversity to carry any genetic information (2). Most biologists believed in those days that if genes were composed of a known substance, it must be protein. However, Erwin Chargaff, who changed his field of research to DNA after reading Avery's paper in 1944, reported in 1949 variations of DNA base composition between species. Furthermore, Chargaff found the ratio between the quantities of the 2 purine bases, namely adenine and thymine. Moreover, the quantities of the 2 pyrimidine bases, guanine and cytosine, also remained at about the same ratio i.e. 1 to 1. The latter finding was a very

important factor in Watson and Crick's determination of the double helical structure of DNA. In the same year, Roger and Colette Vendrely discovered that the nuclei of sex cells contain half as much DNA as do the body cells (1). Later, in 1951, a 31-year-old physical chemist working in the biophysics unit of King's College in London, Rosalind Franklin, distinguished the 2 forms of DNA: the paracrystalline B form and crystalline A form (3). One year later, Rosalind Franklin was able to produce a magnificent X-ray diffraction pattern of the B form of DNA with Raymond Gosling. This finding was recorded in her laboratory notebook in 1953, which clearly stated that the structure of DNA had 2 chains and the molecule had its phosphate groups on the outside. Rather interestingly, 2 weeks later, Watson and Crick built their model of DNA as a double helix. Thus, Rosalind Franklin's unpublished experimental evidence, which had reached Watson and Crick through irregular routes, is claimed to have helped them construct one of the best known molecules of the century. Nowadays, it is widely accepted that Rosalind Franklin had never been aware that they had seen her X-ray photograph, which demonstrated the unmistakable evidence of a helical structure and her precise measurements of the unit cell of the DNA crystal (3). Furthermore, Watson and Crick never told Franklin directly (which they subsequently admitted publically long after her death) that they could not have discovered the double helix structure of DNA in the early months of 1953 without her work. After her early death in 1958 at the age of 37 from ovarian cancer, this confession was first expressed in 1968 by James Watson in his best-selling book *The Double Helix* (4). He was by then a Nobel Laureate (awarded in 1962) in medicine and physiology.

He wrote in his book that “Rosy, of course, did not directly give us her data. For that matter, no one at King’s realized that they were in our hands”. Although in 1953 Nature published 7 papers on the structure of DNA and these reports on DNA structure were written by James Watson and Francis Crick (5,6), Rosalind Franklin and Raymond Gosling (7,8), Maurice Wilkins, W.E. Seeds, Alec Stokes and Herbert Wilson (9,10) and Bertil Jacobson (11), the Nobel prize in medicine was awarded in 1962 to only James Watson, Francis Crick and Maurice Wilkins for their work on DNA.

The unique importance of the finding of the DNA structure is due to the light it sheds on the inheritance of genetic material, replication, repair, diversity and the evolution of species. In a broader sense, its discovery has united genetics with biochemistry, cell biology and physiology. Briefly, the model for the DNA double helix proposed by James Watson and Francis Crick is based on 2 paired DNA strands that are complementary in their nucleotide sequence. The model had striking implications for the process of DNA replication and DNA recombination (12). Before the discovery of DNA’s structure it was impossible to speculate about the molecular mechanisms of DNA replication and recombination, but the discovery of complementary base pairing between DNA strands indicates that 2 strands of a DNA molecule could serve as a template for the synthesis of new complementary strands, the sequence of which would be dictated by the specificity of base pairing. As a result, any part of the sequence can be used either to create or to recognize its partner nucleotide sequence and these 2 functions are central in DNA replication and recombination (12,13). Another important dynamic state of DNA is the restoration of altered DNA to its normal state, which is called DNA repair (14). During evolution there is a fine line between genomic stability and instability and of mutation and repair. Twenty years after the discovery of DNA’s structure, Francis Crick wrote in Nature that “we totally missed the possible role of...(DNA) repair although... I later came to realize that DNA is so precious that probably many distinct repair mechanisms would exist” (15).

Watson and Crick’s double helix model has also prepared the basis for the Human Genome Project, which is the most remarkable project of the century. This project has accumulated a tremendous amount of

information about DNA sequences. It is now time to convert the information into knowledge of organisms.

Finally, as an immunologist, I would like to stress the importance of the discovery of DNA’s structure in the transformation of immunology over the past 50 years. One of the most striking examples is the diversity of antibodies. An individual is capable of making a tremendous number of antibodies, each with a distinct specificity (16). During the maturation of B-lymphocytes a group of short genes are rearranged and come together at the DNA level. This process is caused by the production of many structurally distinct, up to 10^9 , antibodies by B cells. As the rearrangement is mostly random, each lymphocyte makes different choices and thus the result is a broad repertoire of lymphocytes reactive to different antigens (17). The puzzle of antibody diversity cannot be solved without the double helix information.

The celebration of this particular molecule is not only related to its remarkable scientific importance but also to the fact that as Martin Kemp from the Department of the History of Art at Oxford said, “No molecule in the history of science has reached the iconic status of the double helix of DNA. Its image has been imprinted on all aspects of society, from science, art, music, cinema, architecture and advertising” (18). Even for artists, the charm of a form that is both beautiful and full of all kinds of scientific and social significance is quite considerable.

Since the late 1950s DNA has been a part of the daily life. One may come across a sculpture or a Lego model of the DNA double helix. Similarly, Salvador Dali painted DNA in his *Butterfly Landscape, the Great Masturbator in Surrealist Landscape with DNA* (1957-8) (18). Like him, many artists have used the image of DNA in their designs and paintings and DNA was included in the Millennium Collection stamp designed by Mark Curtis and the cosmetic industry recently came up with a perfume named “DNA”.

Corresponding author:

Dicle GÜÇ

Hacettepe University, Oncology Institute,

Department of Basic Oncology

06100,Sıhhiye, Ankara, Turkey

E-mail: dguc@hacettepe.edu.tr

References

1. Olby R. Quiet debut for the double helix. *Nature* 421: 402-405, 2003.
2. McCarty M. Discovering genes are made of DNA. *Nature* 421: 406, 2003.
3. Maddox B. The double helix and the "wronged heroine". *Nature* 421: 407-408, 2003.
4. Watson JD. *The Double Helix: A personal account of the discovery of the structure of DNA* (Atheneum, New York, 1968). Northon Critical Edition (ed. Stent, GS) published by Northon, New York, London, 1980.
5. Watson JD, Crick FHC. A structure for deoxyribose nucleic acid. *Nature* 171: 737-738, 1953.
6. Watson JD, Crick FHC. Genetic implications of the structure of deoxyribonucleic acid. *Nature* 171: 964-967, 1953.
7. Franklin RE, Gosling RG. Molecular configuration in sodium tymonucleate. *Nature* 171: 740-741, 1953.
8. Franklin RE, Gosling RG. Evidence for 2-chain helix in crystalline structure of sodium deoxyribonucleate. *Nature* 172: 156-157, 1953.
9. Wilkins MHF, Stokes AR, Wilson HR. Molecular structure of deoxyribose nucleic acid. *Nature* 171: 738-740, 1953.
10. Wilkins MHF, Seeds WE, Stokes AR et al. Helical structure of crystalline deoxyribose nucleic acid. *Nature* 172: 759-762, 1953.
11. Jacobson B. Hydration structure of sodium deoxyribonucleic acid and its physicochemical properties. *Nature* 172: 666-667, 1953.
12. Alberts B. DNA replication and recombination. *Nature* 421: 431-435, 2003.
13. Cooper GM. *Fundamentals of Molecular Biology, Heredity, Genes and DNA in The Cell: A Molecular Approach*, ASM Press Washington DC, 1996, pp: 87-135.
14. Friedberg EC. DNA damage and repair. *Nature* 421: 436-440, 2003.
15. Crick F. The double helix: a personal view. *Nature* 248: 766-796, 1974.
16. Abbas AK, Lichtman AH. *Antibodies and Antigens in Cellular and Molecular Immunology* (5th Ed). Saunders, Philadelphia, USA, 2003, pp: 43-64.
17. Nossal GV. The double helix and immunology. *Nature* 421: 440-444, 2003.
18. Kemp M. The Mona Lisa of modern science. *Nature* 421: 416-420, 2003.