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Milestones

DNA structure : James Watson and Francis Crick's moment of medical history

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The discovery of DNA (deoxyribose nucleic acid) structure was a giant step in biomedical science. Science is yet to exploit the full potential of the knowledge which came with it but huge strides have been made in all fields of medicine. In the specialty of obstetrics and gynecology, molecular medicine has brought about a sea change in practice. Our understanding of inherited disease and prenatal diagnosis is the area where the impact has been maximal. Diagnosis of infectious disease, understanding of the pathophysiology of obstetric phenomena such as preeclampsia and research are all being shaped by molecular medicine. The double helix structure of DNA (Figure 1) is arguably the most recognizable icon in biology, so it might at first appear strange that two of the three men awarded the Nobel Prize for its discovery were physicists.

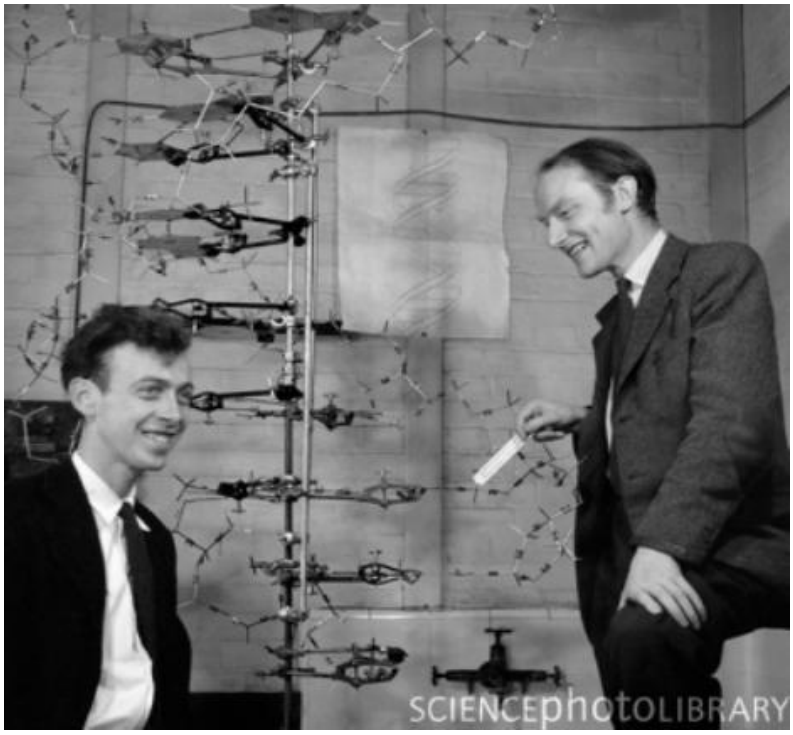

Figure 1. Watson and Crick with their DNA structure model.

In the early 1900s, despite some progress in chromosome research, genes were still very much an abstract concept, and many biologists were still convinced by the idea of an immaterial vital force. In 1935, Delbrück, a German physicist and later a Nobel Prize winner himself, proposed that genes were large molecules, consisting of bonds of thousand of atoms. Building on this concept, Erwin Schrödinger, an Austrian physicist, argued that life could be thought of in terms of storing and passing on biological information. He proposed a mind-expanding metaphor of a 'hereditary code-script' embedded in the molecular fabric of chromosomes. To understand life, then, we would have to identify these molecules, and crack their code. Schrödinger's metaphor of a readable book of life, a decipherable genetic code, might seem obvious now, but at the time this was a sensationally new concept [1]. The presence of DNA was known even in the 1800s. But it was Avery who identified it as the inheritance molecule. In the 1940s, time Maurice Wilkins and Rosalind Franklin, both working at King's College, London, were using X-ray diffraction to study DNA. This work would be the foundation on which Francis Crick and James Watson (Figure 2) would base their work on DNA structure.

Figure 2. James Watson and Francis Crick.

Francis Harry Compton Crick was born on June 8th, 1916, at Northampton, England, being the elder child of Harry Crick and Annie Elizabeth Wilkins. Crick was educated at Northampton Grammar School and at University College, London, obtained a B.Sc. in 1937. He started research for a Ph.D. under Prof E. N. da C. Andrade, but this was interrupted by the outbreak of war in 1939. During the war he worked as a scientist for the British Admiralty, mainly in connection with magnetic and acoustic mines. He left the Admiralty in 1947 to study biology. He became a research student in 1950, being accepted as a member of Caius College, Cambridge, and obtained a Ph.D. in 1954 on a thesis entitled X-ray diffraction: polypeptides and proteins. A critical influence in Crick's career was his friendship, beginning in 1951, with James Watson.

James Dewey Watson was born in Chicago, on April 6th, 1928, as the only son of James D. Watson, a businessman, and Jean Mitchell. His father's ancestors were originally of English descent and had lived in the midwest for several generations. Watson received a B.Sc. degree in Zoology from the University of Chicago. In 1950, he received his Ph.D. degree in Zoology. The subject of his study was the effect of hard X-rays on bacteriophage multiplication. He spent

his first postdoctoral Copenhagen as a Merck Fellow of the National Research Council. A chance meeting with Maurice Wilkins in 1951 stimulated him to change the direction of his research toward the structural chemistry of nucleic acids and proteins. He joined the Cavendish Laboratory at Cambridge in the following year.

In 1953, Linus Pauling, the great American chemist, claimed to have discovered the structure of the DNA molecule, but when Watson saw Pauling's research paper (which had not yet been published) he knew it was wrong. A few days later at King's College in London, Watson saw an X-ray diffraction photograph of the DNA crystal taken by Rosalind Franklin. "The instant I saw the picture, my mouth fell open and my pulse began to race," wrote Watson in his book The Double Helix (1968).[2] The photo convinced him that the DNA molecule must consist of two chains arranged in a paired helix, which resembles a spiral staircase or ladder. Watson and Crick set about developing a stick-and-ball model of DNA's possible structure. The sides of the ladder were made up of alternating molecules of phosphate and the sugar deoxyribose, while each rung on the ladder was composed of a pair of nitrogen-containing bases connected in the middle. At first, the scientists were uncertain how DNA's four bases — A, T, C, and G — link up with each other. Based on Chagraff's rule, they realized that the bases always join up with the same partners - A with T, and C with G. On March 7, 1953, Watson and Crick finished their model, which reached 6 feet tall. "We wish to suggest a structure for the salt of deoxyribose nucleic acid (DNA). This structure has novel features which are of considerable biological interest."[3] Those modest words were an understatement. By the late 1950s, their work had been widely accepted by the scientific community. In 1962, Watson and Crick received the Nobel Prize for Physiology or Medicine with Maurice Wilkins. He had published important crystallography work relating to DNA at the same time as Watson and Crick. Rosalind Franklin, whose photograph provided "a Eureka moment" for Watson, died in 1958 of cancer and could not be share the award.

They went on to receive numerous awards and honors together and individually including the Albert Lasker Award. Crick was awarded the Fellowship of the Royal Society in 1959. He worked on neurons and brain function at the Salk Institute, California. He passed away in 2004. Watson continued work in DNA research and was instrumental in obtaining funding for the Human Genome Project. He lives in California presently.

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