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A success story of DNA double helix

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History is the story of the achievements of men and women, but it records relatively few outstanding names and events. Many important contributions were by people whose names have been forgotten and whose accomplishments have been lost in the longer and deeper shadows cast by those who caught the fancy of the chroniclers. It has been said that in science the credit goes to the one who convinces the world, not to the one who first had the idea. Women are also not the exception here. There are notable examples of exceptional women not being publicly acknowledged for their contributions.

Lise Meitner (1878-1968):

A pioneer of nuclear physics; discovered element Protactinium; conducted experiments that led to fissioning of Uranium.

Similar is the case for Rosalind Franklin (1920-1958) conducted the research central to the discovery of DNA's double-helix structure that led to Watson and Crick being awarded the 1962 Nobel Prize.

Rosalind Elsie Franklin (25 July, 1920 Notting Hill, London-16 April, 1958 Chelsea, London)

She was an English biophysicist and X-ray crystallographer who made important contributions to the understanding of the fine molecular structures of DNA, viruses, coal and graphite.

Background:

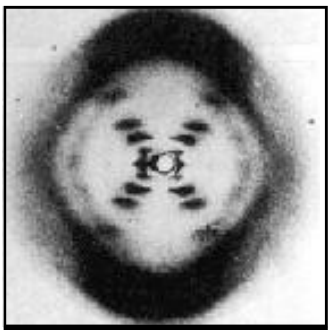
Franklin was born in Notting Hill, London into an affluent and influential British-Jewish family. Her father was Ellis Arthur Franklin (1894-1964), a London merchant banker and her mother was Muriel Frances Waley (1894-1976); she was the elder daughter and second of the family of five children. Franklin was educated at St Paul's Girls' School where she excelled in science, Latin and sport. Her family was actively involved with a Working Men's College, where Ellis Franklin, her father, taught electricity, magnetism and the history of the Great War in the evenings and later became vice principal. Later Franklin's family helped settle Jewish refugees from Europe who had escaped the Nazis.

There is probably no other woman scientist with as much controversy surrounding her life and work as Rosalind Franklin. Franklin was responsible for much of the research and discovery work that led to the understanding of the structure of deoxyribonucleic acid, DNA. Franklin excelled at science and attended one of the few girls' schools in London that taught physics and chemistry. When she was 15, she decided to become a scientist. Her father was decidedly against higher education for women and wanted Rosalind to be a social worker. Ultimately he relented, and in 1938 she enrolled at Newnham College, Cambridge, graduating in 1941. She held a graduate fellowship for a year, but quit in 1942 to work at the British Coal Utilization Research Association, where she made fundamental studies of carbon and graphite microstructures. This work was the basis of her doctorate in physical chemistry, which she earned from Cambridge University in 1945. After Cambridge, she spent three productive years (1947-1950) in Paris at the Laboratoire Central des Services Chimiques de L'Etat, where she learned X-ray diffraction techniques. In 1951, she returned to England as a research associate in John Randall's laboratory at King's College, Cambridge.

It was in Randall's lab that she crossed paths with Maurice Wilkins. She and Wilkins led separate research groups and had separate projects, although both were concerned with DNA. When Randall gave Franklin responsibility for her DNA project, no one had worked on it for months. Wilkins was away at the time, and when he returned he misunderstood her role, behaving as though she were a technical assistant. Both scientists were actually peers. His mistake, acknowledged but never overcome, was not surprising given the climate for women at Cambridge then. Only males were allowed in the university dining rooms, and after hours Franklin's colleagues went to men-only pubs. Rosiland But Franklin persisted on the DNA project. J. D. Bernal called her X-ray photographs of DNA, "the most beautiful X-ray photographs of any substance ever taken." Between 1951 and 1953 Rosalind Franklin came very close to solving the DNA structure. She was beaten to publication by Crick

and Watson in part because of the friction between Wilkins and herself. At one point, Wilkins showed Watson one of Franklin's crystallographic portraits of DNA. When he saw the picture, the solution became apparent to him, and the results went into an article in Nature almost immediately. Franklin's work did appear as a supporting article in the same issue of the journal.

"As a scientist Miss Franklin was distinguished by extreme clarity and perfection in everything she undertook. Her photographs are among the most beautiful X-ray photographs of any substance ever taken. Their excellence was the fruit of extreme care in preparation and mounting of the specimens as well as in the taking of the photographs."



J.D. Bernal

A chemist by training, Franklin had established herself as a world expert in the structure of graphite and other carbon compounds before she moved to London. In James Watson's account of the discovery of the structure of DNA, entitled The Double Helix, Rosalind Franklin was depicted inaccurately as an underling of Maurice Wilkins at King's College. In fact, Maurice Wilkins and Rosalind Franklin were peers. Franklin had discovered that DNA could crystallize into two different forms, an A form and a B form. John Randall gave Franklin the A form and Wilkins the B form, assigning them each the task of elucidating their molecular structure. The technique with which Wilkins and Franklin set out to do this is called X-ray crystallography. With this technique a crystal is exposed to x-rays in order to produce a diffraction pattern. If the crystal is pure enough and the diffraction pattern is acquired very carefully, it is possible to reconstruct the positions of the atoms in the molecules that comprise the basic unit of the crystal called the unit cell. By the early 1950s, scientists were just learning how to do this for biological molecules as complex as DNA. Progress in discerning the structure of DNA was blocked because the A and B forms of DNA were mixed together in preparations, yielding impure crystals and "muddy" diffraction patterns that were near impossible to interpret.

After discovering the existence of the A and B forms of DNA, Rosalind Franklin also succeeded in developing an ingenious and laborious method to separate the two forms, providing the first DNA crystals pure enough to yield interpretable diffraction patterns. She then went on to obtain excellent X-ray diffraction patterns of crystalline B-form DNA and, using a combination of crystallographic theory and chemical reasoning, discovered important basic facts about its structure. She discovered that the sugar-phosphate backbone of DNA lies on the outside of the molecule, not the inside as was previously thought. She discovered the helical structure of DNA has two strands, not three as proposed in competing theories. She gave quantitative details about the shape and size of the double helix. The all- important missing piece of the puzzle, which she could not discover from her data, was how the bases paired on the inside of the helix, and thus the secret of heredity itself. That discovery remained for Watson and Crick to make.

After Randall presented Franklin's data and unpublished conclusions at a routine seminar, aspects of her results were informally communicated to Watson and Crick by Maurice Wilkins and Max Perutz, without her or John Randall's knowledge. It was Watson and Crick who put all the pieces of the puzzle together from a variety of sources including Franklin's results, to build their ultimately correct and complete description of DNA's structure. Their model for the structure of DNA appeared in the journal Nature in April, 1953, alongside Franklin's own report.

Rosalind Franklin never knew that Watson and Crick had gotten access to her results. At the time of the Watson and Crick publication and afterwards, Franklin appears not to have been bitter about their accomplishment. In her own publications about DNA structure, she agreed with their essential conclusions but remained skeptical about some details of their model. Franklin moved on to work on an even more challenging problem: the structure of an entire virus, called the Tobacco Mosaic Virus. Her subsequent publications on this topic would include four more papers in the journal Nature. Rosalind Franklin was friendly with both James Watson and Francis Crick, and communicated regularly with them until her life and career were cut short by cancer in April of 1958, at the age of 37. She died with a reputation around the world for her contributions to knowledge about the structure of carbon compounds and of viruses. After her death, Watson and Crick made abundantly clear in public lectures that they could not have discovered the structure of DNA without her work. However, because the Nobel Prize is not awarded posthumously, Rosalind Franklin could not be cited for her essential role in the discovery of the physical basis of genetic heredity.

Important contributions:

Work on DNA forms:

Rosalind Franklin made crucial contributions to the solution of the structure of DNA. She discovered the B

form, recognized that two states of the DNA molecule existed and defined conditions for the transition.

Work on tobacco mosaic virus:

Using the method of isomorphous replacement, she showed that the virus particle was not solid, as had been previously thought, but actually a hollow tube. Her work showed that the ribonucleic acid was not to be found in the central cavity but embedded in the protein.

Work on carbons:

In a series of beautifully executed researches, she discovered the fundamental distinction between carbons that turned into graphite on heating and those that did not and further related this difference to the chemical constitution of the molecules from which the chars were made.

Illness and death:

In the summer of 1956, while on a work related trip to the USA, Franklin first began to suspect a health problem. An operation in September of the same year revealed two tumors in her abdomen. After this period and other periods of hospitalization, Franklin spent time convalescing with various friends and family. These included Anne Sayre, Crick and his wife Odile, with whom Franklin had formed a strong friendship. Even while undergoing cancer treatment Franklin continued to work and her group continued to produce results, seven papers in 1956 and a further six in 1957.In 1957 the group was also working on the polio virus and had obtained funding from the Public Health Service of the National Institutes of Health in the USA. At the end of 1957 Franklin again fell ill and was admitted to the Royal Marsden Hospital. She returned to work in January 1958 and was given a promotion to *Research Associate in Biophysics*. She fell ill again on the 30th of March and died on 16 April 1958 in London, of bronchopneumonia, secondary carcinomatosis and carcinoma of the ovary. Exposure to X-ray radiation is sometimes considered a possible factor in her illness. Her death certificate read: A Research Scientist, Spinster, Daughter of Ellis Arthur Franklin, a Banker.

Rosalind Franklin is described as the “dark lady of DNA” by Brenda Maddox, who has written book on Franklin, saying “Franklin was instrumental in discovering structure of DNA, but she wasn’t altogether ignored.”