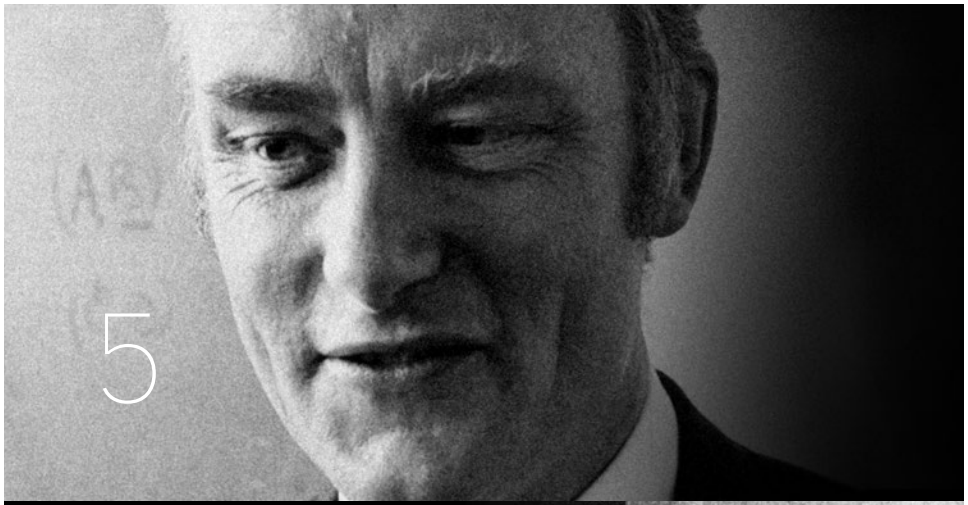

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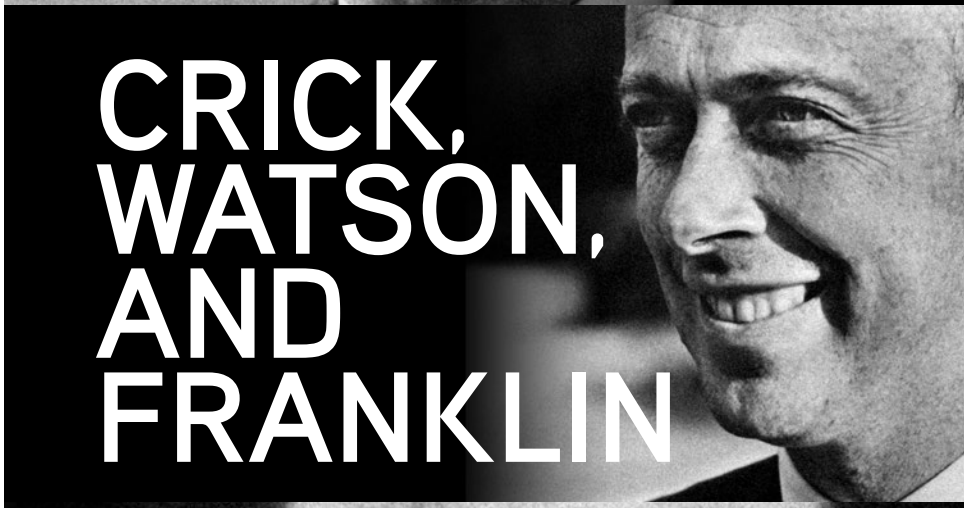
CRICK, WATSON, AND FRANKLIN



BIOGRAPHY

1220L

BIG HISTORY PROJECT

Rosalind Franklin

Born
July 25, 1920
London

Died
April 16, 1958
London

Francis Crick

Born
June 8, 1916
Northampton, England

Died
July 28, 2004
San Diego, California

James Watson

Born
April 6, 1928
Chicago, Illinois

CRICK, WATSON, AND FRANKLIN

THE RACE TO DISCOVER THE STRUCTURE OF DNA

By Cynthia Stokes Brown

In 1953, three English biochemists helped unlock the mystery of life by determining the double helix structure of the DNA molecule. Found in all life on Earth, DNA contains the information by which an organism regenerates its cells and passes traits to its offspring.

Setting the Stage

Despite his success in formulating the theory of natural selection, Charles Darwin did not yet understand how characteristics are passed from parent organisms to their offspring with the slight changes that make evolution possible and identify each individual.

By the middle of the twentieth century this was still not well understood. The first part of the century had seen major breakthroughs in physics, such as Einstein's Theory of Relativity and atomic bombs that used the energy of nuclear fusion. After World War II, scientists turned to understanding the physical basis (atomic and molecular) of biological phenomena.

In the 1950s, biochemists realized that DNA, short for deoxyribonucleic acid, delivered the instructions for copying a new organism. A yard of DNA is folded and packed into the nucleus of every cell in pairs called "chromosomes," with one exception: in the reproductive cells, where the pieces of DNA are not paired.

DNA has three constituents: 1) a type of sugar called "ribose"; 2) a phosphate (phosphorous surrounded by oxygen) responsible for its acidity; and 3) four kinds of bases — adenine (A), thymine (T), guanine (G), and cytosine (C). Since these four bases seemed too simple to be able to pass on all the information needed to create a new organism, biochemists were baffled about DNA's structure and how it worked. However, these four bases combine like letters of an alphabet to describe complex variations in genetic traits.

The question became how to study the DNA molecule. Biochemists believed that understanding its structure would reveal how the molecule coded the instructions for copying a new organism. They began taking X-ray images of crystals of DNA, believing that its crystallization meant it must have a regular structure. The pattern of the X-rays bouncing off atoms (a phenomenon called "diffraction") gave information about their location in the molecule. One of the pioneers of this technique, called "X-ray crystallography," was Linus Pauling, who worked at the California Institute of Technology in Pasadena. In the early 1950s, Pauling, a prominent chemist doing molecular

research in the States, seemed a likely candidate to unlock the mystery of life, since he had already concluded that the general shape of DNA must be a helix, or spiral.

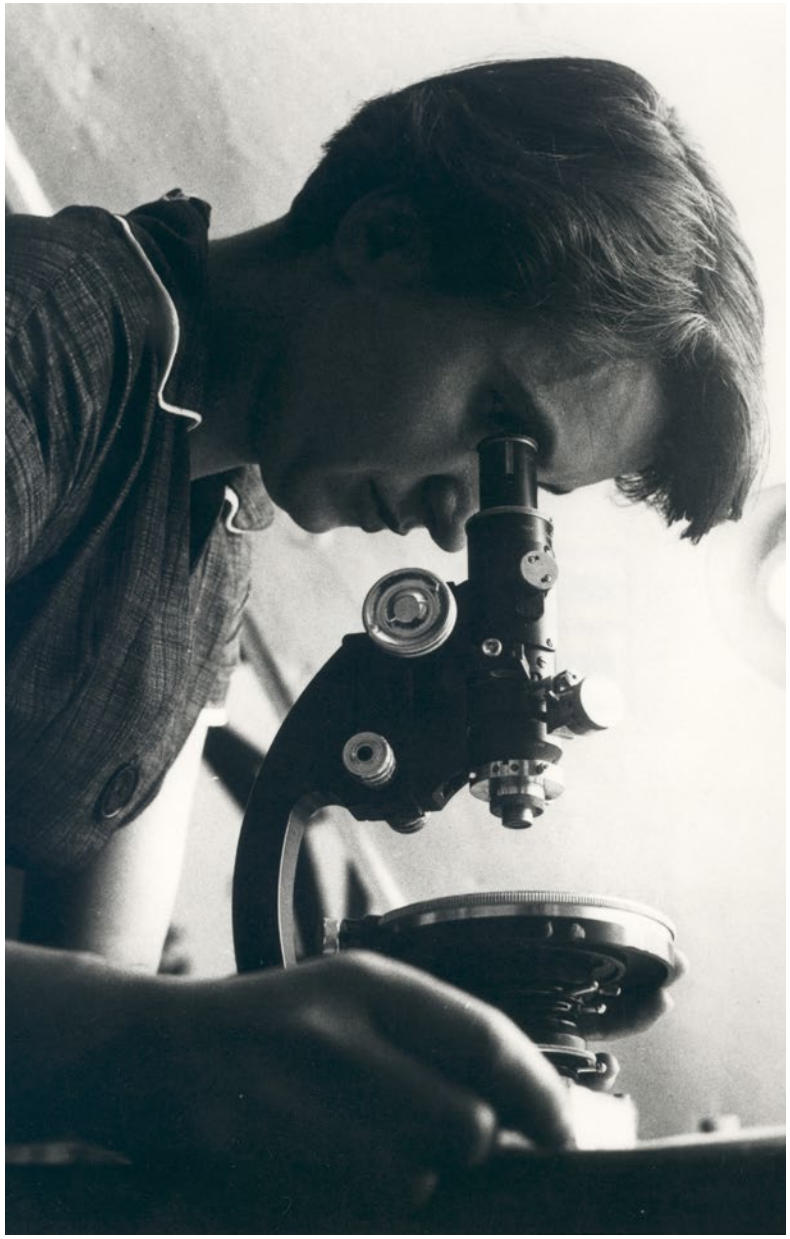
The race

The victory, however, went to three people working in England, in one of the great scientific races of all time. One, Rosalind Franklin, was working at King's College at the University of London. The other two, James Watson and Francis Crick, were friends and lab mates some 50 miles away at the Cavendish Laboratory at Cambridge University, where they worked cooperatively and shared their ideas.

Franklin was from a wealthy, influential family in London. She had earned her PhD in 1945 from Cambridge in physical chemistry. Starting at King's College in 1951 at the age of 31, she was focused on studying DNA. She became extremely skilled in X-ray crystallography, able to produce clear and accurate diffraction images of DNA crystals by using fine-focus X-ray equipment and pure DNA samples.

Over in Cambridge, biochemists were supposed to leave the study of DNA to the lab at King's College. Francis Crick, age 35 in 1951, was working on his PhD in the crystallography of proteins. He had grown up in a small English village and, since he had failed to qualify for Cambridge, took his undergraduate degree in physics from the University of London. Watson, only 23 in 1951, was at Cambridge as a post doctorate fellow in biology with limited knowledge of chemistry. He had grown up in Chicago, performed on the national radio show "Whiz Kids," entered the University of Chicago at age 15, and secured his doctorate from the University of Indiana at just 22. He was at the Cambridge lab to learn crystallography.

Between 1951 and January 1953, Franklin reasoned through her precise X-ray diffraction images that: 1) DNA takes two forms (shorter-dryer and longer-wetter), 2) the sugar-phosphate backbones must be on the outside, and 3) the molecule looks the same upside down or right side up. In late 1952, she



Rosalind Franklin working at King's College in London

recorded an especially clear X-ray diffraction image that her colleague, Maurice Wilkins, later showed to Watson in January 1953 without telling Franklin or asking her permission. Franklin and Wilkins did not always communicate well, so his actions were perhaps not surprising.

Watson knew at once from seeing Franklin's photograph that DNA had to be a helix with certain dimensions. He was so excited that he returned to his lab to draw up plans for models that the machine shop would construct out of sheet metal and wire.

In building their models, Watson and Crick had to find the answers to several questions. How many strands did the helix have? Which direction did the strands run? Were they on the inside or the outside? How were the four chemical bases arranged?

While Franklin believed the answers would come with more X-ray images of better quality, Watson and Crick recognized they were racing against Linus Pauling for a solution and thought that making a model would speed up the answers. First, they tried using two strands, putting them in the center of the model with the bases on the outside; however, this did not produce a chemically acceptable structure.

Next, they played around with the shapes of the four bases, using paper models and combining them in different ways. Finally, they visualized a structure that solved the puzzle: If two of the bases were bonded in pairs (G with C), they took up the same space as the other pair (A with T). Hence, they could be arranged like steps on a spiral staircase inside of two strands of sugar-phosphates running in opposite directions.

These insights occurred to Crick and Watson between February 4 and 28, 1953, when they announced at lunch in their usual pub that they had found the secret of life.

The news gets out

The April 25, 1953, issue of *Nature* published Crick and Watson's 900-word article, "A Structure for Deoxyribose Nucleic Acid." Wilkins and Franklin, who both accepted Crick and Watson's solution, wrote accompanying articles. By the 1960s, scientists generally embraced the double helix as the structure of DNA, and in 1962, Wilkins, Watson, and Crick received the Nobel Prize in medicine/physiology for their work.

Franklin could not share in the prize as it cannot be granted to someone who has passed away. She had died from ovarian cancer at the age of 37 on April 16, 1958, in London. She had a family history of cancer, but her exposure to X-rays may have contributed to her death. And in any case, she may not have had the chance for the award had she been alive. Crick and Watson

James Watson and Francis Crick in 1959

never told Franklin that they had used her images. She was mentioned only in passing by Crick and Watson in *Nature*. Nor did Watson explain this in his popular account of their discovery, *The Double Helix* (1968).

It wasn't until much later that Watson finally admitted in public that he and Crick could not have found the double helix in 1953 without Franklin's experimental work. If she had survived, would she have been acknowledged and shared in the prize?

In their 1953 article, Watson and Crick did not discuss how DNA copies itself. They simply included this sentence: "It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material."

Five weeks after their first article in *Nature*, Crick and Watson published another article proposing the idea that, to make a copy, the double helix unzips, or separates, into two strands — each a backbone of sugar-phosphates with the four bases attached in some sequence. Then the cell uses each strand as a template to assemble another DNA strand from free-floating complementary bases: A picks up T, while C picks up G. This would result in two identical DNA molecules, one a copy of the other. Occasional mistakes in copying enable evolution to occur and each organism to be unique. This idea has been confirmed, while the means for carrying it out have proved to be immensely complex.

Crick continued his research in England until 1976, when he moved to the Salk Institute for Biological Studies in La Jolla, California, where he died in 2004. Watson returned to the United States, researching at Harvard from 1956 to 1976. He helped establish the Human Genome Project in the early 1990s and served as president of the Cold Spring Harbor Laboratory on Long Island, New York, until his retirement in 2007.

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