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Rosalind Franklin (1920-1958)

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Photo 51 and the unveiling of DNA

DNA has been known for quite some time. In 1869, the Swiss biochemist Johann Miescher did a series of experiments on a cell type that was then abundantly available: pus cells. From their nucleus, he extracted a phosphoric substance he called *nuclein*. The function of this substance, later called deoxyribonucleic acid (DNA), was a mystery. Toward the end of the 1940's, it was discovered that it had to be an unbranched chain molecule. Erwin Chargaff found out that it always contained equal amounts of A and T (adenine and thymine), and equal amounts of G and C (guanine and cytosine). Those bases therefore had to be coupled somehow to one another.

In the meantime, Oswald Avery discovered that DNA, at least in bacteria, was the carrier of genetic information. When scientists realized DNA might well be the source code of life itself – including in human beings – they fervently started looking for its structure. The greatest chemist of those days, the American Linus Pauling, proposed an alpha helix structure in 1951, but unfortunately this did

not match the X-ray diffraction analysis. In January 1953 he proposed a different DNA model – a triple spiral – but this too was incorrect. Eventually, two young scientists from Cambridge solved the puzzle. In April 1953, James Watson and Francis Crick published their double helix model in the prestigious journal Nature. In 1962, they received the Nobel Prize in Medicine for it. Missing from the ceremony however, was a young woman who had nevertheless played a crucial role with her "X-ray-photo 51". Her name was Rosalind Franklin.

Rosalind Franklin

Rosalind was born on July 25th, 1920, in a middle class British-Jewish family. After primary school, she went to St. Paul's Girls School, one of the few girls' schools where physics and chemistry was taught. When she was fifteen years old, she knew what she wanted to become: scientist. But her father thought higher education did not suit a woman, so he refused to pay for a university degree. Luckily, Rosalind found an ally in her aunt. When her mother also supported her choice, her father finally agreed.

In 1938 Rosalind studied physical chemistry at the Newham College in Cambridge. After her degree, the Second World War immediately provided her with a research project. To utilise the coal supply as efficiently as possible in war time, she was appointed by the British Coal Utilisation Research Association to study the physio-chemical properties of this fossil fuel. This led to a thesis in 1945, which awarded her with a PhD. One of her colleagues was a French girl who had fled the Nazi terror in France. Now that the war was over, she wanted to go back to Paris and she asked Rosalind if she fancied joining her there. Because Rosalind didn't have any other projects, she accepted the offer. In Paris she worked under the direction of professor Jacques Mering in the "Laboratoire Central des Services Chimiques de l'Etat". It was a pleasant work environment and professor Mering developed a little crush on her. But his knowledge of X-ray diffraction analysis pleased her even more. In three years' time, Rosalind learned the techniques necessary to study the three-dimensional structure of complicated molecules using X-rays.

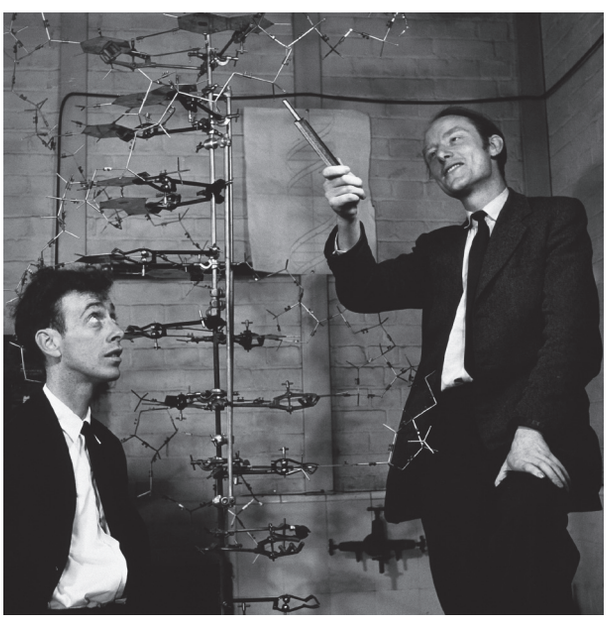

Fig. 2. — James Watson and Francis Crick

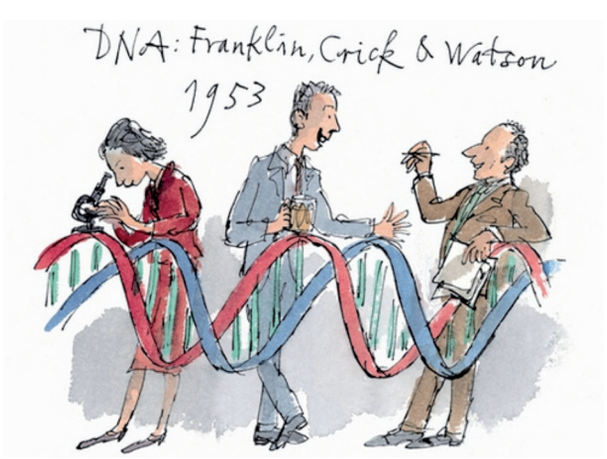

Fig. 3. — Cartoon by Quentin Blake

Victorian London

Back in London, she applied to King's College in 1948, in the department of Sir John Randall. Given her experience in X-ray diffraction analysis, she was hired immediately. Randall confirmed her appointment in a letter, but he failed to mention a certain Maurice Wilkins, who had been working for some years now in the same experimental division. When Wilkins returned from holidays, he suddenly found himself eye to eye with a young unknown woman, in *his* lab, fiddling with *his* equipment! He asked her if she was the new assistant, but when Rosalind answered that professor Randall had hired her to adjust the X-ray diffraction technique, Wilkins almost exploded at the scene. Giving away his job, or even worse, *sharing* his job with a woman? Never!

The race to fame

In the race to figure out the DNA structure, many scientists besides Linus Pauling were in the running. Among them were two young, then still unknown chemists from Cambridge, James Watson and Francis Crick. They were well aware of everything there was to know about DNA at that time, but they

Fig. 4. — Rosalind in the laboratory in Paris

didn't conduct experimental research themselves. When Pauling presented his triple helix model, they crafted a 3D model with wire and clothe pins, but they could take it down again after having heard Rosalind Franklin at a seminar. With her X-ray diffraction analysis, she had discovered that DNA could not be a triple helix chain. It was a double helix. When Rosalind revealed at the end of her lecture that she had already notified Linus Pauling of these findings, Watson and Crick realised they had no time to lose. In order to be quicker than their redoubtable competitor, they had to act fast. Immediately they rebuilt their triple helix model to a double helix, even though they didn't know what to do with the protruding base pairs A-T and G-C. No matter how much they turned or flipped these purines, their monstrous palisade didn't reveal its secrets. An important piece was missing.

Photo 51

While Watson and Crick were feverishly putting together their model in Cambridge, Rosalind was quietly researching further the X-ray diffraction properties of DNA. One day, she succeeded in taking a very clear photo. The central "X" and the expanding dots in "Photo 51" pointed her strongly towards the conclusion that DNA had to be a double helix. And the base pairs A-T and G-C weren't located on the outside of the structure, but on the inside. Theoretically, she was now the first to conceptualise the structure of DNA, but as a fundamental scientist she remained cautious. Before publishing her idea, she wanted to gather some extra evidence. What she had overlooked though, was that her aggrieved colleague Maurice Wilkins, eager for vengeance, had been secretly transferring her notes and results to his friends at Cambridge. When Wilkins one day – without her knowing – showed

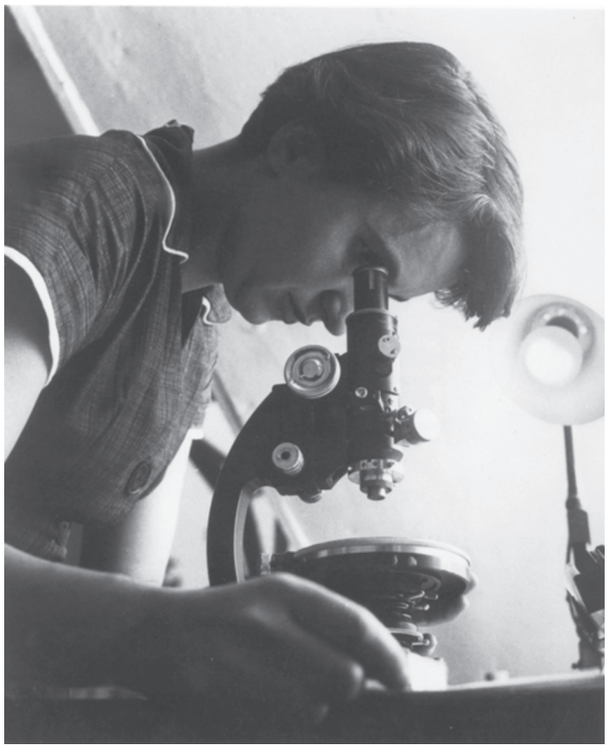

Fig. 5. — First Class Scientist Rosalind Franklin

them the "photo 51", Watson instantly got a *Eureka-erlebnis*. This was it! This was the missing piece.

What Rosalind hadn't dared to do, the Cambridge boys had no problem with. In the next issue of Nature, they published their DNA model, which later proved to be the right one. They became world famous. Watson and Crick had outrun their competition, Linus Pauling. And Rosalind too. In their article, her crucial "photo 51" isn't mentioned at all. They did include an uninformative foot note: "We have also been stimulated by a knowledge of the general nature of the unpublished experimental results and ideas of Dr. M. H. F. Wilkins, Dr. R. E. Franklin and their co-workers at King's College, London."

When John Randall, the head of the department of Experimental Research at King's College, found out that two young chemists from Cambridge had taken all the credits, he tried to save what could still be saved. He insisted that Nature published an article of his team in the same issue, describing the experimental data that he, Wilkins and Rosalind Franklin had discovered. Cambridge might have taken the credit, but it had been their X-ray diffraction research that had substantially contributed to the research.

Birkbeck

In the fall of that year, Rosalind received an offer to work with John Bernal in Birkbeck. She gladly

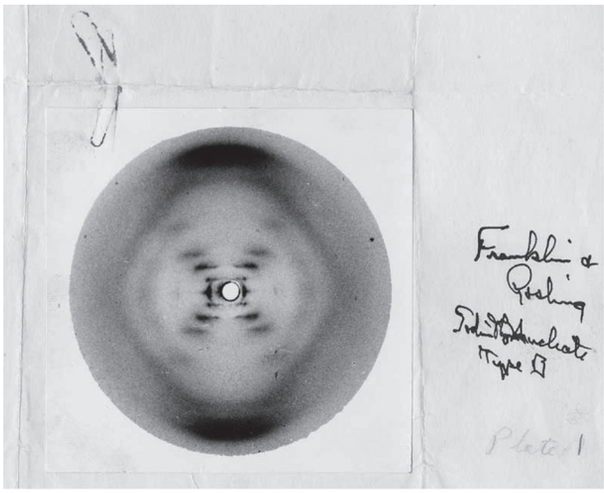

Fig. 6. — The famous photo 51

took this opportunity to flee the hostile environment at King's College London, and especially its incarnation, Maurice Wilkins. But additionally, John Bernal offered her an even greater challenge: to decipher the tobacco mosaic virus (TMV). Quickly, Rosalind got results and published in Nature again. In an article of 1955, she stated that all TMV particles are of the same length. This was in contradiction with the view of one of the most eminent virologists of those days, Normal Pirie, but it turned out her observation was right. The laboratory of Birkbeck might not have been as well equipped as London's, it produced some remarkable results. Even more so when Rosalind started to collaborate with a couple of passionate chemists, among which Aaron Klug, who would receive the Nobel Prize in Chemistry in 1982.

The woman in Rosalind

First and foremost, Rosalind was a scientist. One of the purest breed. She had the brains and the curiosity necessary to investigate each unexplored territory. She was very experienced and continued to refine her techniques. In her DNA research, she only worked with the purest extracts and always knew exactly where to found them. In 1953, she was the only one who would have been able to shoot that flawless *photo 51*. But she was a woman, and in conservative England, this was a handicap. Men in those days didn't know how to handle women, let alone women who read novels by Albert Camus, listened to Mahler's symphonies and knew more about X-ray diffraction than they did! In their exclusive clubs, refectories and smoking salons, such an unattainable woman could only be referred to as "that frigid girl". But Rosalind was far from frigid. In her spare time, she liked to dance, swim and hike in the mountains. People who knew her a bit better, knew that she could be joyful and elated, and that she loved children. On top of that, she certainly wasn't unattractive. Her Parisian professor wasn't the only one of her colleagues who fell in love with her. She never reciprocated these feelings, though. Usually these men were already married, or like professor Mering, had a couple of mistresses on the side. For as far as we know, Rosalind was never rancorous because of the foul play that had occurred behind her back. With Watson and Crick, she continued to have friendly relations. James Watson even supported her wholeheartedly when she asked for a stipend to work with Aaron Klug. With Francis Crick too, she maintained a friendly correspondence in the years 1956 and 1957. Crick's wife even became her best friend. The only one she didn't want to have anything to do with anymore, was this prototype of the Victorian bungler and dirty spy, Maurice Wilkins.

Last years

In the laboratory of Birkbeck, Cupid finally struck. Rosalind fell in love with an American researcher, Don Casper. Unfortunately, the romance was short-lived. During a journey to America, where she had been invited to give some lectures, she felt a lump in her lower abdomen. Back in London, it turned out to be bilateral ovarian cancer. She had surgery, but the tumour had metastasized already. In an era without chemotherapy, she knew she didn't have long. Because her mother reacted rather hysterically, she decided to move in with friends

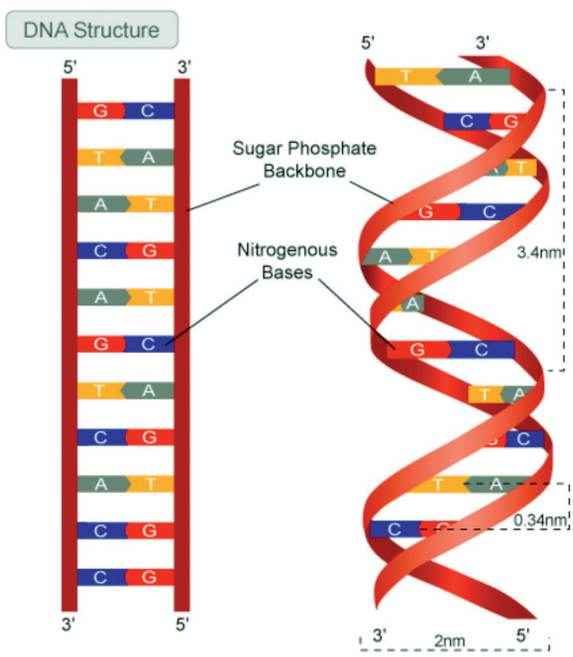

Fig. 7. — The DNA structure

like Francis Crick and his wife Odile. Despite her sad fate, Rosalind kept on working. Together with her team she published seven more articles in 1956 and six more in 1957. But when she turned to X-ray diffraction analysis of the poliovirus, she had to give up. A lifelong exposure to X-rays had eventually gotten the upper hand. She died on April 16th, 1958 in Chelsea, London.

P.S.

In his autobiography, "The Double Helix", Watson quite undervalued Rosalind's role in the discovery of the DNA structure. On top of that, he painted a rather unflattering picture of "Rozy", as he called her somewhat contemptuously. Rozy was naïve, frigid, didn't use lipstick and her dresses were off-putting. Later, he regretted this. In the end, both Watson and Crick had to admit that they would never have discovered the *source code of life* without that remarkable and clarifying *photo 51*.