

My Letter From Francis Crick by George Johnson

(originally posted on my blog for Discover Magazine's website, 4/19/13)

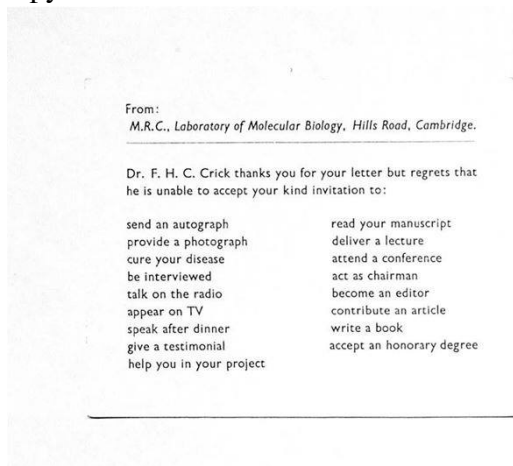
Earlier this year, the 23-karat gold medal awarded to Francis Crick was auctioned off for £1.3 million, or more than \$2 million. When I heard the news, I thought it seemed a little tacky. Then I went on to read that Crick's family will donate 20 percent of the money to the establishment of the Francis Crick Institute in London. That took out some of the sting.

Not long afterward another bit of Crick memorabilia went on the auction block at Christie's: a letter, dated March 19, 1953 from Crick to his 12-year-old son, Michael, who was away at boarding school. It went for £3.45 million or about \$5.3 million. Half will go to the Salk Institute in La Jolla, where Crick worked for many years.

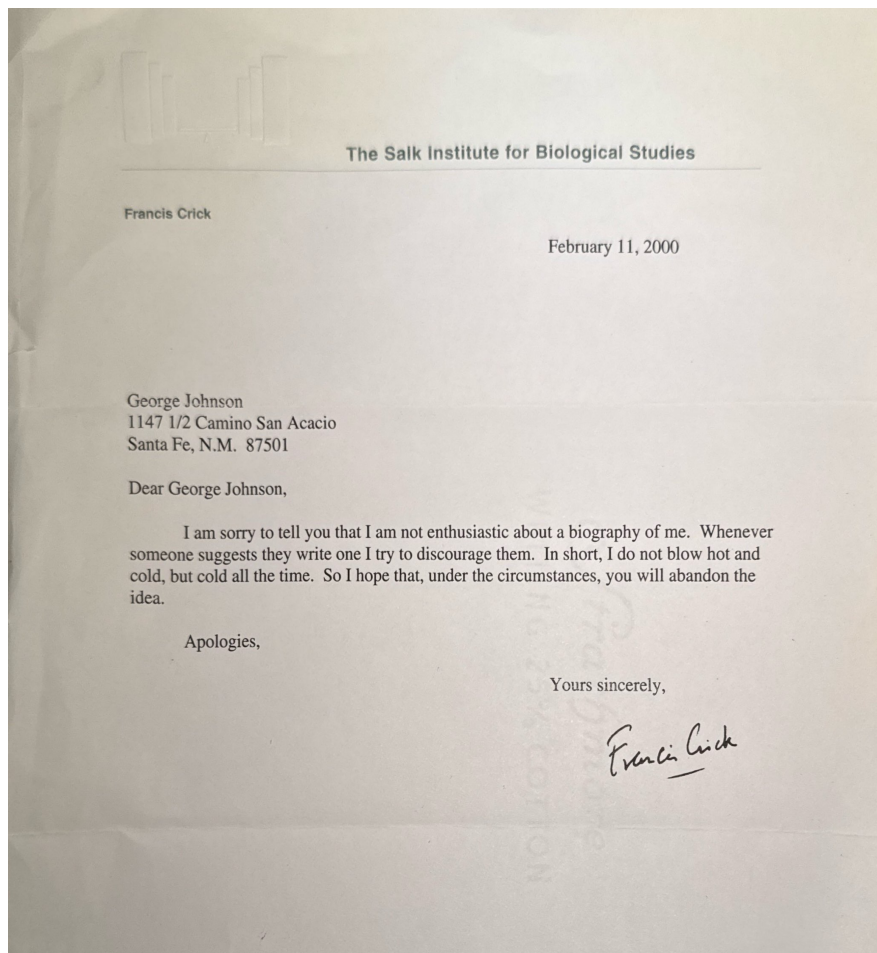
It is easy to see why the letter was worth so much more than the piece of gold. In just a few hundred words, Crick provides as crisp a description of DNA as you will every see, complete with his hand-drawn sketch of the double helix and other rough diagrams. It was a discovery clear enough for a 12-year-old to understand, and one that completely transformed the life sciences.

I have my own letter from Crick, long buried in a file drawer in my office, though I doubt it would fetch much on the market. In the year 2000 after my biography of Murray Gell-Mann was published, I heard from a reader in Pasadena. He knew Crick, and he was urging me to write his biography. He offered to ease the way by approaching the great man himself. I wasn't certain that I was ready to take on another huge project but I followed up with a letter, sounding Crick out about the idea.

I was spared the postcard Crick was famous for using to fend off any and all requests. Here is a copy from the Francis Crick Archive at the Wellcome Library:



But I did receive a short reply:



And so I did. Nine years later Robert Olby, a historian of science, published *Francis Crick: Hunter of Life's Secrets*.

Brenda Maddox is now doing Watson's life story. She is also the author of *Rosalind Franklin: The Dark Lady of DNA*, which probably did more than anything to bring recognition to Franklin — both for the important role her x-ray crystallographic work played in the discovery of the double helix and for the condescending way she was treated by Watson and other colleagues. Many people were surprised last month when, in a short essay on DNA's 60th anniversary, she ended like this:

Watson has been much criticized for his portrayal of the “terrible Rosie” in *The Double Helix* but, as Franklin's biographer, my answer to critics is that if it weren't for Watson, no one would have heard of Rosalind Franklin. . . .

I guess it is natural for a biographer's allegiances to shift with a change of subjects. We won't really know until her book is published.

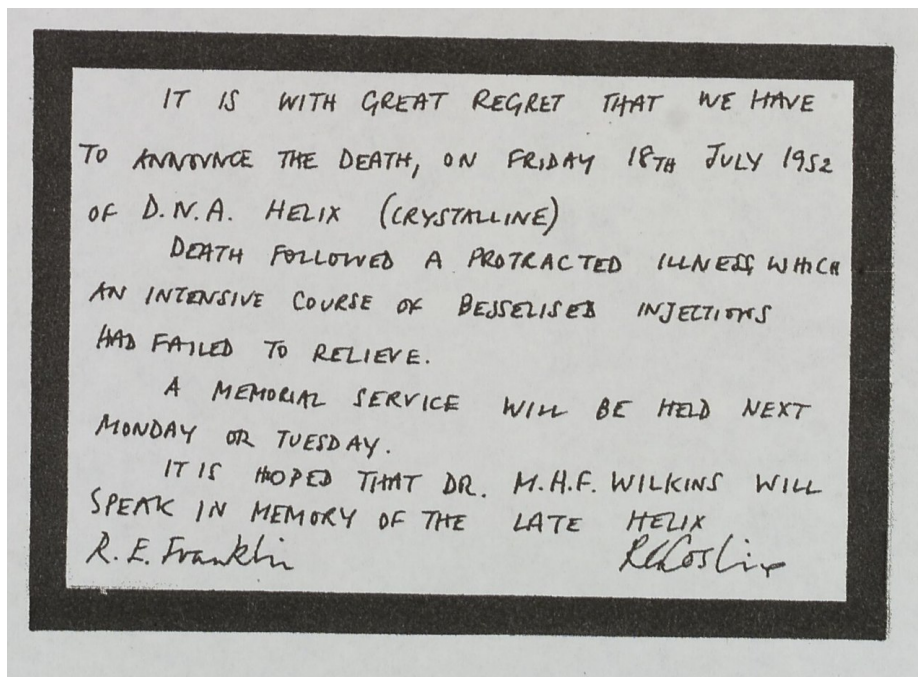
Meanwhile I was reminded of a remarkable section in Judson's *The Eighth Day of Creation* where he recreates, through Franklin's journal and other sources, what she knew and when she knew it, every step along the way. He writes of her "grievous slowness of intuitive response," of her working "head down and doggedly, ingeniously struggling in the wrong direction." "It is easy to feel great sympathy with Franklin," he concludes. "The fact remains that she never made the inductive leap."

I went back and reread those passages a couple of nights ago and then got a copy of Maddox's book from the local library. I'm still trying to reconcile the two accounts and will write more about that in my next installment. – George Johnson, talaya.net

On DNA's Anniversary: How Rosalind Franklin Missed the Helix

(originally posted on my blog on Discover Magazine's website, 4/25/13)

Less than a year before Watson and Crick's paper, "A Structure for Deoxyribose Nucleic Acid," was published in *Nature*, 60 years ago today, Rosalind Franklin sent around a hand-lettered obituary:



Wellcome Collection

Led astray by her own evidence, she had missed, just barely, making the greatest discovery in the history of biology: the coiled, interlaced structure that explained with such clarity the working of the gene. "The secret of life," Crick called it.

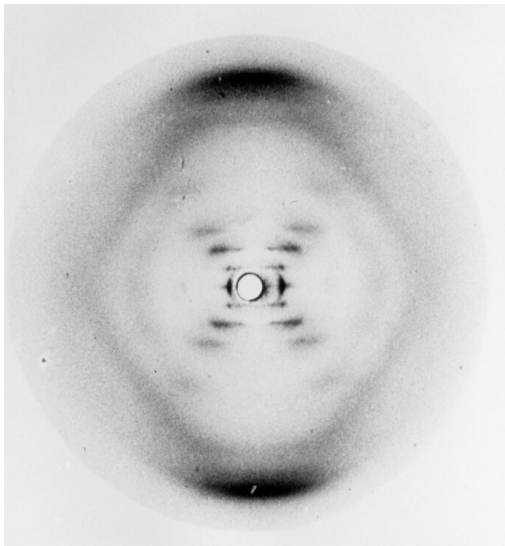
Gosling, the other signatory, was Franklin's assistant at King's College in London, and Wilkins was her boss and *bête noire*. "Besselised" refers to Bessel functions, a mathematical tool

used to analyze the photographic images she so expertly produced of DNA. But the most significant word in her mocking postcard was the one in parentheses: crystalline.

Several months earlier, having mastered better than anyone a technique called x-ray crystallography, she had taken the clearest pictures yet of the molecule. It came in two forms, depending on whether it was crystallized (shape A) or dissolved in water (shape B). It was the longer, stretched-out wet form, her Photo 51, that went on to become legendary. Horace Freeland Judson describes it in *The Eighth Day of Creation*:

The overall pattern was a huge blurry diamond. The top and bottom points of the diamond were capped by heavily exposed, dark arcs. From the bull's-eye, a striking arrangement of short, horizontal smears stepped out along the diagonals in the shape of an X or a maltese cross. The pattern shouted helix.

The question that has dogged historians ever since is why Franklin didn't shout out the same. Instead she put image B aside, concentrating instead on the far less certain pattern in image A. No matter how hard she looked, she couldn't see a helix there.



Franklin's Photo 51. King's College London

She bristled when Crick, working with Watson at the Cavendish Laboratory in Cambridge, told her she was allowing herself to be misled by ambiguous markings and that both forms must be helical. But she couldn't be persuaded. Cautious by nature, she believed in holding back on interpretation and grand theories until all the data were gathered and understood, the seeming contradictions resolved. Her style was to work from the bottom up, meticulously trying to piece together the big picture.

She thought it was rash and premature that Crick and Watson, with their top-down approach, were enthusiastically building models — castles in the air — before they had laid the foundation.

As they put together their sheet-metal and wire sculpture, the details, they believed, could be filled in along the way.

By now Crick was already puzzling over what he saw as the next key issue: How are the nucleotide bases (what we now think of as the DNA letters) zipped together in pairs? He assumed it would be a matter of like with like — that adenine would stick to adenine, thymine to thymine, cytosine to cytosine, guanine to guanine. Then a mathematician told him that his calculations showed the pairing was complementary: A-T, C-G. Crick also finally saw the significance of Chargaff ratios. In his analysis of nucleic acid, Erwin Chargaff at Columbia had shown that A and T and C and G exist in roughly the same proportions. Suddenly it all made sense: two interlocking helical templates forming a molecule that could carry information, and that could replicate.

Over a span of about 40 pages, Judson explains the reasoning with a satisfying verve and turns the realizations and false leads into an absorbing drama. At first Watson had the helix inside out. Then he tried to cram together, like mismatched puzzle pieces, the wrong forms for the bases. In the final weeks before the discovery, another contender, Linus Pauling in Pasadena, had convinced himself that DNA was a triple helix. (Watson and Crick had been up that cul-de-sac before.) Meanwhile Franklin had become intent on proving that DNA — the crystal, at least (it's not entirely clear what she was thinking) — was shaped like a figure 8. All the while her image B remained on a shelf, in a filing cabinet — wherever it was kept — ignored month after month until Wilkins showed it to Watson, resulting in his famous epiphany. A few weeks later he and Crick had the structure.

After negotiations between both labs, papers by Wilkins and by Franklin and Gosling appeared in the same issue of *Nature* along with the one by Watson and Crick. (They can all be found on a website at *Nature*, and an annotated version of the Watson-Crick paper is at the Exploratorium's site.) Toward the end of their paper, they flatly state that “We were not aware of the details of the results presented [by the King's scientists] when we devised our structure, which rests mainly though not entirely on published experimental data and stereochemical arguments.” Yet they go on to write in an acknowledgment, three paragraphs later: “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.”

The sentences seem to contradict each other, and in any case Watson made a point, in his book *The Double Helix*, to describe the pivotal moment when he saw Photo 51.

So the controversy continues. Was it ethical for Wilkins to show Watson his colleague's work without asking her first? Should she have been invited to be a coauthor on the historic paper? Watson hardly helped his case with his belittling comments about Franklin in *The Double Helix*.

In Brenda Maddox's biography, *Rosalind Franklin: The Dark Lady of DNA* (it was Wilkins who called her that) she makes a strong argument that her subject knew all along that the B form of DNA was helical. But she didn't advertise the fact or begin to see the significance until shortly before Watson and Crick made their breakthrough. With a little more time she might have gotten the structure first. Or maybe Wilkins would have done so if Franklin hadn't left him with the impression that a helical structure had been ruled out. After the discovery was made, she figured

out how the crystalline A form was just a foreshortened version of the B. Like so many things it was clear in retrospect.

During the last week or so I've reread Judson's account of that year before the discovery and then the relevant pages in Maddox's biography and Robert Olby's detailed history, *The Path to the Double Helix*. There are many other wrinkles to the story — the “gentlemen's agreement” by the Cavendish not to tread on King's turf, the role of Max Perutz as another conduit between the two laboratories. All of this was hashed out during the 50th anniversary in 2003 and it will be rehashed again for the 70th. That is how fascinating a story it is, revealing how human curiosity vies with human competitiveness in the unfolding of great science. – George Johnson, talaya.net