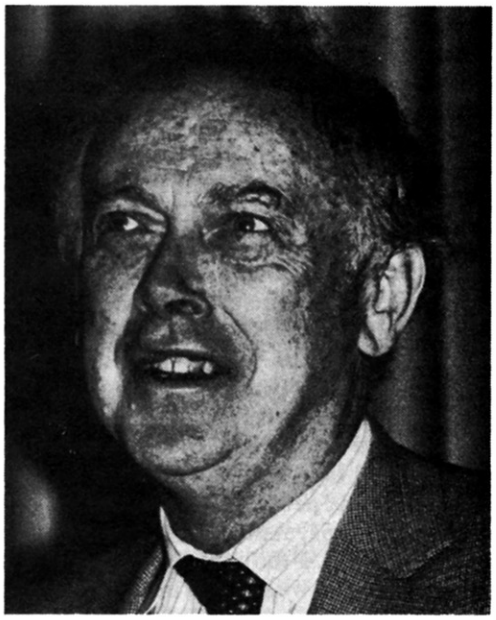
Nature conference



Jim Watson, in his introduction to the conference, looked back . . .

WHY thirty years and not, say, twenty years or ten years? Well, it's pretty clear why it couldn't be ten years, because we waited 9½ years to get the Nobel Prize. Fifteen years wouldn't have had any meaning, as the big event occurred after thirteen years, in 1966, when the genetic code was solved. Then repressors came along, but that wasn't enough for a big celebration. And then twenty — we didn't know it at the time, but that was the real year, because that was when we came to recombinant DNA. It was made practical by Boyer and Cohen. People ask me "Why did the Swedes take nine years to give you the Nobel Prize if it was so important?" But they still haven't given it to Boyer and Cohen.

Nature did celebrate twenty-one years, and that was really very nice, because Francis [Crick] wrote and, in particular, Linus [Pauling] wrote. But we couldn't sell the twenty-fifth anniversary very big, because we were still mad at each other. We couldn't work on tumour viruses, because of the regulation of recombinant-DNA research. And it's really only now, in year thirty, that we're free to do exactly as we want.

Now, I guess, people like me have lots of debts to acknowledge — mostly to people that those here really didn't know. But there were two unique patrons — people who protect you if you're trying to do something different. One was the Rockefeller Foundation. It really started the thing. It gave money in 1933 to begin the first Cold Spring Harbor Symposium, and it gave a lot of money to Caltech and it gave money to the Medical Research Council (MRC). It gave money to Indiana University. It gave money to Copenhagen, when I was with Herman Kalckar. The Rockefeller Foundation did this because of one man, Warren Weaver, a mathematician from the University of Chicago, president of the University of Wisconsin, and . . . a fine man. It was his belief that helped Linus Pauling and George Beadle to talk about how chemistry was going to revolutionize biology. Weaver provided a spirit in which younger people could think.

The second patron was MRC. Harold Himsworth supported the MRC laboratory in its earliest days and Sidney Cattell, my better, saw that the new laboratory was built, without which Cambridge couldn't have been the outstanding place it still is today.

The second kind of patron is more personal. We had Sir Lawrence Bragg. As the Cavendish Professor, he could assign space. And he assigned some space to Max Perutz and then to John Kendrew so that there were six people in Cambridge when I arrived in 1951. And, as I recount in *The Double Helix*, I thought Bragg was just a stuffy old man when I met him. But he was a fine man. He had a really keen interest in science, and he was certainly Francis's only competition at that time — in the sense that he was a theoretician. And he had a difficult time, because most people thought that it was his father who had been the clever one, whereas it was the younger Bragg who'd made the running. When he came to the Cavendish, people said how dreadful it was that he was not a nuclear physicist or even a low-temperature physicist, but just a crystallographer. So his support of us was very important. I showed him several manuscripts, and he really was very helpful.

Then there was the patronage given to Francis and me by John Kendrew and Max Perutz. Francis was Max's research student and I was John Kendrew's. And when I was going to lose my fellowship for coming to Cambridge, they dug up enough money for me to stay in Cambridge.

But I guess I owe most of all to Francis, who really did look after me, and who often tried to keep me from being silly. I wasn't as silly as he thought, but he was so sensible that I had occasionally to say things I didn't believe, to see if I could trap him. And I sometimes did.

I don't think the whole thing would have worked if the Cricks hadn't cooked so many meals for me, or made me feel at home in Cambridge by seeing that I didn't cut my hair for quite a while. And then seeing that I wore a tie. And that I got an English suit. And giving me the good advice that I shouldn't look like an American. I followed their rules to the point where it made it difficult sometimes to go home.

I couldn't have got anywhere without Francis, so I really felt a little strange coming back here for this meeting, because it's without Francis. It could have been Crick without Watson, but certainly not Watson without Crick.

I wrote *The Double Helix* because it was a good story. Some people claimed they didn't recognize me in it, but others thought they recognized me too well. Originally, it had the title *Honest Jim*, but some people objected because they thought I was proclaiming myself as the Honest Truth. So then I changed it to *Base Pairs*, and that didn't go over either, so the book ended up with the title *The Double Helix*. I had this great idea of a picture of me looking at Francis and Maurice [Wilkins] looking at Rosalind [Franklin] on the cover of *Base Pairs* — a kind of *Kind Hearts and Coronets* arrangement. But it ended up a little more sensible.

Rosalind Franklin was a very intelligent woman, but she really had no reason for believing that DNA was particularly important. She was trained in physical chemistry. I don't think she'd ever spent any length of time with people who thought DNA was important. And she certainly didn't talk to Maurice [Wilkins] or to John Randall, then the professor at Kings. And then the time came when he moved her out of DNA and sent her over to Bernal, and she had to write up the papers.

As Aaron Klug has explained in *Nature*, she came very close to the structure of DNA. She really had accepted that it was a helix, but we didn't know that. She was moving towards the idea that there were two chains, but she never built models. Now if she could have had just two hours with Francis, and she could have been convinced that he was right, not just a loudmouth, I think she would have gone back to her laboratory and built models. She'd have solved the structure of DNA. But she was really prepared to give up working on DNA, and she wouldn't have agreed to give up if she'd thought it was important. So that was why she didn't get the answer.

Probably none of you knows how much she liked Francis. Afterwards she came to him to talk. She did that very beautiful work on tobacco mosaic virus (TMV) and when she had her operation for ovarian cancer, which she knew was very serious, she came and stayed with the Cricks to recuperate. She was pretty ill, but she was supported strongly by Don Caspar, and less so by me, and we got her a National Institutes of Health grant that let her do the TMV work when the Agricultural Research Council (ARC) turned her down after she'd told the head of ARC that he was an idiot. He was an idiot. When she wanted a diffractometer, he pointed out that there was one in Aberdeen. So she told him what an idiot he was and then they didn't support her. She wasn't a diplomatic person but when you got to know her she was fine to deal with.

Linus [Pauling] didn't deserve to get the structure. He really didn't read the literature. And he didn't talk to anyone either. He'd even forgotten his own paper with Max Delbruck which said that a gene should replicate by complementarity. He seems to consider that he should have got the structure because he was so bright, but really he didn't deserve it.

Now he might have got it because Alex Rich arrived at Caltech and began to take X-ray photographs at just about the time that we proposed our model. I think it was

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inevitable that the structure would have been solved within about a year. The momentum was there, and they knew that DNA was important.

But I have no guilt feelings. Both Francis and I were products of a tradition that wanted to solve the problem, right through. I'd been trained in the phage group, for which self-replication was the key problem. And Francis was the heir to the tradition established here in England that molecular structure is important, and if you work out bigger and bigger structures, you'll learn something important.

What happened when we got the structure? Well, we wrote the paper for *Nature* and then we realized that the final throw-away line might have been too cute and that we'd better write a longer paper. So, so that some third person wouldn't write down these trivial ideas and claim credit for them, we wrote the second *Nature* paper called "The genetical applications of the structure of DNA". And then Francis started to talk. I mean he'd always talked. And then Sydney [Brenner] came over. On about the first occasion I saw Sydney, we talked for about six hours non-stop. Sydney had a few bright friends in Oxford who talked about DNA, but they didn't have expert pictures and didn't do anything about it. Sydney was then a research student with Hinshelwood, who was a kind of Lamarckian and . . . a strange man. And Sydney was doing a PhD thesis that was as dull as Francis's, on bacteriophage T4. But he knew the phage was important.

He took me aside one day and said "Jim, you don't realize how important the work you've done is". I think I did, but I was also scared — it might not be right. One had this sort of feeling because of the Cambridge biochemists who were calling it the WC structure. When Francis got a request to speak on BBC radio, I said that he could do it if the broadcast went out on the External Services and if it wasn't heard in England. So his voice talking about DNA and its importance was heard only outside England. But then I realized that it was the end of an era. I'd been raised at courses on H.J. Muller, and I'd heard what genes might be and how they might self-replicate. So when we saw the complementary structure of DNA, that was the final solution. We didn't see it, as we now see it, as the beginning.

Both Francis and I had no doubts that DNA was the gene. But most people did. And again, you might say, "Why didn't Avery get the Nobel Prize?" Because most people didn't take him seriously. Because you could always argue that his observations were limited to bacteria, or that [the transformation of *Pneumococcus* that he described was caused by] a protein resistant to proteases and that the DNA was just scaffolding. Only when they saw the double helix did people stop asking what the gene was.

The first thing I worried about was whether the strands would come apart quickly enough and how to explain [Arthur] Kornberg's discovery that the chains run in opposite directions. But I doubt whether Francis and I combined spent more than ten hours worrying whether the structure was right, whether they would take it away from us or something like that. So it was very satisfying when we saw that the replication scheme seemed to be right, even though [L.F.] Cavalieri came along and said we should use a four-chain model.

What happened next? There was the area of the genetic code, or how information was included in DNA. That was dominated by Francis and Sydney, Khorana and a few others, but I'd say the work here at Cambridge was the intellectual high-point of that whole thing. Then we were all dominated by the biochemistry of the central dogma [DNA makes RNA makes protein] and we all wanted to find the enzymes that did all those steps. That was an era when we were the new enzymologists. But when Francis and I saw the structure, we'd never thought in terms of an enzyme. We even thought that because it's a template, you might not need those enzymes. But now, of course, there's this great RNA splicing story without enzymes that makes one think that we weren't totally mad. But it was far out, and the person who used to argue with us most about enzymes was Peter Mitchell, which was interesting because [in his later work] Peter managed to do away with the need for several enzymes.

Without first class biochemistry of this sort, from first class conventional biochemists such as Lippman and Ochoa, we wouldn't be here today, because the enzymes were necessary. But then we also needed the wonderful molecular genetics which came from people such as Benzer, Sydney [Brenner], Jacob and Monod and which finally led to Mark [Ptashne] and Wally [Gilbert] and the repressor story.

But then we didn't know what to do next. Many of us moved into tumour viruses, hoping that what had worked for phage and bacteria would work for tumour viruses in animal cells. It's chilling to think of where we'd be if the cloning of DNA hadn't come along. We would be stuck so far back that it wouldn't be much fun. Even there we owe an enormous amount to a genetics approach that has really made us think about plasmids and so on until, finally, recombinant DNA came along.

But then we were involved with the question of whether we had something so powerful that we shouldn't do it. We'd gone through that. And [the fuss about the control of recombinant-DNA research] is now so far back that I don't really feel mad. I always regarded the regulation of recombinant-DNA research as a black comedy, and said so. But some people thought the concern was genuine. It was genuine for some, but for others it was really the theatre of the absurd. And it's over. What a relief! □

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