DNA's golden jubilee

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50 Years of DNA

Foreword by Phil Campbell, edited by

Julie Clayton and Carina Dennis

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Since the beginning of the year, we have heard many times that in April 1953, *Nature* published three consecutive papers that signalled a new era in biology: the era of DNA.

Nature rightly cele-

brated the fiftieth anniversary of this event by preparing a special supplement (23 January 2003) containing the original papers, together with interesting historical perspectives and topical overviews of the current state of DNA research in different branches of biology. Those who missed this special issue may be glad to learn that Nature Publishing Group has prepared a greatly expanded version that includes such extras as interviews with James Watson and Maurice Wilkins. Compiled by Julie Clayton and Carina Dennis, *50 Years of DNA* is a superbly illustrated, carefully researched and well-written DNA jubilee book. Julie Clayton has written ten introductory chapters that start with a historical background and end with discussions on the moral implications of human cloning. Carina Dennis has commissioned and edited up-to-date reviews on DNA by leading scientists in the field. Of course, it is difficult to avoid mistakes in enterprises like these, and the first one is prominently exposed on the cover of the book: an attractive computer-generated image of DNA with 20 base pairs per turn. There are other graphic lapses inside the book, like the classical mistake of presenting DNA as a left-handed helix. We should, however, concentrate on the text.

For me, and probably many other readers who are interested in the history of science, this book provides new insights into understanding what really happened in the first few months of 1953, and who we should remember as providing the decisive data required to elucidate the structure of DNA. Clayton's detailed description of the main events between 1951 and 1953, which directly contributed to the discovery of the structure, is complemented by Brenda Maddox' description of Rosalind Franklin's contributions, while Watson and Wilkins offer their personal recollections. Clayton introduces readers to the complex interactions that occurred between the three research groups that published the historic papers. James Watson and Francis Crick, at the Cavendish Laboratory at Cambridge, were very interested in the structure of DNA but did not do DNA experimental work themselves. Two groups at King's College, London—one led by Maurice Wilkins and the other by Rosalind Franklin—both used X-ray diffraction analysis of DNA fibres to get insights into the structure of DNA. It was Wilkins who started the project at King's College and obtained interesting X-ray DNA-diffraction patterns, but they lacked the necessary clarity to conclude, for example, the symmetry of the unit cell. When Franklin joined King's College in January 1951 after a postdoctoral stay in Paris, her earlier experience in obtaining X-ray diffraction data, and also her exceptional experimental skills, allowed her to obtain much better DNA diffractograms. Rightly or not, Franklin felt possessive of her own results and did not want Wilkins to analyse her data. She wanted to solve the DNA puzzle herself, or rather together with her doctoral student Raymond Gosling. Even today, determining the three-dimensional structure of biomolecules from their X-ray diffraction pattern is a complex task that requires computers and special software, so one can imagine how difficult it was 50 years ago. Despite these difficulties, Franklin was advancing in her analysis and concluded that the symmetry of unit cells in DNA fibres is of the type 'face centred monoclinic'. She included this information in a formal

scientific report for a reviewing committee. This report was sent to, among others, Max Perutz, a superior of Watson and Crick at the Cavendish Laboratory. By this time, relations between Franklin and Wilkins had deteriorated, but Wilkins maintained good relations with Watson and Crick. Towards the end of 1952, Franklin decided to move to Birkbeck College, London, but before moving she wrote three papers on DNA. In late January 1953, she agreed that Gosling could give the DNA data to Wilkins. Soon after, Watson visited Wilkins, who showed him the best DNA diffraction pattern obtained by Franklin. Watson was stunned by the quality of the data and had a long discussion with Wilkins about their possible interpretations. A few days later, Watson started building a model of DNA, attempting to make it consistent with the recently seen X-ray pattern. However, there were too many unknown parameters to solve the puzzle. At this point, Perutz gave Franklin's scientific report, which contained the symmetry assignment of the DNA fibres, to Watson and Crick. Crick immediately recognized that this symmetry indicated that the two DNA strands are antiparallel. With this additional information, Watson tried again to build a model that, in addition, incorporated Ervin Chargaff's observation that in DNA, numbers of adenines and thymines are equal, as are the numbers of guanines and cytosines. Watson tried to match adenines with thymines and guanines with cytosines, but this did not work. At this point, another lucky coincidence occurred. Jerry Donohue, who worked in the same room, noticed that Watson was using formulae of bases in their enol forms, as suggested by contemporary textbooks. However, Donohue, who was a former student of Linus Pauling, knew that bases exist in keto forms. After this correction, Watson had no problems in matching As with Ts and Gs with Cs (although he proposed only two hydrogen bonds for a GC pair), and thus completed the whole model. On 28 February, the model of DNA was built, just four weeks after Watson first saw Franklin's unpublished X-ray data. The race to solve the structure of DNA was therefore won by Watson and Crick.

In 1962, Watson, Crick and Wilkins shared a Nobel Prize for their momentous discovery. Sadly, Franklin died of cancer in 1957 at the young age of 37, and could not even be considered for the Prize, as it is not awarded posthumously. One would expect, however, that history and human memory would place Franklin as one of discoverers of DNA structure. But this is not the case, as Franklin's contributions were not correctly acknowledged by the winners of the race to DNA glory. In their first *Nature* paper, Watson and Crick stated that their model was devised without knowing the details of Franklin's work. They omitted to mention, though, that while they did not know the details, they knew the principal findings of her unpublished work. Later, in 1968, Watson published his best-selling book *The Double Helix* and presented Franklin as a scientist who obstructed, rather than hastened, the revelation of DNA structure. Even in the recent jubilee interview, Watson stated again that he could have solved the DNA structure without ever seeing any of Franklin's photographs, and that the symmetry assignment of DNA was correctly interpreted by himself and Crick, but not by Franklin. Watson even says that 1947 X-ray pictures obtained by William Astbury at the University of Leeds already contained all the necessary information. Conversely, it is known that, in 1952, Watson's attempts to build the DNA model on the basis of

Astbury's data resulted in a fiasco, as the structure had three DNA strands with bases outside and phosphates inside. Therefore, Astbury's data were clearly not sufficient to arrive at the correct DNA model. As Watson admits, only the high-quality picture by Franklin prompted him to start model-building again. Questioned by Clayton, Watson estimates that it may have taken three to six months of further work until Franklin could deduce the structure of DNA. This answer by Watson automatically raises the question: How much more time would it have taken Watson to build a correct model if Franklin's unpublished DNA X-ray pictures were not shown to him, and if the symmetry assignment was not leaked to him from Franklin's report? It seems to me that it would have taken much more than three to six months. Who would then have discovered the DNA structure? Watson was not asked this question, but he already provided the answer by estimating how much more time Rosalind Franklin would have needed to solve the puzzle.

The second part of the book symbolically spans 50 years of DNA research by starting with the three 1953 DNA papers in their original form, and ending with topical reviews on principal current domains of DNA research. We learn from a historical perspective by Robert Olby that the initial reception of the double helix was very cold. Following the *Nature* publications, only one

British newspaper reported the discovery of the DNA structure, and this was only in the context of a public lecture given by Nobel Prize laureate Sir Lawrence Bragg, the director of Cavendish Laboratory, who tried to popularize the idea that originated in his laboratory. In fact, reading the original papers, one may understand why this was the case. Watson and Crick's paper does not show the structure of base pairs, and all biological implications of their structure are contained in what is certainly the most famous scientific understatement: "It has not escaped our notice that the specific pairing we have postulated immediately suggests a possible copying mechanism for the genetic material".

Finally, we are brought back to the twenty-first century by feature articles divided into two sections: the first devoted to implications of DNA knowledge on medicine and society and the second reporting the actual state of our DNA knowledge from all aspects. These splendid feature articles are written by luminaries of their respective fields. On the whole, *50 Years of DNA* should find its place on the desks of all those who are interested in history, the current state of DNA research and its future.

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