Obituary

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by Jean Thomas
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Francis Crick OM FRS (1916–2004)

Francis Crick, who died on 28 July 2004 in La Jolla, California, is best known for his co-discovery of the structure of DNA, with Jim Watson, in 1953 — a story told many times. In Crick's lifetime this led to a revolution in biology, and has laid the foundations for much of modern medicine, genetics and forensic science.

The laconic and much-quoted last sentence of the 1953 *Nature* article on base-pairing in the double helix, "It has not escaped our attention that the specific pairing that we have postulated immediately suggests a possible copying mechanism for the genetic material.", encapsulated Crick and Watson's profound contribution to the understanding of inheritance. Five weeks later, their second paper in *Nature* elaborated on this. Exactly 50 years later, the first draft of the human genome was published (one third of this being determined by John Sulston and his colleagues at the Wellcome Trust's Sanger Centre in Hinxton, Cambridge).

However, Francis Crick's contributions to biology over more than 20 years in Cambridge extended beyond DNA structure with his work on elucidation of the genetic code. He focused on the relationship between the linear sequence of DNA and the linear sequence of proteins that had been shown earlier for insulin in a landmark contribution by Fred Sanger. This led Crick to postulate the existence of 'adaptor molecules', nucleic acids that would work through base-pairing and assemble amino acids in the correct sequence, corresponding to the sequence of the DNA bases. Transfer RNAs (tRNAs) were discovered soon afterwards by Mahlon Hoagland and Paul Zamecnik in the USA. In 1961, through the work of Sydney Brenner, also in the Medical Research Council (MRC) Laboratory of Molecular Biology in Cambridge, in collaboration with Francois Jacob and Matthew Meselson, messenger RNA (mRNA) was discovered; this was the 'missing link' that carried the nucleic acid sequence from the nucleus to the cytoplasm for translation into protein. In the same year, Crick, Brenner and their colleagues reported in a remarkable paper in *Nature* that the code is a triplet code: genes are translated three bases (a codon) at a time. Marshall Nirenberg and Heinrich Matthaei went on to decipher the code, showing which codons corresponded to which amino acids. Crick, in his 'wobble hypothesis', explained the structural relationship between codons in DNA and anticodons in tRNA. These landmark discoveries form the core of molecular biology.

Francis Harry Compton Crick was born in 1916 at Northampton, and was educated at Northampton Grammar School, Mill Hill School and University College, London (UCL). He graduated in physics in 1937 and started a PhD at UCL to study the viscosity of water at high temperatures. His studies were disrupted by the outbreak of the second world war, when he joined the Admiralty to work mainly on countermeasures to acoustic and magnetic mines. After the war, like many other physicists of that time, he decided to switch to biology, and at the end of the war, with a research studentship from the MRC, he moved (in 1947) to the Strangeways Research Laboratory in Cambridge, then a prominent centre for cell-biology research, where he again studied viscosity — this time of cell cytoplasm. In 1949 he joined Max Perutz and John Kendrew in the recently-founded MRC Unit in the Cavendish Laboratory in the University

of Cambridge (the forerunner of the present MRC Laboratory of Molecular Biology). His PhD project there, under the supervision of Max Perutz, was on X-ray crystallography of horse and ox haemoglobin. Crick soon made his first theoretical contribution, with William Cochran and Vladimir Vand, by formulating the general theory of X-ray diffraction by a helical molecule, and went on to deduce the existence of coiled coils (α-helices coiled around each other) from the diffraction patterns of proteins, as did Linus Pauling and Paul Corey in the USA more or less simultaneously. Two years into Crick's PhD studies in protein crystallography, Jim Watson arrived in the Unit, as a postdoctoral fellow. He was a young and enthusiastic biologist with an interest in trying to find out the structure of DNA. Crick readily became involved, alongside his project on protein structure, and the rest, as they say, is history. The pair did no experimental work on DNA. Crick came to the collaboration with his background in X-ray diffraction, and Watson with his knowledge of phage and bacteria genetics; they also knew from the work of Edwin Chargaff that there were equal amounts of adenine and thymine, and of guanine and cytosine, in DNA. The critical piece of evidence leading to the crucial insight by Watson and Crick, as has been widely discussed, was Rosalind Franklin's diffraction pattern of DNA provided by her colleague Maurice Wilkins; both Franklin and Wilkins were at King's College London. The story of the elucidation of the structure of DNA by the unique combination of Watson and Crick is told in Watson's personal account *The Double Helix*, later the basis of a BBC film (*Life Story*, 1987). The structure of DNA was published in 1953.

Crick received his PhD in 1954 for a thesis entitled "X-ray diffraction: polypeptides and proteins". In 1959, he was elected a Fellow of the Royal Society, and, in 1962, he and Watson shared with Wilkins (Franklin had meanwhile died of cancer) the Nobel Prize for Physiology or Medicine "for their discoveries concerning the molecular structure of nucleic acids and its significance for information transfer in living material".

Watson and Crick went their separate ways after the determination of the structure of DNA, apart from a collaboration on the structure of small viruses. Watson returned to the USA, and Crick embarked on a highly productive collaboration with Sydney Brenner, who had joined the MRC Unit in 1957, leading to a second round of seminal discoveries, on the genetic code, as outlined above. Crick subsequently also became interested in other major problems: how gradients of morphogens might cause patterning in development; and in chromosome structure.

In 1977, he left Cambridge with his wife Odile for the Salk Institute in California to pursue interests in neuroscience. Characteristically, he attacked another major problem – the nature of consciousness – for which he was convinced there was a cellular and biochemical basis. He continued to work on this major and difficult problem until his death from cancer. His ideas are elaborated in his last book, *The Astonishing Hypothesis: the scientific search for the soul* (1994) (which followed *Of Molecules and Men*, 1966, and *What Mad Pursuit*, 1988). Crick remained a British citizen, and, in 1991, was appointed to the highly select Order of Merit.

Francis Crick was a larger than life character. He spoke rapidly, and rather loudly, and had an infectious and reverberating laugh, and a lively sense of humour. His formidable intellect and clear thinking was obvious. He would instantly spot sloppy thinking — as many a hapless seminar speaker found out. He was a unique personality, as well as a major figure in the history of science. It was a disappointment that in 2003 Francis was not well enough to be able to travel to Cambridge to join Jim Watson for the celebration — one of many worldwide — of the discovery of the structure of DNA there, 50 years earlier. But Francis appeared on videotape to deliver his message. And the old magic was still there.