

Discovering life on omics plane: the genius of Frederick Sanger

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Frederick Sanger (13 August 1918–19 November 2013), is an immortal reference in this ‘omics’ world. Indeed, he was one of the greatest biochemists, and was highly appreciated for winning the Nobel Prize in Chemistry twice¹. Till now, he is the only person to have been honoured with the Nobel Prize in Chemistry twice, and one among the only four two-time Nobel laureates after Marie Curie (Physics, 1903 and Chemistry, 1911), Linus Pauling (Chemistry, 1954 and Peace, 1962) and John Bardeen (Physics, 1956 and 1972)². His groundbreaking research on the structure of insulin got him the first Nobel Prize in Chemistry in 1958. According to ISI *Web of Science*, Sanger’s Nobel Prize-winning paper ‘DNA sequencing with chain-terminating inhibitors’³ was cited 65,274 times by June 2014. Another novel publication ‘Sequence and organization of the human mitochondrial genome’⁴ was cited 7731 times. He exclaimed ‘I felt I would be much more interested in and much better at something where I could really work on a problem’. Indeed his pioneering work on molecular structure of insulin has not only unravelled the possibilities of curing diseases at the molecular level as we know today, but also motivated many biological scientists to go beyond the contemporary imagination.

Sanger was born at Rendcombe, United Kingdom, where he pursued his schooling at Bryanston School and obtained his B A degree in natural sciences (1939) at St John’s College, Cambridge. He started his Ph D in October 1940 under the supervision of N. W. ‘Bill’ Pirie. His project was to investigate whether edible protein could be obtained from grass. But within a month, Pirie left the department and A. Neuberger was assigned as his new mentor. He changed his thesis title and worked on the topic ‘The metabolism of the amino acid lysine in the animal body’. He was awarded the doctorate degree in 1943 and was granted Beit Memorial Fellowship for medical research (1944–51) and since 1951, he was a permanent member of the external staff of the Medical Research Council (MRC). He was also the Head of the Division of Protein Chemi-

stry in MRC Laboratory for Molecular Biology at Cambridge.

Sanger was the first person to perform complete amino acid sequencing of the two polypeptide chains of bovine insulin⁵. He concluded that the two polypeptide chains of the protein insulin had a specific amino acid sequence and that every protein had a unique sequence. Prior to his work there was a strong belief that proteins were amorphous in nature. Through his groundbreaking work, Sanger concluded that protein molecules have a defined chemical composition⁶. For this contribution he was awarded the Nobel Prize in Chemistry in 1958. This discovery was a pathfinder at that time and it laid the foundation for proteomic-based research.

Later, Sanger and colleagues (1977) developed the ‘dideoxy’ chain-termination method for DNA sequencing, which is also referred as ‘Sanger’s method of DNA sequencing’. This technique enables rapid and accurate sequencing of long stretches of DNA⁷. The immense application of this easy and reliable technique earned him the second Nobel Prize in Chemistry (1980) jointly with Paul Berg (Stanford University) and Walter Gilbert (Harvard University). He was rightfully called the ‘father of genomics’. In 1977, Sanger for the first time



Figure 1. Sanger analyzing a genome map (source: <http://www.telegraph.co.uk/news/obituaries/science-obituaries/1046-2574/Frederick-Sanger-OM.html>)

sequenced the complete genome of a bacteriophage Φ X174 and also sequenced the human mitochondrial genome⁸ (Figure 1). ‘Sanger’s sequencing’ was effectively adopted in the Human Genome Project (2000) which decoded the three-billion-letters human genetic code.

Sanger was a dedicated researcher who inspired the budding scientists by advocating that ‘Scientific research is one of the most exciting and rewarding occupations’. He emphasized that ‘Through science it is possible to make a permanent contribution towards improvement and enrichment of human life and it is these pursuits we are engaged in’. In 1992, the Wellcome Trust and MRC founded the Sanger Institute in his honour (Figure 2). The Sanger Institute is regarded as one of the pioneer DNA sequencing centres of the Human Genome Project, including sequencing of other organisms.

Sanger has published many books and research papers in prestigious journals worldwide. He has also bagged several awards and honours (Figure 3).

The sole autobiographical article by Sanger was written five years after his retirement, which opens with the self-disparaging statement ‘I was not academically brilliant’ and also exclaimed about himself as ‘the three main activities involved in scientific research, thinking, talking and doing, I much prefer the last and am probably best at it. I am all right at the thinking, but not much good at the talking’. His modest autobiography had clearly no mention of the various awards and prizes bestowed on him. Sanger also turned down the offer of knighthood as he was against the idea of being addressed as ‘Sir’. He modestly



Figure 2. Sanger Institute, Cambridge, United Kingdom (source: <http://www.nbbj.com/work/wellcome-trust-sanger-institute-genome-campus-expansion/>).

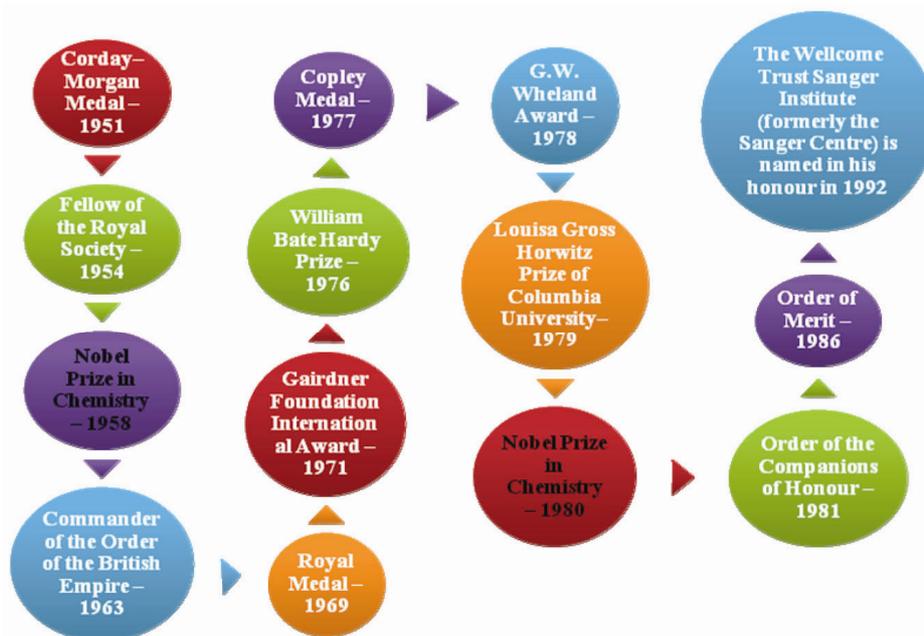


Figure 3. Major achievements of Frederick Sanger in chronological order.

stated ‘A knighthood makes you different, doesn’t it, and I don’t want to be different’, reflecting his humility⁹.

His demise (19 November 2013) was a great loss to the scientific world. Jeremy Farrar, the new director of Wellcome Trust, quoted ‘Fred can fairly be called the father of the genomic era: his work laid the foundations of humanity’s ability to read and understand the genetic code, which has revolutionized biology and is today contributing to transformative improvements in healthcare’. Sanger will be remembered and cherished for several eras for his invention of the two critical technical advances – for sequencing pro-

teins and nucleic acids – which opened up the field of molecular genetics.

1. The Nobel Prize in Chemistry 1980: Frederick Sanger – autobiography. Nobel-prize.org (accessed on 10 October 2010).
2. Sanger, F., *Nature*, 2014, **505**, 27.
3. Sanger, F., Nicklen, S. and Coulson, A. R., *Proc. Natl. Acad. Sci. USA*, 1977, **74**(12), 5463–5467.
4. Sanger, F. *et al.*, *Nature*, 1981, **290**, 457–465.
5. Sanger, F., *Annu. Rev. Biochem.*, 1988, **57**, 1–28.
6. Sanger, F. and Tuppy, H., *Biochem. J.*, 1951, **49**(4), 481–490.

7. Sanger, F., *Science*, 1959, **129**, 1340–1344.
8. Nobel lecture, Medical Research Council Laboratory of Molecular Biology, Cambridge, England, 8 December 1980.
9. Sanger, F. and Dowding, M. (eds), *Selected Papers of Frederick Sanger: With Commentaries* (Series in 20th Century Biology), World Scientific, Singapore, 1996, p.662.

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