Obituary

Charles M. Steinberg (1932–99)

On 17 September, Charley Steinberg died in Basel, Switzerland, of leukaemia that developed after a long-drawn-out illness. His name is not in the usual list of Heroes of the Molecular Biological Revolution, but to those who were fortunate enough to have come under his spell he was perhaps the supreme master of them all. Indeed, it is a sign of his special kind of mastery that he does not figure in the list.

Born in Montgomery, Alabama, Steinberg graduated from Vanderbilt University, Tennessee, in 1954. He was then drawn to Caltech by Max Delbrück (who, having himself worked at Vanderbilt during the Second World War, used to claim that Steinberg was the best thing ever to have come out of that university). During the next few years, the biology department at Caltech was the home for an astonishing array of graduate students and postdoctoral fellows — Edgar and Epstein, Streisinger, Meselson and Stahl, Drake, Rubin and Temin, and many others, all of whom were to make major contributions to the foundations of molecular genetics. But each would surely have agreed that Steinberg was the intellectual giant in their midst. Indeed when the physicist Richard Feynman decided that, for a while, he would try his hand at biology, he chose Steinberg (still a graduate student) to be his tutor and supervisor.

During those years at Caltech, Steinberg played a central role in two important acts of clarification. Certain bacteriophages had been shown to undergo genetic recombination when multiplying in their host. At that time nothing was known about the relation between DNA replication and recombination, and much effort therefore went into trying to unravel the mysteries of the phage-infected cell. Finally, in 1958 Steinberg and Frank Stahl produced a precise and elegant analysis that showed that phage genetics could not, in principle, show what kinds of interaction were going on between replicating DNA molecules, and this put a stop to much fruitless speculation.

Steinberg's other contribution was in his part in identifying and characterizing the different kinds of conditional lethal mutations in phage T4. The study of these mutations was crucial in elucidating the relation between DNA sequence, the genetic code and the nature of genes. It was during this collective work by Delbrück's students that Steinberg told Harris Bernstein that, if he would help count culture plates, they would name any discovery after Bernstein's mother. This is why one of the three (suppressible) nonsense codons is now called amber (*Bernstein* in German).

After Steinberg completed his PhD thesis, Delbrück took him in 1961 to Cologne to help in the attempt to import the non-hierarchical American style to a German university. After two years, Delbrück returned to Caltech and Steinberg moved to the biology division at Oak Ridge, Tennessee. While there he was able to show the local experts (who had failed in their efforts) how to prepare the other radioactive isotope of phosphorus, ^{33}P, that was needed to resolve certain questions about the mechanism of DNA inactivation by ^{32}P and ^{3}H decay. Later, it was the availability of two distinguishable radioisotopes of phosphorus that allowed Hamilton Smith to put different labels into the two strands of DNA and determine the mechanism of action of the class II restriction enzymes that were to prove to be nature's gift to sequencers.

In 1970, Niels Jerne became head of the new Hofmann-LaRoche Institute of Immunology in Basel. He immediately recruited Steinberg to be one of its first tenured members of staff and to serve as intellectual watchdog for the institute (to place some restriction on Steinberg's critical instincts, Jerne also put him in charge of complaints). During the next 20 years, the institute must have exceeded its creators' fondest hopes, for it was largely responsible for showing that antibody diversity is generated first by the shuffling of segments of genes to give multiple permutations and combinations, and second by high levels of random mutation selectively directed to what are called the hypervariable regions of antibodies.

Steinberg played a crucial part in each of these discoveries. Unfortunately, that was not obvious from a casual reading of the literature because, after doing much of the work, he usually chose to retreat into his role as unseen advisor. When first Jerne and then Susumu Tonegawa were awarded Nobel prizes for their work on antibody formation, many felt that Steinberg could well have shared in one or other of the prizes. His contribution is there for all to see, however, in the clarity of the annual reports of the institute. Until 1995, Steinberg wrote a dazzling introduction to each report and edited each laboratory's contribution. If you want to observe a fine scientific mind at work, read those reports.

A self-effacing influence in genetics and immunology

Once upon a time, Steinberg's erstwhile student, The Famous Physicist, was talking to the director of the Oak Ridge National Laboratory. Feynman remarked that he knew a clever fellow at Oak Ridge named Charley Steinberg, who was the smartest guy he had ever met. When the director got back to Oak Ridge he asked about this Steinberg person and learned that he was one of the more influential scientists in the biology division. But Steinberg never put himself forward because he despised self-promotion in others.

To young scientists, who have to work in a world where survival depends on continued visibility, such a self-effacing life devoted to precision and excellence must seem scarcely believable. Yet, to all those friends and associates who constantly sought his advice, Steinberg represented the ideal combination of brilliance and integrity. For him nothing was difficult. And perhaps for that reason he chose to give credit to everyone but himself.

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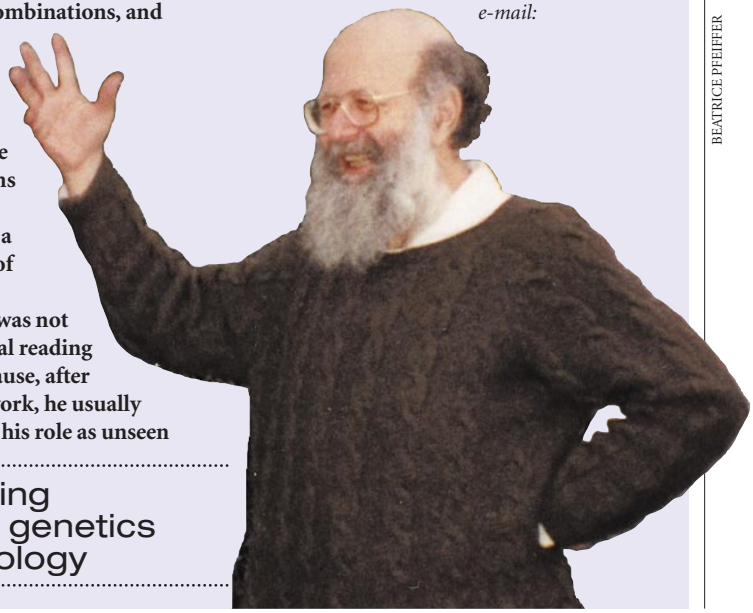

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