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BOOK REVIEW

An uncommon farmer

George Beadle, an Uncommon Farmer: the Emergence of Genetics in the 20th Century
P Berg and M Singer
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Reviewed by R Roskoski

George Beadle (1903–1989), the focus for this survey of genetics, lived through much of the period during which genetics changed from an abstract to a molecular science. Moreover, Beadle was instrumental in this transition. The authors obtained their information from numerous archives of papers, letters, documents, and numerous interviews that are cited in the appendix.

Beadle was reared on a farm near Wahoo, Nebraska. He took care of his chores in the early morning before walking 2 miles to a one-room schoolhouse. One of the themes of this biography is that Beadle used the traits that he learned as a farm boy throughout his entire life. Hershel K Mitchell noted that Beadle maintained his hands on style as the chairman of the biology division at Cal Tech where he taught laboratory courses. 'He walked around to see what needed doing. I think that was the farmer coming out …And if there was a spill of water or something, he would be the first one in there with a mop and mop bucket.'

Beadle graduated from the University of Nebraska in 1926 and received his PhD from Cornell University in 1931. Beadle's first Cornell paper was on the *asynaptic* maize gene. It was coauthored with Barbara McClintock, another graduate student and future Nobel Laureate. McClintock was 1 year ahead of Beadle, and the book notes that her mind worked rapidly. To the chagrin of her fellow students, she often provided the correct interpretation of their data before they had an opportunity to formulate an explanation for themselves. Beadle did his postdoctoral work at Cal Tech where he continued his work on maize and began work on crossing over in *Drosophila*. The director of the biology division was Thomas Hunt Morgan, the leading geneticist in the world at the time.

Beadle spent 1935 in Paris working on eye-color mutants in *Drosophila* with Boris Ephrussi with whom he worked at Cal Tech the previous year. They showed that eye pigments were formed by a linear sequence of reactions and that genes were important in development, which was revolutionary at the time. Beadle went to Harvard as assistant professor in 1936. He would stay for only a year because 'Harvard was too formal for a Wahoo farm boy.' Midway through the year, Beadle received an offer to go to Stanford as a tenured professor. Beadle asked EM East, a distinguished Harvard professor, for advice. East told Beadle 'Stanford isn't any good, it never was any good, and it will never be any good.' Despite this advice, Beadle accepted the offer.

Following up on his studies with Ephrussi, Beadle sought the collaboration of a biochemist to identify a chemical intermediate in eye pigment biosynthesis in *Drosophila*, and Edward L Tatum joined Beadle at Stanford. However, they were scooped by Adolph Butenandt in 1939, who identified the intermediate as kynurenine, a tryptophan metabolite. Instead of using genetics to study the metabolism of unknown compounds, Beadle had the idea of examining known metabolic pathways in *Neurospora*. This idea came to him while he attended a formal class lecture given by Tatum in comparative biochemistry in the winter quarter of 1940–1941. They identified mutants that required amino acids and other compounds for growth, and they were able to determine which step in their synthesis was blocked. Beadle went to Cal Tech to recruit people to his group at Stanford. His seminar describing the nutritional mutants of *Neurospora* was spellbinding, and several Cal Tech graduates joined Beadle at Stanford.

Norman H Horowitz characterized the Stanford years during 1942–1946 as a scientific paradise. This work was the first to unite genetics and biochemistry, which Beadle called biochemical genetics. For the first time it was possible to relate genes directly with enzymes and the reactions they catalyze. Genetics was no longer preoccupied solely with experiments that examined the transmission of genes from one generation to the next, a focus that began with the Morgan tradition.

Beadle thought of genes as nucleoproteins with the proteins as the primary source of genetic information. He wrote that the gene was a 'master molecule or template in directing the final conformation of the protein molecule as it is put together from its component parts.' In the 1940 s, Lewis Stadler and, independently, Alexander Hollaender demonstrated that ultraviolet light produces gene mutations with an efficiency that corresponds to its absorption by DNA. Beadle explained this away by suggesting that the nucleic acid acted as a conduit for passing the energy of the radiation to protein. Ostwald Avery's work demonstrated that DNA is the transforming principle, but these experiments were open to question. Alfred Mirsky, at the Rockefeller Institute and the home of Avery, argued that the DNA was contaminated with protein, and the gene resides in protein. Another interpretation was that the DNA served as a mutagen and changed the structure of the 'real' gene. Another caveat with Avery's work was the question of whether bacteria actually contained genes!

Beadle wanted to combine biochemistry and genetics, but this was not possible at Stanford because the biochemists were not interested in genetics. Linus Pauling, chairman of the chemistry division at Cal Tech, wanted Beadle to head up the biology division. Beadle became its chairman in 1946 and recruited a group of faculty including four future Nobel Prize recipients (Max Delbruck, Renato Dulbecco, Edward Lewis, and Roger Sperry). After the Watson–Crick DNA double helix was described in 1953, Beadle invited Watson to join the biology division as a senior research fellow with Max Delbrück as mentor. By the spring of 1954, Delbrück abdicated his responsibility for Watson, writing Beadle that Watson was 'ruthlessly egocentric in scientific matters', and Delbruck faulted Watson for 'publishing prematurely, putting his name as senior author, accepting too many public lecture obligations, etc.' Delbruck was furious at Beadle ' for having played up so much to Watson.' Delbruck refused to support Watson with his grant funds, and instead supported Niels Jerne (who became a Nobel Laureate in 1984).

Beadle and Tatum received half of the Nobel Prize for Medicine or Physiology in 1958 for their discovery that genes act by regulating definite chemical events. They formulated the one gene-one enzyme hypothesis. Many biologists could not accept the notion that each gene has only one function, preferring instead the long-held idea that a gene contributes to an organism's traits in multiple ways. As noted above, Beadle thought of genes as nucleoproteins with the proteins as the primary source of genetic information. This was one of the few times that his intuition failed him. Joshua Lederberg, a Tatum student, received the other half of the prize.

The authors tell the story of Beadle's tenure as Chancellor of the University of Chicago from 1961–1968. His first official act at his inauguration was to confer an honorary degree to James Watson, a University graduate. Beadle was successful at fund raising, and some of these funds were used for building a much-needed library. Ironically, the library was built on the site of Stagg Field, where, before being dropped, Chicago had been among the powerhouses in intercollegiate football. Jay Berwanger, who was a University of Chicago athlete, won the first Heisman trophy in 1935.

One question that the authors raise is why is George Beadle not more widely known by today's biology students? Perhaps the scientific community should be more generous in naming ideas after scientists. We have Mendelian genetics, the centimorgan, the Watson–Crick structure of DNA, the Meselson–Stahl experiment, and the Hershey–Chase experiment as reminders. Perhaps more eponymous labels would keep scientific architects fresh in the minds of students of all ages. Including Beadle's 'one gene–one enzyme' hypothesis and its various modifications may aid in understanding the development of biological information transfer for today's students.

I highly recommend this book and hope that it will introduce many biologists and geneticists to the farm boy from Wahoo. It includes insightful descriptions of how genetic experiments with corn, *Drosophila*, and *Neurospora* are performed, and how the resulting data are interpreted. It also provides a fascinating assessment of geneticists from Mendel to Morgan to McClintock and to Beadle and a bevy of their collaborators and competitors.

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