Hermann J. Muller

The Nobel Prize in Physiology or Medicine 1946

Biography

Hermann Joseph Muller was born in New York City on December 21, 1890. His grandparents on his father's side were of artisan and professional background and, though at first Catholics, had emigrated from the Rhineland during the wave of reaction of 1848 to seek the greater freedom of America. His father, born in New York, had continued the grandfather's art metal works (the first in the U.S.A.), but was not by inclination a business man, and, although he died in 1900, he early awoke in the boy a lively interest in the nature of the universe and in the process of evolution, as well as in the welfare of men in general. The boy's mother, Frances Lyons Muller, had also been born in New York City. Her parents had come from Britain, but were in the main descended from Spanish and Portuguese Jews who, as an after-effect of the Inquisition, had settled generations earlier in England and Ireland. She, as well as the father, encouraged in the boy a broad sympathy, an interest in living things, and a love of nature.

He was brought up in Harlem, first attending public school there and later Morris High School (also public) in the Bronx. There he and his classmates Lester Thompson and Edgar Altenburg founded what was perhaps the first high-school science club. Though his family (mother, sister Ada, and himself) had very limited means, they were fortunate in usually being able to spend their summers in the country while he was of school age. But he was enabled to attend a first class college - Columbia - only through the unexpected award of a scholarship (the Cooper-Hewitt), automatically granted to him in 1907 on the basis of entrance examination grades. He spent his summers, during his college years, at such jobs as bank runners and hotel clerk (the latter at $25 a month, plus board, for a 14-hour work-day).

At Columbia College he was before the end of his first year fascinated by the subject of biology. Reading by himself in the summer of 1908 R.H. Lock's (1906) book on genetics, his interests became centered in that field. Courses soon afterwards taken under E. B. Wilson influenced him profoundly, as did also his reading, independently of courses, of works by Jacques Loeb and by other writers on experimental biology and physiology. In I909 he founded a students' biology club, which was participated in, among others, by Altenburg, and by two students, Bridges and Sturtevant, who had entered Columbia a year later.

For his first two years of graduate work, since there was no opening offered to him in zoology, he managed to obtain a scholarship (1910-1911) and then a teaching fellowship (1911-1912) in physiology, the latter at Cornell Medical College, while keeping up with genetics on the side and doing various extra jobs, such as teaching English to foreigners in night school. Finally, however, he obtained a teaching assistantship in zoology at Columbia (1912-1915). The first summer (1911) of graduate work was spent in studies at Woods Hole, the rest in laboratory teaching at Columbia. During these five years he was seriously overworked. In all this period he was chiefly interested in the *Drosophila* work which Morgan had opened up, and from 1910 on he closely followed this research and was an intimate member of the group, although he did not have opportunity for much experimental work of his own on this material until 1912. Then he was able to begin his investigation of the simultaneous inter-relationships of many linked genes, which supported the theory of crossing-over and constituted his thesis. At the same time he undertook his analysis of variable, multiple-factor, characters by means of the device of «marker genes». This extended the validity both of chromosomal inheritance and of gene stability, and led later (1916) to his theory of balanced lethals.

Called to the Rice Institute, Houston, as Instructor, by Julian Huxley, he taught varied biological courses (1915-1918), and began studies on mutation. During this time and the two years following, when he was again at Columbia (1918-1920), now as instructor, he elaborated methods for quantitative mutation study. Altenburg, who had meanwhile moved to the Rice Institute, and he, partly in collaboration, obtained the first results in this field (1918-1919), including evidence that made probable an effect of temperature. He then (1920) returned to Texas, this time to the University, at Austin, as Associate Professor, and from 1925 on as Professor, teaching mainly genetics and evolution, and doing research mainly on mutation. He formulated in 1918, 1920, 1921, and 1926 the chief principles of spontaneous gene mutation as now recognized, including those of most mutations being detrimental and recessive, and being point effects of ultramicroscopic

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physico-chemical accidents arising in the course of random molecular motions (thermal agitation). At the same time he put forward the conception of the gene as constituting the basis of life, as well as of evolution, by virtue of its possessing the property of reproducing its own changes, and he represented this phenomenon as the cardinal problem of living matter.

In late 1926 he obtained critical evidence of the abundant production of gene mutations and chromosome changes by X-rays (published 1927). This opened the door to numerous researches, many of them carried on with the aid of students and co-workers, both at his own and other institutions, in the twenty years that followed. These have been briefly outlined in his Nobel Lecture, since they, together with the first discovery of the effect, constitute the work for which the Nobel Award was granted. They include studies on the mechanisms of the gene mutation effects and of the structural changes, on the roles which each kind of changes, when spontaneously occurring, play in evolution, and on the properties of genes and of chromosome parts (e.g. eu- versus hetero-chromatin), as disclosed by studies in which the chromosomes were broken and rearranged.

This later work was carried on at a succession of places. In 1932 he was awarded a Guggenheim Fellowship and for a year worked at Oscar Vogt's institute in Berlin, in Timoféeff's department of genetics. At the request of N. I. Vavilov, he then spent 3 1/2 years as Senior Geneticist at the Institute of Genetics of the Academy of Sciences of the U.S.S.R., first in Leningrad later (1934-1937) in Moscow, with a considerable staff of co-workers. With the rise of the Lysenko anti-genetics movement, he moved to the Institute of Animal Genetics, University of Edinburgh (1937-1940); here numerous graduate students, largely from India, took part. Then, from 1940 to 1945, I he did both teaching and research at Amherst College, being professor ad I interim there from 1942 to 1945. At Amherst he completed a large-scale experiment showing the relationship of ageing to spontaneous mutations. Finally, in 1945, he accepted a professorship in the Zoology Department at Indiana University, Bloomington, Indiana. Here he is again devoting his time chiefly to work on radiation-induced mutations, using them on the one hand for purposes of genetic analysis and on the other hand in the study of how radiation produces its biological effects.

One group of studies, participated in by J. I. and Ruby M. Valencia, I. H. Herskowitz, I. I. Oster, S. Zimmering, S. Abrahamson, A. Schalet, J. D. Telfer, Helen U. Meyer, Sara Frye, Helen Byers, and others, has been concerned with the influence on mutation frequency in the fruit fly *Drosophila* of diverse conditions and agents, when these were used before, after, or with radiation, or without radiation, on the influence of dose-rate and total dose of the radiation, and on the relative sensitivities of different cell stages to induced or natural mutagenesis. The types of mutations studied included «point» changes and both minute and gross structural changes of chromosomes. In another group of studies, since carried much further by E. A. Carlson, the interrelations among independently arisen mutations of the same gene were studied intensively, their intra-genic arrangement determined, and principles governing their functional interactions worked out.

The incidence of radiation damage to the bodies of the individuals that have themselves been exposed, as manifested in a long-term mortality or, in other words, life-span shortening or accelerated «ageing», was also investigated, first by I. I. Oster and then by W. Ostertag and Helen U. Meyer in collaboration with Muller. Evidence was obtained that these effects are for the most part consequences of losses of chromosomes from dividing somatic cells, after these chromosomes have been broken by the radiation. Natural ageing, however, gave evidence of not being caused in this way.

Another group of researches, also carried out with cooperation from students, more especially Margaret Lieb and S. L. Campbell, had concerned itself with problems of dominance and related subjects. It was shown that most mutant genes are incompletely recessive (not «overdominant») and are acted upon by selection while heterozygous. Studies of dominance in relation to «dosage compensation» disclosed that selection usually acts with high precision, tending to establish homozygous «normal» types. Most genetic variation within populations was deduced to depend on the recurrence of detrimental mutations which, balanced by selective elimination, constitute a «load». Estimates of this load were formed for both *Drosophila* and man (in the latter case in cooperation with Drs. Newton E. Morton and James F. Crow of the University of Wisconsin).

Included in the studies were calculations concerned with both the «spontaneous» and the radiation-induced mutation frequencies, and of the consequences of selection. Estimates were made of the effects of changes in mutation frequency, on the one hand, and of selection pressure, on the other hand, on the load. It was shown that eugenic policies are needed to avoid genetic degeneration in man as well as to bring about the genetic enhancement called for by his advances in technology and in other aspects of his culture. It was pointed out that modern reproductive technologies, such as germ-cell banks, and liberalized mores now make possible the exercise of voluntary germinal choice in human reproduction, and that this procedure affords the practical solution necessary to enable cultural evolution to promote the biological evolution of man instead of perverting it.

Prof. Muller will retire from Indiana University, in June, 1964, to take an appointment at the Institute for Advanced Learning in the Medical Sciences, The City of Hope, Duarte, California - for one year.

Muller has contributed over 300 articles on biological subjects to the scientific publications of learned societies. His principal books are *The Mechanism of Mendelian Heredity* with T. H. Morgan and others, 1915 and 1922, *Out of the Night - a Biologist's View of the Future,* 1935, 1936, and 1938, and *Genetics, Medicine and Man* with C. C. Little and L. H. Snyder, 1947.

He was President of the 8th International Congress of Genetics in 1948 and of the American Humanist Association during 1956-1958. He has received Doctor of Science degrees from the Universities of Edinburgh (1940), Columbia (1949) and Chicago (1959), the honorary Doctor of Medicine from Jefferson Medical College (1963), the Annual Award of the American Association for Advancement of Science (1927), the Kimber Genetics Award (1955) and the Darwin-Wallace Commemoration Medal (1958). He was Pilgrim Trust Lecturer (Royal Society) and Messenger Lecturer (Cornell University) in 1945, and was designated Humanist of the Year by the American Humanist Association in 1963. He has also received honorary memberships and fellowships of many learned societies in the United States, England, Scotland, Sweden, Denmark, India, Japan, Italy, etc.

Muller married his first wife, formerly Jessie M. Jacobs, in 1923 - they had one son, David Eugene. In 1939 he married Dorothea Kantorowicz - they have one daugther, Helen Juliette.

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Hermann J. Muller died on April 5, 1967.