MARSHALL W. NIRENBERG

NIRENBERG, MARSHALL W(ARREN) Apr. 10, 1927- Biochemist

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Man's scientific understanding of the fundamental nature of life took a giant stride forward in 1961 when Dr. Marshall W. Nirenberg discovered a procedure for deciphering the "genetic code" in living cells. His findings then and his continuing research have opened the gates for other scientists to vast areas of knowledge about the processes of all life on earth, its origin, evolution, and future. Almost equally vast is the speculation over the eventual rewards and dangers to man when his mastery of the genetic code gives him the power to influence heredity. Since 1957 Nirenberg has been associated with the National Institutes of Health of the Department of Health, Education, and Welfare, and since 1962 he has been chief of the section of biochemical genetics of the National Heart Institute.

Marshall Warren Nirenberg was born on April 10, 1927 in New York City. His family moved to Orlando, Florida when he was ten years old, and he has always thought of Florida as home. As a student at the University of Florida in Gainesville, he was attracted to biochemistry while working with Dr. R. L. Shirley and Dr. George K. Davis of the Nutrition Laboratory. Biochemistry was then almost unknown to the undergraduate courses, and Nirenberg recalls getting a good introduction at the laboratory to radioisotope techniques that proved important to him in investigating the structures of organic compounds. He was an assistant in the department of biology from 1945 to 1947 and a teaching assistant there the following year. He obtained his B.S. degree in 1948. His fraternity at the university was Pi Lambda Phi.

While taking graduate courses at the University of Florida, Nirenberg worked as a research associate at the Nutrition Laboratory in 1951-52. For his M.Sc. degree in biology, which he received in 1952, he made a study of certain insects in Alachua County. Dr. Lewis Berner, who was directing Nirenberg's research, recognized his deeper inclination and helped him decide to seek his Ph.D. degree in biochemistry. From 1952 to 1956 he held a teaching fellowship in the department of biological chemistry at the University of Michigan. Then as a research fellow in 1956-57, he completed his dissertation on the subject of hexose uptake in ascites tumor cells. The University of Michigan awarded him the Ph.D. degree in biochemistry in 1957.

A postdoctoral fellowship of the American Cancer Society for further work in biochemistry, under the sponsorship of Dr. DeWitt Stetten, Jr., brought Nirenberg to the National Institutes of Health in Bethesda, Maryland in 1957. During the next few years at the National Institute of Arthritis and Metabolic Diseases, Nirenberg doggedly pursued his research into the yet illegible hieroglyphics of life's code. When his American Cancer Society fellowship expired in 1959, he continued at the institute under a fellowship of the Public Health Service, and in 1960 he became a research biochemist in the institute's section of metabolic enzymes.

The fruits of his research were summed up in a paper on the genetic code that Nirenberg delivered at the International Congress of Biochemistry in August 1961 in Moscow. The paper had an electrifying impact on his fellow-scientists and was followed up by two reports published in the October issue of the *Proceedings of the National Academy of Sciences.* In these Nirenberg described how he and Dr. J. Heinrich Matthaei, a visiting scientist from West Germany, performed the milestone experiment that cracked the genetic code. But although he had stirred the world of biochemistry, Nirenberg remained unknown to the general public until December 1961, when news of his discoveries appeared in the press.

The chemical "language" used to describe Nirenberg's findings is a metaphorical means of expressing the way that every living cell passes along its genetic message. The storehouse of genetic information, which he has helped to unlock, is a chemical called DNA (deoxyribonucleic acid). Another chemical, RNA (ribonucleic acid), serves as a kind of messenger and transmits the information out of the original cell. Through the co-operation of the two acids, specific proteins are manufactured that are basic to the development of new cells. Genetic information is transmitted in the form of a code made up of precise quantities of four nucleic acids: A (adenine), T (thymine), G (guanine), and C (cytosine). From this genetic "alphabet" words and sentences are formed, and their sequence determines each genetic trait.

Dr. Nirenberg looked for clues to the code in the making of protein. He mixed a batch of chemicals containing all the amino acids, excluding from them the DNA, RNA, and other components. Then he added an artificial RNA made up only of uracil, coded as UUU. "By adding radioactive carbon 14 to one amino acid at a time in each mixture," as George Eagle explained in the Washington *Post* (January 3, 1965), "Nirenberg found that the amino acid directed into protein by UUU is phenylalanine." This was the first word translated from the genetic code. A similar experiment was performed later in the year by a New York University group led by the Nobel Prize winner Dr. Severo Ochoa. In January 1962 Ochoa announced that he and his colleagues had determined the coding for nineteen of the twenty known amino acids and had predicted the base code for the last one. Nirenberg immediately announced substantial agreement with those findings for the fifteen amino acids his team had deciphered.

Scientists everywhere hailed Nirenberg's feat as the most important development in molecular biology since the two Nobel Prize winners, James Dewey Watson and Francis H. C. Crick, demonstrated the double-spiral structure of DNA back in 1953. Crick declared that the entire coding problem would be solved within a year —a prediction that proved to be too optimistic. Nirenberg pointed out that many other scientists in all parts of the world were adding fragments of knowledge that would help to unravel the life process. Later, when singled out for awards, he insisted to the press that at least thirteen biochemists at the National Institutes of Health share the credit with him, including Philip Leder and Merton Bernfield, who were most closely associated with him in the work on the genetic code.

At a symposium on the chemistry of heredity in April 1962, in Atlantic City, a record-breaking audience of 3,000 biologists and chemists heard Nirenberg report how he made his system turn out tobacco virus proteins. In co-operation with Dr. Heinz Fraenkel-Conrat and Dr. Akira Tsugita of the University of California, he fed tobacco virus RNA into a mixture of amino acids derived from wrung-out sewage bacteria whose code of life had been destroyed. Soon the "brainless" bacteria turned out tobacco virus proteins—something that only a tobacco leaf could do before. In a similar way, biochemists at the Rockefeller Institute have made Dr. Nirenberg's system turn out hemoglobin, the protein pigment of red blood cells of vertebrates.

In 1962 Dr. Nirenberg was appointed chief of the section of biochemical genetics of the National Heart Institute. Addressing a symposium at the Institute of Microbiology, Rutgers University, in September 1962, he disclosed that earlier in the year he and his associates had worked out three-letter combinations for each of the twenty amino acids. Many scientists at the symposium shared the belief that the genetic code of life is more complicated than it was thought the year before. Nirenberg supported this view by presenting evidence that in addition to the twenty three-letter words for the amino acids, there are some twenty-five other designations for them in the code. In his opinion, the newly discovered complexity in the genetic code represented a step forward, since it meant that the understanding of the code was nearer reality and less of a laboratory ideal. He expressed his belief that the code would be broken in the near future.

The next step in the deciphering of the code was made public at a gathering of the world's leading biochemists in New York on July 30, 1964. Nirenberg described how he and his colleagues combined the chemical code symbols into a three-letter "word" and then put all the "words" into the test tubes with ribosomes, amino acids, and the proper enzymes. Each of the GUU "words," it turned out, called for the amino acid named valine. Thus Nirenberg found out a code word that carried a specific order. George Eagle of the Washington *Post* reported that Nirenberg has revealed that codes can be read and written in sequence by adding radioactive material to see which component comes up first, second, and third. According to Nirenberg, his group was "just zooming" through the translation in sequence. But he said that biochemists in the molecular field still could not read long genetic messages—only fragments.

The discoveries resulting from Nirenberg's pure research are bound to have startling implications for the world outside his laboratory, and hardly any area of life will remain unaffected by them. His research might eventually tell doctors enough about the construction of diseased cells to help wipe out diabetes, cancer, and other illnesses. The pattern of RNA has already been further clarified by Robert W. Holley and others, and its function, particularly in the process of memory, is already being investigated. Mastery of the genetic code would permit not only the improvement of the lot of individuals but also the slowing down of the aging process, the correction of genetic defects, and the changing of heredity. Although most scientists look at these prospects with exhilaration, some have sounded sober warnings. Thus the Nobel Prize winner Arne Tiselius has cautioned against tampering with life, mind control, and heredity abuse.

Against this background of awesome opportunities and dangers, Nirenberg takes a cautious and realistic position. He calls his group's work "enlightened trial and error" and prefers to speak of his immediate task in the laboratory. In his view, a long and tedious building of the foundations of basic biological knowledge is necessary before any of the medical and other implications can begin to be understood. "Ultimately one hopes," he wrote in an article for *Scientific American* (March 1963), "that cell-free systems will shed light on genetic control mechanisms. Such mechanisms, still undiscovered, permit the selective retrieval of genetic information." He believes that the genetic code is essentially universal on this planet and is used even by species on opposite ends of the evolutionary scale.

The National Academy of Sciences gave Dr. Nirenberg its award for distinguished research in molecular biology in 1962, including a $5,000 grant to continue his work. Other honors followed: the Paul Lewis Award in Enzyme Chemistry of the American Chemical Society in 1963 and the Modern Medicine Award in 1964. On February 8, 1965 President Lyndon B. Johnson presented Nirenberg with one of eleven National Medals of Science. He is a member of the American Society of Biological Chemists, American Chemical Society, Biophysical Society, Washington Academy of Sciences, and Sigma Xi, the science honor society. His articles have appeared in *Science, Scientific American,* the *Proceedings of the National Academy of Sciences,* and other professional periodicals.

Modest about his scientific achievements, Nirenberg prefers anonymity. According to one interviewer, "He shies away from talk about cancer cures, controlled heredity, and the possibility of international honors." He is six feet three inches tall, slender, and dark-haired. The scientist is said to look ten years younger than his age. His wife, the former Perola Zaltzman, met him when she was a graduate exchange student from Brazil on a fellowship at the National Institutes of Health. Mrs. Nirenberg now works in the clinical endocrinology branch of the National Heart Institute. They live in Bethesda near the institute. Dr. Nirenberg likes to return to his laboratory in the evening to pursue an interesting idea far into the night. His sense of urgency about his work has made him appreciate the way the United States has supported scientific research. He has visited laboratories in many other countries, but "nowhere else in the world," he has said, "do the researchers get the support of anything like the National Health Institutes. Without this kind of help we would be many, many years behind where we are now."

References

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