Robert Holley—1968 Nobel Laureate

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The 1968 Nobel Prize for physiology or medicine was shared by 3 scientists, Robert W. Holley, Har Gobind Khorana (1922-), and Marshall W. Nirenberg (1927-), for research that helped to explain how genetic components of the cell nucleus control the synthesis of proteins. Holley was the first scientist to determine exactly the internal structure of a strand of one of the nucleic acids that helps build protein in living cells according to a genetic master plan. He developed techniques for determining the structure of nucleic acids and determined the complete nucleotide sequence of alanine transfer ribonucleic acid (tRNA). Khorana, working at the University of Wisconsin in Madison, developed methods for investigating the structure of nucleic acids and provided the codons (sequences of nucleotides that code for amino acids) for several amino acids. Nirenberg, working at the National Institutes of Health in Bethesda, Md, developed the procedure for deciphering the genetic code in living cells. The work of these 3 laureates contributed substantially to the understanding of genetic mechanisms and protein synthesis.

Holley was born on January 28, 1922, in Urbana, Ill. Both his parents were schoolteachers. He received his early education in the public school systems of Illinois, California, and Idaho. After graduating from Urbana High School in 1938, he entered the University of Illinois at Urbana and received a BA degree in chemistry in 1942.

During World War II, Holley joined the US Office of Research and Development and worked at Cornell University in Ithaca, NY. He was part of the team that, from 1944 to 1946, first synthesized penicillin. After the war, he was appointed a National Research Council Fellow at Cornell University and completed his formal education there, receiving his PhD degree in biochemistry in 1947.

After receiving his doctorate, Holley was awarded a fellowship from the American Chemical Society, which enabled him to spend 1 year (1947-1948) doing postdoctoral research at Washington State College in Pullman. In 1948, he returned to Cornell University as an assistant professor of organic chemistry, doing research at the New York State Agricultural Experiment Station, a branch of Cornell University located in Geneva, NY. In 1957, he was appointed research chemist at the US Plant, Soil, and Nutrition Laboratory at Cornell University, and in 1964, he was promoted to professor of biochemistry and named chairman of the department. During these years, he began to study the biochemistry of the nucleic acids. Except for a sabbatical leave, Holley remained at Cornell University from 1948 to 1966.

In 1966, Holley was awarded a National Science Foundation Fellowship and spent a year doing research at the Salk Institute for Biological Studies in La Jolla, Calif. In 1968, Holley was named American Cancer Society Professor of Molecular Biology and was a resident fellow at the Salk Institute. In 1969, he was named adjunct professor of the University of California at San Diego.

Holley was granted a 1-year sabbatical from Cornell University in 1955 to work at the California Institute of Technology (Caltech) in Pasadena as a Guggenheim Fellow doing research with biochemist and molecular biologist James Frederick Bonner (1910-1996). Holley began his prize-winning work at Caltech in 1955-1956 and completed it as a research chemist at Cornell University. He returned to Cornell University in 1957 and spent 3 years isolating 1 g of alanine tRNA from 90 kg of yeast. On March 19, 1965, Holley and colleagues announced in *Science* that they had identified the complete sequence of 77 nucleotides of alanine tRNA. They had determined the composition of tRNA that incorporates the amino acid alanine into protein molecules. This feat—the first determination of the sequence of nucleotides in a nucleic acid—required digesting the molecules with enzymes, identifying the pieces, and figuring out how they fit together. Since that work, all tRNAs have been shown to have a similar structure.

Holley died of lung cancer on February 11, 1993, at the age of 71 years in Los Gatos, about 8 miles southwest of San Jose, Calif. Besides the Nobel Prize, he was awarded the Distinguished Service Award of the US Department of Agriculture (1965), the Lasker Award (1965), and the US Steel Foundation Award of the National Academy of Sciences (1967). He was honored on a stamp issued in 2000 by the Palau Islands that includes a portrait of Khorana, one of his Nobel Prize cowinners.