Summary of Dr. Marshall W. Nirenberg's Work

The thousands of different proteins which are found in nature are composed of only 20 or so subunits, called amino acids, the exact characteristics of each protein molecule being determined by the number, kinds and arrangement of amino acids within the molecule. The production of proteins is directed by the genes, which are made up largely of deoxyribonucleic acid (DNA). Every living cell, and hence all living things, are what they are primarily because of the proteins they contain. A specific protein is made at the direction of a code which is contained within the DNA molecule and is determined by the sequential arrangement of subunits within it.

DNA does not act directly in protein synthesis but goes through an intermediary, ribonucleic acid (RNA), implanting the code in RNA. The messenger RNA, which is thus formed can be one of a great variety of patterns corresponding to one of an equally great variety of DNA molecules. The subunits of both DNA and RNA, called nucleotides, in turn contain still simpler substances belonging to the chemical classifications of purines and pyrimidines combined with sugar and phosphoric acid. The names of the nucleotides are derived from the four possible purines and pyrimidines, which in the case of RNA are adenine, guanine, uracil and cytosine. It is the composition and arrangement of the nucleotides which dictate the final composition of the protein molecule.

In 1959 Marshall Nirenberg began studies at the National Institutes of Health on protein synthesis in cell-free systems, and with amazing rapidity reported a series of observations which are now known throughout the world. He started by preparing from the bacterium, E. coli, a cell-free system which synthesized protein in the presence of amino acids and energy sources (ATP). Then, he showed for the first time that messenger RNA is required for cell-free protein synthesis.

Synthetic RNA and natural RNA prepared from a virus, greatly stimulated cell-free protein synthesis. Dr. Nirenberg discovered a synthetic RNA containing only a single pyrimidine, uracil, serves as a template for the cell-free synthesis of the protein containing only one amino acid, phenylalanine. This single experiment may be said to have "cracked the genetic code."

Further experiments with other synthetic RNAs containing various proportions of purines and pyrimidines revealed codes for essentially all the known amino acids normally present in protein.

Although the base composition of RNA codons and many properties of the genetic code were clarified with the use of synthetic polynucleotides, the sequence of the bases within each codon remained unknown. More recently, a general method of great simplicity was found by Nirenberg and co-workers for determining the base sequence of codons. With this it was demonstrated directly that since tri- but not dinucleotides serve as templates in this system, a triplet code exists.

The sequences of virtually all codons have now been determined by Dr. Nirenberg's laboratory. It has been shown that the patterns of synonym codons differ markedly in both template activity and specificity. The biological consequences of these and other findings remain to be assessed. It would seem logical, however, that some synonym codons must play special roles in protein synthesis, such as specifying the beginning or end of the genetic message; others may be necessary for the synthesis of certain proteins or may selectively influence the rate of protein synthesis.

Studies are now in progress in Dr. Nirenberg's laboratory to define possible consequences of selective modification of components required for codon recognition. Particular attention is being focused upon mechanisms which may selectively control the rate of protein synthesis during viral infection and embryonic differentiation.

Dr. Nirenberg has deciphered the genetic code. His work has given us understanding of much of the mysterious way information is coded into the nucleic acids and used to direct the incorporation of specific amino acids into proteins. It represents a major contribution toward understanding on a molecular basis how the chemicals of the cell nucleus carry the hereditary message from one generation to the next.