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Nobel Prize in Medicines 1968


Robert W. Holley


Har Gobind Khorana


Marshall W. Nirenberg

The Nobel Prize in Physiology or Medicine 1968 was awarded jointly to Robert W. Holley, Har Gobind Khorana and Marshall W. Nirenberg "for their interpretation of the genetic code and its function in protein synthesis"

During the fall of 1868, exactly 100 years ago, a young Swiss physician by the name of Friedrich Miescher isolated a new type of compound from cell nuclei. He called this compound nuclein; today we call it nucleic acid. Two years earlier, unbeknownst to Miescher, a Czech monk, Gregor Mendel, in the town of Brno finished a series of experiments which eventually turned out to be closely connected with Miescher's discovery. From very simple experiments with peas Mendel discovered that our inheritance is packaged into many independent genes. Mendel's work marked the beginning of genetics as a science.

Nucleic acids and genes - originally two widely separated concepts - together form the basis for this year's Nobel Prize for medicine, for Holley's, Khorana's and Nirenberg's investigations on the genetic code, also called the code of life.

During the 19th century the Nobel Prize had not been established. Had the prize existed it is unlikely that it would have been awarded for the discoveries of nucleic acids and genes. Miescher's

results were published in extenso only after his death in 1890. Mendel reported his observations in a first publication in 1866, which received little attention and was soon forgotten.

For a long time no connection between genes and nucleic acids could be seen. 25 Years ago nucleic acid research was considered a rather dull and exclusive area which interested few scientists. One of the interested few was Einar Hammarsten, professor at the Karolinska Institute. His foresight served at an early stage as a stimulus for important contributions by several Swedish scientists, in particular Torbjörn Caspersson - who demonstrated the biological importance of nucleic acids.

Nucleic acid research came of age in 1944. In this year the American scientist Avery succeeded in transferring a hereditable property from one bacterium to another with the aid of pure nucleic acid, and in so doing demonstrated that genes are made up of nucleic acids. Avery's discovery marked the beginning of a new branch of science which has come to be called molecular biology and which, up to the present time, has been concerned mainly with the biochemistry of genetics. The vitality of molecular biology is attested by the fact that today's prize is the fifth Nobel Prize in medicine since 1958 awarded to research in this area.

What then is the genetic code and why is it called the code of life? Nucleic acids are very complicated molecules, but their structure shows certain regularities. They are constructed from a limited amount of smaller building blocks. If we compare a nucleic acid with a language, we can think of the building blocks as the letters of the alphabet of the language. With this analogy, we may say that the language of nucleic acids in the cell describes our inherited traits. It tells us if our eyes and those of our children are blue or brown, if we are healthy or sick.

There also exists a second language in our cells: the language of proteins, written in the alphabet of proteins. A single cell contains many thousands of proteins which perform all the chemical reactions required for the normal life of the organism. The synthesis of each protein is directed by a particular nucleic acid. A brown-eyed child receives from its parents nucleic acids which have the ability to direct the formation of proteins required for the synthesis of dark pigment of the eye. It is the chemical structure of the nucleic acid which determines the chemical structure of the protein; the alphabet of nucleic acids dictates the alphabet of proteins. The genetic code is the dictionary which gives us the translation of one alphabet into the other.

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When the hieroglyphs were deciphered the archeologists made use of the Rosetta Stone which contains the same alphabet written with Greek and Egyptian letters. In theory one could use the same method for deciphering the genetic code by comparing the chemical structure of a particular nucleic acid with that of the corresponding protein, letter by letter. However, this is not possible for technical reasons.

In this situation Nirenberg arrived at a very simple and ingenious solution: he realized that the biochemist had a decisive advantage over the archeologist since he could construct in the test tube a system which uses a nucleic acid as template for the formation of a protein. Such a system can be compared with a translation-machine which is fed by the scientist with a sentence written in the alphabet of nucleic acids; the machine then translates the sentence into the protein alphabet. Nirenberg synthesized a very simple nucleic acid, composed of a chain of only a single repeating letter. Using this nucleic acid the system produced a protein which also contained a single letter, now written in the protein alphabet. In this way Nirenberg had both deciphered the first hieroglyph and shown how the machinery of the cell can be used for the translation of the genetic code in general. After that, the field moved extremely rapidly. Nirenberg reported his first results in August 1961. Less than five years later all the details of the genetic code were established, mainly from the work of Nirenberg and Khorana.

Much of the final work was done by Khorana. During many years he had systematically devised methods which led to the synthesis of well defined nucleic acids, giant molecules with every building block in its exact position. Khorana's synthetic nucleic acids were a pre-requisite for the final solution of the genetic code.

What is the mechanism for the translation of the code within the cell? This question was successfully attacked by Holley. He is one of the discoverers of a special type of nucleic acid which has been called transfer-RNA. This nucleic acid has the capacity to read off the genetic code and to transform it to the protein alphabet. After many years' work Holley succeeded in preparing a transfer-RNA in pure form and, finally, in 1965, established its exact chemical structure. Holley's work represents the first determination of the complete chemical structure of a biologically active nucleic acid.

The interpretation of the genetic code and the elucidation of its function are the highlights of the last 20 years' explosive evolution of molecular biology which has led to an understanding of

the details of the mechanism of inheritance. So far the work can be described as basic research. However, through this work we can now begin to understand the causes of many diseases in which heredity plays an important role.

Dr. Holley, Dr. Khorana, Dr. Nirenberg. At the end of his Nobel lecture, Edward Tatum in 1958 looked into his crystal ball and tried to predict some of the future developments in molecular biology. He suggested among other things that the solution of the genetic code might come during the lifetime of at least some of the members of his audience. This appeared to be a bold prophecy at that time. In reality it took less than three years before the first letters of the code were deciphered and, because of the ingenuity of you three, the nature of the code and much of its function in protein synthesis were known within less than eight years. Together you have written the most exciting chapter in modern biology.

It is now a great pleasure for me to congratulate you on behalf of the Karolinska Institute and to ask you to receive this year's Prize for Medicine from the hands of His Majesty the King.

For more details please visit:

http://www.nobelprize.org/nobel_prizes/medicine/laureates/1968/press.html