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Nobel Prize in Medicines 1959

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Arthur Kornberg

The Nobel Prize in Physiology or Medicine 1959 was awarded jointly to Severo Ochoa and Arthur Kornberg "for their discovery of the mechanisms in the biological synthesis of ribonucleic acid and deoxyribonucleic acid"

To maa man vaere hvis livet skal lykkes, «There must be two if life shall succeed», is the theme of a sentimental old Danish song. The author had in mind man and woman, but she probably did not know how right she was from a more elementary biological viewpoint. Two principles are necessary so that «life» shall «succeed». One consists of proteins, the other of nucleic acids. The analogy is more than just a play upon words. Just as man and woman are responsible for the regeneration of mankind, likewise is the interplay between proteins and nucleic acids the only, and universally repeated basic mechanism of life. In the long series of substances which build up viruses, bacteria, plants, and animals, everything else might vary, but the proteins and nucleic acids are always present as the life-supporting elements. These both show certain principal characteristics. Their molecules are very large, and are built up from thousands of smaller units linked together in chains - just like a string of pearls - which have a tendency to form helices. Single helices

join together in complicated threads which can contain proteins or nucleic acids or both. In the mixed «super molecules», the reactions of life proceed in the subtle pattern of the intimately associated strands.

The proteins contain amino acids as their elementary part. In the whole of Nature on this earth, there are found only some twenty amino acids in proteins. The elementary parts of the nucleic acids, the nucleotides, consist of nitrogenous bases, sugar, and phosphoric acid. There are found in Nature practically no more than eight of these most important nucleotides, all of which contain phosphoric acid, but in which the nitrogenous base may be one of five different kinds. The sugar can be of two different kinds, one of which, «ribose», contains one more oxygen atom than the other, «deoxyribose». This seemingly insignificant difference in a single atom produces a remarkably great effect. Nucleic acids are divided into two different series because of this characteristic. These series have widely different functions, so widely different in fact, that this is the reason why we have two Prize Winners on the stage today.

«Deoxyribonucleic acids», which Arthur Kornberg has now synthesized, are mainly present as the hereditary substance in chromosomes. The «ribonucleic acids», which Severo Ochoa has synthesized, have other functions, such as to assist in the synthesis of proteins. The Swedish scientist Torbjörn Caspersson has played an important role in demonstrating this last fact. From his and other research-workers' discoveries, it has been possible to conclude that nucleic acids assist in the synthesis of protein. The exact chemical mechanism, however, is as yet unknown. Inasmuch as nucleic acids and proteins are the two main principles of life, it seemed highly probable that, vice versa, the proteins should take part in the rebuilding of nucleic acids. This seems so much the more probable when we realize that proteins, in the form of enzymes, take part in practically every chemical reaction in the biological world. It is to the everlasting credit of Ochoa and Kornberg to have clarified this fundamental mechanism by preparing proteins that build up nucleic acids in test tubes.

For proteins it has been proved, and for the nucleic acids it is highly probable, that the order of the different building blocks in the chains is by no means left to chance, but on the contrary is planned in detail for each kind of molecule and for each kind of living organism.

It is this regulated order between the building blocks that always makes human children grow up to be human beings, and the serpent's offspring grow up to be serpents. It is disturbances in this regulated order which change the hereditary factors and allows the variations of species over thousands of years. The almost infinite possibilities to combine the building blocks in different ways makes it possible to vary the form in which life appears on our earth. Let me give a comparable example. By different combinations of the 28 letters in our alphabet, we can write everything that can be expressed in our own language, as well as in all other languages. The building blocks of the proteins, the amino acids, are approximately equal in number to the letters of the alphabet. The protein molecules can be compared with words with 100, 1,000, or even 10,000 letters. It is clear that Nature here has been generous with the possibility to make different combinations amounting to astronomical figures. But here, another factor might be brought up. The differences between the amino acids are necessary not only to produce the possibilities for variation, but also to enable the proteins, by their enzymatic activity, to regulate the different aspects of metabolism. Even the two types of nucleic acids with 4 different nucleotides in each, when made up from 100 to 10,000 nucleotide units in each molecule, give a fantastic number of possible combinations. Thus it would seem as if it were too heroic an enterprise to try to find out the procedure whereby Nature forms such complicated substances as nucleic acids with such an unerring accuracy in placing each building block.

A few years ago, Ochoa and Kornberg, each in his own laboratory, started to investigate the problem. The development turned for Ochoa's part in a direction that made him work with systems that produced ribonucleic acids, while for Kornberg it led him to investigate the formation of deoxyribonucleic acids. They have both, in a series of

outstanding investigations, without direct cooperation, but nevertheless, as personal friends probably profiting from each other's results, reached the goal at the same time. As everyone else, they were able to make use of results obtained by preceding research workers, among whom I can only mention a few. It might be of interest to mention that uric acid, the first representative of the purines (a class of nitrogenous bases that form part of the nucleic acids) was discovered in Sweden in 1776 simultaneously by both Carl Wilhelm Scheele and Torbern Bergman. It is a curious parallel to the shared Nobel Award of today, and a reminder of Sweden's great era in the science of chemistry. The German scientist Albrecht Kossel received the Nobel Prize in 1910 for his elucidation of the chemistry of the nitrogenous bases of the nucleic acids, whereas the English scientist Alexander Todd clarified in detail the chemical properties of the nucleic acids, and received the Nobel Prize for Chemistry in 1957. But what really enabled Ochoa and Kornberg to succeed was their own excellent previous work in related fields. Both have worked with bacteria from which they have made preparations of a high degree of purity, Ochoa from an acetic acid bacterium, and Kornberg from the coli bacterium. Ochoa's enzyme produces ribonucleic acids from ribonucleotides having twice the ratio of phosphoric acid residues as that contained in ribonucleic acid. The ribonucleic acid is formed by splitting out half of the phosphoric acid residues, and linking the nucleotides together to form large molecules, which, as far as we can prove today, do not differ in any way from natural nucleic acids. Kornberg's enzyme produces deoxyribonucleic acids in a similar, but not identical fashion. Both have arrived at the same, principally important result that in order to make the reaction start, it is necessary to add in the beginning a small amount of nucleic acid to act as a template. Otherwise the enzymes do not «know» which kind of nucleic acid they are to produce. As soon as they get a template to act as a guide, they start, just like a skilled type-setter, to copy the «manuscript» they have received. Here one recognizes life's own principle that like creates like. Even though several research workers had earlier suspected that such a mechanism was involved, the actual experimental proof is of greatest importance. Furthermore, Ochoa's enzyme has

given us the possibility of enzymatically synthesizing simplified nucleic acids of great interest.

To give an idea of where the discoveries that are being honored today may lead to in the near future, I want to mention one example. Other scientists, especially S. S. Cohen in the U.S.A., have shown that the nucleic acid of a certain bacteriophage, T_2, which is a kind of bacterial virus, contains a somewhat chemically different nitrogenous base. If bacteria are infected with T_2 phage, this different nucleic acid is soon produced in the bacteria. Kornberg succeeded in explaining the mechanism in detail. T_2 phage behaves like the worst kind of usurper. Within four minutes it produces a number of enzymes which destroy a nucleotide necessary for the bacterium's normal production of nucleic acids, and rebuilds it to the different nucleotide of the T_2 phage, and thereby destroys the bacteria.

We are sure to witness in the near future several important discoveries in biochemistry, virus research, genetics, and cancer research as a consequence of the work of Ochoa and Kornberg. They have helped us to advance quite some distance on the road to understanding the mechanism of life.

Professor Severo Ochoa, Professor Arthur Kornberg, dear friends and colleagues. Some 130 years ago, Friedrich Wöhler, in the laboratory of Berzelius, synthesized urea from inorganic matter. This event occurred in the heart of this city of Stockholm, less than half a mile from where we are now standing. He thus overbridged the first gap between living and dead material. You have now made the second fundamental discovery on this pathway, the synthesis in test tubes of one of the two basic principles of life.

On behalf of the Caroline Institute, I extend to you our warm congratulations, and ask you to receive this year's Nobel Prize for Physiology or Medicine from the hands of His Majesty the King.

For more details please visit:

http://www.nobelprize.org/nobel_prizes/medicine/laureates/1959/press.html