DNA: ITS HISTORY AND POTENTIAL

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A brief history of the discovery of nucleic acid is given.

Specificity of DNA synthesis is amazing and the sequence of amino acids in proteins as a result of DNA coding is most precise. Rather than being the master chemical, DNA is the servant of the cell. Thus its operation is repressed by the cell until needed.

Reasons for not being carried away by false hope of altering genes controlling our own body and mental traits are given, most important of which is lack of specificity of any irradiation or chemical mutagen. These all tend to be random in their effect. Thus we cannot "tell" a nitrite ion which of about 2500 adenine bases it should change to guanine.

As we continue to learn more of the complexity of the DNA-RNA system we should be ever more impressed by Psalm 139:14, "Man is fearfully and wonderfully made." Surely such a complexly integrated system could only have been created by a wisdom far superior to our own. Unbelieving man, willfully stubborn, prefers to believe this marvelous system could have evolved from properties inherent in the neutron. How much more reasonable to accept the clear proclamation "In the beginning God created . . ."

First isolation of nucleic acid from the nuclei of cells, now known as deoxyribonucleic acid (DNA), was accomplished by a medically-trained Swiss physiological chemist, Friedrich Miescher, in 1869.[1] This work was performed in the laboratory of Hoppe-Seyler at Tubingen. Hoppe-Seyler was one of the outstanding chemists of that era, and Miescher's accomplishment was so significant that Hoppe-Seyler held up publication of results for two years until Miescher's work could be fully confirmed.

Because of their availability, Miescher used pus cells from discarded bandages as his source of cells. He first isolated the cell nuclei, and from these he extracted a grey-white powder which he later called "nuclein."

Miescher next turned to the sperm of Rhine salmon as a source of nuclein. He isolated what he recognized as a salt-like compound formed by the combination of a nitrogen-rich base and a phosphorus-rich acid, his nuclein. The base he called protamin", and he developed a method for isolating it. The purified nuclein had a phosphorus content of 9.6%, and after acid hydrolysis, all of the phosphorus was recovered in the form of phosphoric acid.

Miescher also investigated sperm of frogs, carp, and bulls. He detected nuclein in all of them. He pointed out that nuclein seemed to be the genetically active chemical which had been postulated as being present in spermatozoa.

From about 1875, other workers became active in this field, and by 1900 all of the major bases which occur in nucleic acid had been isolated. Later it became apparent that there were two types of nucleic acid, differing in origin and composition. The nucleic acid from yeast or from wheat embryo was hydrolyzed to yield four bases, adenine, guanine, cytosine and uracil, phosphoric acid and a sugar identified in 1909 by Levene as the pentose, ribose.

From thymus was isolated the other type of nucleic acid, from which was obtained the four bases, adenine, guanine, cytosine, and thymine, phosphoric acid and a pentose sugar identified by Levene in 1930 as deoxyribose. Today the type of nuleic acid containing the base, uracil, and the sugar, ribose, is known as ribonucleic acid (RNA), and the other type containing thymine and deoxyribose is known as deoxyribonucleic acid (DNA).

During the decade 1940-1950, results indicated that DNA is almost always found in the cell nucleus as part of the chromosomes, while RNA is mainly found in cytoplasm. It is now known that cell nuclei, as well as the cytoplasm, contain both DNA and RNA. It was found that nucleic acid is a polymer consisting of thousands of sub-units. These sub-units are called nucleotides. The nucleotides are composed

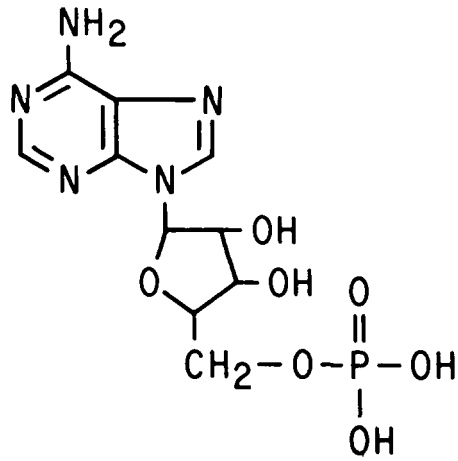

Figure 1. Adenylic acid, a nucleotide.

of a base, either a purine or a pyrimidine, linked to a sugar, either ribose or deoxyribose, depending upon the type of nucleic acid, and the sugar in turn is linked to phosphoric acid. One such nucleotide, adenylic acid, is shown in Figure 1.

The sub-units, or nucleotides, of nucleic acid are joined through phospho di-ester bonds, the phosphate being combined with the 3'-hydroxyl of one sugar and the 5'-hydroxyl of the sugar of the adjacent unit. This "backbone" structure is shown schematically in Figure 2.

Molecular weight values range up to 2,000,000 or more for RNA (tobacco mosaic virus RNA contains about 6600 nucleotides and has a molecular weight of 2,000,000) to 10,000,000 and higher for DNA.

The almost forgotten suggestion by Miescher that nucleic acid might play a central role in inheritance was confirmed by Avery and co-workers in 1944[2]. They extracted DNA from "smooth" or encapsulated pneumococcus bacteria and added it to the culture of "rough" or unencapsulated pneumococci. A new generation of "smooth" bacteria was produced which continued to produce the "smooth" type. The DNA from the "smooth" type had been incorporated into the genetic material of the "rough" type, converting it permanently to the "smooth" type. This established that genes are composed of DNA. This event gave great impetus to research into all aspects of DNA.

In 1950, Chargaff[3] recorded the fact that among the bases of DNA the amount of adenine was always equal to thymine and guanine was always equal to cytosine (in molar quantities). This observation provided one of the keys to the structure proposed for DNA in 1953 by Watson and Crick. In that year, Watson and Crick[4], combining the data of Chargaff and X-ray crystallographic data, proposed for DNA the structure that is now widely accepted.

Watson-Crick Model

According to the proposal of Watson and Crick, DNA exists in the form of a double-stranded helix, the two helical chains being coiled about a common axis. They proposed that one chain of the double helix is the complement of the other, with adenine in each chain pairing with thymine of the other, and guanine in each chain pairing with cytosine of the other. The two chains of the double helix are held together by hydrogen bonds between the purine bases (adenine and guanine) and the pyrimidine bases (cytosine and thymine).

A purine is always paired with a pyrimidine, because two purines would occupy too much space to allow a regular helix, and two pyrimidines would occupy too little. Because of stereochemical relationships, adenine always pairs with thymine and guanine with cytosine. The base pairing of a section of two complementary DNA strands is shown in Figure 3.

From the structure proposed for DNA implications could be drawn concerning its replication by the cell. These implications were published by Watson and Crick[5] a few months after their paper on the structure of DNA.

They proposed that prior to replication, the hydrogen bonds holding the double-stranded helix of DNA together are broken, and the two chains unwind and separate. Each chain then acts as a template for the formation onto itself of a new complementary chain, so that eventually two pairs of chains are formed where only one existed before.

After the two original strands have separated, along each of these intact chains are assembled free nucleotides (these nucleotides at this stage are in the form of triphosphates). This assemblage takes place according to the base pairing pattern described above. That is, every place in the intact chain where adenine occurs, a nucleotide containing thymine will become loosely attached by hydrogen bonds; where guanine occurs in the intact chain, the nucleotide containing cytosine will become attached by hydrogen bonds, etc.

When the nucleotides have been assembled in place along the intact chain, the enzyme DNA polymerase joins the free nucleotides together by forming regular chemical bonds between them to form the new DNA strand. The result is a

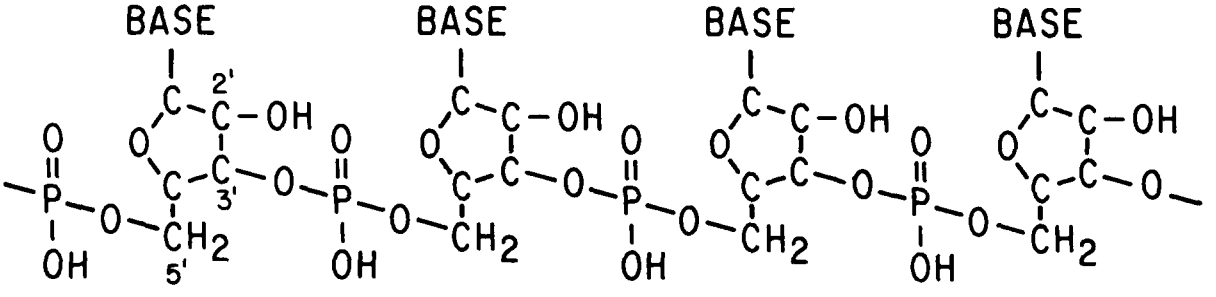

Figure 2. Schematic representation of nucleotide arrangement in nucleic acid.

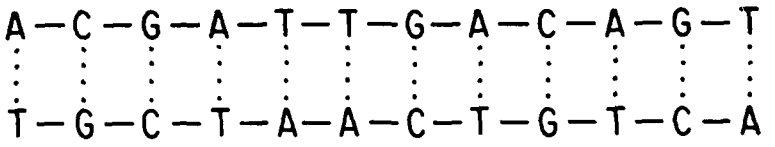

Figure 3. Base pairing in DNA (A=adenine, G=guanine, T=thymine, C=cytosine).

double-stranded DNA helix, one strand having been derived intact from the previously existing DNA and the second having been formed from the nucleotide sub-units.

DNA Replicated by Cell

It should be pointed out here that DNA does **not** replicate itself. **It is replicated by the cell.** DNA does furnish important information for its replication in the form of the sequence of its individual nucleotides, but the complex apparatus in the cell is required to synthesize copies of DNA. The cell synthesizes the sub-units or nucleotides that are polymerized to form DNA.

The cell, through the complex apparatus designed for this purpose, supplies the energy required for the synthesis to take place. A certain concentration of magnesium is required and, of course, the presence of the enzyme DNA polymerase, in the absence of which no synthesis would take place, is an absolute necessity.

Here evolutionists are faced with a dilemma, The presence of a protein, the enzyme DNA polymerase, is indispensible for the synthesis of DNA. On the other hand, the information required for the synthesis of all proteins is contained in DNA. In an evolutionary scheme, which could have come first? Protein is required for DNA synthesis, and DNA is required for protein synthesis. Which preceded the other? The best answer seems to be that neither arose before the other, but both have existed together from the very beginning.

It is now believed that most genetic information resides in DNA. This information is contained in the form of a "genetic code" built into the DNA molecule. This genetic code is fashioned from the sequence of the bases in DNA. What this code is, and how this information is transmitted so that a protein with a fixed and specific structure is synthesized, I will not attempt to explain here. Nevertheless, there is a message built into each DNA molecule, and this message is used to dictate the structure of every other molecule in the cell.

Complexity of Apparatus

I must emphasize the extreme complexity of the apparatus required to transfer the message or code in a structural gene into a specific protein molecule:

The code in the gene (which is DNA, of course) is used to construct a messenger RNA molecule in which is encoded the message necessary to determine the specific amino acid sequence of the protein.

The cell must synthesize the sub-units (nucleotides) for the RNA (after first synthesizing the sub-units for each nucleotide, which include the individual bases and the ribose).

The cell must synthesize the sub-units, or amino acids which are eventually polymerized to form the protein. Each amino acid must be activated by an enzyme specific for that amino acid. Each amino acid is then combined with another type of RNA, known as soluble RNA or s-RNA.

There is a specific s-RNA for each individual amino acid. There is yet another type of RNA known as ribosomal RNA. Under the influence of the messenger RNA, the ribosomes are assembled into units known as polyribosomes.

Under the direction of the message contained in the messenger RNA while it is in contact with polyribosomes, the amino acid-s-RNA complexes are used to form the protein. Other enzymes and key molecules are required for this.

During all of this, the complex energy producing apparatus of the cell is used to furnish the energy required for the many syntheses.

A brief description as the one above may leave one more confused than enlightened, yet it does emphasize the tremendously complex apparatus that is required to synthesize a protein molecule in the living cell. Four types of nucleic acid are involved–DNA, messenger RNA, soluble RNA, and ribosomal RNA. In the synthesis proper, about 30 different enzymes are involved, and if we include the synthesis of the sub-units and of the energy producing apparatus, hundreds of different enzymes are required.

The specificity of the synthesis is amazing. The sequence of the sub-units, or amino acids, in each protein molecule is very definite and precise. Along the complex pathway from DNA to protein molecule, which involves the interaction of many different molecules and includes passage from the nucleus to the cytoplasm, where polyribosomes are found, the code contained in the DNA is perfectly transcribed into the structure of the protein molecule.

The DNA serves two purposes in the cell. In DNA is encoded the information which, on

demand of the cell, is converted by the cell into the message necessary for the production of other complex molecules and structures of the cell. The DNA also serves as the genetic unit of the cell, its replication serving as the means of transferring to the daughter cell all of the information encoded in the parent DNA.

DNA: Master or Servant?

What of DNA? Is it the "master chemical," the "secret of life?" Is it true, as claimed by Jukes[6], that "the purpose of life is the perpetuation of a base sequence?" It seems inescapable to me that DNA, rather than being the master of the cell, is the servant of the cell. DNA is kept under strict regulation by the cell. Its operation or message is repressed by the cell until needed. Derepression follows, and when the need for the message, or the molecule produced by this message, is no longer needed, the gene is once more repressed.

When the cell replicates, and before cell division takes place, it reproduces a second set of DNA molecules and from this constructs a second set of chromosomes. The parent cell utilizes its replication of DNA to pass on to the daughter cell the genetic information contained in the parent cell. While DNA occupies a key position in the cell, it is only one of many important features of the cell. Commoner[7] has aptly stated that, rather than DNA being the secret of life, "life is the secret of DNA."

Williams[8] stated in his review of Juke's book, mentioned above, that in this book we have witnessed "the deification of a molecule." There is a widespread tendency today among scientists and laymen alike to prostrate themselves before an altar upon which is enshrined DNA.

Many believe that the solving of the genetic code will open up a marvelous new future for man whereby he will be able to "control his own evolution." Such a belief rests in ignorance. The solving of the genetic code would eliminate only one of many problems involved in understanding how the numerous features of life are uniquely determined. Even if we understood all of this, how to alter DNA specifically in order to bring about a desirable change would remain an insuperable difficulty.

The first problem involved in altering our genetic make-up is the fact that the carriers of the genes, the chromosomes, are located in the nuclei of the egg and sperm cells. In order to subject this material to treatment, some means must be devised for removing it from the egg or sperm and replacing it, after treatment, with retention of viability by the egg or sperm.

Today we have some understanding about the relative positions of a few of the many thousands of genes in some microorganisms. By their linkage we can determine whether or not they occupy adjacent positions on the chromosome. We do not have the slightest idea where their actual positions on the chromosome are, however, and have no way at present of determining this. Even if we knew which gene is which, how could one particular gene be separated from among the tens of thousands present?

If, in the future, we could devise a method for removing a particular gene for treatment in order to alter it, several practical impossibilities would yet stand in the way of altering our genetic properties selectively.

In each gene there are thousands of nucleotides, or sub-units. A change in only one of these thousands of sub-units causes profound changes in the genetic properties of the gene. We do not have the slightest idea, however, what effect on an organism will be caused by a specific change at some point in the gene.

In a recent series of newspaper articles, Professor James Bonner of the California Institute of Technology was quoted as saying that in the future man will so control his own genetics that, for instance, if a person wants four arms, he can have four arms. Some of his speculations even went beyond this.

If we alter one of the genes governing the arms, however, what do we get—four arms, short arms, long arms, or no arms at all? The almost certain result would be some crippling effect, for in spite of the claims of evolutionists. all mutations are in the nature of injuries. If man ever begins to tinker with his genes, he had better construct many additional institutions to house the monsters that result.

It could also be pointed out that most, if not all, of our characteristics are polygenetic, that is, they are under the control of not one but a number of genes. For instance, eye color in *Drosophila* is under the control of 15 genes. The desirable alteration of a certain characteristic, if that is possible at all, most likely would require changes in more than one particular gene. Precisely coordinated changes in several genes would probably be required.

Great Difficulty Remains

If all the above problems were solved, which seems incredible, one insuperable difficulty would yet remain. In each gene there are thousands of nucleotides, but only four different kinds of bases. In a gene of 10,000 nucleotides, there would be, on the average, 2500 of each of the four different kinds of bases.

Let us say we knew that to bring about a specific desirable change, we had to change the adenine, at position 5263 of the chain, to a

guanine. If a chemical or irradiation or some other kind of treatment were used, how could the effect of that treatment be limited to position 5263 without affecting one of the other 2499 adenines in this DNA? It could not.

Chemical action, irradiation, or other mutagenic treatments are completely random in effect. We cannot "tell" a nitrite ion which base to attack. Since these treatments are by their very nature random in effect, it is obvious that they can never be utilized to bring about a specific change in the genetic material.

Other possible means of altering genetic properties could be discussed with much the same results. In spite of the bold claims of Dr. Bonner and others, man will have to get along with the two arms he has, as well as with the other features with which he is endowed. Man is "fearfully and wonderfully made" (Psalm 139:14), the product of the Master Planner. If we can learn to preserve that creation in reasonably good health for three score and ten, we will do well.

As we learn more and more about DNA and how it functions in the cell, we should view this great master plan with awesome wonder. Its complexities and intricacies are beyond our comprehension; the results of the plan, marvelous. Who is it that conceived and brought this into being? Unbelieving man, willingly ignorant, prefers to believe it was inherent in the properties of the neutron. It seems to me immeasurably more reasonable to accept the clear proclamation of Scripture, "In the beginning God created. . . .". The purpose of life is not, as Jukes claims, to perpetuate a base sequence, but the purpose of DNA is to perpetuate life.

References

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