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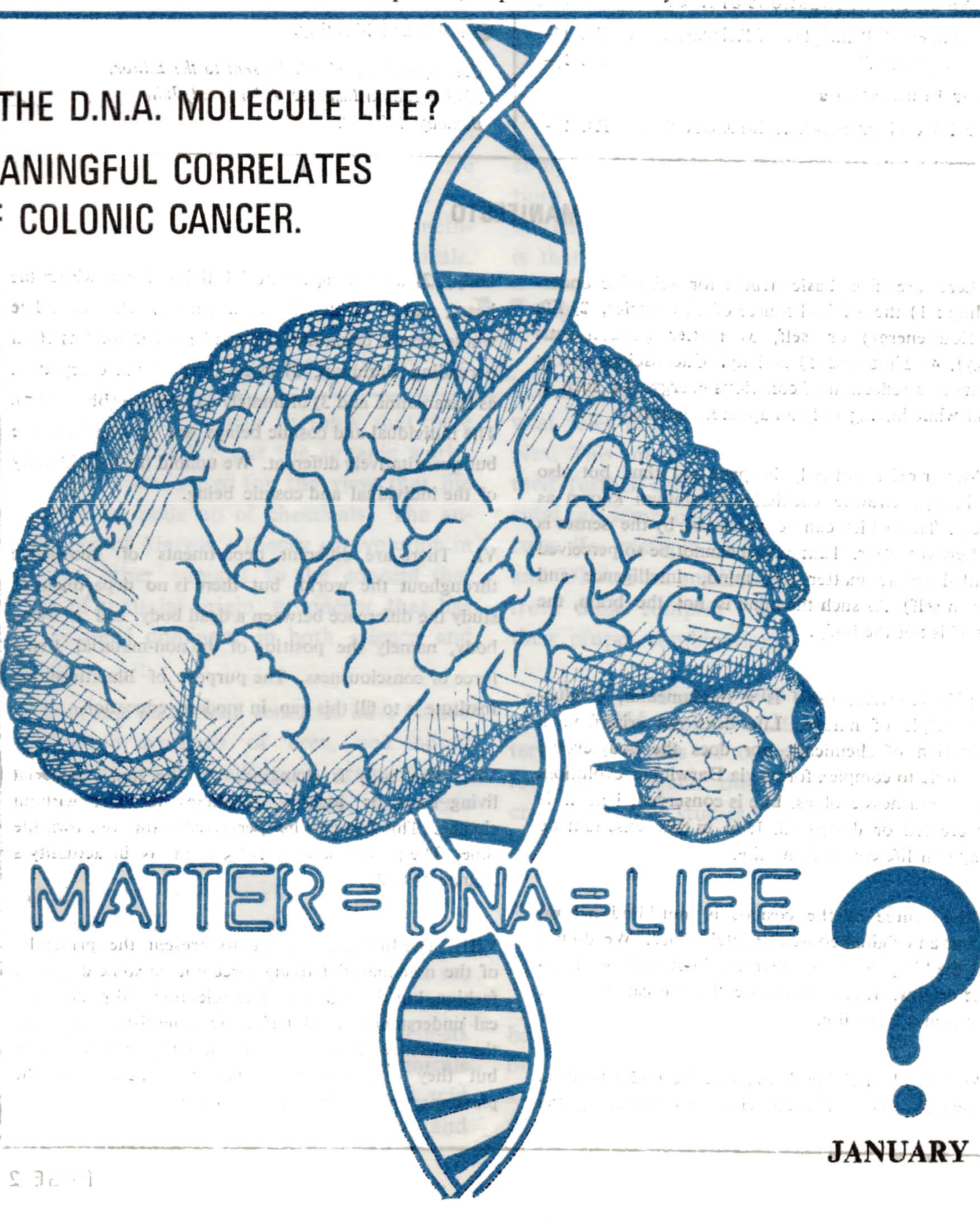

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IS THE D. N. A. MOLECULE LIFE?

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UNTIL the nineteenth century, chemists thought that whatever happened in a living system could not be reproduced in the laboratory; In other words, inorganic matter composing living material bodies. The prevailing view was that a non-physical vital energy was operating in the living system. In 1828, however, the German chemist Friedrich Wohler announced the laboratory synthesis of urea from ammonium cynate, an inorganic compound. Urea is an end organic by-product forming the major solid component of mammalian urine. Wohler's synthesis of urea profoundly influenced the minds of chemiststoward adopting a materialistic view of life. By the late 1850's, Pierre Berthelot reported the production of such organic compounds as alcohols, acetylene, methane and benzene from inorganic chemicals. Gradually, chemists, began to think that there was nothing unusual about the organic world. Thus the way was paved for the view that life itself must be made up of chemicals. The announcement of Darwin's theory of evolution in 1859 lent further support to the concept that life was of material origin, a concept that has since remained dominant in both science and philosophy.

About one and a half centuries have passed since Wohler's synthesis of urea, and indeed organic chemistry has advanced tremendously since that time. Synthetic fibers, synthetic rubber, synthetic dyes, chemotherapeutic agents, synthetic pesticides, synthetic glass and synthetic liquid crystals are some of the major products of synthetic organic chemistry.

Similarly, during the last fifty years or so, many advances have been made in the fields of cell biology and molecular biology. Chemists and biochemists have identified many chemicals such as lipids, proteins, deoxyribonucleic acid (DNA), ribonucleic acid (RNA), hormones and coenzymes inside the cells constituting living material bodies. Many scientists believe that the DNA molecule holds the ultimate explanation of life. It is their genuine hope that once this DNA molecule, the so-called master molecule, is assembled step by step from its constituent atomic elements-carbon (C), hydrogen (H), nitrogen (N), oxygen (O), and phosphorus (P), their goal of synthesizing life in the test tube will be achieved. This will finally prove that life is, after all, nothing but a system of chemicals. But is the DNA molecule really the essence of life ?

We would like to argue that no matter how complex they may be, all molecules or collections of molecules, including DNA, are dead matter. What scientists know and agree upon is that the majority of the molecules playing vital roles in living systems are extremely complex. This much is correct. We question only their further conclusion that if complex molecules can somehow be made from simple molecules (for example, proteins from amino acids, and DNA from nucleotides) then life will arise from these complex molecules by virtue of their proper combinations.

Let us briefly examine the chemistry of the cellular DNA molecule. It consists of two interwined strands of complementary structures forming a regular double helix. From X-ray crystallographic studies the diameter of the helix is found to be approximately 20 A°, and each strand makes a complete turn every 34 A° (or every 10 nucleotides).[2] Strings made of alternate groups of phosphate and sugar (deoxyribose) form the backbone of the two strands. Each phosphate group links to deoxyribose, a five-car bon chain sugar. The sugar in turn links to one of two possible bases of purine (guanine or adenine) or two possible bases of pyrimidine (thymine or cytosine) through hydrogen bonds.

Adenine (A) is always paired with thymine (T), and guanine (G) with cytosine (C), for conformational reasons and because of the donor-acceptor natures of the hydrogen bonding groups. As a stereochemical consequence of this strict base pairing, the two polynucleotide chains run in opposite directions. Although hydrogen bonding between other base pairs is possible, it leads to nucleotide pairs which have the wrong external geometry and do not fit into the regular doublehelical structure.

This strict requirement of base pairing is responsible for the systematic replication process of DNA. Geneticists commonly assume that DNA is the carrier of the genetic information of the cell. It duplicates itself before cell division to provide each daughter cell with a complete set of DNA molecules. DNA replication involves strand separation, and each separated strand forms the template for the condensation of a complementary strand. This is commonly called the Watson-Crick mechanism.

GAP CAN BE BRIDGED BY FAITH

Descriptions such as this of DNA and its replication mechanism are commonly given as though they provided a complete description of the most fundamental processes of life- a final mechanical, stey-by-step breakdown of these life processes into understandable chemical terms. However, this is far from true. An enormous gulf lies between the few simple chemical facts known about DNA and the actual functioning of a cell. All that science actually knows about DNA are a few relations between inanimate chemicals. The gap between this knowledge and an actual chemical understanding of life is bridged only by faith.

To illustrate this, let us consider a few features of the cellular reproduction process. According to Watson, the replication and maintenance of DNA requires at least four different kinds of enzymes : endonuclease, exonuclease, DNA polymerase, and polynucleotide ligase [3]. These are all practically unknown at present. The one which seems to be best understood, DNA polymerase is estimated to contain some 1,100 amino acid subunits, but the arrangement of these subunits is still unknown. It is thought DNA polymerase is involved in the cellular replication of DNA. However, there is also evidence that this enzyme is involved in the repair of damaged DNA instead, and that in bacteria other, unknown enzymes in the cell membrane are required for replication.[4]

The replication process is thus very poorly understood. For example, the single chromosome of E. coli is thought to be a loop of double-stranded DNA some 500 times longer than the cell itself. Due to its spiral nature, this tangled loop must spin on its axis some 360,000 times in the course of a single replication, and the two loops must be neatly separated. In order to account for this, biochemists have postulated many different molecular mechanisms, but none of these are clearly understood [5]. This is just one of many examples that we could cite.

Although we may imagine that the cell is nothing more than an elaborate chemical machine, we actually do not at all know how this machine works. We have no idea how the large scale actions of a cell (what to speak of a multicellular organism) can be reduced to the reactions of molecules. Indeed, we do not even fully understand the chemical interactions of water molecules. The operations of enzymes composed of 1,100 amino acids are certainly a mystery.

The assumption that the cell is a machine running according to simple push-pull laws is therefore, simply a matter of faith. It may be imagined that thousands of reactions of the form Ai–Bi–Ci can combine to create an elaborate chemical automation surpassing even the most sophisticated man-made computers. However, in contemplating this analogy we should consider that even the most detailed knowledge of the intricate functioning of a computer would be incomplete unless it entailed an understanding of the programmer. In like manner, it is quite possible in the context of current knowledge that other laws are involved in the operation of cells that are unknown to modern chemistry.

The most that can be said at present is that the knowledge of the biochemists is a knowledge of chemical reactions; it cannot be claimed that it constitutes an understanding of life.

As a further example, consider the recently reported synthesis of the E. coli gene that codes for tyrosine transfer ribonucleic acid (tRNA)[6] This gene has only 126 nucleotides, and commercially synthesized nucleotides are used as the starting materials for the gene's synthesis. The nucleotides are chemically hooked to form di-tri, and tetranucleotides. These units are further chemically assembled into dioxyribooligonucleotide segments of 10 to 15 units. The segments that possess complementary base sequences are enzymatically connected with DNA ligase to form larger duplexes, which are themselves finally connected enzymatically to complete the synthesis. (It is not a total chemical synthesis, in the sense that the natural enzyme has to be used to join the larger units.)

A gene is taken as a fundamental unit of heredity. According to geneticists, everything from the color of rose petals to the shape and color of human eyes is determined by genes. It has been reported that the functioning of this artificial gene could be detected in a living cell. These are quite significant findings so far as chemical knowledge is concerned. They suggest the possibility that a geneticist will be able to manipulate genes chemically, replacing defective ones with healthy ones. This does not, however, demonstrate that genes are completely responsible for life. Rather, it simply indicates that cells make use of messages coded in chemical form and that our technology may enable us to take advantage of this medium of information storage.

At this stage of scientific knowledge, all the experimental techniques and tools needed to synthesize most of the chemicals primarily found in living cells (for example, proteins, hormones, lipids, carbohydrates, vitamins and genes) are available. Yet scientists are nowhere near to constructing a complete "synthetic living cell" in the test tube. The great hope expressed by many molecular biologists about a quarter century ago (after the historic discovery of the double helical structure of DNA by Watson and Crick) seems to have faded away in the midst of new discoveries.

Indeed, the findings of the biochemists, far from proving that life is a chemical phenomenon, have strongly demonstrated that the present scientific understanding of life is inadequate. In Darwin's time the cell appeared to be little more than a simple bag of organic compounds that one might readily hope to describe in chemical terms. In the majority encountered in recent biochemical investigations, however, it has been shown that this hope is unrealistic. Modern science is far from having understood the principles of life.

Szent–Gyorgyi, the Nobel–prize winning chemist, thus remarked : "In my search for the secret of life, I ended up with atoms and electrons which have no life at all. Somewhere along the line, life has run out through my fingers. So, in my old age, I am now retracing my steps. .".[7] This is the basic point we would like to emphasize. Atoms and molecules are lifeless. A gene or a DNA molecule is not life, and a protein molecule is not life. Indeed, we propose that a collection of these molecules is also not life. The recent announcement of Khorana's synthetic gene is not different from that of Wohler's synthesis of urea in 1828 as far as our understanding of life is concerned. ☐

1. Watson, J. D. and Crick, F. **NATURE** 171, 964, (1953)
2. Watson, J. D. **MOLECULAR BIOLOGY OF THE GENE** P. 261
3. Ibid. p. 281
4. Ibid. pp. 295–296
5. Ibid. pp. 282–292
6. **CHEM. ENG. NEWS**, 54(No. 39), 27(1976)
7. **BIOLOGY TODAY** Del Mar, California : CRM Books, 1972, p. xxiv