Key Molecule for the Evolution of Life—Nucleic Acid

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1. DNA and RNA

It is well-known widely that the double helix DNA is the genetic material itself. However, another nucleic acid called RNA (Fig. 1) is not so popular as DNA. The function of RNA is often compared with that of DNA as follows. DNA is the important original while RNA is the copy of it, in other words, blue print.

As indicated in Fig. 1, DNA and RNA are chemically very similar. We can logically say that both are, naturally, very similar because of the relation between the original and the copy. In the present organisms, however, DNA is always the record medium of the genetic information. On the other hand, RNA is versatile: the record medium (messenger RNA), information conversion material transfer molecule (transfer RNA), catalytic activity (ribozyme/ribosomal RNA), regulatory molecule (miRNA) and etc. RNA has really various functions as mentioned above while DNA is specialized for conveying information. Many viruses consist of RNA as their genetic material (RNA genome). This type, as readers may know, includes notorious SARS (Severe Acute Respiratory Syndrome) and HIV (Human Immunodeficiency Virus).

2. Discovery of Ribozyme

As a fruit of molecular biology, RNA was discovered to be functioning in the broader range of life than DNA. Nevertheless, RNA has been thought to be a supporting actor on the stage of life. As compared with DNA, RNA is more unstable and much susceptible to acid, generating the negative image as a substance.

Thus, DNA was thought to be a beauty in the closeted room, while RNA a parlor maid. In 1980s, however, since Cech and Altman discovered that RNA has a function of catalytic activity and termed as ribozyme, scientists have greatly changed their look at this molecule.

Up to this discovery, all of the catalytic activities were believed to be intrinsic to the protein called "enzyme". So it's quite natural that the scientists all over the world had been terribly surprised. This discovery gave an impetus to the theory that RNA is the very molecule that had worked for the evolution of life in the early days (RNA World Hypothesis). Consequently, DNA is considered to be derived from RNA. At present researches on this track are appearing and giving the support to 'RNA world hypothesis'. Then we have to clarify the reason why the discovery of ribozyme did lead to that sort of hypothesis.

3. Chemical Evolution and Nucleic Acids

In the latter half of 1970s Eigen and his colleagues advocated the hypercycle theory to explain the process of chemical evolution that is believed to have occurred at the early stage of the evolution of life. Chemical evolution represents the concept that before the cell-based organism of the present days, the functional and self-replicating molecules had appeared and evolved so as to proliferate the molecule itself. This concept is based on the study on the life cycle of RNA virus (Qβ). It was hypothesized that a molecular system (=hypercycle) is able to continually proliferate by itself as an interplay between the information molecule (≒RNA) and the function molecule (≒protein). The discovery of ribozyme proved that a single molecule of RNA can play both roles of 'information' and 'function'.

Inspired by this discovery, scientists began to consider that, at the early phase of chemical evolution, solely RNA molecule could have evolved to various functional ones before the emergence of protein. It is exactly 'RNA world'. In 1990s exploiting the technique of in vitro selection and simulating the evolution process, RNA molecules of function have been generated. In such experiments, usually, RNA molecules of around 100 bases were produced with a function. That is partly because RNA molecules of a too long sequence, make too many diversity to be exhaustively searched.

Note that a sequence of 100 bases have a diversity of $4^{100} = 10^{60}$. It proved possible to obtain such molecules with a satisfactory function from the limited number of molecules. Interestingly, the transfer RNA, working in the current organisms, is just around this size. From the recent studies, it has become clear that even the DNA molecule can have the function of catalytic activity. These facts show that nucleic acid (RNA/DNA) is really a great superstar who can take a charge of both information and function and

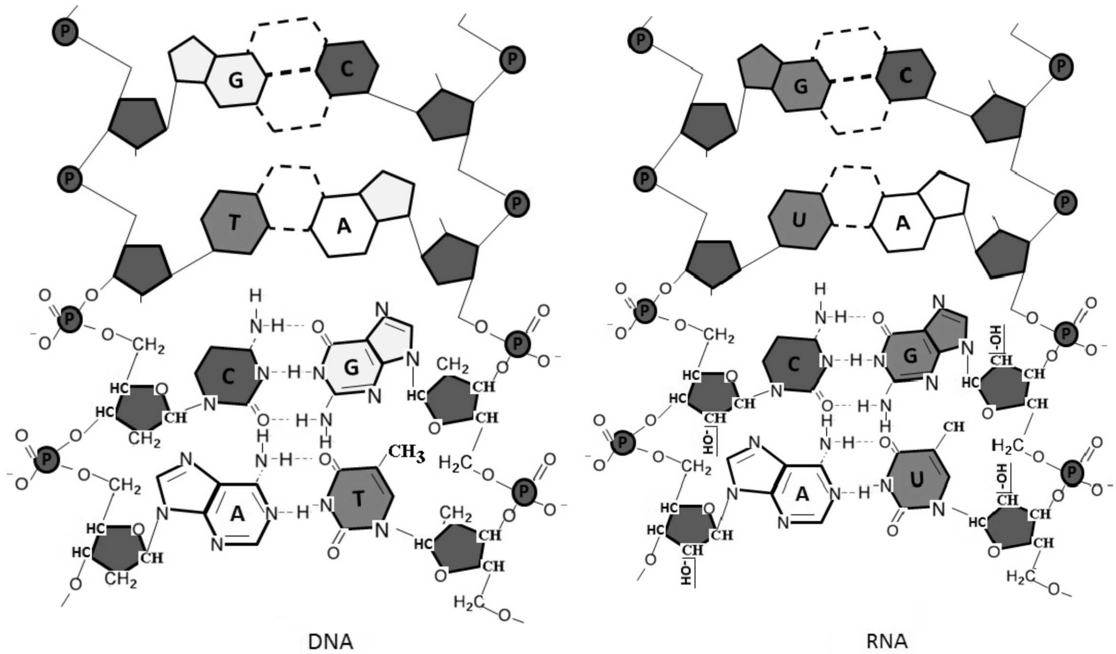

Fig. 1. Molecular Structures of DNA and RNA. As the molecular structure, DNA and RNA are very much alike each other. Few differences are: RNA has an additional OH in the sugar moiety if compared with DNA, and RNA is built up by the use of uracil base whereas DNA built up of thymine. The difference between thymine and uracil is methyl-modified or not. In organisms, such slight differences are strictly discriminated. Importantly, [G and C] and [A and T (U in RNA)] make pairs of bases. This is so-called Watson-Crick (WC) base-pairing. The relations are "complementary" to each other. The basis of inheritance resides just here. The dotted line in this figure indicates a weak binding of hydrogen bond.

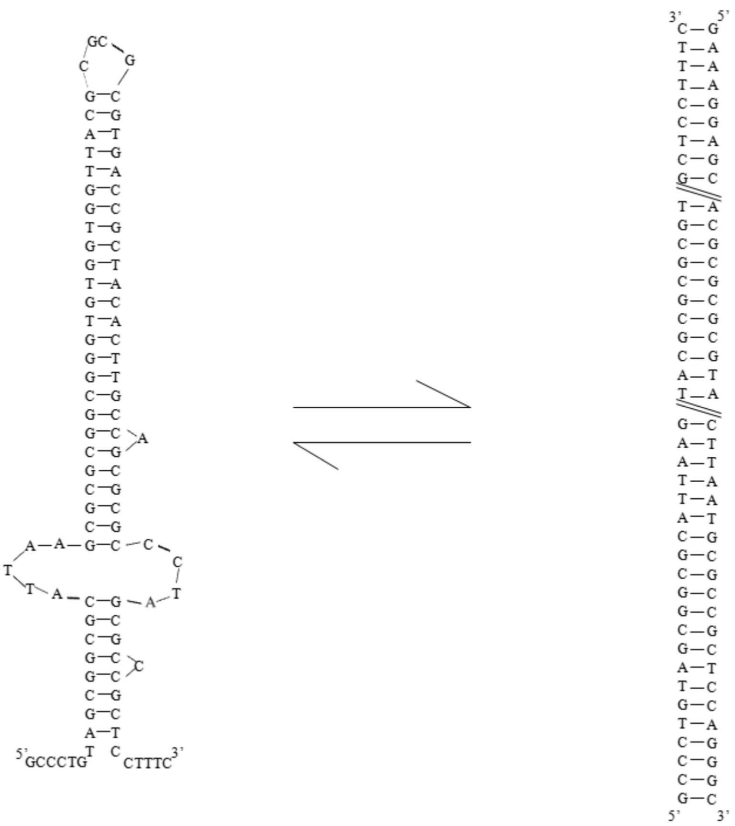

Fig. 2. Nucleic acids with the structure of single and double strands. This Figure stands for the morphology-generating part of DNA (that of DNA type virus fd). In the single strand structure, the virus fd can take the hairpin loop structure (left), providing the scaffold for wearing coat proteins. When the complementary strand appears or is synthesized, the virus fd DNA can make the double helix structure (right). The hairpin structure consists of WC base-pairings but is relatively unstable as compared with that of the double strand. In RNA, it is known that the part of non-base-paring is usually responsible for the catalytic activity.

considered to have played a very important role in the early stages of chemical evolution.

4. Dual Functions of Nucleic Acid

Next, why the nucleic acid could play so important roles of both information and function? Rationally speaking, the secret must be within the molecule structure. In fact we can find the answer for it by considering that the nucleic acid can take both states of "single strand and double strand". For example, as per Fig. 2, the DNA of virus fd, a parasite on the bacteria *Escherichia coli*, takes two different forms and functions; i.e. single strand and double strand. In single strand, it takes a so-called hairpin loop structure while in the double strand, the DNA of virus fd takes a double helix structure which has a nature of complementarity, that is each step of the double helix consists of two complementary bases; G and C or A and T. What is interesting is that the hairpin loop regions of a single strand DNA also contain the double helix structure (see Fig. 2). The function of double helix is exclusively specialized in preservation and transmission of information. On the other hand, the hairpin loop structure can perform the catalytic activity and other functions.

The principle of structure formation lies in the base-pairing for both of double helix and hairpin loop structures. The former can be said to be a complete type of the base-pairing and the latter an incomplete type of the same. It is really beautiful that the same molecule makes a flexible change of structure in order to achieve the different work, that is, information and function.

In the course of evolution, it is a minimum requirement to keep molecules functional and informational to reproduce themselves for 4 billions (4,000,000,000) of years. RNA fulfilled this requirement surprisingly nicely.

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