

It was an RNA world...

All living organisms share a number of properties. One is that all consist of similar organic compounds; second, that all the proteins found in present-day organisms consist of the same 20 amino acids; and third, that all living organisms carry their genetic information in nucleic acids—DNA and RNA—and use essentially the same genetic code. These properties seem to imply that the common ancestral cell stored genetic information in nucleic acids that specified the composition of all needed proteins, and, furthermore, that they relied on proteins to direct many of the reactions required for self-perpetuation. How did this mutually dependent system of proteins and nucleic acids come into being? Leslie Orgel, Francis Crick, and Carl Woese have postulated that RNA may have come first and established what is now called the **RNA world**—a world in which RNA catalyzed all the reactions necessary for a precursor of the common ancestral cell to survive and replicate. They also suggest that RNA could have developed the ability to link amino acids together into proteins. To do this, RNA would have to replicate itself without the presence of proteins and also would have to have the capability to catalyze every step of protein synthesis.

Why is RNA believed to be the originator of the genetic control system rather than DNA? One reason is that the ribonucleotides in RNA are more easily synthesized abiotically than the deoxyribonucleotides in DNA. In addition, RNA is single stranded and DNA is double stranded. It is easier to envision ways in which DNA could evolve from RNA and then, being more stable, could take over RNA's role as the repository of genetic information. Today, however, RNA synthesis in cells is catalyzed by a whole array of enzymes working together. Since such enzymes would not have been present in the primordial soup, how could replication occur? Recently it has been found that some present-day RNAs have catalytic activity. Called **ribozymes** (Fig. 1), these RNA molecules catalyze specific reactions involving other RNA molecules, such as the cutting of an RNA chain at certain sites. Other RNAs carry on self-splicing: they catalyze the removal of specific nucleotide sequences and then join together the resulting pieces. It is likely that the first organic catalysts were RNA molecules. At an early stage of evolution, then, RNA may have served as both genes and catalysts, only later giving up those roles to DNA and enzymes. This would allow living systems to use the more versatile proteins rather than RNA as enzymes and structural elements.

How could the ability of RNA to direct protein synthesis evolve? Just how a correlation between nucleotide sequences in nucleic acids and amino acid sequences in proteins could have arisen remains a mystery. Some ancient RNA systems may have had the capability to catalyze the synthesis of primitive proteins. The key may lie in RNA's structure; because it is single-stranded, different parts of the chain can join by complementary base pairing to produce a molecule that has a precise three-dimensional shape (Fig. 2). Perhaps the R groups of different amino acids formed weak attachments with specific sites on particular RNA molecules; once in position the amino acids could more easily be joined together to form a polypeptide (Fig. 3). Studies of ribosomes have provided experimental support of this hypothesis, because it has been found that it is probably the RNA in ribosomes, not the protein, that catalyzes formation of the peptide bonds. Whatever the mechanism, RNA somehow became involved very early in evolution in directing protein synthesis. In all living cells it plays a key role in this process: it is messenger RNA that provides the instructions for sequence of amino acids; it is transfer RNAs that bring the amino acids to the messenger RNA; and it is on the ribosomes, which are themselves composed largely of RNA, that protein synthesis takes place.

Another problem with the RNA-world hypothesis yet to be explained is how self-replicating RNA was created. The simplest hypothesis is that the nucleotides were formed when direct chemical reactions joined ribose with nucleic acid bases and phosphate (all of which could have been available in the "prebiotic soup"). Next, these ribonucleotides spontaneously joined to form polymers, one of which happened to be capable of engineering its own

reproduction (Fig. 4). This is an attractive hypothesis but experimental support is lacking. As of now, no one has produced an original polymer without help from proteins, nor has anyone been able to copy a complementary strand to yield a duplicate of the first template without help from proteins. Work on the problem is continuing. Because synthesizing nucleotides and achieving replication has proven to be so difficult under prebiotic conditions, some investigators are suggesting that RNA was not the first self-replicating molecule on the earth, but that another system came first and RNA took over from this molecule.

Whether RNA arose spontaneously or replaced some earlier genetic system, its development was probably the key event in the evolution of life. Finally, probably by reverse transcription, DNA came to code for RNA and DNA became the final repository for the genetic information (Fig.5). DNA, because it is double-stranded, is more stable than RNA, making replication errors less likely.

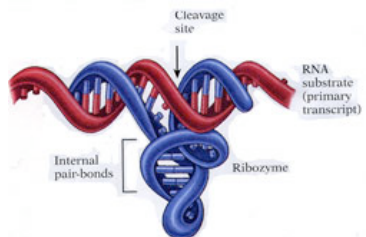


Fig. 1. The 39-nucleotide **ribozymes** (blue) and mRNA (red) that aid in intron editing bind to the target site on the primary transcript and then cleave a particular bond.

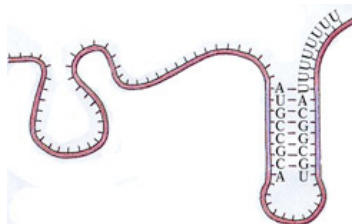


Fig. 2. **The folded structure of an RNA molecule.** Complementary base pairing between parts of an RNA molecule gives each molecule a unique, folded shape.

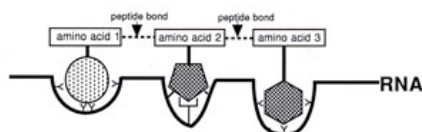


Fig. 3. Amino acids are trapped in clefts of an RNA molecule to form protein.

Fig. 4. **Abiotic replication of RNA.** Short chains of RNA could have formed abiotically in the primitive soup (A). If RNA is added to a mixture of activated nucleotides, the nucleotides will join weakly to the RNA by complementary base pairing (B). Polymerization of the complementary chain could have taken place under the conditions that existed on the early earth. The complementary chain could then act as a template for making RNA molecules identical to the original (C). Each molecule can act as a template for making many copies.

Fig. 5. **Evolution of genetic systems.** (A) The first cells probably used RNA for storage of genetic information. The RNA could have been self-replicating, if the raw materials and an energy source were present. (B) Some self-replicating RNA systems may have developed the ability to catalyze the synthesis of simple proteins, and a primitive form of translation evolved. (C) Finally, DNA, which is more stable than RNA, became the final repository for genetic information and came to code for RNA. Proteins became the major catalysts of the cell, and RNA functions as the middleman between the two.

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