Enzymatic Cleavage of RNA by RNA

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The discovery and characterization of the catalytic RNA subunit of the enzyme ribonuclease P of Escherichia coli is described.

KEY WORDS: RNA; RNase; ribonuclease P.

INTRODUCTION

The transfer of genetic information from nucleic acid to protein inside cells can be represented as shown in Fig. 1. This simple scheme reflects accurately the fact that the information contained in the linear arrangement of the nucleotides in DNA is copied accurately into the linear arrangement of nucleotides in RNA which, in turn, is translated by machinery inside the cell into proteins, the macromolecules responsible for governing many of the important biochemical processes in vivo. The straightforward transfer of information from DNA to protein is carried out by a class of molecules called messenger RNAs (mRNAs). The diagram shown does not elaborate on the properties of other RNA molecules that are transcribed from DNA, namely transfer RNA (tRNA) and ribosomal RNA (rRNA) and many other minor species of RNA found in vivo that had no identifiable function prior to 1976, nor does it indicate that the information in DNA and RNA can be replicated as daughter DNA and RNA molecules, respectively (see Crick, 1970, for further discussion).

Ribosomes are complexes which, in Escherichia coli, are made of about 50 proteins and three RNA molecules. It is on these particles that mRNA directs the synthesis of protein from free amino acids. tRNA molecules (Fig. 2) perform an adaptor function in the sense that they match particular amino acids to groups of three specific nucleotides on the mRNA to be translated and ensure that the growing polypeptide (protein) chain contains the right linear sequence of amino
Fig. 1. A representation of the flow of information inside cells from DNA to protein. This diagram is not a complete representation of the central dogma (see Crick, 1970).

acid subunits. Thus, rRNA and tRNA participate in the process of information transfer inside cells but they clearly do so in a comparatively complex manner.

My work on RNA began as a study of certain mutants that disrupt the ability of tRNA molecules to function normally during translation (Altman, 1971). This research, in turn, led to the identification of another RNA molecule that had, unexpectedly, all the properties of an enzyme (Guerrier-Takada et al., 1983). Aside from its intrinsic interest to students of catalysis and enzymology, our finding of an enzymatic activity associated with RNA has stimulated reconsideration of the role of RNA in biochemical systems today (see Cech, 1987, and Altman, 1989, for reviews) as illustrated in Fig. 1, and of the nature of complex

Fig. 2. A diagram illustrating the folding of the yeast tRNA\textsuperscript{Pho} molecule. The ribose-phosphate backbone is drawn as a continuous ribbon and internal hydrogen-bonding is indicated by crossbars. Positions of single bases are indicated by bars that are intentionally shortened. The anticodon and acceptor arms are shaded (Reprinted with permission from Watson, J. D., Hopkins, N. H., Roberts, J. W., Steitz, J. A. and Weiner, A. M., Molecular Biology of the Gene, 4th ed., Benjamin/Cummings, Menlo Park, 1987).