RNA World Hypothesis and General Information on RNA in Eukaryotic and Prokaryotic Organisms

RNA WORLD HYPOTHESIS

Addresses the fundamental dilemma inherent to the Central Dogma of Molecular Biology with respect to the beginning of life.

-How was protein produced without the DNA code?
-How was DNA produced without the catalytic activity of proteins?

DNA ---> RNA ---> Protein

Three basic assumptions:
1. At some time, genetic continuity was assured by the replication of RNA
2. Base pairing was the key to replication
3. Proteins were not involved in RNA replication.

Evidence for the Theory:
1. Catalytic activity for RNA:
-self splicing introns
-RNase P and catalytic RNA (ribozymes)
-peptide bond formation is catalyzed by rRNA
-short polymerization of RNA

2. Structural diversity:
-DNA is mostly inert and predominantly in the B-form and is acted upon by proteins
-RNA adopts extensive secondary - tertiary structures indistinguishable from proteins.

RNA ---> DNA ---> RNA ---> Protein

"RNA World Hypothesis"

Although RNA is best known for its role in translating genetic information into proteins, it serves many other functions in the cell, especially in relation to the regulation of gene expression and other basic cellular functions.

Over the last 10+ years, specific endonuclease/ligation processes and template functions have been identified for cellular RNAs and in many cases have been associated with important cellular processes involving RNAs and RNA processing.

In addition, the advent of methods for in vitro selection of RNAs (artificial evolution) with particular catalytic or binding processes strongly suggests RNAs as catalysts (ribozymes) are functionally quite plastic and that much of modern metabolism may have been distantly derived from a biochemistry centered on RNA rather than on protein catalysis.

Remants of such metabolism or important roles for RNA molecules are currently present in many processes:

Ribonucleotide based co-factors

RNA primers in DNA replication

Role of RNAs in RNA splicing and processing

Autocatytic splicing

Role of RNA in protein synthesis: tRNA and catalytic role of ribosomal RNA

Biosynthesis of ribonucleotides and then subsequent conversion to Deoxyribonucleotides

Other template functions in telomere maintenance and RNA editing

rRNA methylation (template)

DNA methylation (template/intermediate?)

Interest in these processes derives not only from interest in basic structure and function of RNA molecules and the role these molecules currently play in regulation of gene expression and other cellular processes, but also from the view that some of these processes likely represent "molecular fossils" of the "RNA World“
and as such provide a window into understanding the evolution of life, early life forms, and the overall potential or capabilities molecules have (RNA or other) for carrying out certain fundamental biochemical or cellular processes

RNA world

Overall, studies indicate that RNA molecules are capable of preforming the essential elements of living organisms :

1. self-replication (from in vitro selection experiments)

2. multiple catalytic functions including

a. cutting, joining, and moving around pieces of RNA molecules (existing functions)

b. making and breaking peptide bonds = synthesis and degradation of proteins (existing functions and from in vitro selection experiments)

c. can made nucleotides and other catalytic functions

3. informational template (several existing functions)

The capabilities as well as the function and role of RNA molecules in cellular processes suggest that early life forms may have been RNA based and that the first life forms may have evolved from an "RNA World" = **RNA WORLD HYPOTHESIS**