what is ribozyme ?

- A **ribozyme** (ribonucleic acid enzyme) is an RNA molecule that is capable of performing specific biochemical reactions, similar to the action of protein enzymes.

RIBOZYMES

- RIBOZYMES are *RNA* possessing *catalytic* activity.
- The first Ribozymes were discovered in the *1980*s by *Thomas R. Cech* and *Sidney altman*.
- The term "ribozyme" was first introduced by *kelly kurger* et al. in *1982*

Characteristic features of RNA molecule are:

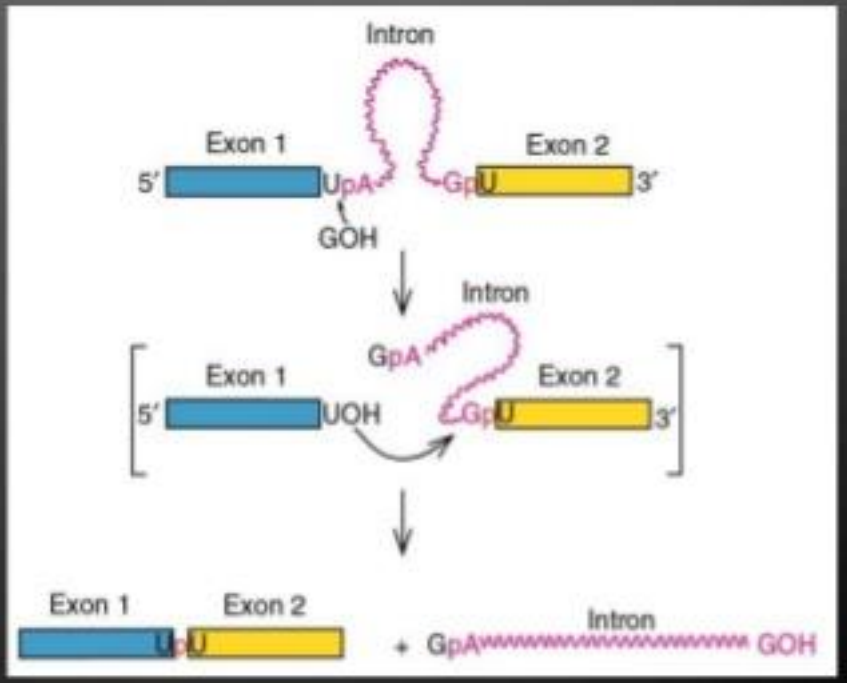
- An enzyme that uses RNA as a substrate
- AN RNA with enzymatic activity
- An enzyme that catalyzes the association between the large and small ribosomal subunits
- An enzyme that synthesizes RNA as part of the transcription process
- An enzyme that synthesizes RNA primers during DNA replication

Group I Intron Splicing :

- Group I intron ribozymes constitute one of the main classes of ribozymes.
- Found in bacteria, lower eukaryotes and higher plants.
- Group I introns are also found inserted into genes of a wide variety of bacteriophages of Gram-positive bacteria.
- However, their distribution in the phage of Gram-negative bacteria is mainly limited to the T4, T-even and T7-like like bacteriophages.

Mechanism:

The group I splicing reaction requires a guanine residue cofactor, the 3' OH group of guanosine is used as a nucleophile. The 3' OH group attacks the 5' phosphate of the intron and a new phosphordiester bond is formed. The 3' OH of the exon that is displaced now acts as the nucleophile in a similar reaction at the 3' end of the intron. So the intron is precisely excised and exons are joined together.

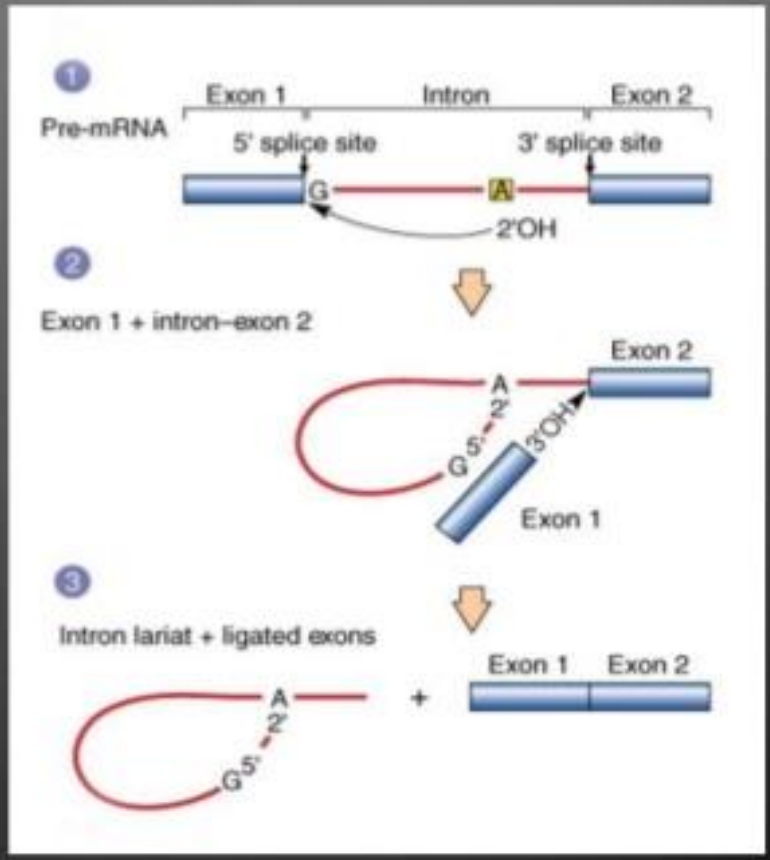


Group II Intron Splicing :

- Group II introns have been found in bacteria and in the mitochondrial and chloroplast genomes of fungi, plants, protists, and an annelid worm.

Mechanism:

The 2'OH of a specific adenosine acts as a nucleophile and attacks the 5' splice site creating a branched intron structure. The 3' OH of the 5' exon attacks the 3' splice site, ligating the exons and releasing the intron as a lariat structure.

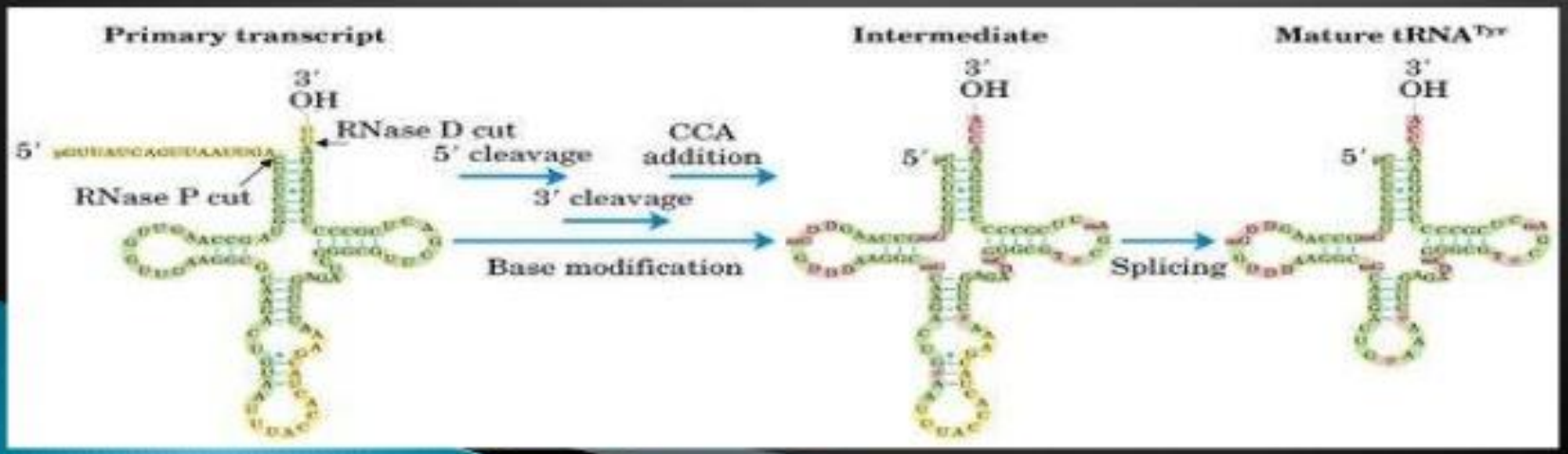


RNase P :

- Ribonuclease P (RNaseP), a ribonucleoprotein, is an essential tRNA processing enzyme found in all living organisms. Since its discovery almost 40 years ago, research on RNase P has led to the discovery of the catalytic properties of RNA, and of the only known, naturally occurring RNA enzymes.

Mechanism:

- All RNase P enzymes are ribonucleoproteins [bacteria: 1RNA + 1 protein subunit; eukaryotes: 1 RNA + many protein subunits (11 in human)],
- In Ribonulease – P, protein component is facilitates binding between RNase and t-RNA substrate.
- Requires divalent metal ions (like Mg^{2+}) for its activity.
- Endo-ribonuclease responsible for generating 5' end of matured tRNA molecules.
- Cleavage via nucleophilic attack on the phosphodiester bond leaving a 5'-phosphate and 3'-hydroxyl at the cleavage site.



GROUP I intron splicing

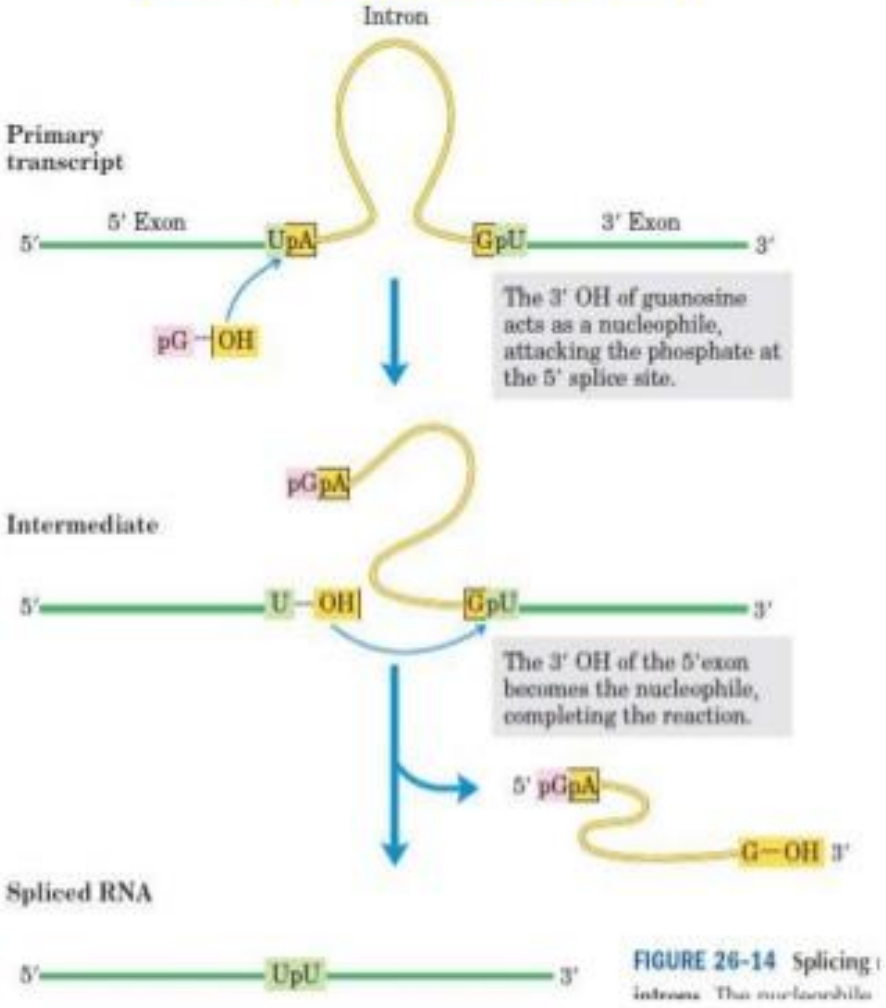


FIGURE 26-14 Splicing i
introns. The nucleophile

GROUP II intron splicing

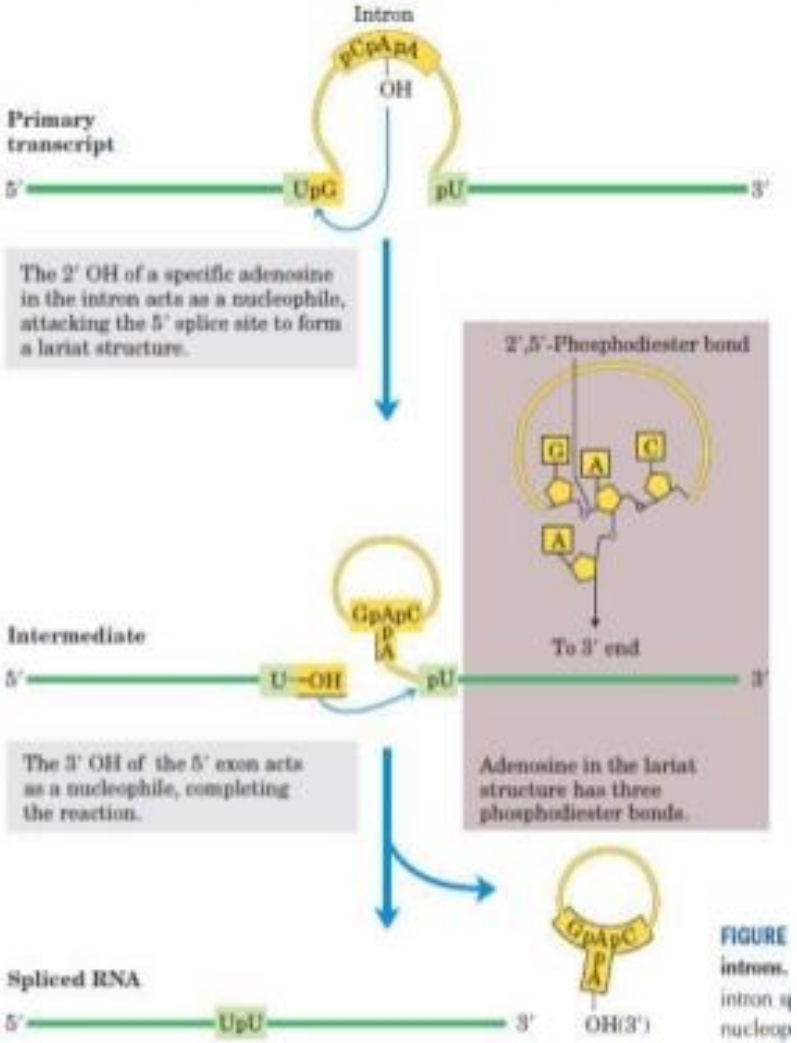


FIGURE
introns.
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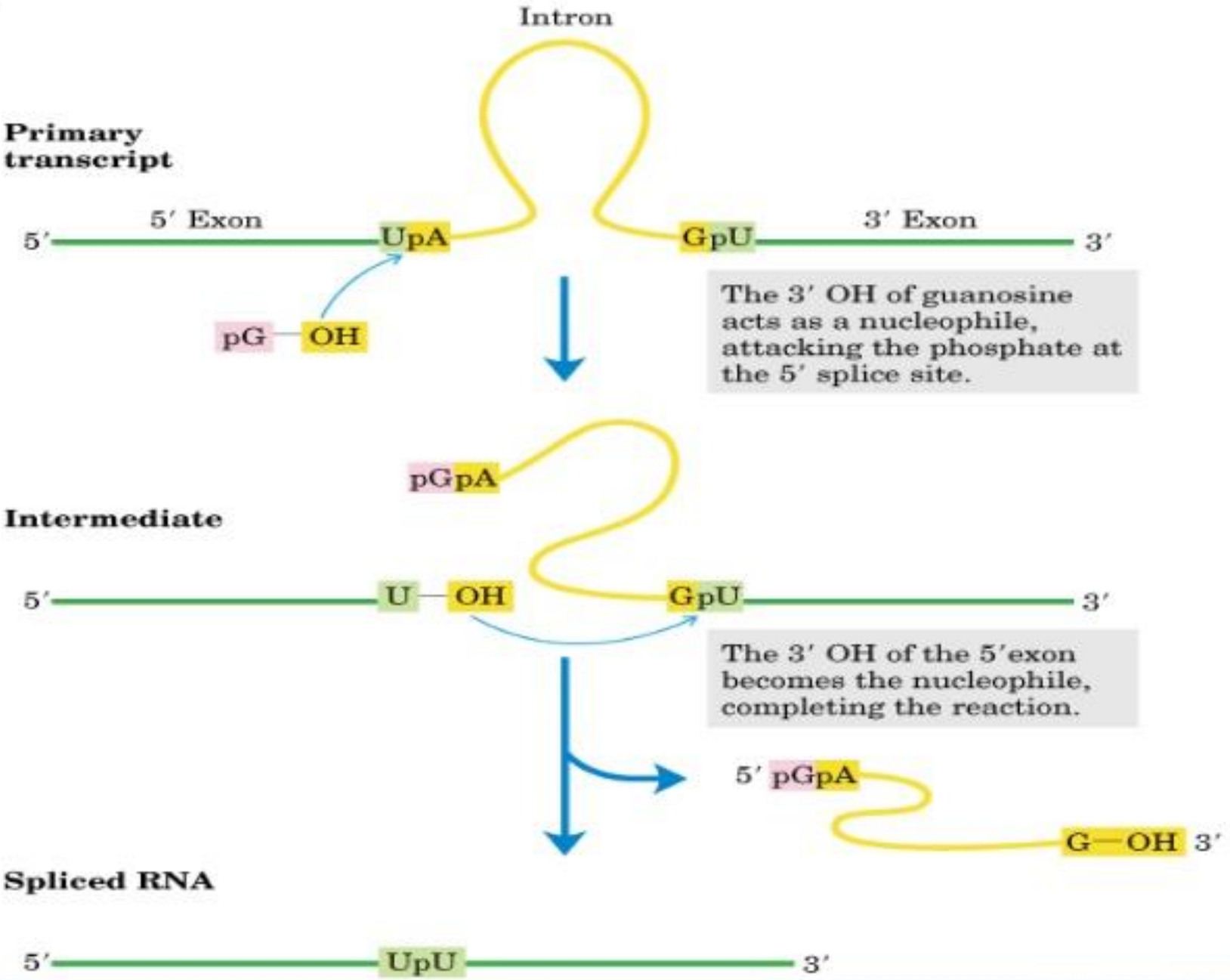
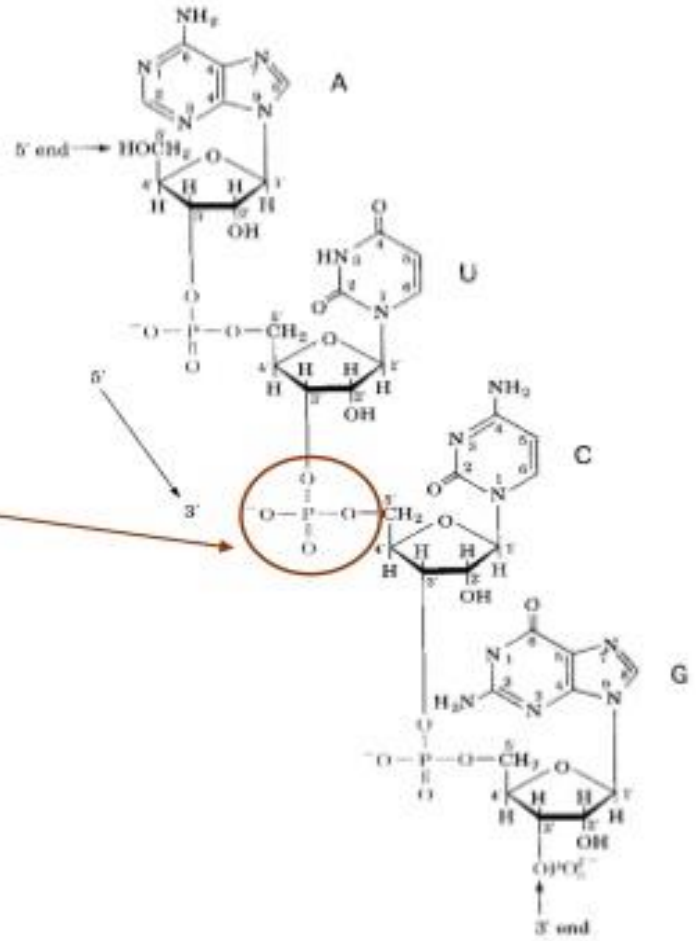

Intron
Primary transcript
5′ Exon
5′
UpA
GpU
3′ Exon
3′
pG
OH
The 3′ OH of guanosine acts as a nucleophile, attacking the phosphate at the 5′ splice site.
pGpA
Intermediate
5′
U
OH
GpU
3′
The 3′ OH of the 5′exon becomes the nucleophile, completing the reaction.
5′ pGpA
G
OH
3′
Spliced RNA
5′
UpU
3′

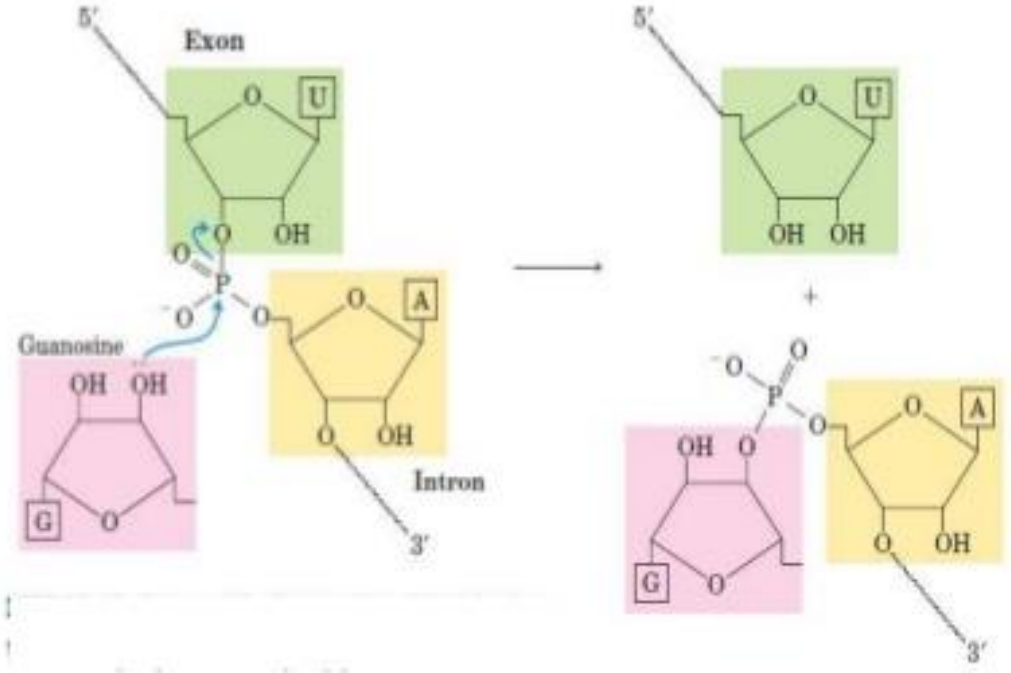
RIBOZYME:

- RNA possessing catalytic activity
- Increases the rate and specificity of:
  - phosphodiester bond cleavage
  - peptide bond synthesis
- Widespread occurrence in nature – from viruses to humans



1. Self-splicing introns

This is a transesterification reaction in which the guanosine hydroxyl group attacks the phosphodiester bond between the 3′ end of the first exon and the first nucleotide of the intron.

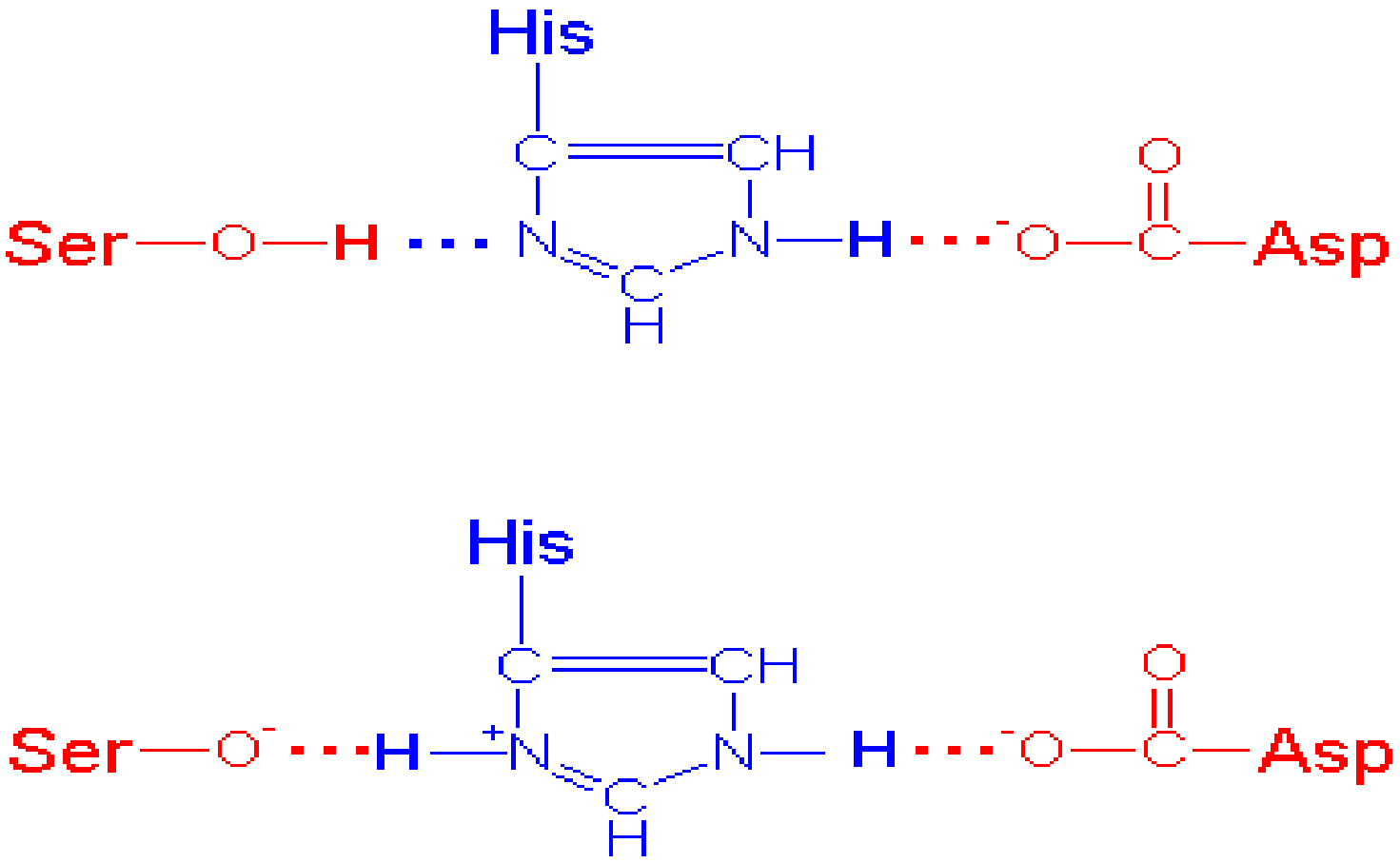


The guanosine remains attached to the 5′ end of the intron. Then, the 3′ end of the liberated exon attacks the extremity of base 413 from the intron to bring together the exon's two ends

Charge relay network

The serine in the triad is much more reactive then other serines in the protein. The serine hydroksyl is normally protonated at neutral pH, but in the enzyme Ser-195 (Ser-221) is hydrogen-bonded to His-57 (His-64), which is further hydrogen-bonded to Asp-102 (Asp-32). These three amino acids are often referred to as a **catalytic triad**.

As the serine oxygen attacks the carbonyl carbon of a peptide bond, the hydrogen-bonded His functions as a general base to abstract the serine proton, and the negatively charged Asp stabilizes the positive charge that forms on the His residue. This prevents the development of a very unstable positive charge on the serine hydroxyl and increase its nucleophilicity. The residues of the catalytic triad form a **charge-transfer relay network**.



Scheme of the charge-transfer relay network