Structure of tRNA

In 1965, Robert Holley for the first time gave the detailed structure of tRNA of alanine ($tRNA^{ala}$ or alanyl tRNA. He shared the Nobel prize for medicine with Khorana and Nirenberg in 1968. $tRNA^{ala}$ is a small molecule, 77 nucleotide long, 10 of which were modified bases. After that structure of many other tRNA molecules were described. After going through the structure of many other tRNA molecules, a general structure of tRNA can be derived.

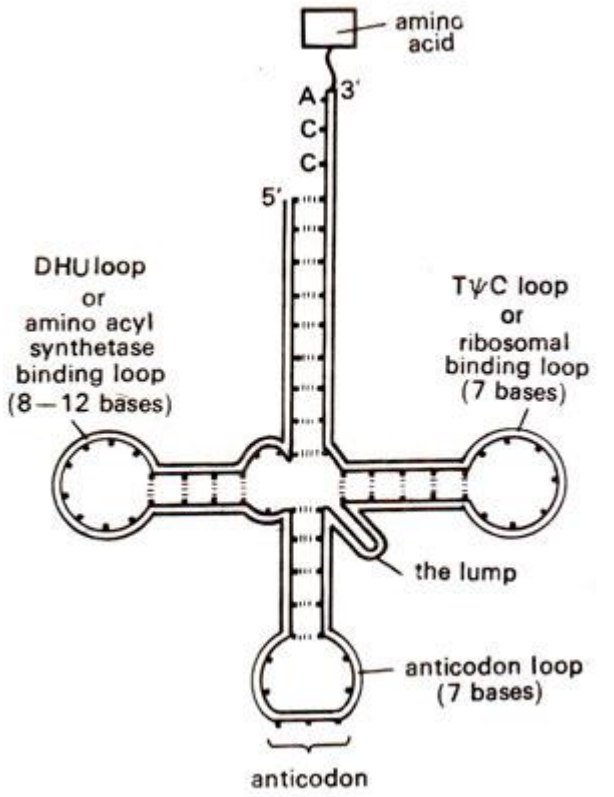
General structure of tRNA molecule:

1. These are small molecules containing 73 to 93 nucleotides.
2. Approximately 10% of the bases are modified bases, enzymatically modified post transcriptionally.
3. Most of the tRNAs have GMP at the 5' end and all have –CCA at the 3' end.
4. All tRNA molecules have nucleotide sequences in one part of the mol. That are complimentary to sequence located in other parts of the molecule. Because of this, all tRNA mols. become folded in a secondary structure which resemble clover leaf and called 'Clover leaf model.'

Clover leaf model: represents 2D structure of tRNA

According to this model, there are four/more double helical regions :

1. Amino acid acceptor arm (AA acceptor arm) : A double helical arm that has a single stranded region – 3' acceptor end of tRNA
2. Anticodon arm – It invariably contains a loop at the end which is composed of 7 nucleotides, middle three of which constitute anticodons which interacts with the codons of the mRNA.
3. T arm or TΨC arm ending in a loop (7 nucleotides). It is ribosome binding loop.
4. D arm/DHU arm with 8-12 nucleotides loop. This is aminoacyl synthetase binding loop.



Many of the abnormal bases are present in these loops which disrupts the normal pairing and consequently a loop is formed.

There is a highly variable region, variable loop/extra arm present between T arm and anticodon arm. Based on the number of bases in these loops, there are 2 classes of tRNA :

Class I tRNA – small loop of 3-5 nucleotides only. 75% of tRNA belong to this class.

Class II tRNA – large variable loop with 13-21 nucleotides, e.g., serine and leucine tRNA.

The bases in the tRNA can be :

1. Invarient – At a particular position, there will always be the same base, e.g.,14 = A, 18 = G,19 = G, 53,54,55,56,58 = G, T, Ψ, C, A; 3'end = CCA

2. Semi-varient - Either Pu or Py at any particular position; 11= Py, 15 = Pu, 24 = Pu, 48 = Py
3. Varient

3-D structure of tRNA:

tRNA was available in crystalline form in 1968 and the 3-D structure was studied by x-ray crystallography. Most acceptable model was proposed by S.H.Kim (1973). According to him, 3-D structure of tRNA takes the shape of letter L. It can be easily derived from 2-D structure by condensing 4 arms of the clover leaf into two major domains –

i. Acceptor arm – TΨC minihelix and

ii. Anticodon arm – D arm biloop.

The -CCA stem projects out. The individual tRNAscan also be distinguished on the basis of differences in the angle of 2 arms of the L shaped structure. **Tertiary interactions between the TΨC- and D-loop** form the corner of the L-shape and stabilize the structure.

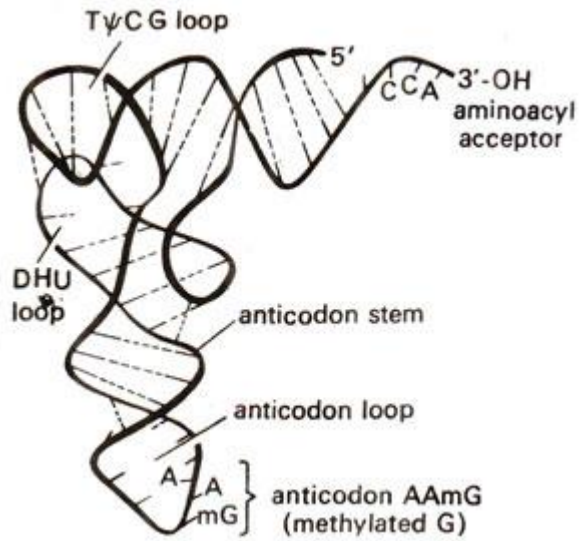


Fig : 3-D structure of tRNA molecule

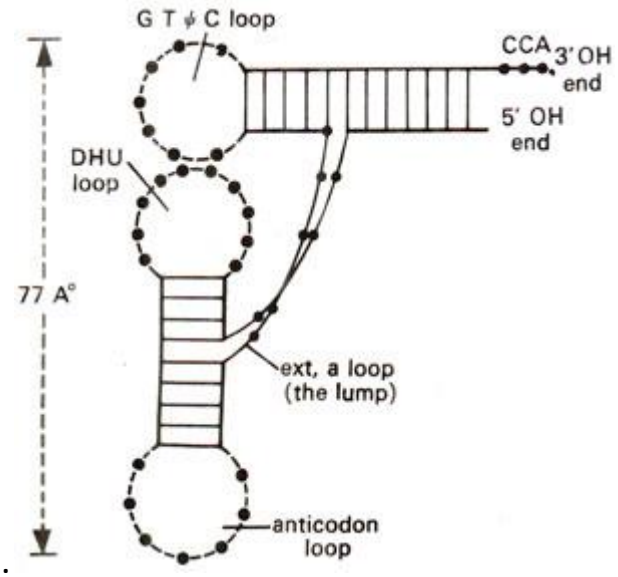


Fig : Simplified diagrammatic representation of L-shaped 3-D structure

(Modified nucleotides : Most tRNAs contain modified nucleotides, which are added post-transcriptionally by specific enzymes. Common modifications include isomerisation of uridines into pseudouridines (Ψ), methylation of either the ribose and/or the base, thiolation, reduction of uridines into dihydrouridines (D).)

Types of tRNA

A tRNA can be classified based on the amino acid it carries, giving rise to 20 different tRNAs. Alternatively, they can also be grouped based on their anticodon. There are 64 possible codons arising from a combination of four nucleotides. Of these, 3 are stop codons that signal the end of translation. This gives rise to a situation where one amino acid is represented by multiple codons and the AATS, as well as the tRNAs have to accommodate this redundancy. However, very few species have exactly 61 tRNAs, which gives rise to the question of how every codon is recognized by a specific tRNA. In many species, the number far exceeds 61 and different tRNAs carrying the same anticodon could display varying efficiency in translation, adding a layer of regulation to the process of protein synthesis.

tRNAs interact with codons on the mRNA through their anticodon loop. Base pairing between the codon and anticodon ensures specificity during translation. However, the first base of the anticodon, that pairs with the ‘wobble’ or third position in a codon is often modified to allow the tRNA to hydrogen bond with three, instead of one base. Thus a single tRNA has the option of recognizing and base pairing with three codons, which code for the same amino acid. There are 20 AATS, one for each amino acid. This group of enzymes can recognize all the anticodons representing a particular amino acid and therefore act as the second arm of the machinery that handles genetic code redundancy.

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