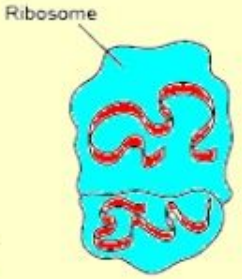
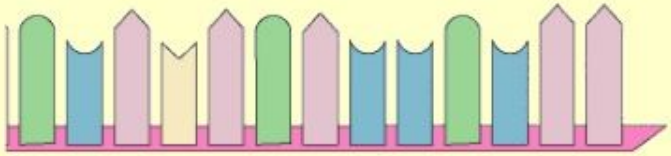
3 KINDS OF RNA HELP WITH INFO TRANSFER FOR PROTEIN SYNTHESIS

RIBOSOMAL RNA (rRNA)
Combines with proteins to form ribosomes



TRANSFER RNA (tRNA)
Matches m-RNA codon to add correct amino acids during protein synthesis

MESSENGER RNA (mRNA)
carries code from DNA to ribosomes

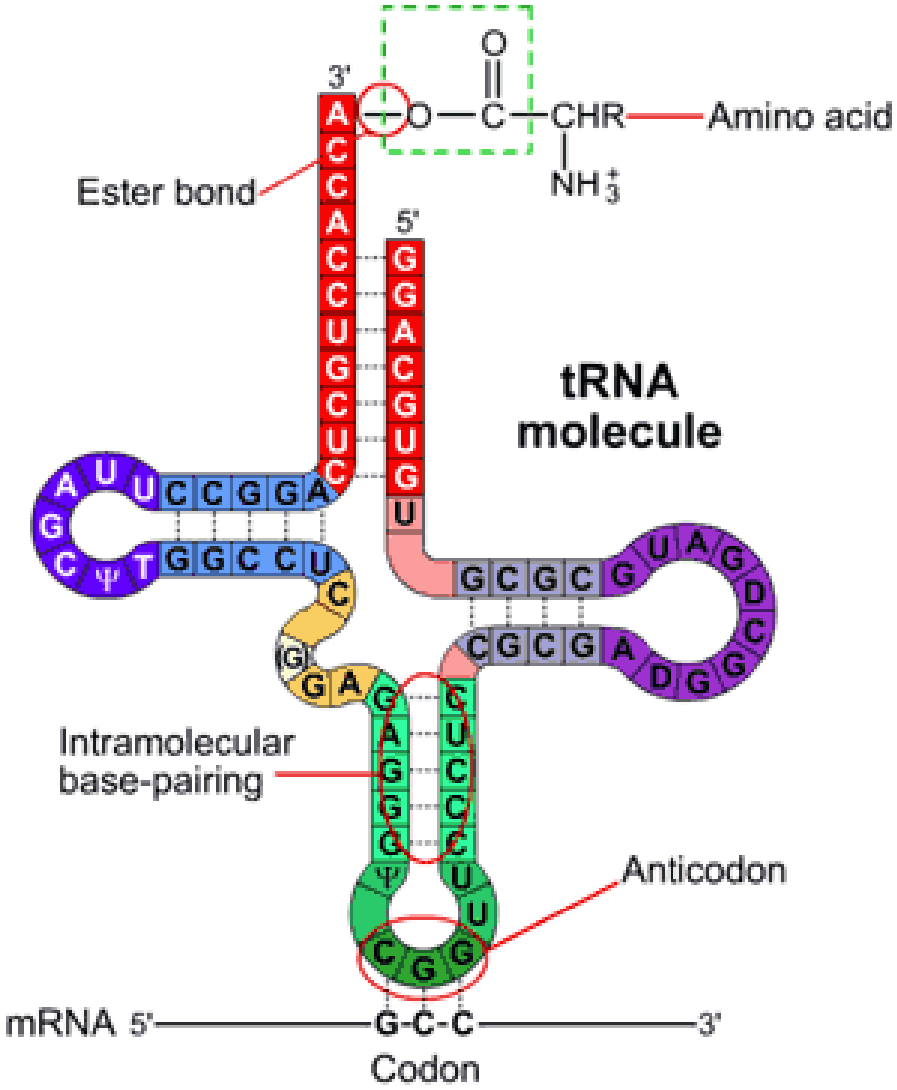


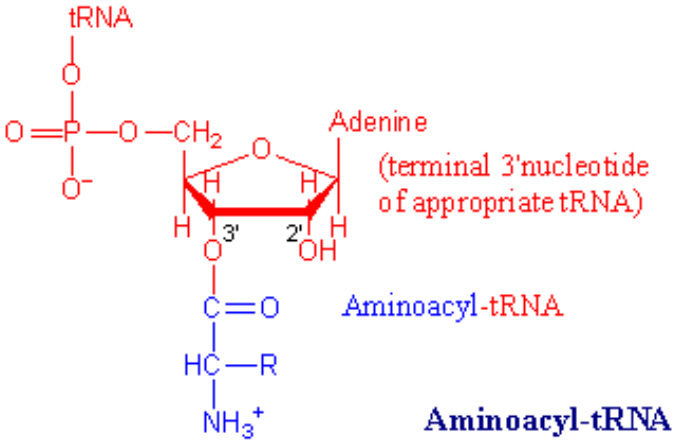
rRNA and t-RNA images from © Pearson Education Inc, publishing as Pearson Prentice Hall. All rights reserved
mRNA image from http://wps.prenhall.com/wps/media/tmp/labeling/1140654_dyn.gif

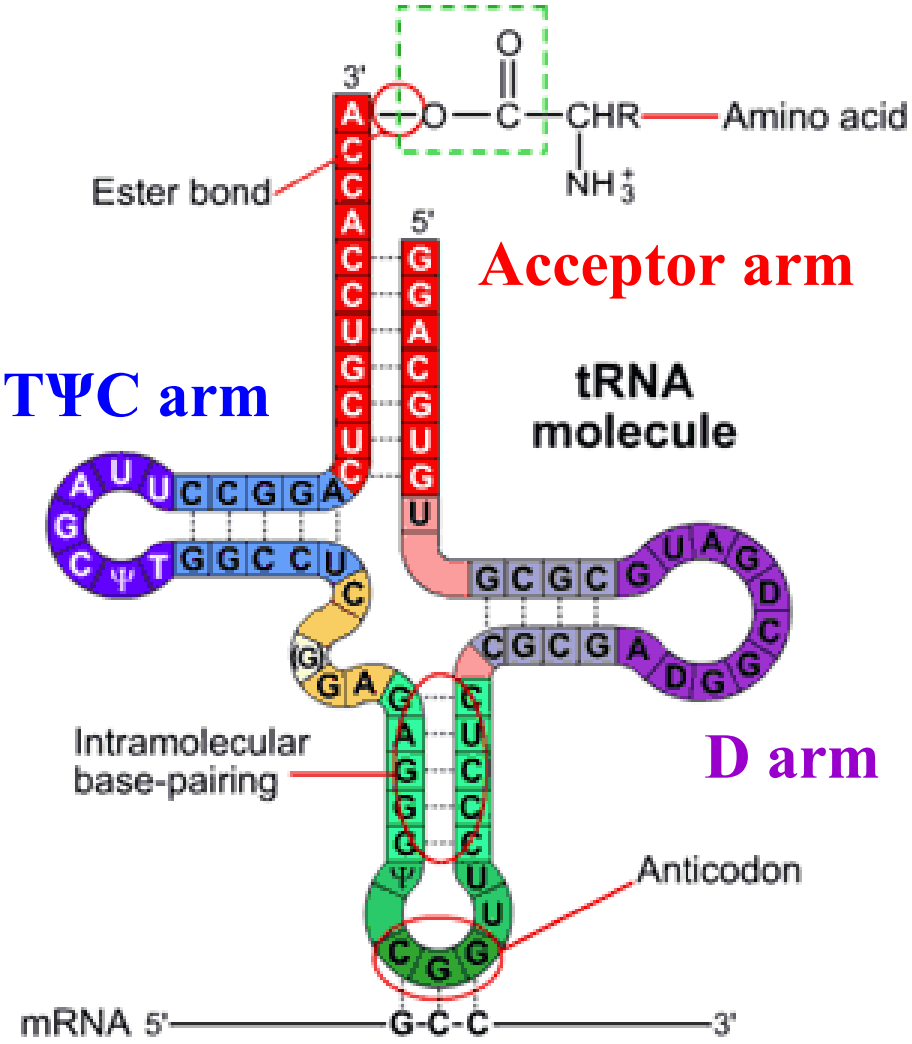
Transfer RNA (tRNA)

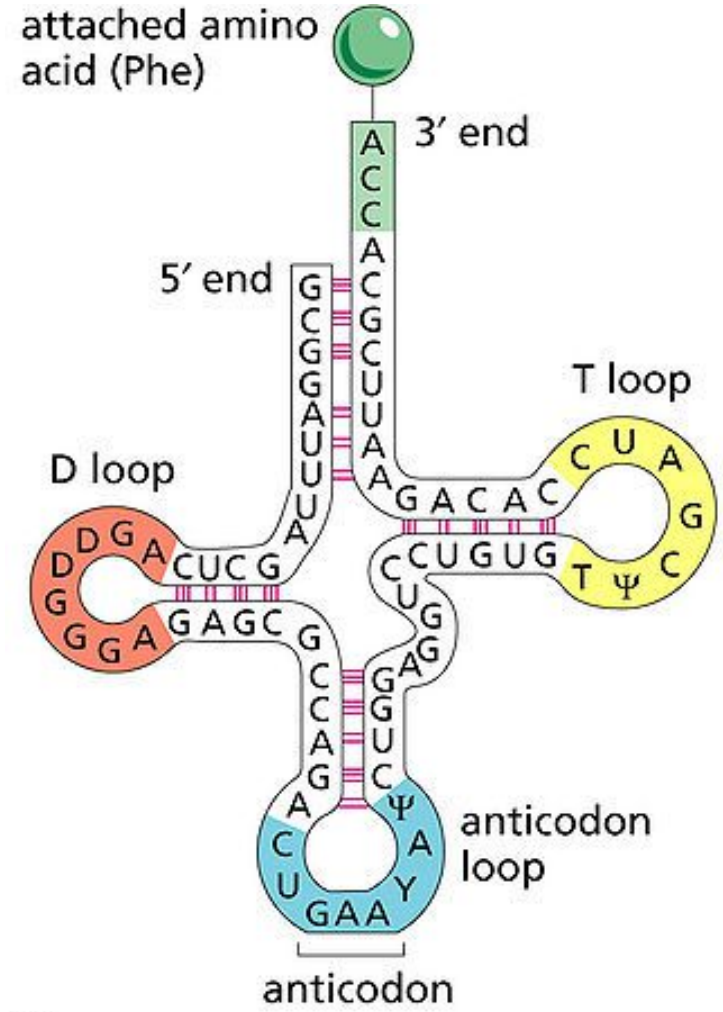
Transfer RNA (abbreviated tRNA) is a small RNA (usually about 74-95 nucleotides) that transfers a specific amino acid to a growing polypeptide chain at the ribosomal site of protein synthesis during translation.

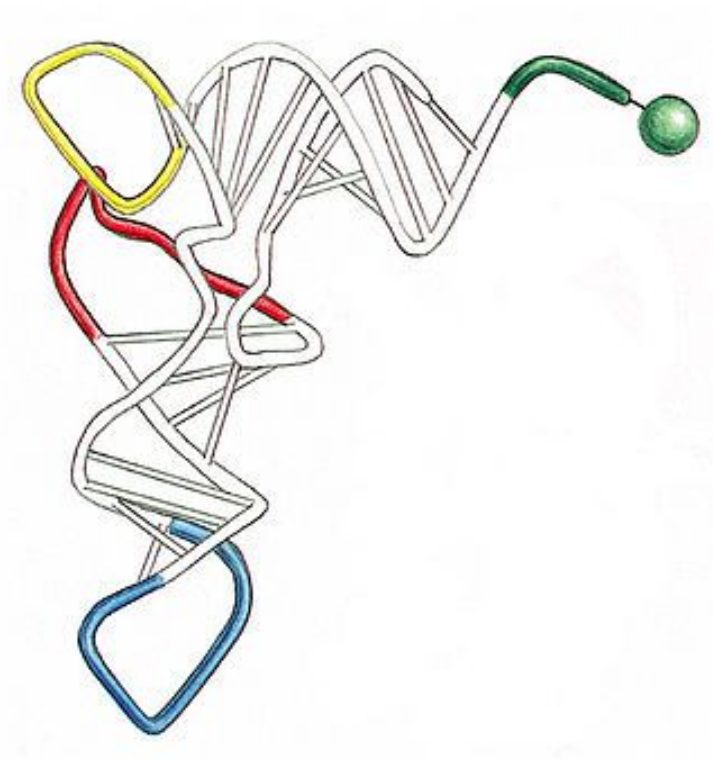
The tRNA is an adaptor Made to recognize both the amino acid on one side and the codon on the other side



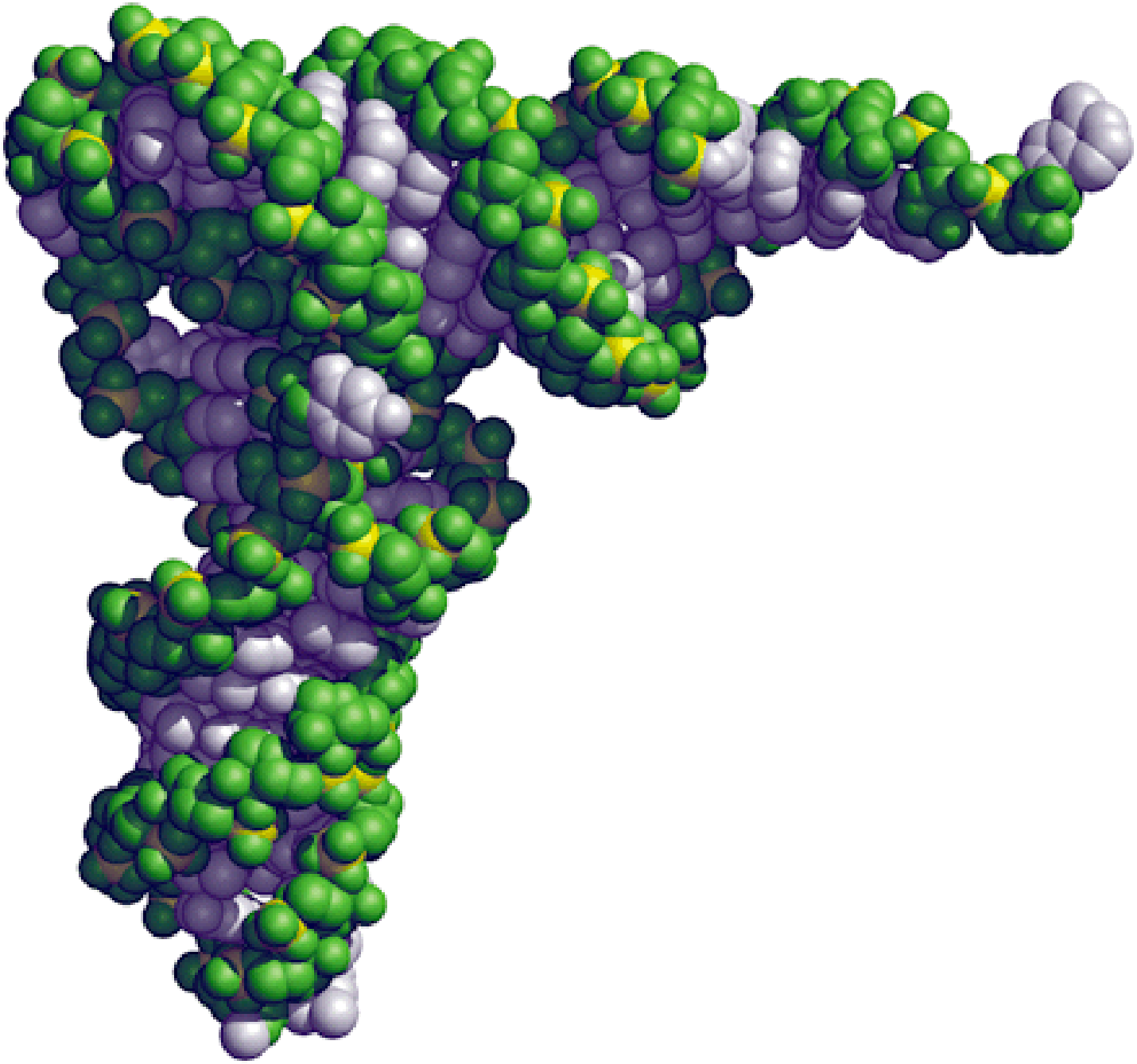



3'
5'
Ester bond
Amino acid
Acceptor arm
TΨC arm
tRNA molecule
D arm
Intramolecular base-pairing
Anticodon
mRNA 5'
3'
Anticodon arm





The tRNA is folded into a compact L shaped tertiary structure, with the amino acid at one end and the anticodon on the other end



tRNA Contains Modified Bases
(81 examples of modified bases in tRNAs have been reported.)

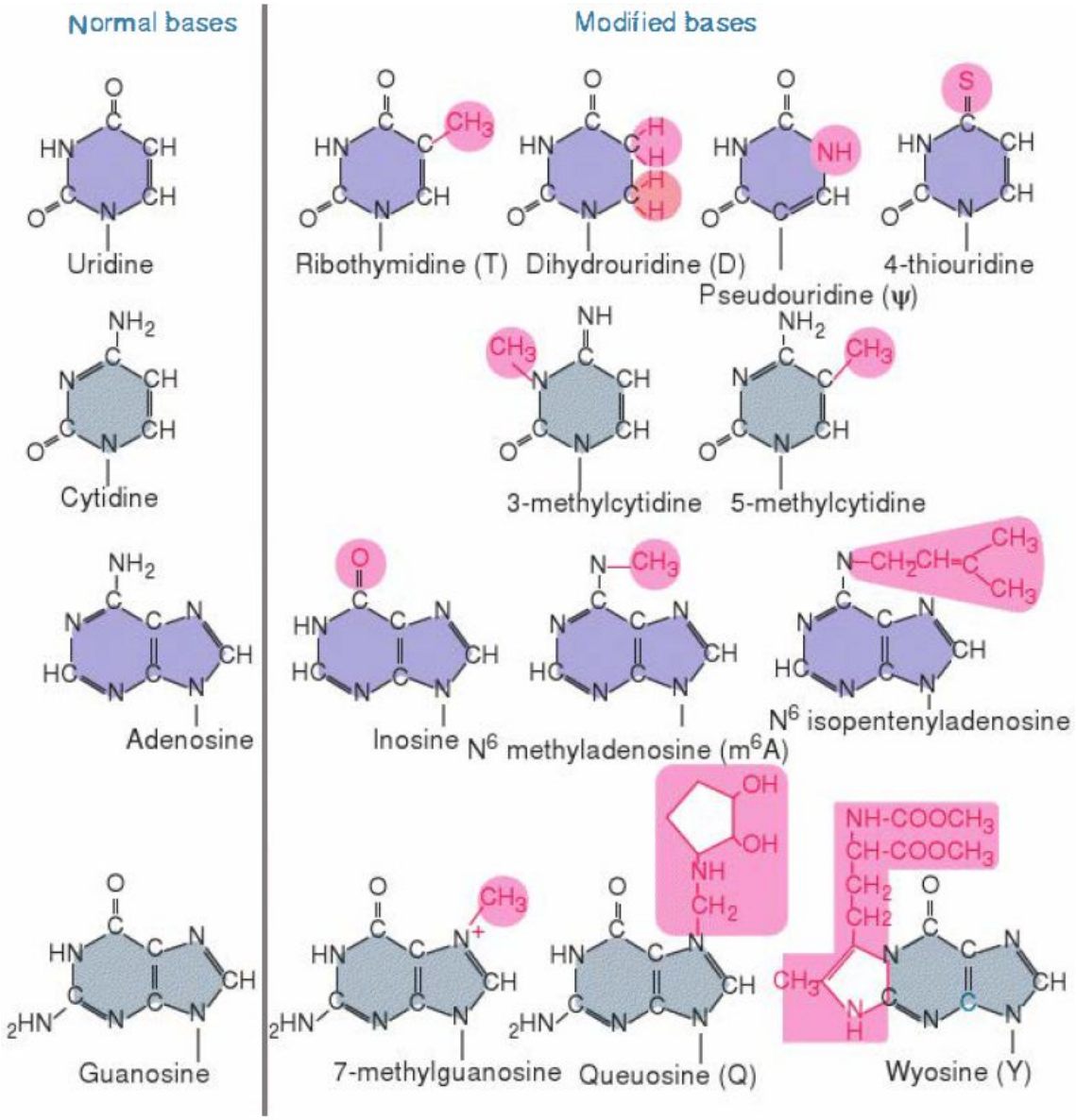


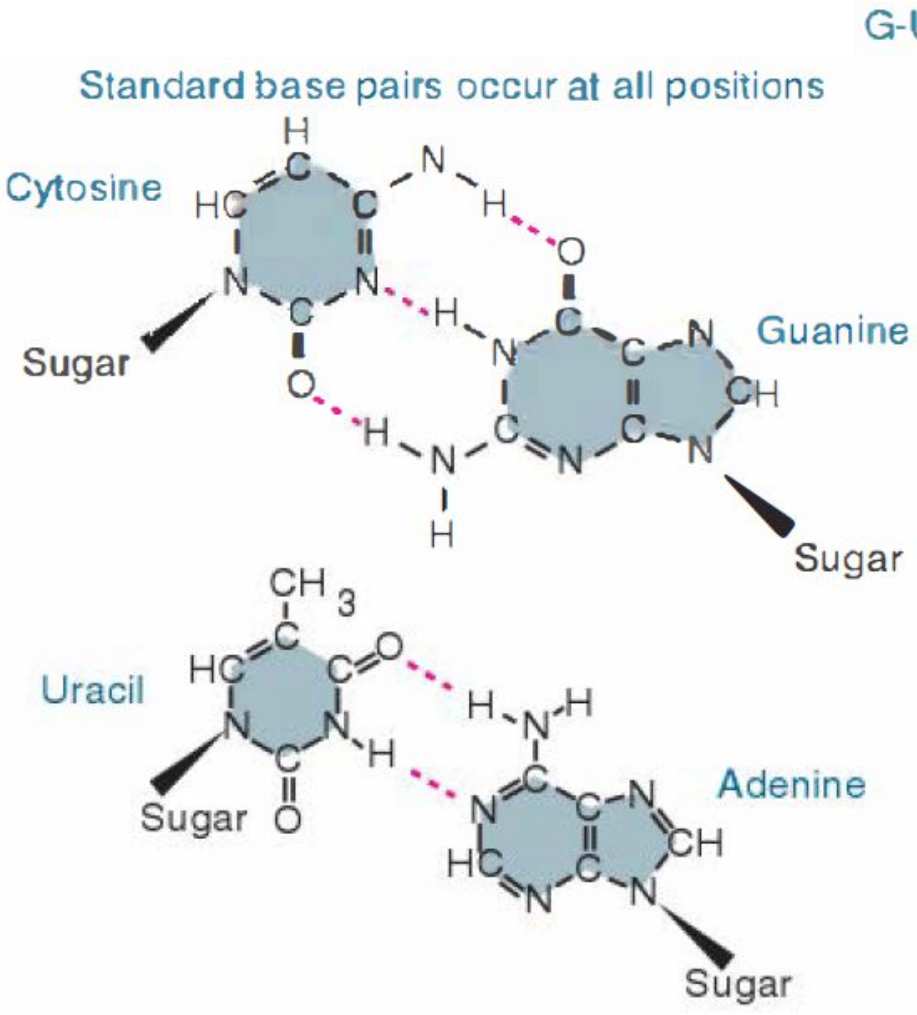
FIGURE 25.7 All four bases in tRNA can be modified.

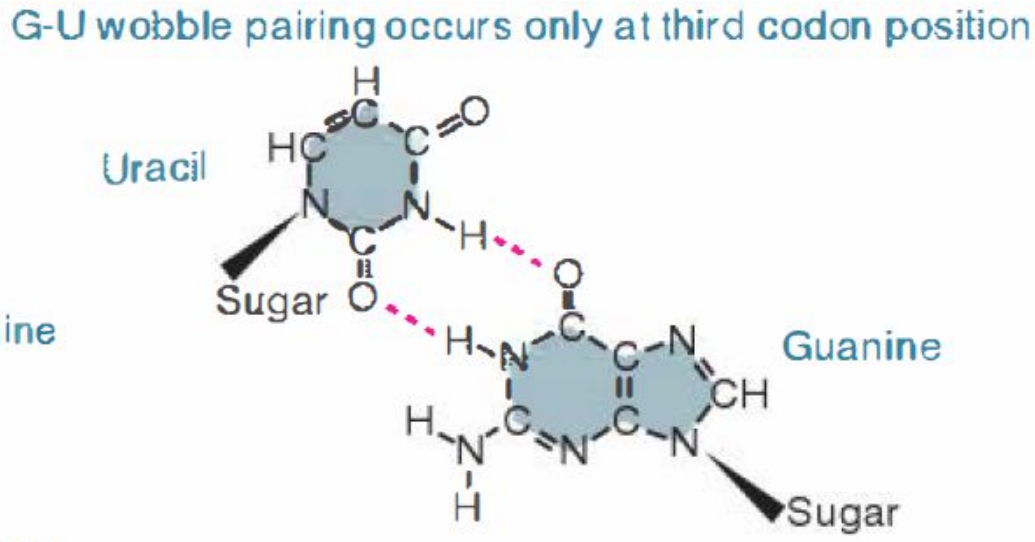
"Wobble"
Tentennamento
Vacillamento
Oscillazione

A wobble base pair is a G-U and I-U / I-A / I-C pair fundamental in RNA secondary structure. Its thermodynamic stability is comparable to that of the Watson-Crick base pair.

The fact that there are 61 amino-acid-coding codons and roughly 40 tRNA molecules presented a problem; in 1966 Francis Crick proposed the Wobble hypothesis to account for this. He postulated that the 5' base on the anti-codon was not as spatially confined as the other two bases, and could thus have non-standard base pairing. This would account for 60 codons for 40 tRNA.

FIGURE 25.4 Wobble in base pairing allows G-U pairs to form between the third base of the codon and the first base of the anticodon.





Codon-anticodon pairing can involve A G/U (wobble) pairing in third position

Base in first position of anticodon	Base(s) recognized in third position of codon
U	A or G
C	G only
A	U only
G	C or U

FIGURE 25.5 Codon–anticodon pairing involves wobbling at the third position.

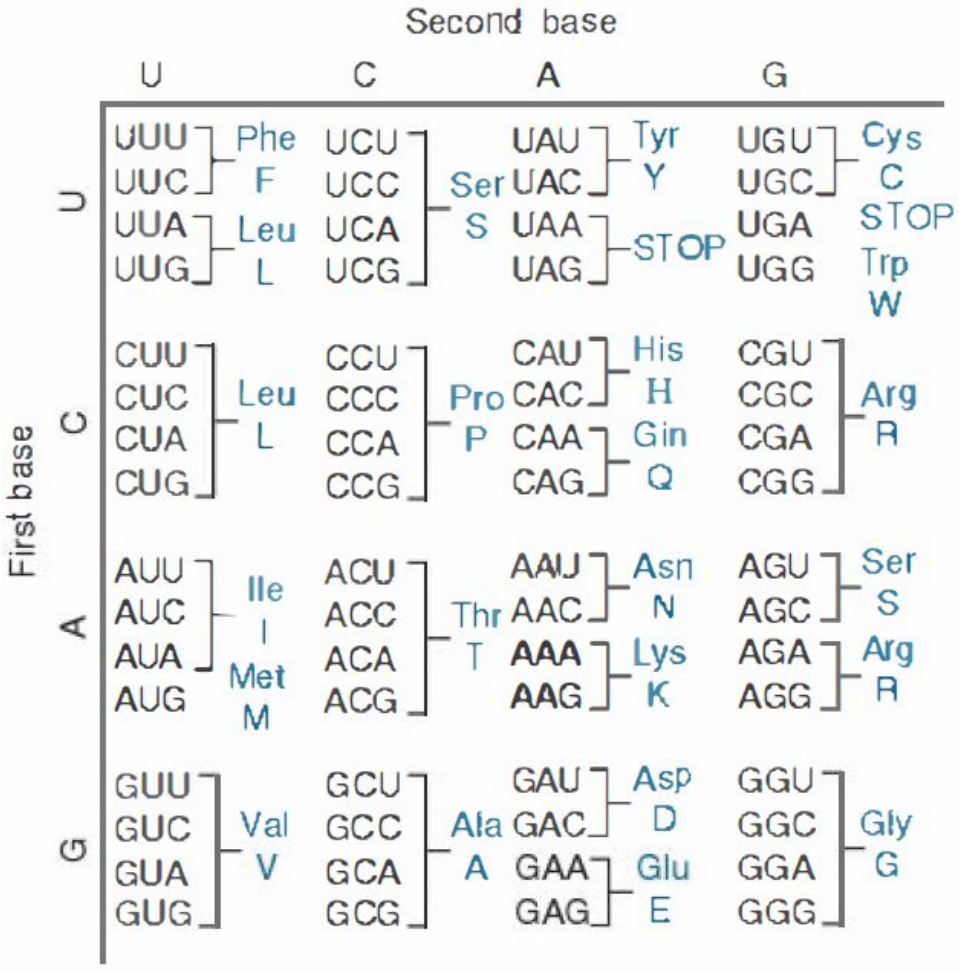


FIGURE 25.1 All the triplet codons have meaning: 61 represent amino acids and 3 cause termination (stop codons).

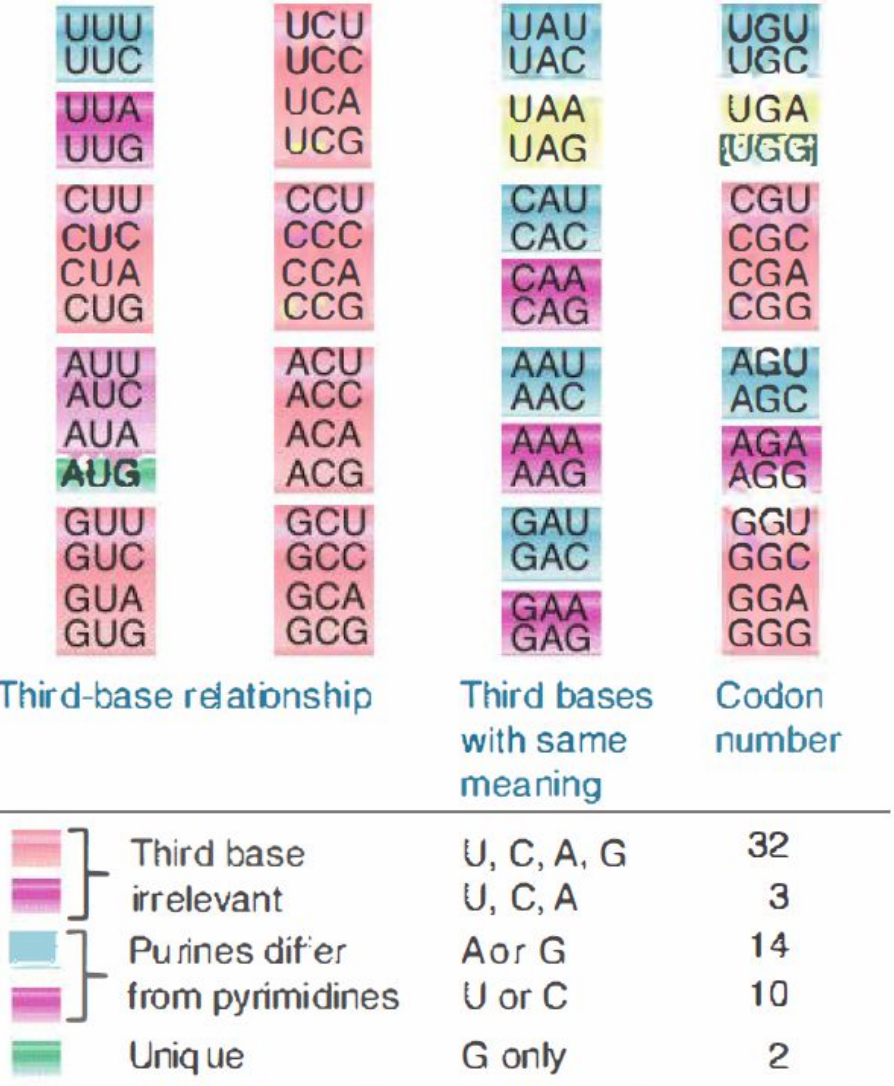


FIGURE 25.3 Third bases have the least influence on codon meanings. Boxes indicate groups of codons within which third-base degeneracy ensures that the meaning is the same.

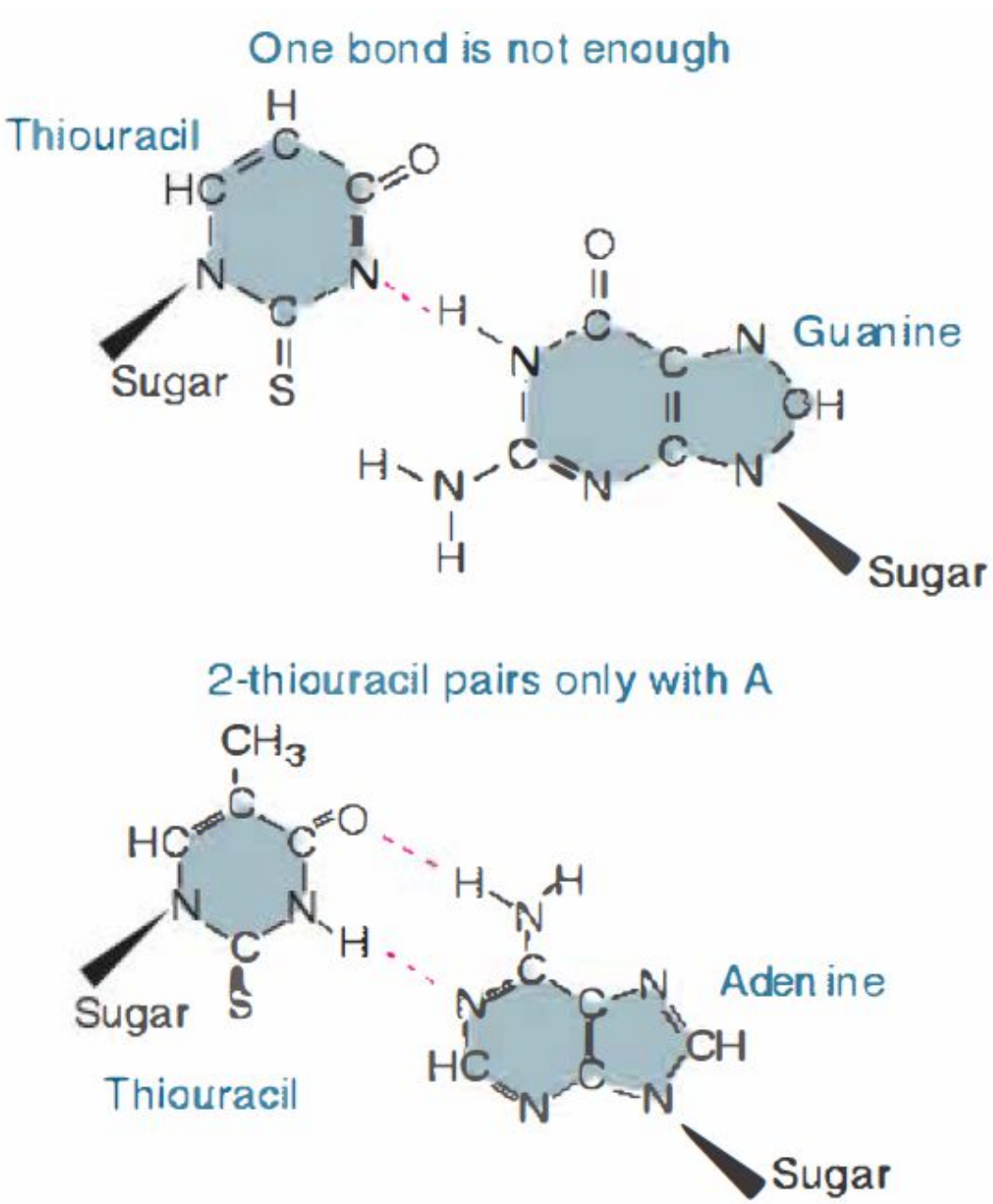


FIGURE 25.9 Modification to 2-thiouridine restricts pairing to A alone because only one H-bond can form with G.

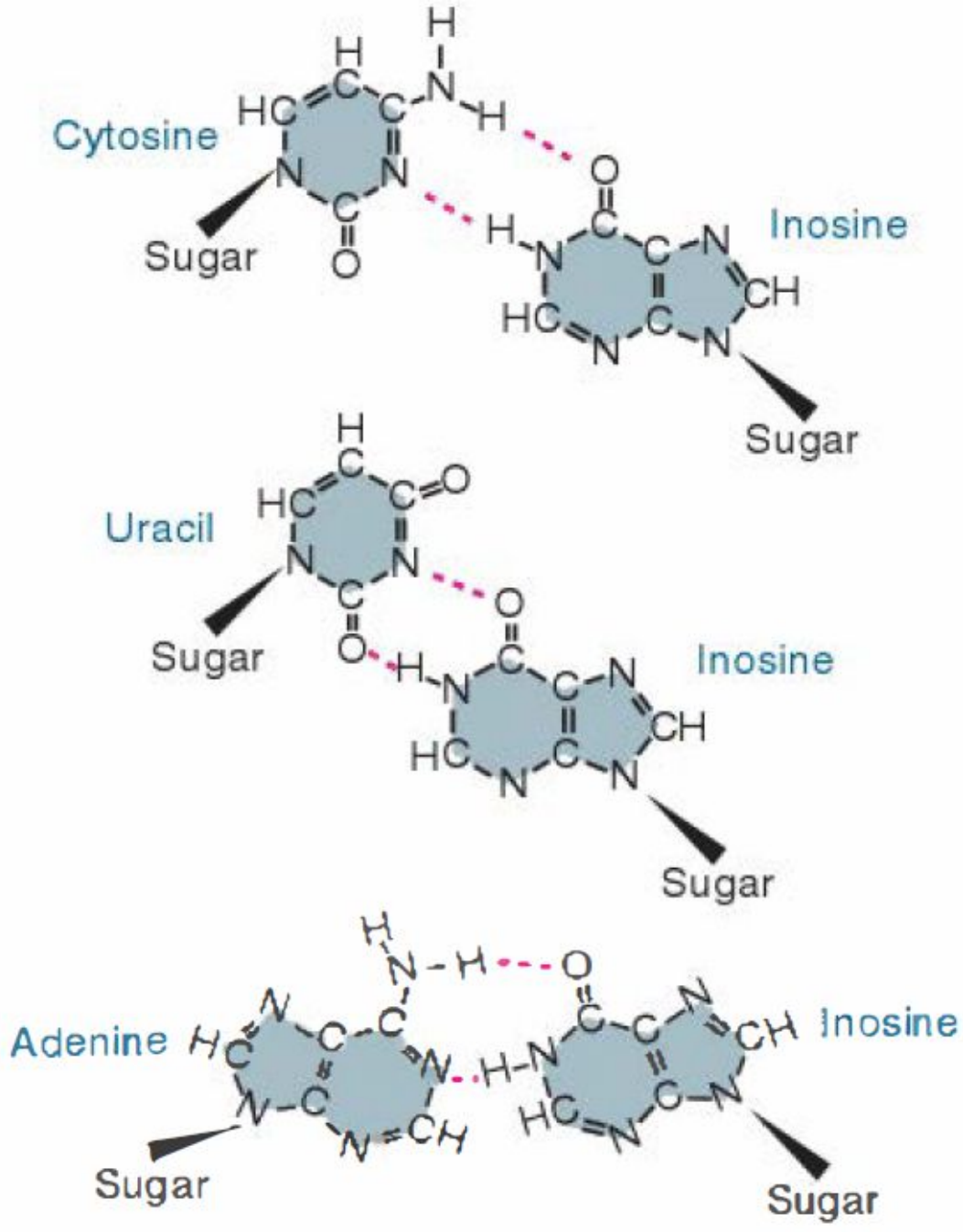


FIGURE 25.8 Inosine can pair with any U, C, or A.

The modification of some bases of the anticodon allows different pairings

Modified base in the first position of the anticodon	Recognized bases in the third position of the codon
I	C / U / A
tio-U	A

Amminoacil-tRNA synthesis

- **Starting from the amino acid and the tRNA (aminoacil-tRNA synthase)**
- **By modification of some aminoacil-tRNA already synthetized**

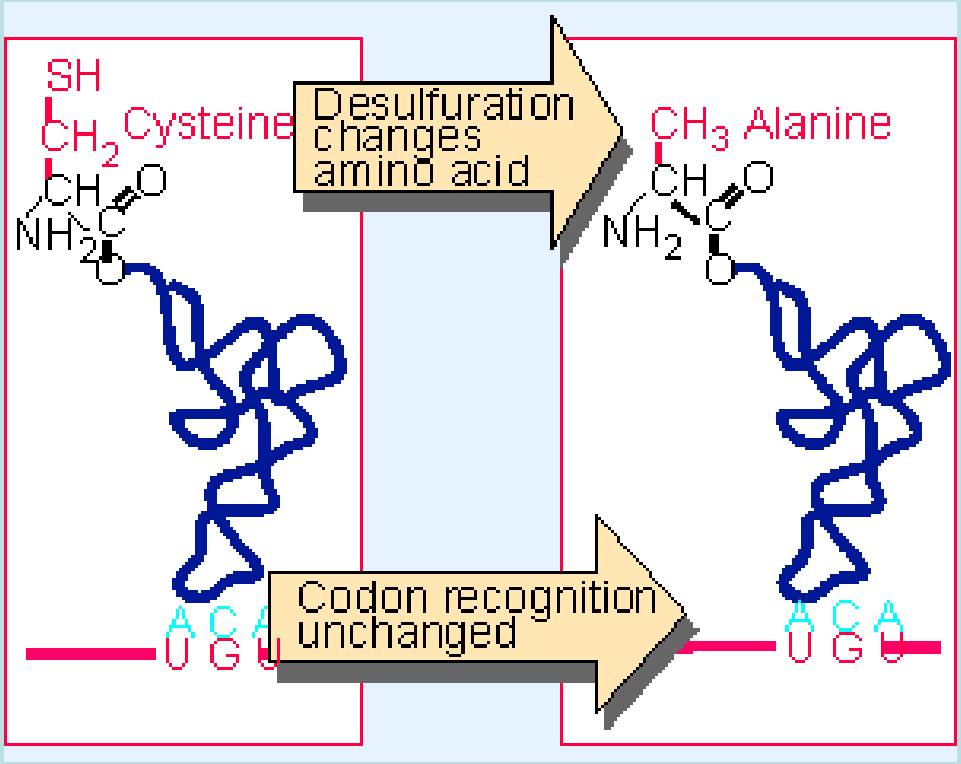


Figure 5.6 The meaning of tRNA is determined by its anticodon and not by its amino acid.

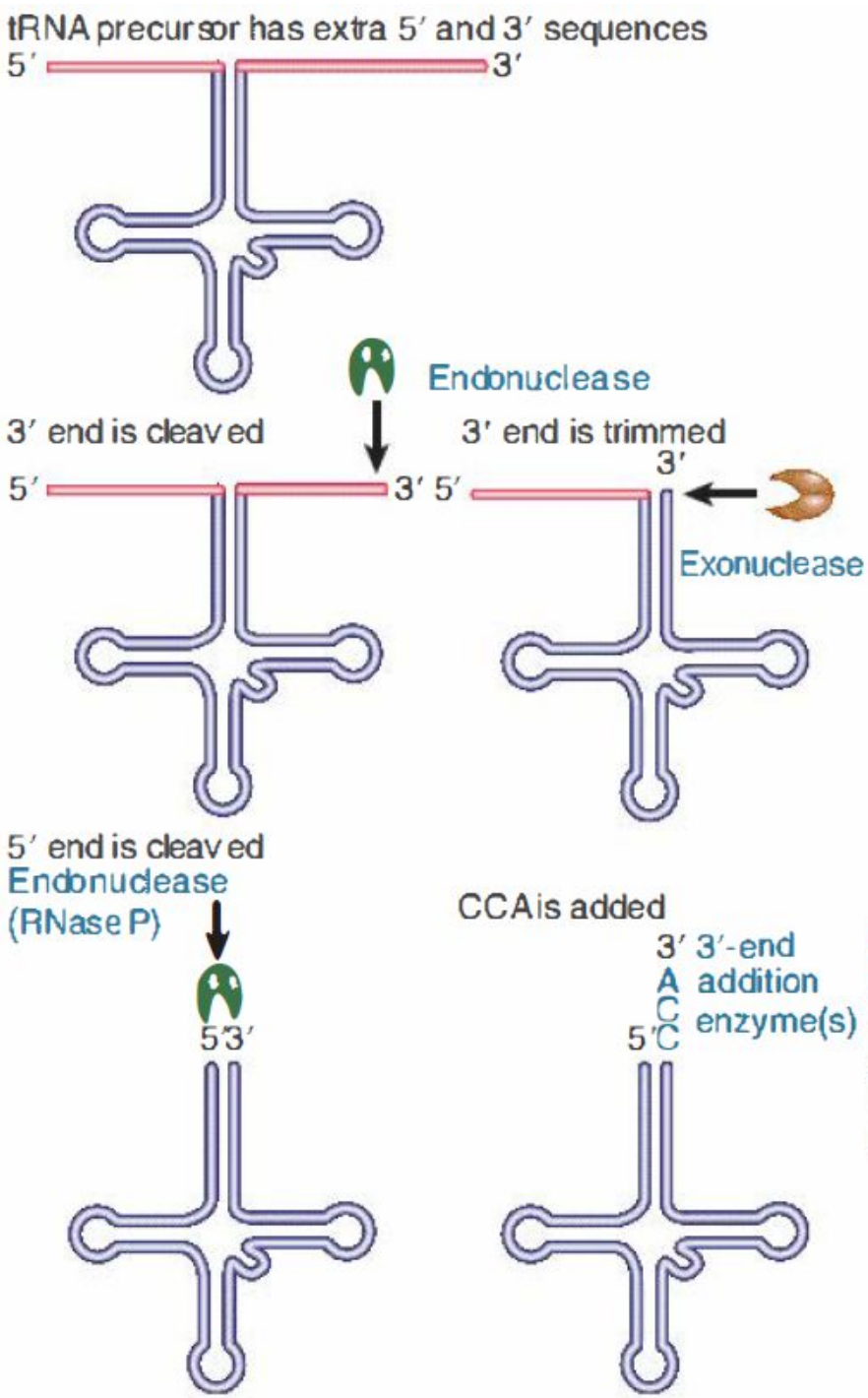
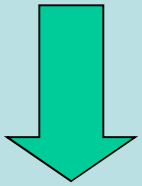
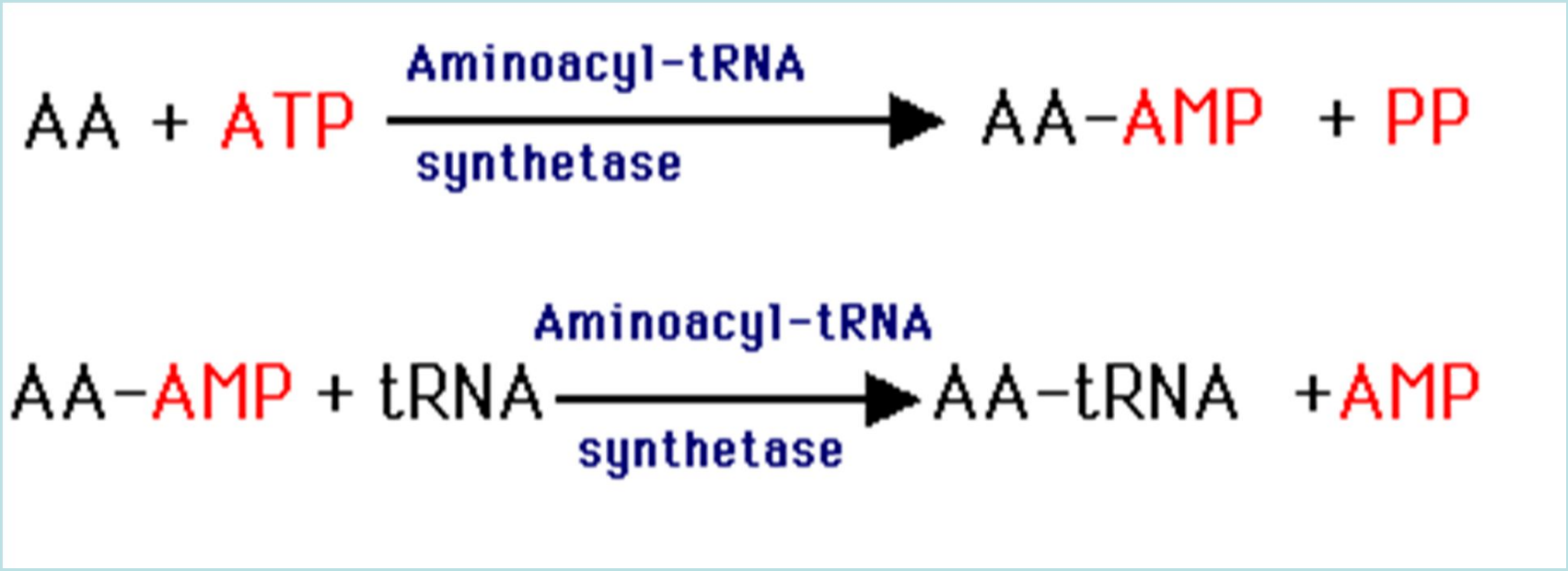


FIGURE 25.6 The tRNA 3′ end is generated by cutting (endonucleolytic) and trimming (exonucleolytic) reactions, followed by addition of CCA when this sequence is not encoded; the 5′ end is generated by a precise endonucleolytic cleavage.

tRNA loading



The aminoacil-tRNA synthase


AA + ATP
Aminoacyl-tRNA
synthetase
AA-AMP + PP
AA-AMP + tRNA
Aminoacyl-tRNA
synthetase
AA-tRNA +AMP

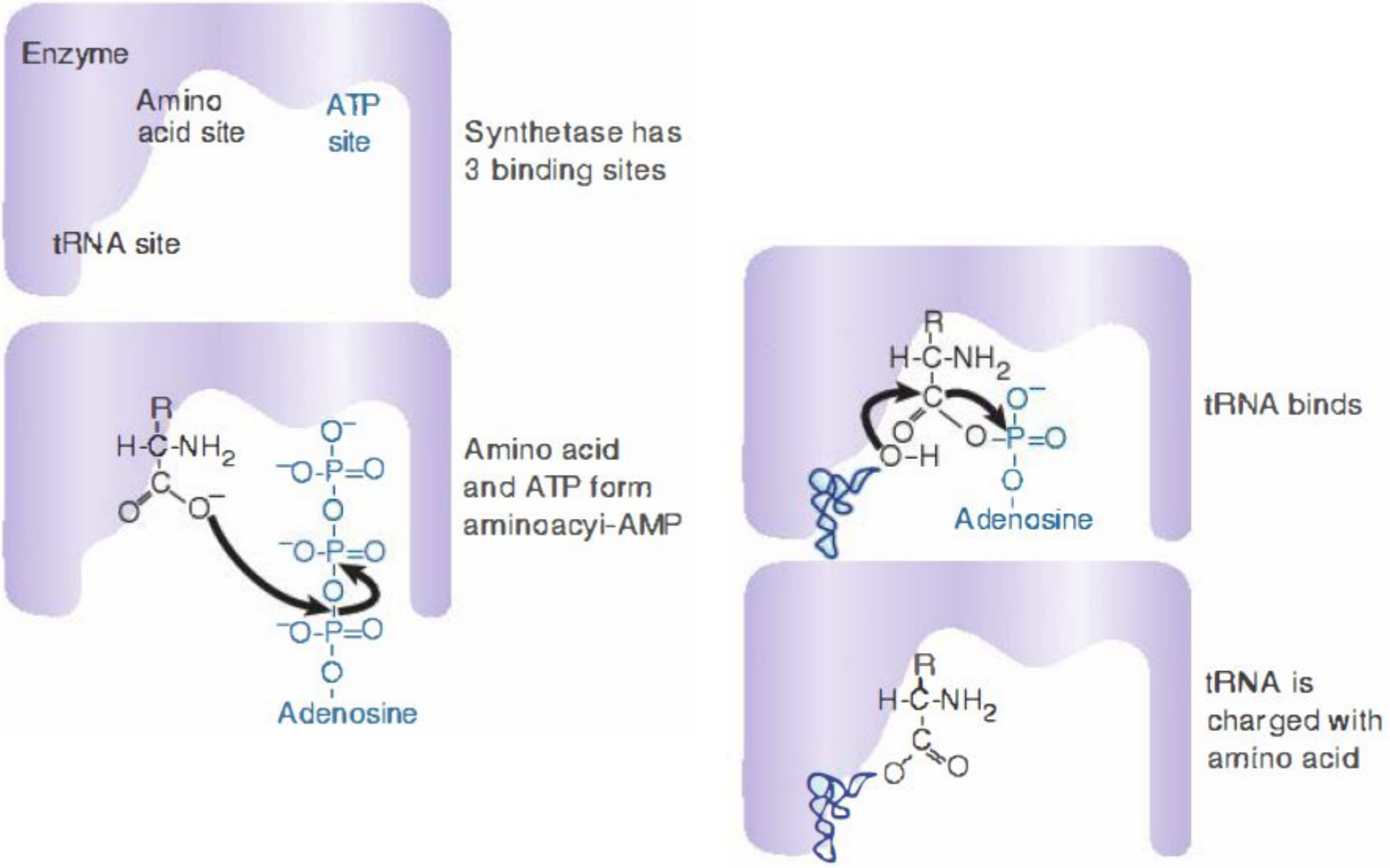
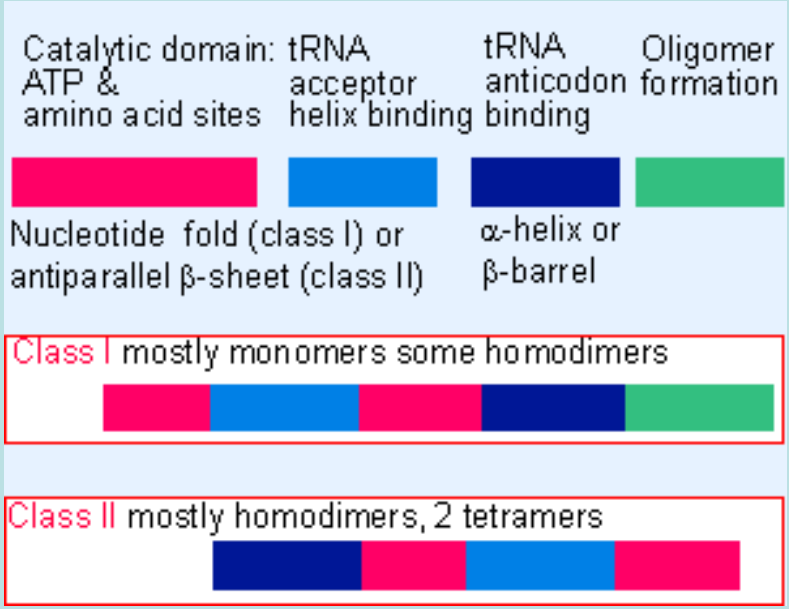
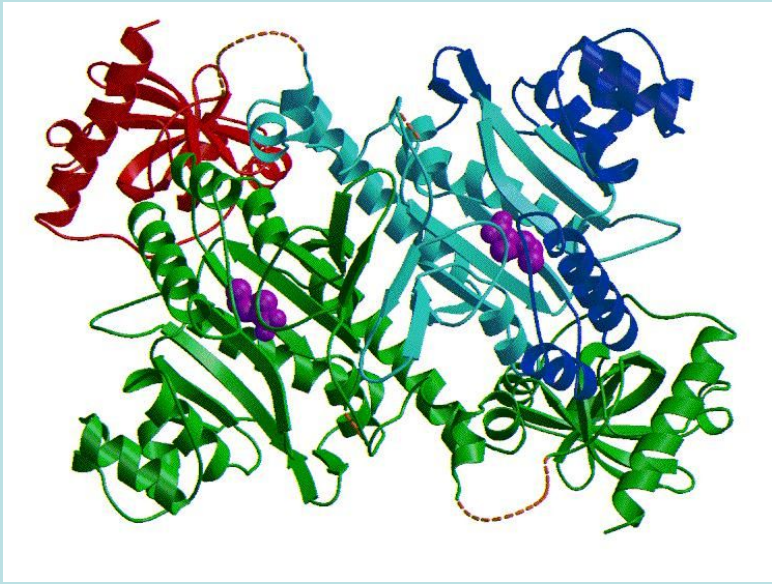


FIGURE 25.13 An aminoacyl-tRNA synthetase charges tRNA with an amino acid.

Figure 7.11 **An aminoacyl-tRNA synthetase contains three or four regions with different functions. (Only multimeric synthetases possess an oligomerization domain.)**





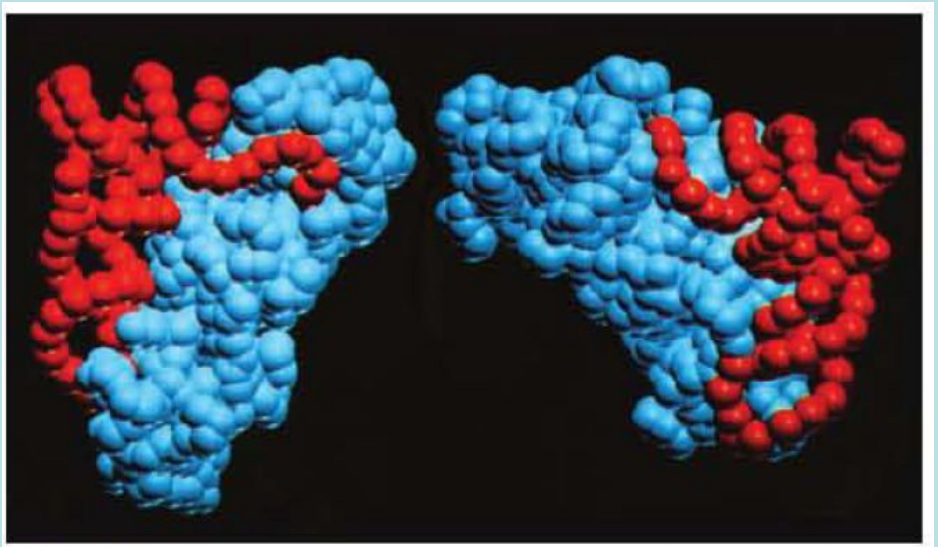
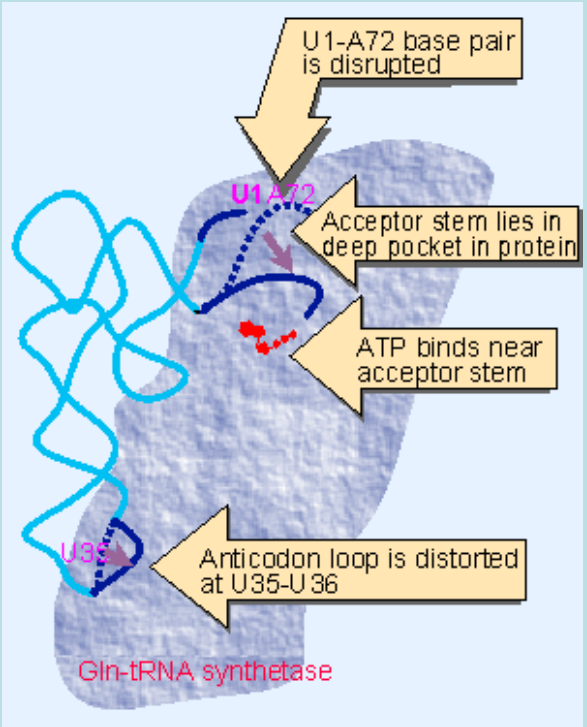
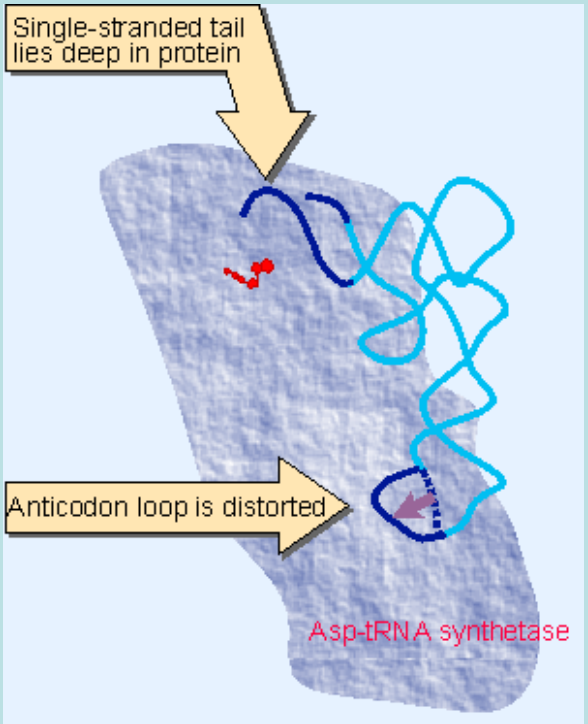


FIGURE 25.16 Crystal structures show that class I and class II aminoacyl-tRNA synthetases bind the opposite faces of their tRNA substrates. The tRNA is shown in red and the protein in blue. Photo courtesy of Dino Moras, Institute of Genetics and Molecular and Cellular Biology.



A class I tRNA synthetase contacts tRNA at the minor groove of the acceptor stem and at the anticodon.

A class II aminoacyl-tRNA synthetase contacts tRNA at the major groove of the acceptor helix and at the anticodon loop.



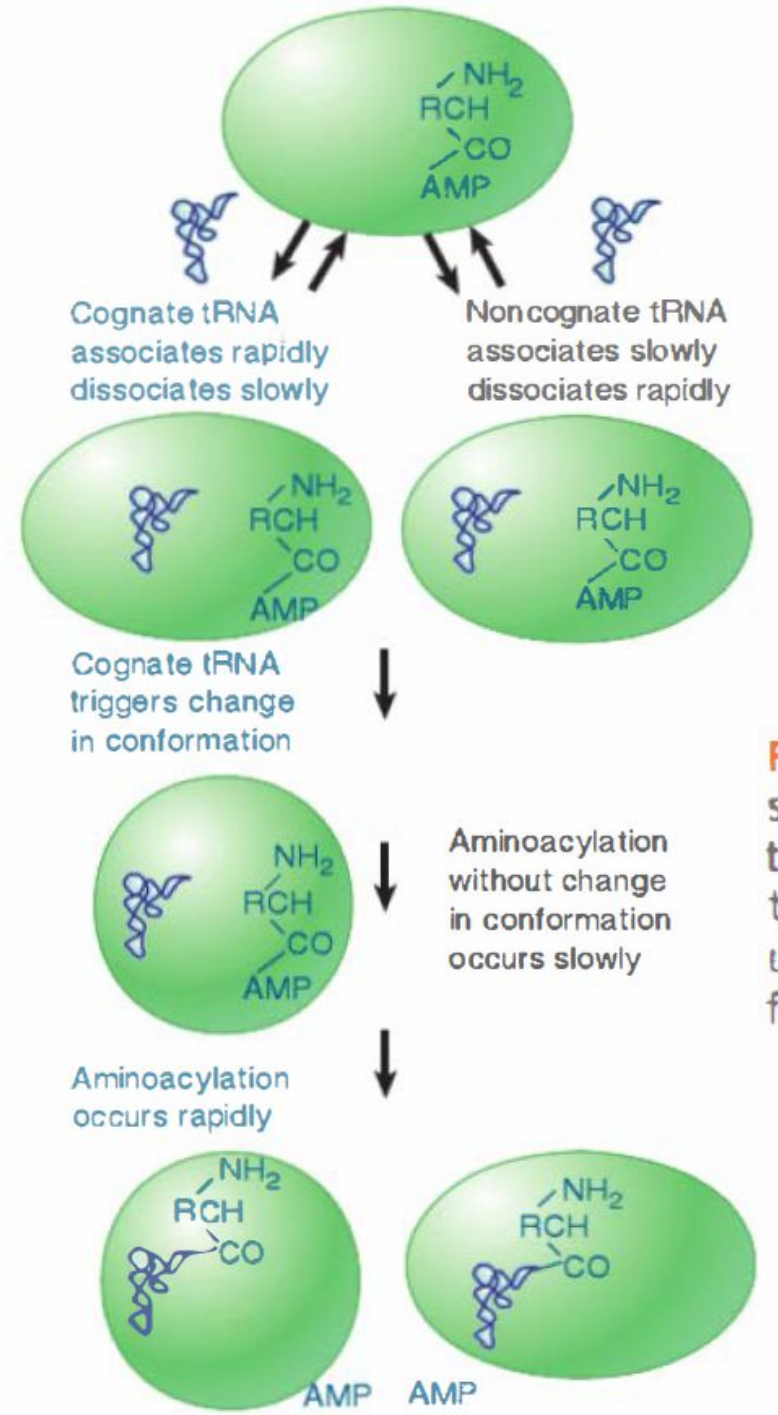


FIGURE 25.17 Aminoacylation of cognate tRNAs by synthetase is based in part on greater affinities for these types, coupled with weak affinities for noncognate types. In addition, noncognate tRNAs are unable to fully undergo the induced-fit conformational changes required for the later catalytic steps.

Specificity of amino acid-tRNA pairing is controlled by proofreading reactions that hydrolyze incorrectly formed aminoacyl adenylates and aminoacyl-tRNAs:

- **a conformational change can cause the hydrolysis of the a.a.-adenylate**
- **the a.a. transfer on the tRNA can be followed by an hydrolysis**

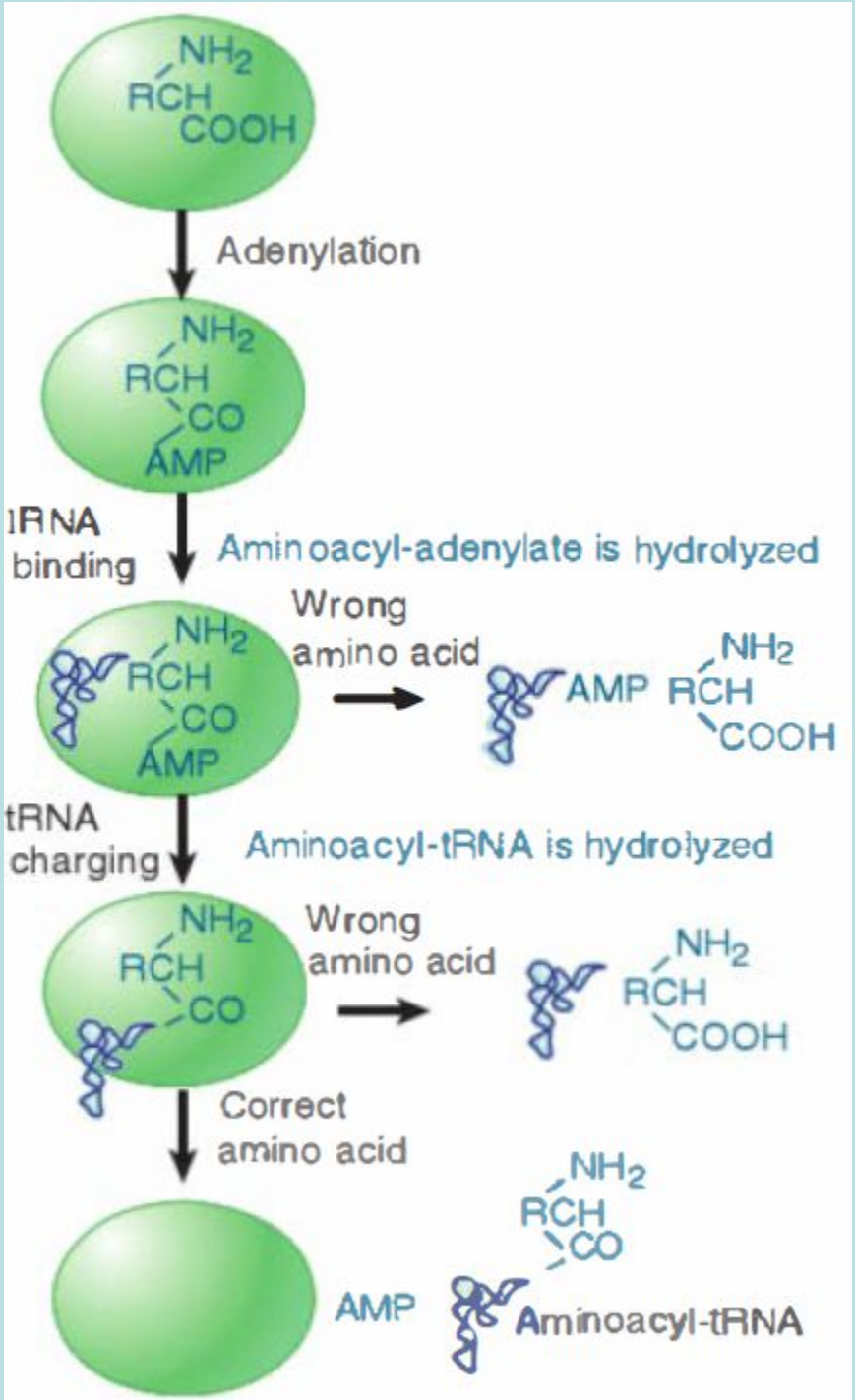


Figure 7.17 The accuracy of charging $tRNA^{Ile}$ by its synthetase depends on error control at two stages.

Step	Frequency of Error
Activation of valine to Val-AMP^{Ile}	1/225
Release of Val-tRNA	1/270
Overall rate of error	1/225 x 1/270 = 1/60,000

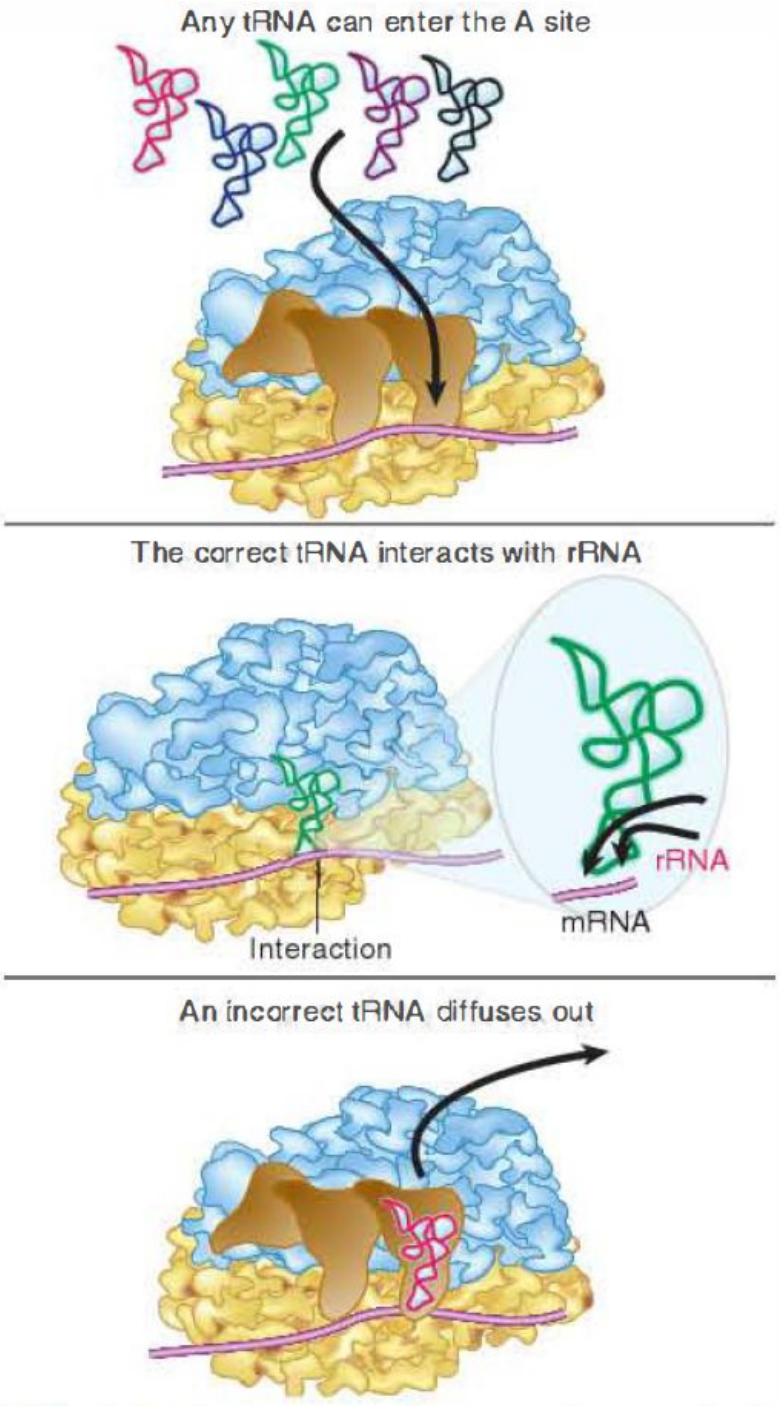


FIGURE 25.24 Any aminoacyl-tRNA can be placed in the A site (by EF-Tu), but only one that pairs with the anti-codon can make stabilizing contacts with rRNA. In the absence of these contacts, the aminoacyl-tRNA diffuses out of the A site.