Genetic Code

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Genetic Code

- The genetic code is formed of a collection of codons (triplets of nucleotides) that constitute the structure of different mRNAs.

- In a codon, since each position of the 3 may be occupied by one of four bases (uracil, cytosine, adenine, or guanine), there are 4^3 = 64 possible codons.

- Actually, 61 of these codons code for the 20 amino acids used for protein synthesis.

Genetic Code

- Most of the amino acids are encoded by more than one codon.

- **The remaining 3 codons (UAA, UAG, UGA) indicate termination of the peptide chain (terminator or stop or non-sense codons).**

- **There is one specific initiation codon (AUG) for methionine.**

	Second Letter			
First Letter	U	C	A	G	Third Letter
U	UUU ⎤ Phe UUC ⎦ UUA ⎤ Leu UUG ⎦	UCU ⎤ UCC ⎥ Ser UCA ⎥ UCG ⎦	UAU ⎤ Tyr UAC ⎦ UAA **Stop** UAG **Stop**	UGU ⎤ Cys UGC ⎦ UGA **Stop** UCG Trp	U C A G
C	CUU ⎤ CUC ⎥ Leu CUA ⎥ CUG ⎦	CCU ⎤ CCC ⎥ Pro CCA ⎥ CCG ⎦	CAU ⎤ His CAC ⎦ CAA ⎤ Gln CAG ⎦	CGU ⎤ CGC ⎥ Arg CGA ⎥ CGG ⎦	U C A G
A	AUU ⎤ AUC ⎥ Ile AUA ⎦ AUG Met └Start	ACU ⎤ ACC ⎥ Thr ACA ⎥ ACG ⎦	AAU ⎤ Asn AAC ⎦ AAA ⎤ Lys AAG ⎦	AGU ⎤ Ser AGC ⎦ AGA ⎤ Arg AGG ⎦	U C A G
G	GUU ⎤ GUC ⎥ Val GUA ⎥ GUG ⎦	GCU ⎤ GCC ⎥ Ala GCA ⎥ GCG ⎦	GAU ⎤ Asp GAC ⎦ GAA ⎤ Glu GAG ⎦	GGU ⎤ GGC ⎥ Gly GGA ⎥ GGG ⎦	U C A G

Characteristics of Genetic Code

- **Specificity:** The genetic code is **specific** (unambiguous), each codon codes for only one amino acids.

- **Near Universality:** With the intriguing exception of a few minor variations in mitochondria, some bacteria, and some single-celled eukaryotes, amino acid codons are identical in all species examined so far. Human beings, E. coli, tobacco plants, amphibians, and viruses share the same genetic code.
    - This suggests that all life-forms have a common evolutionary ancestor, whose genetic code has been preserved throughout biological evolution.

Amino acid	Number of codons	Amino acid	Number of codons
Met	1	Tyr	2
Trp	1	Ile	3
Asn	2	Ala	4
Asp	2	Gly	4
Cys	2	Pro	4
Gln	2	Thr	4
Glu	2	Val	4
His	2	Arg	6
Lys	2	Leu	6
Phe	2	Ser	6

Characteristics of Genetic Code

- **Degeneracy (redundancy)**: A given amino acid may have more than one codon and are termed *synonym codons* e.g., leucine has 6 codons. Only methionine & tryptophane have one codon each.

- In general, the third nitrogenous base of the codon is less specific than the first two in the base pairing between the codon and its specific anticodon (wobble theory) e.g., glycine has the codons GGU, GGC, GGA and GGG.

    Since most organisms have fewer than 45 species of tRNA, some tRNA species must pair with more than one codon.

In 1966, Francis Crick proposed the **Wobble Hypothesis** to account for this.
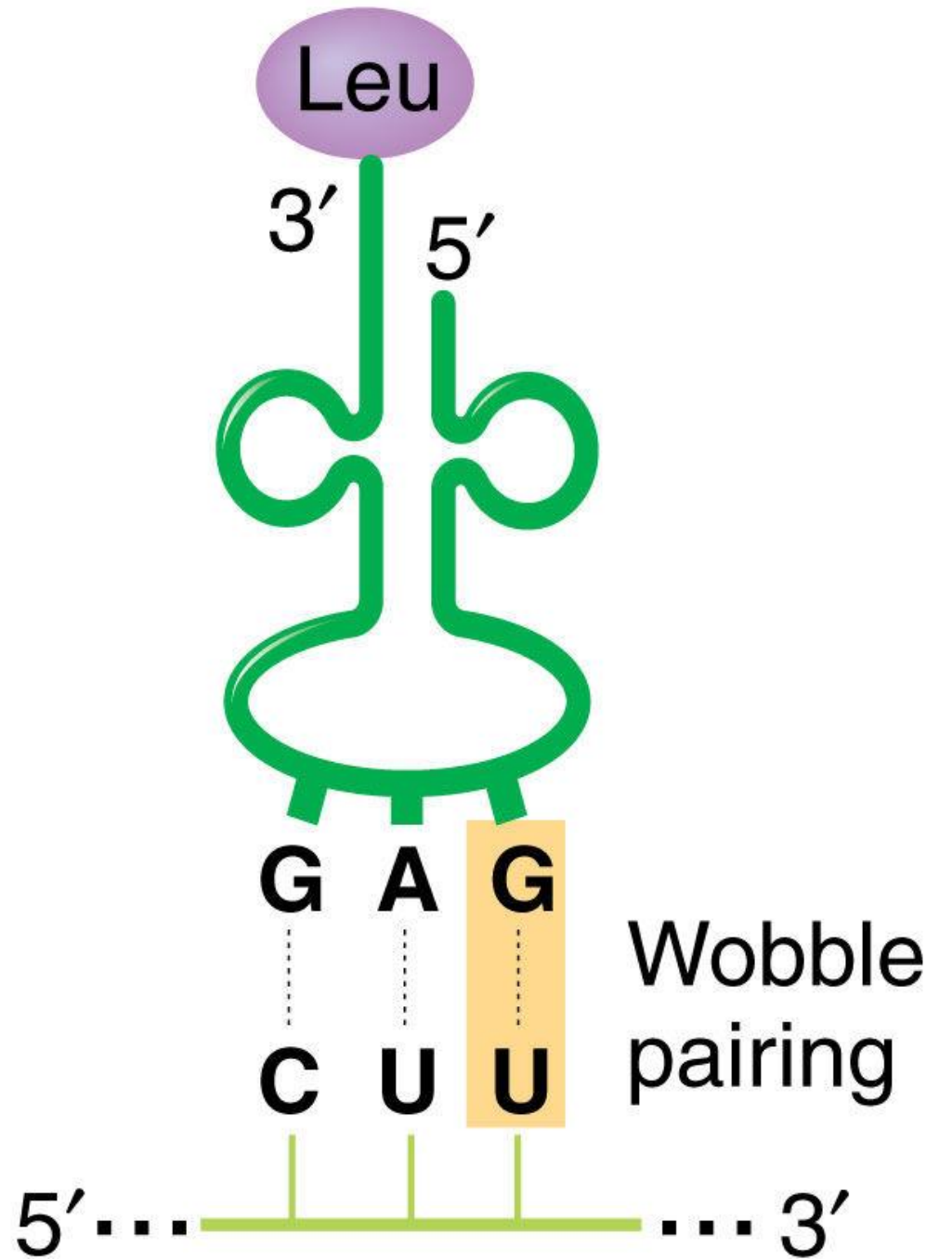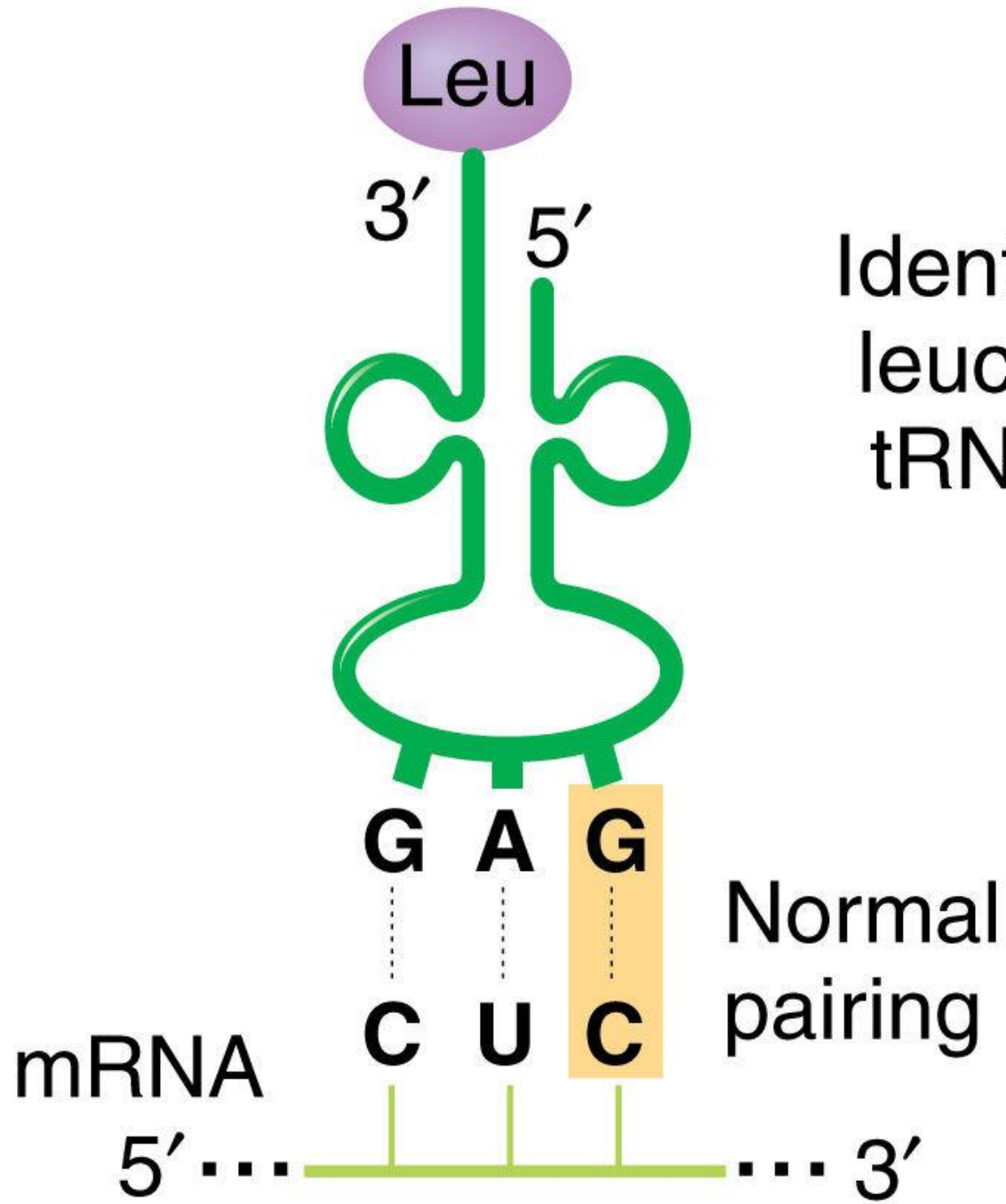
Characteristics of Genetic Code

- **If the anticodon triplet of a tRNA recognized only one codon triplet through Watson-Crick base pairing at all three positions, cells would have a different tRNA for each amino acid codon.**

- **This is not the case, however, because the anticodons in some tRNAs include the nucleotide inosinate (designated I), which contains the uncommon base hypoxanthine.**

Since most organisms have fewer than 45 species of tRNA, some tRNA species must pair with more than one codon.

The ribosome binds **new tRNA** molecules and **amino acids** as it moves along the mRNA.

Leu

3′ 5′
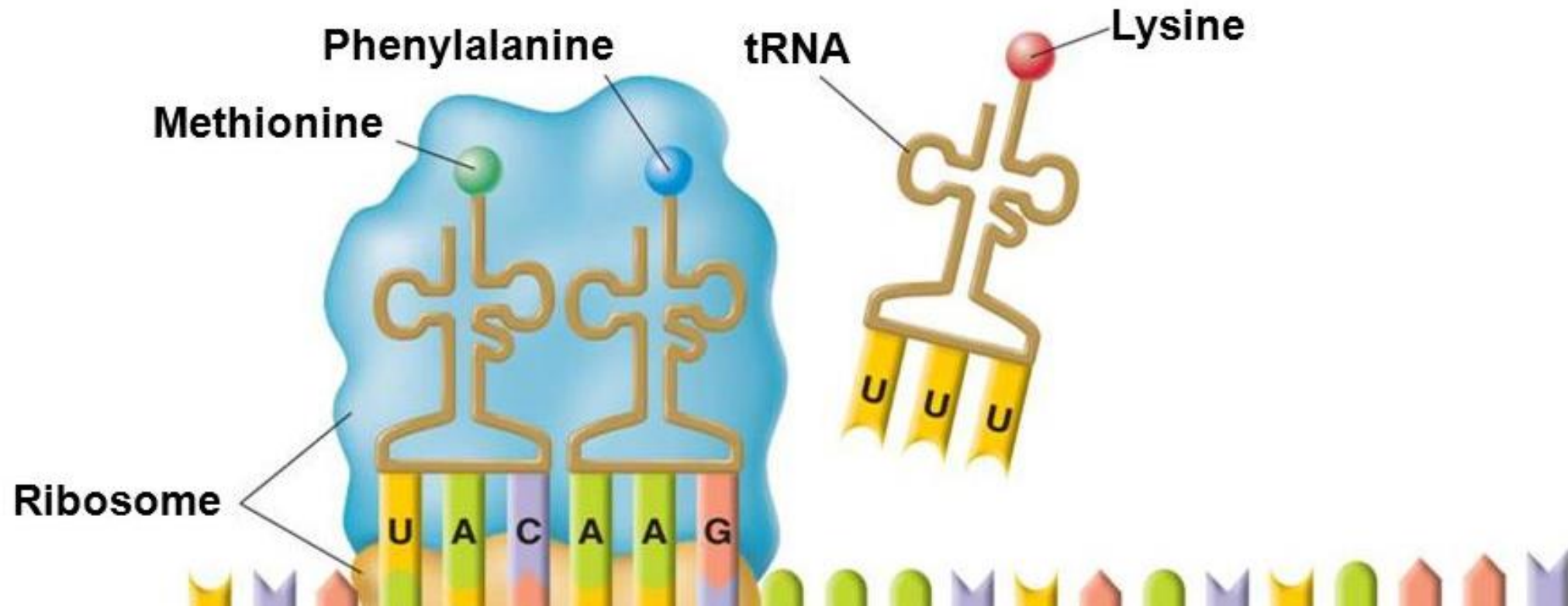
Identical
leucine
tRNAs

Leu

3′ 5′

G A G

Normal
pairing

C U C

mRNA

5′ ··· ··· 3′

G A G

Wobble
pairing

C U U

5′ ··· ··· 3′

The Wobble Hypothesis

The wobble hypothesis is explained by the following:

1. The **first two bases** of an mRNA codon always form strong Watson-Crick base pairs with the corresponding bases of the tRNA anticodon and confer most of the coding specificity.

The Wobble Hypothesis

The wobble hypothesis is explained by the following:

2. The first base of the anticodon (reading in the 5'→3' direction; this pairs with the third base of the codon) determines the number of codons recognized by the tRNA.

- When the first base of the anticodon is C or A, base pairing is specific and only one codon is recognized by that tRNA.
- When the first base is U or G, binding is less specific and two different codons may be read.
- When inosine (I) is the first (wobble) nucleotide of an anticodon, three different codons can be recognized — the maximum number for any tRNA.

The Wobble Hypothesis

The wobble hypothesis is explained by the following:

3. When an amino acid is specified by several different codons, the codons that **differ in either of the first two bases** require **different tRNAs.**

4. A minimum of 32 tRNAs are required to translate all 61 codons (31 to encode the amino acids, 1 for initiation).

The Wobble Hypothesis

Inosinate can form hydrogen bonds with three different nucleotides — A, U, and C — although these pairings are much weaker than the hydrogen bonds of Watson-Crick base pairs G≡C and A=U.

Example: In yeast, one tRNA^{Arg} has the anticodon (5')ICG, which recognizes three arginine codons: (5')CGA, (5')CGU, and (5')CGC.
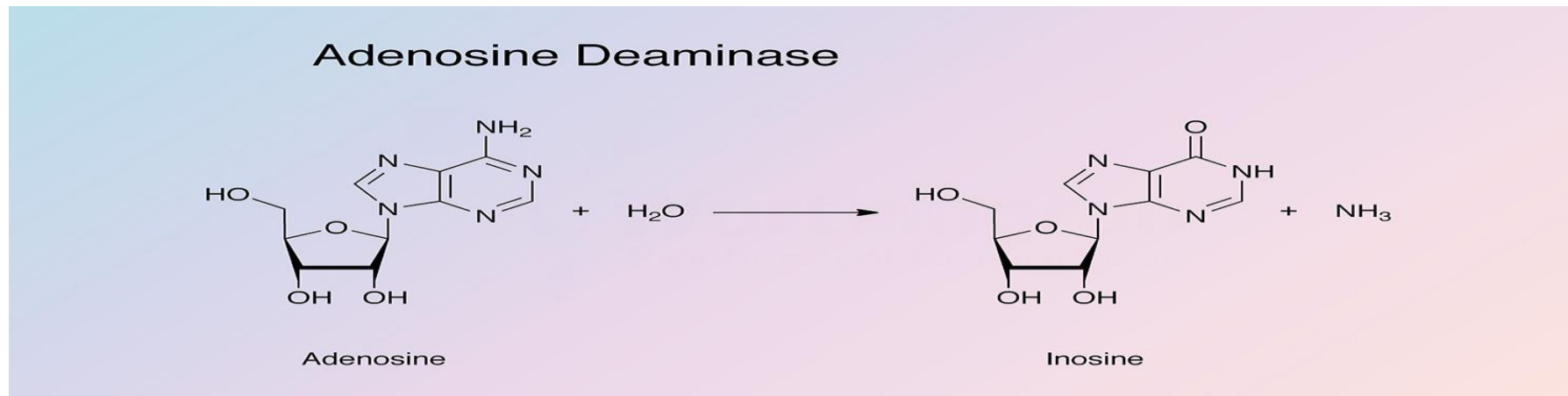
The first two bases are identical (CG) and form strong Watson-Crick base pairs with the corresponding bases of the anticodon, but the third base (A, U, or C) forms rather weak hydrogen bonds with the I residue at the first position of the anticodon.
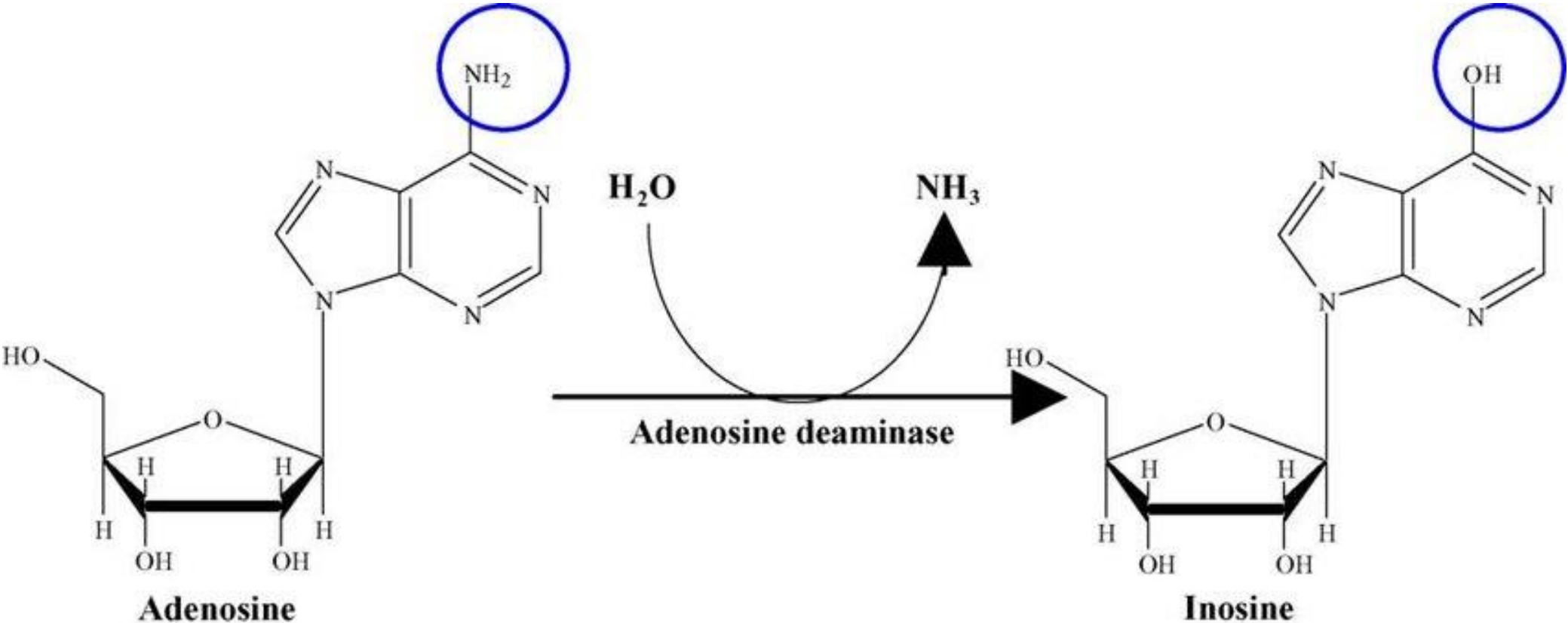
Wobble Base

TABLE 9-1   Wobble Base-pairing Rules

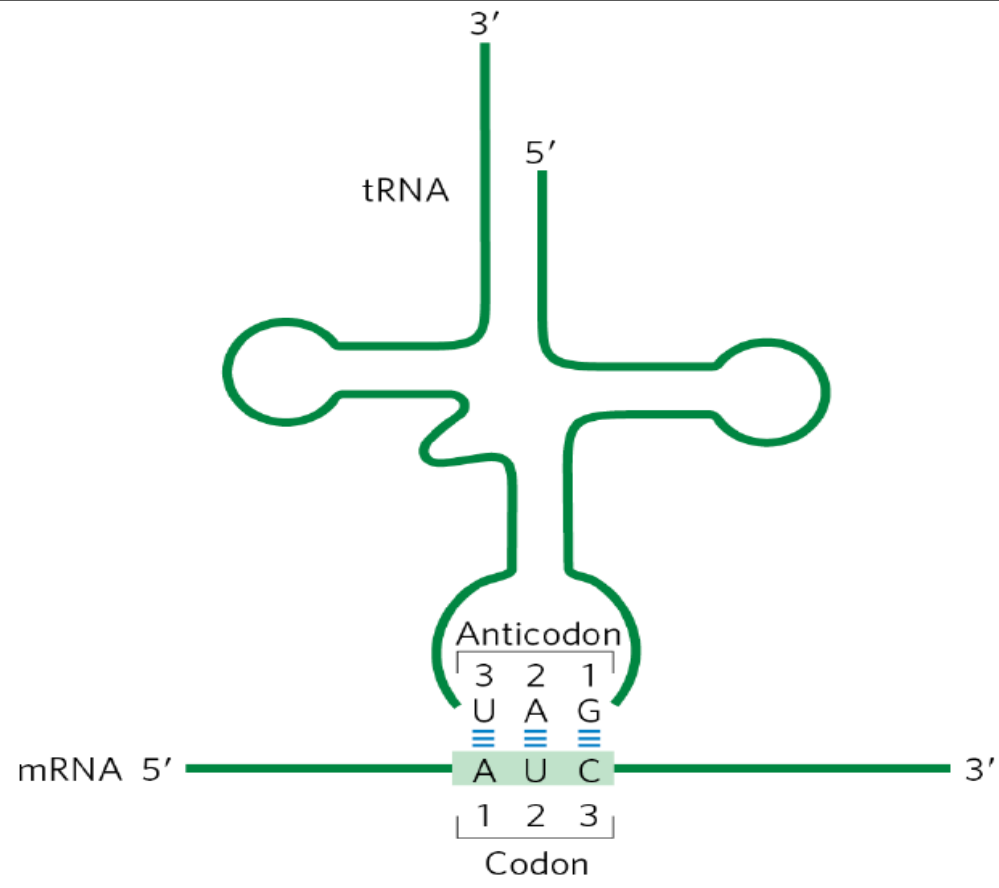| 5' end of anticodon	3' end of codon
A	U
C	G
G	C or U
U	A or G
I (inosine)	A, C, or U

Wobble base pairs are shown in red.

I is the nucleoside Inosine that is formed in tRNA by the removal of an amino group from adenosine. A process that is carried out by an enzyme called anticodon deaminase.

Adenosine Deaminase

Adenosine + H₂O → Inosine + NH₃

Wobble Base

Adenosine + H_2O → (Adenosine deaminase) → Inosine + NH_3

Adenosine

Inosine

tRNA

3′

5′

Anticodon

3	2	1
U	A	G

mRNA 5′

A	U	C	3′

1	2	3

Codon

(a)

	3	2	1		3	2	1		3	2	1	
Anticodon	(3′) G – C – **I**				G – C – **I**				G – C – **I**	(5′)		
Codon	(5′) C – G – **A**				C – G – **U**				C – G – **C**	(3′)		
	1	2	3		1	2	3		1	2	3	

(b)

Characteristics of Genetic Code
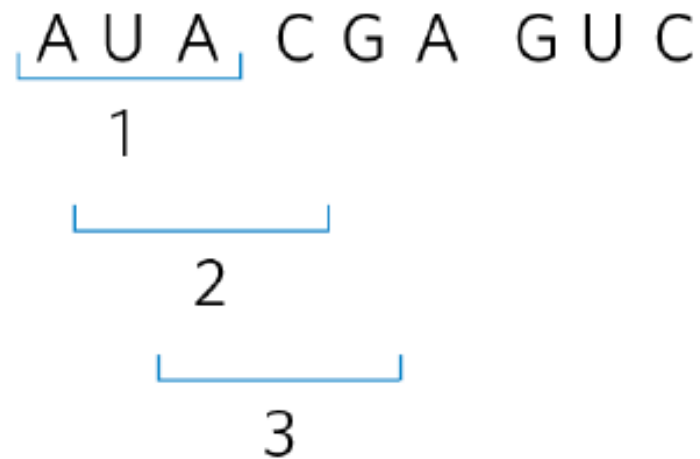
➤ **Non-overlapping and commaless:**

The genetic code is non-overlapping and commaless, that is, the code is read from a fixed starting point as a continuous sequence of bases, taken three at a time.

❖ For example, AGCUGGAUACAU is read as AGC/UGG/AUA/CAU without any "punctuation" between the codons.

Characteristics of Genetic Code

➢**Reading frames**: usually one reading frame will produce a functional protein, the codons are read from a specific starting point (initiating codon) on the mRNA as a continuous uninterrupted sequence of bases taken 3 at a time.

➢**Unidirectional**: The letters in each codon are written from 5\ -end to the 3\ -end and codons on mRNA are written and read also from 5\-end to the 3\-end.

Characteristics of Genetic Code

➢**The genetic code functions via linker molecules.** The tRNAs are the crucial adaptor, matching amino acids with DNA codons.

Thank you ☺