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Unit-IV

TOPIC: Genetic Code, Wobble Hypothesis

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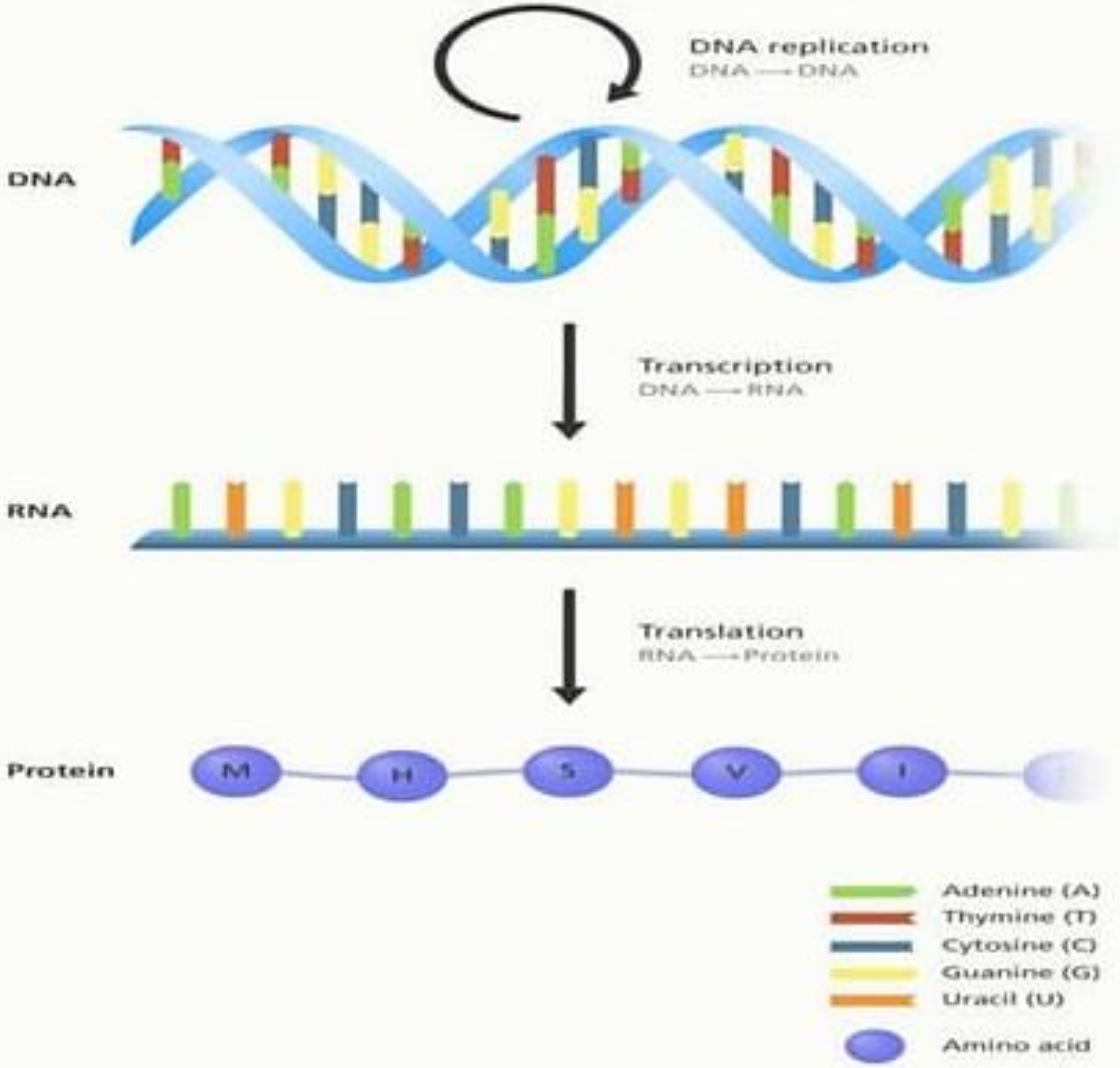
GENETIC CODE – FEATURES & CHARACTER , WOBBLE HYPOTHESIS

CENTRAL DOGMA

- The “Central Dogma” is the process by which instructions in DNA are converted into functional product .
- First proposed by Francis Crick in 1958.
- It explains the flow of genetic information from **DNA** ⟶ **RNA** ⟶ **protein**
- The process by which DNA instructions are converted into the functional product is called gene expression.
- Gene expression has two key stages **transcription** and **translation**



An illustration showing the flow of information between DNA, RNA and protein.

GENETIC CODE

- Genetic code is the sequence of nucleotides in DNA and RNA that determines the amino acid sequence of proteins .
- The term was given by **GEORGE GAMOW.**
- George Gamow postulated that a three letter code must be employed to encode the 20 standard amino acid used by living cells to build proteins.

GEORGE GAMOW

INTRODUCTION OF GENETIC CODE

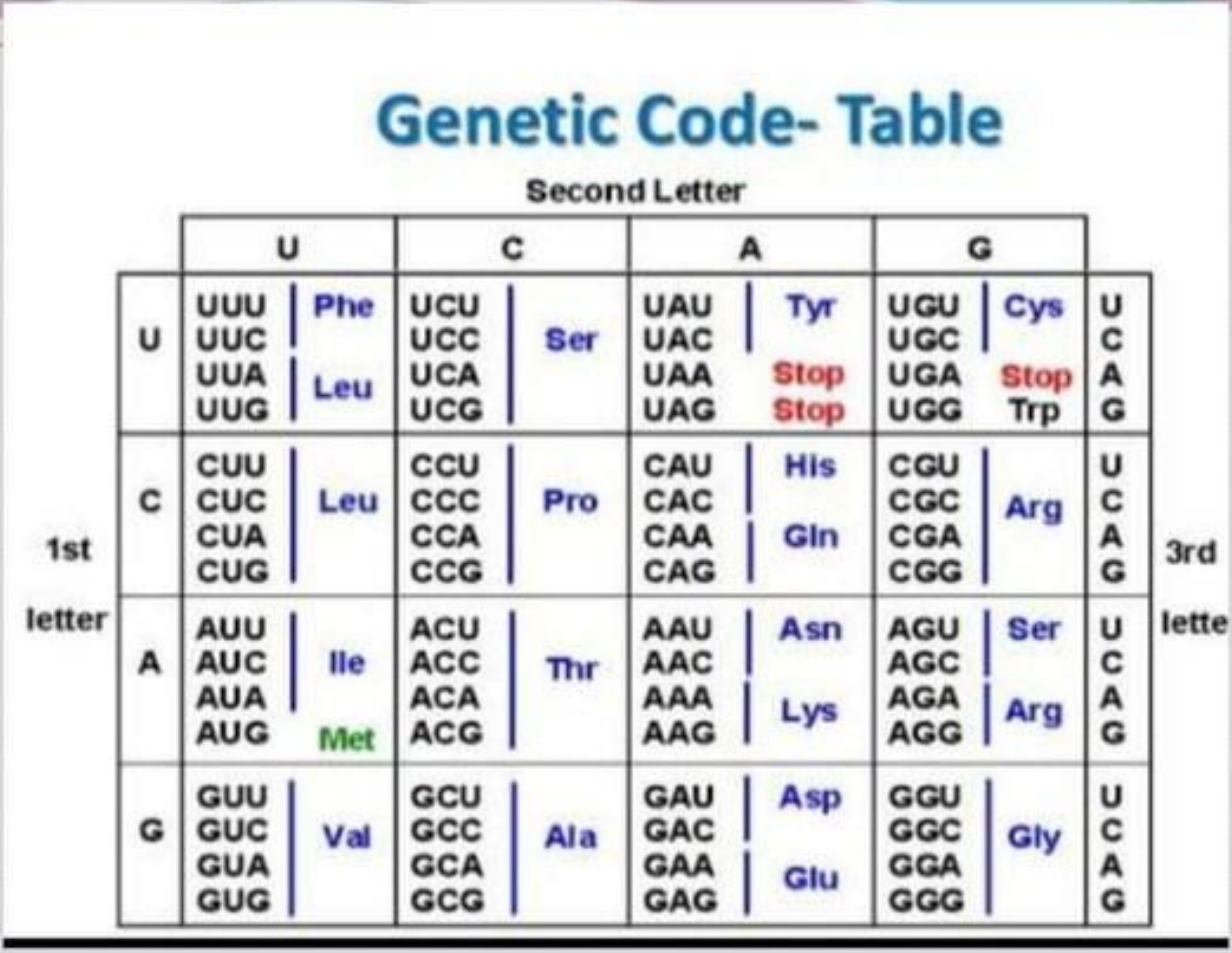
- RNA is composed of four nucleotides : adenine(A), guanine(G), cytosine (C), and uracil(U).
- Three adjacent nucleotides constitute a unit known as **codon,** which codes for an amino acid.
- The collection of codons is called **genetic code**.
- There are 64 possible codons , 3 of which do not code for amino acids but indicate the end of protein.
- The remaining 61 codons specify 20 amino acids that make up protein

- Each codon should have 3 nucleotides to impart specificity to each of the amino acid for specific codon.

  1 nucleotide – 4 combinations

  2 nucleotides- 16 combinations

  3 nucleotides- 64 combinations.



Genetic Code- Table

Second Letter

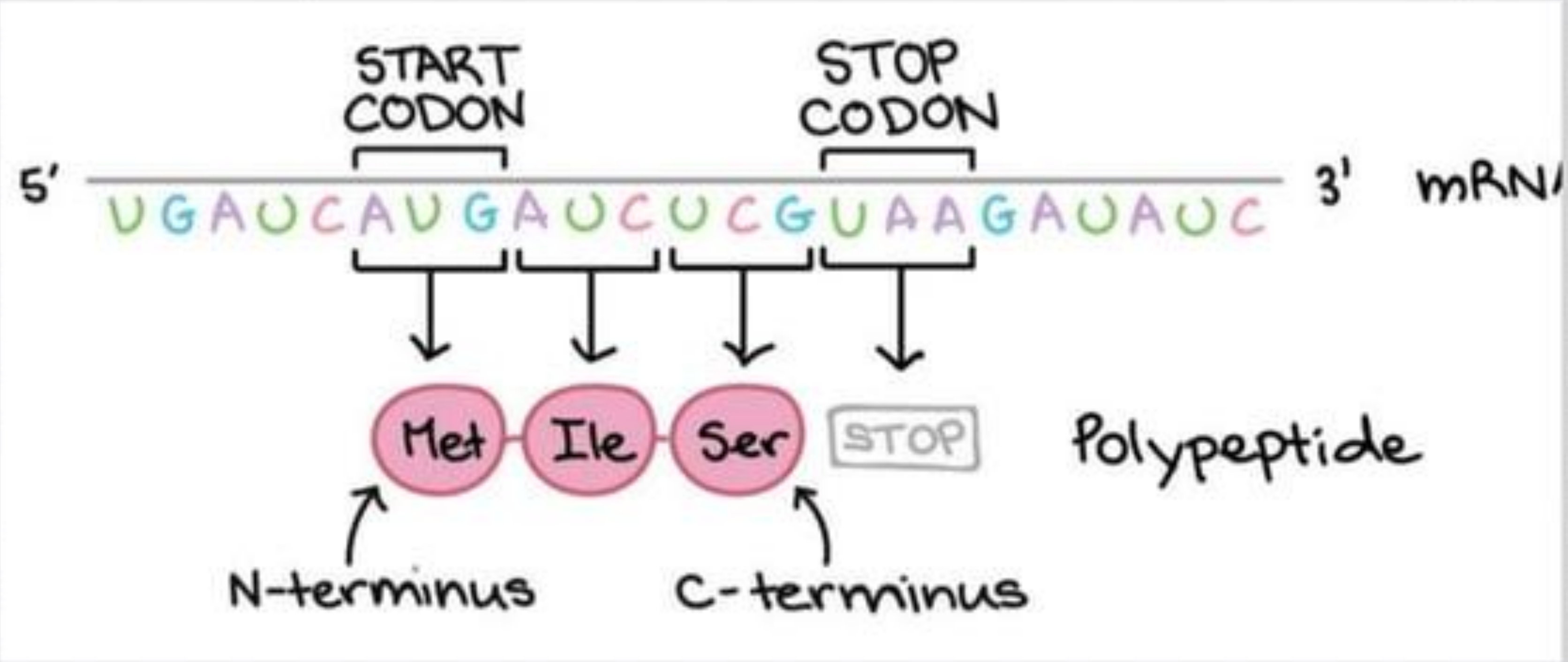
1st letter	U		C		A		G		3rd lette
U	UUU	Phe	UCU	Ser	UAU	Tyr	UGU	Cys	U
	UUC		UCC		UAC		UGC		C
	UUA	Leu	UCA		UAA	Stop	UGA	Stop	A
	UUG		UCG		UAG	Stop	UGG	Trp	G
C	CUU	Leu	CCU	Pro	CAU	His	CGU	Arg	U
	CUC		CCC		CAC		CGC		C
	CUA		CCA		CAA	Gln	CGA		A
	CUG		CCG		CAG		CGG		G
A	AUU	Ile	ACU	Thr	AAU	Asn	AGU	Ser	U
	AUC		ACC		AAC		AGC		C
	AUA		ACA		AAA	Lys	AGA	Arg	A
	AUG	Met	ACG		AAG		AGG		G
G	GUU	Val	GCU	Ala	GAU	Asp	GGU	Gly	U
	GUC		GCC		GAC		GGC		C
	GUA		GCA		GAA	Glu	GGA		A
	GUG		GCG		GAG		GGG		G

CODONS

- Cells decode mRNAs by reading their nucleotides in groups of 3 , called codons.
- **FEATURES:**
  1. Most codons specify an amino acid.
  2. Three “stop” codons mark the end of protein
  3. One “start” codon AUG , marks the beginning of a protein and also encodes the amino acid methionine.

TYPES OF CODON

- Sense codons
- Signal codons
  - Start codons
  - Stop codons
- Sense codon – Codon that codes for amino acid.
- Signal codon: codons that code for signal during protein synthesis . Eg: AUG, UAA, UAG, UGA.
  - There are two types of signal codons:
    - Terminating codon
    - Initating codon



SIGNAL CODONS

- **TERMINATING CODONS**: UAA, UAG &UGA are termination codons or nonsense codons & are often referred to as amber, ochre & opal codons.
- **INITIATING CODONS**: AUG is the intiation codon . It codes for the first amino acid in all proteins.

  At the starting point it codes for methionine in eukaryotes & formyl methionine in prokaryotes.

CHARACTERISTICS OF GENETIC CODE

1. Triplet nature.
2. Degeneracy.
3. Non overlapping.
4. Commaless.
5. Non ambiguity.
6. Universality.
7. Polarity.

POLARITY:

- Singlet and doublet codes are not adequate to code for 20 amino acids, therrefore, it was pointed out that triplet code is minimum required.

DEGENERACY:

- The code degenerates which means that the same amino acid is coded by more than one base triplet.
- Degeneracy does not imply lack of specificity in protein synthesis.
- It merely means that a particular amino acid can be directed to its place in peptide chain by more than one base triplets.
- The code degeneracy is basically of 2 types: partial and complete.

- In partial degenercy , the first two nucleotides are identical but the third nucleotide of the degenerate codon differs. Eg: CUU and CUC code for leucine.
- Complete degeneracy occurs when any of the 4 bases can take third position and still code for the same amino acid. Eg: UCU, UCC,UCA,UCG all code for serine.

➢ **NON-OVERLAPPING**:

- Genetic code is non overlapping i.e adjacent codons do not overlap.

- A non overlapping codon means that the same letter is not used for two different codons in other words no single base can take part in the formation of more than one codon.

- **COMMALESS**:

- The genetic code is commaless . There is no signal to indicate the end of one codon and the beginning of the next

NON AMBIGUITY:

- Non ambiguous code means that there is no ambiguity about a particular codon.
- A particular codon will always code for the same amino acid.
- While the same amino acid can be coded by more than one codon , the same codon shall not code for two or more different amino acids.

- **UNIVERSALITY**:
  - Universality of the code means that the same sequences of 3 bases encode the same amino acids in all life forms .
  - The code is base don work conducted on bacterium E.coli but it is valid for other organisms.
  - Exceptions: Yeast, mitochondria, mycoplasma.
- **POLARITY**:
  - Genetic code has polarity i.e the code is always read in firex direction 5' to 3'.

- It is apparent that if the code is read in opposite direction i.e 3’ to 5’ , it would specify 2 different proteins , since the codon would have reversed base sequence.

WOBBLE HYPOTHESIS

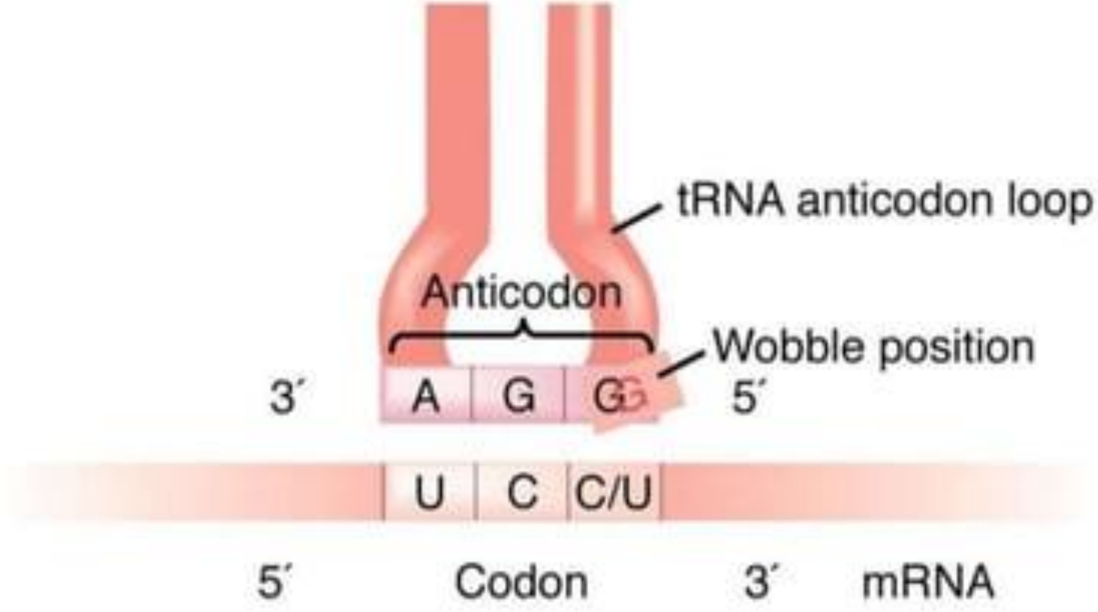
- Wobble means to ''**sway** ''or ''**move unsteadily**''.
- According to this hypothesis ,only the first two bases of codon have precise pairing with the bases of the anticodon of tRNA, while the pairing between the third bases of codon and anticodon may wobble.
- The phenomenon permits a single tRNA to recoganize more than one coodon. Therefore although there are 61 codons for amino acids , the number of tRNA is far less.

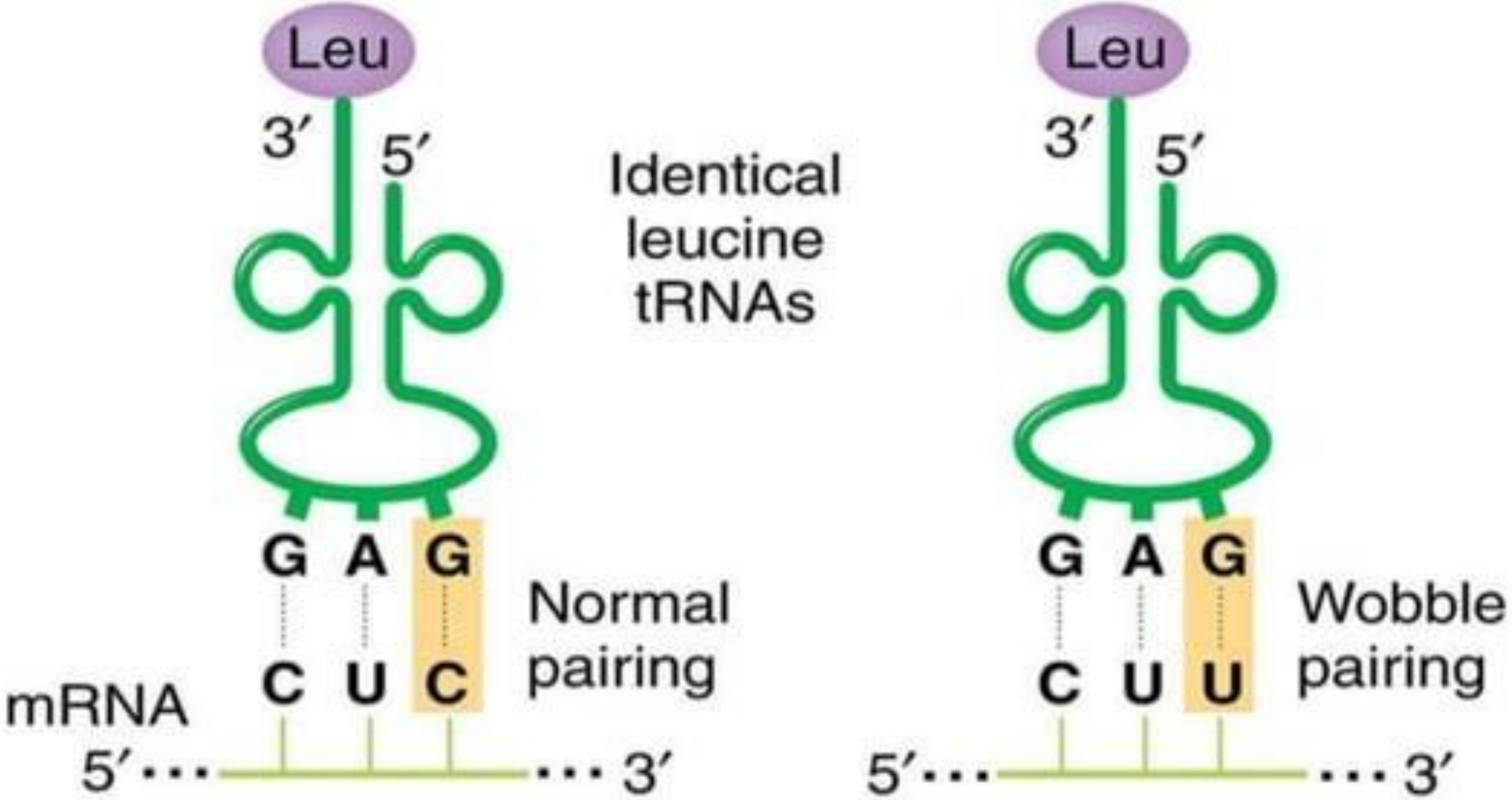
- The wobble states that the base at 5’ end of the anticodon is not spatially confined as the other two bases allowing it to form hydrogen bonds with any of several bases located at 3’ end of codon.

- **HISTORY:** Hypothesis proposed by **Francis Crick** in **1966** to explain the observed degeneracy in the third position of a codon.

The Wobble Hypothesis

- UCC and UCU both code for serine




Leu
3′
5′
Identical leucine tRNAs
Leu
3′
5′
G A G
C U C
Normal pairing
mRNA
5′···
···3′
G A G
C U U
Wobble pairing
5′···
···3′

SIGNIFICANCE OF WOBBLE HYPOTHESIS

- Wobble base pairs are fundamental in RNA secondary structure and are critical for the proper translation of genetic code
- Wobbling allows faster dissociation of tRNA from mRNA and also protein synthesis.
- The existence of wobble minimizes the damage that can be caused by misreading the code.

BIOLOGICAL SIGNIFICANCE OF DEGENERACY OF GENETIC CODE

- If the code were not degenerate , 20 codons would designate amino acids and 44 would lead to chain termination.
- The probability of mutating chain termination would therefore be much higher with a non degenerate codon.

MUTATIONS AND GENETIC CODE

- Mutations results in change of nucleotide sequences in the DNA& RNA.
- Effect of mutations is on translation through alteration in codons. Some mutations are harmful.
- Some of them are:

A. Point mutations - Silent, misense , nonsense

B. Frame shift mutations.

- **POINT MUTATION**: The replacement of one base pair by another results in point mutation.
- **Silent mutation**: There are no detectable effects in silent mutation.
- **Mis sense mutation**: The changed base may code for a different amino acid.
- **Nonsense mutation**: The codon with the altered base may become termination(or nonsense) codon.

- **FRAMESHIFT MUTATION**: These occur when one or more base pair is inserted in or deleted from DNA.

CONCLUSION

Despite these differences , all known species codes are very similar to each other and the coding mechanism is the same for all organisms; three base codons ,tRNA, ribosomes, reading the code in the same direction and translating the code 3 letters at a time into sequence of amino acids.

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THANK YOU