

WOBBLE HYPOTHESIS

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INTRODUCTION




The Wobble Hypothesis explains why multiple codons can code for a single amino acid. One tRNA molecule can recognise and bind to more than one codon, due to the less-precise base pairs that can arise between the 3rd base of the codon and the base at the 1st position on the anticodon.

WOBBLE HYPOTHESIS

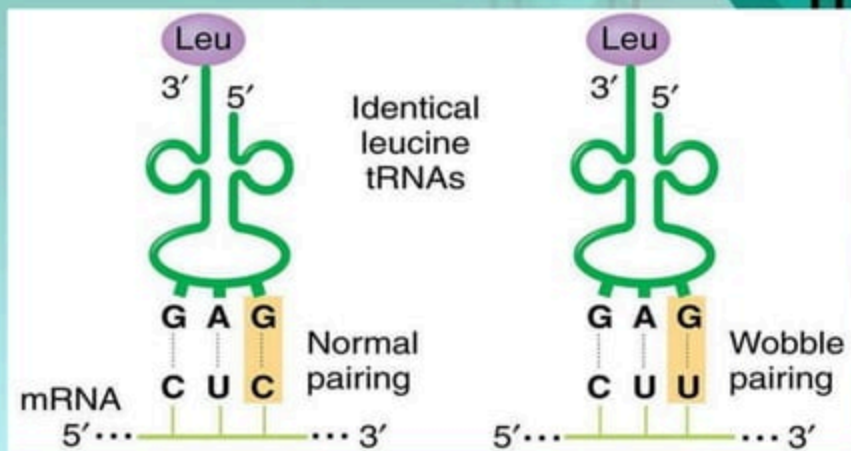


- There are more than one codon for one amino acid. This is called degeneracy of genetic code.
- To explain the possible cause of degeneracy of codons, in 1966, Francis Crick proposed “the Wobble hypothesis”.
- According to this hypothesis, only the first two bases of the codon have a precise pairing 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 recognize more than one codon. Therefore, although there are 61 codons for amino acids, the number of tRNA is far less (around 40) which is due to wobbling.



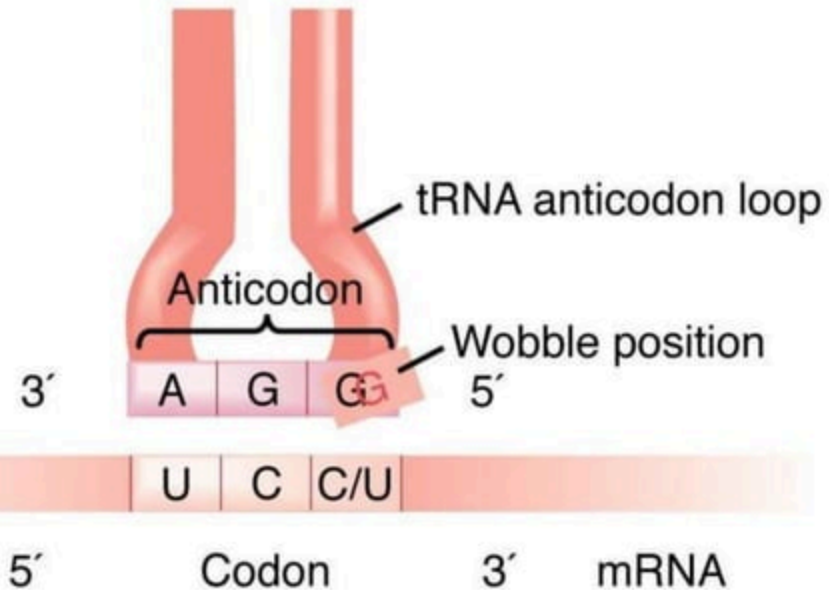
The wobble hypothesis states that the base at 5' end of the anticodon is not spatially confined as the other two bases allowing it to form hydrogen bonds with any of several bases located at the 3' end of a codon. This leads to the following conclusions:

- The first two bases of the codon make normal (canonical) H-bond pairs with the 2nd and 3rd bases of the anticodon.
- At the remaining position, less stringent rules apply and non-canonical pairing may occur. The wobble hypothesis thus proposes a more flexible set of base-pairing rules at the third position of the codon.
- The relaxed base-pairing requirement, or “wobble,” allows the anticodon of a single form of tRNA to pair with more than one triplet in mRNA.
- The rules: first base U can recognize A or G, first base G can recognize U or C, and first base I can recognize U, C or A.



- Crick's hypothesis hence predicts that the initial two ribonucleotides of triplet codes are often more critical than the third member in attracting the correct tRNA.

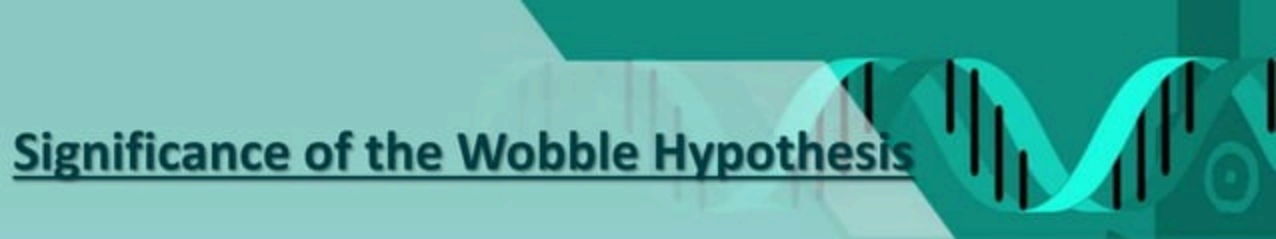
Wobble base pairs



WOBBLE BASE PAIRS

- A wobble base pair is a pairing between two nucleotides in RNA molecules that does not follow Watson-Crick base pair rules.
- The four main wobble base pairs are guanine-uracil (G-U), hypoxanthine-uracil (I-U), hypoxanthine-adenine (I-A), and hypoxanthine-cytosine (I-C).
- In order to maintain consistency of nucleic acid nomenclature, “I” is used for hypoxanthine because hypoxanthine is the nucleobase of inosine.
- Inosine displays the true qualities of wobble, in that if that is the first nucleotide in the anticodon then any of three bases in the original codon can be matched with the tRNA.

Significance of the Wobble Hypothesis



- Our bodies have a limited amount of tRNAs and wobble allows for broad specificity.
- Wobble base pairs have been shown to facilitate many biological functions, most clearly proven in the bacterium *Escherichia coli*.
- The thermodynamic stability of a wobble base pair is comparable to that of a Watson-Crick base pair.
- Wobble base pairs are fundamental in RNA secondary structure and are critical for the proper translation of the 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 a misreading of the code; for example, if the Leu codon CUU were misread CUC or CUA or CUG during transcription of mRNA, the codon would still be translated as Leu during protein synthesis.


Flexible Base Pairing at the 3rd Position of the “codon-anticodon duplex”

- If A is at the 3rd position in the codon it can base pair with U or I, if either of these is present at the 1st position in the anticodon.
- If U is at the 3rd position in the codon it can base pair with A, G or I, if either of these is present at the 1st position in the anticodon.
- If G is at the 3rd position in the codon it can base pair with C or U, if either of these is present at the 1st position in the anticodon.
- If C is at the 3rd position in the codon it can base pair with G or I, if either of these is present at the 1st position in the anticodon.

Reasons Why More Flexible Base Pairing Rules Occur

- The 16S RNA in the 30S ribosomal subunit possesses a means of examining whether the standard Watson-Crick base pairs have formed between the 1st codon base and the 3rd anticodon base, as well as between the 2nd codon base and the 2nd anticodon base.
- However, there is no system to check whether the 3rd codon base and the 1st anticodon base are complimentary to one another and this amounts to the more lenient base-pairing that is witnessed exclusively at the 3rd position

The Consequent Degeneracy of the Genetic Code



- The Wobble Hypothesis explains why multiple codons can code for a single amino acid. One tRNA molecule can recognise and bind to more than one codon, due to the less-precise base pairs that can arise between the 3rd base of the codon and the base at the 1st position on the anticodon.
- This hence explains why more codons exist than there are specific tRNA molecules .
- The Wobble Hypothesis also illustrates why the only variability between many codons, that encode the same amino acid, is their 3rd base

CONCLUSION

The Wobble Hypothesis, by Francis Crick, states that the 3rd base in an mRNA codon can undergo non-Watson-Crick base pairing with the 1st base of a tRNA anticodon. The mRNA codon's first 2 bases form Hydrogen bonds with their corresponding bases on the tRNA anticodon in the usual Watson-Crick manner, in that they only form base pairs with complementary bases. However, the formation of Hydrogen bonds between the 3rd base on the codon and the 1st base on the anticodon can potentially occur in a non-Watson-Crick manner. Therefore different base pairs to those usually seen can form at this position.