Gene Translation:RNA -> Protein

How does a particular sequence of **nucleotides** specify a particular sequence of **amino acids**?

The answer: by means of **transfer RNA** molecules, each specific for one amino acid and for a particular **triplet** of nucleotides in messenger RNA (mRNA) called a **codon**. The family of tRNA molecules enables the codons in a mRNA molecule to be **translated** into the sequence of amino acids in the protein. At least one kind of tRNA is present for each of the 20 amino acids used in protein synthesis. (Some amino acids employ the services of two or three different tRNAs, so most cells contain as many as 32 different kinds of tRNA.) The amino acid is attached to the appropriate tRNA by an activating enzyme (one of 20 **aminoacyl-tRNA synthetases**) specific for that amino acid as well as for the tRNA assigned to it.

Each kind of tRNA has a sequence of 3 unpaired nucleotides — the **anticodon** — which can bind, following the rules of base pairing, to the complementary triplet of nucleotides — the **codon** — in a **messenger RNA** (**mRNA**) molecule. Just as DNA replication and transcription involve base pairing of nucleotides running in opposite direction, so the reading of codons in mRNA (5' -> 3') requires that the anticodons bind in the opposite direction.

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Anticodon:  3' CGA  5'
Codon:      5' GCU  3'
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The RNA Codons

Second nucleotide					
	U	**C**	**A**	**G**	
U	UUU **Phenylalanine**	UCU **Serine**	UAU **Tyrosine**	UGU **Cysteine**	**U**

	(Phe)	(Ser)	(Tyr)	(Cys)	
	UUC Phe	UCC Ser	UAC Tyr	UGC Cys	**C**
	UUA **Leucine** (Leu)	UCA Ser	UAA **STOP**	UGA **STOP**	**A**
	UUG Leu	UCG Ser	UAG **STOP**	UGG **Tryptophan** (Trp)	**G**
C	CUU **Leucine** (Leu)	CCU **Proline** (Pro)	CAU **Histidine** (His)	CGU **Arginine** (Arg)	**U**
	CUC Leu	CCC Pro	CAC His	CGC Arg	**C**
	CUA Leu	CCA Pro	CAA **Glutamine** (Gln)	CGA Arg	**A**
	CUG Leu	CCG Pro	CAG Gln	CGG Arg	**G**
A	AUU **Isoleucine** (Ile)	ACU **Threonine** (Thr)	AAU **Asparagine** (Asn)	AGU **Serine** (Ser)	**U**
	AUC Ile	ACC Thr	AAC Asn	AGC Ser	**C**
	AUA Ile	ACA Thr	AAA **Lysine** (Lys)	AGA **Arginine** (Arg)	**A**
	AUG **Methionine** (Met) or **START**	ACG Thr	AAG Lys	AGG Arg	**G**
G	GUU **Valine** Val	GCU **Alanine**	GAU **Aspartic**	GGU **Glycine**	**U**

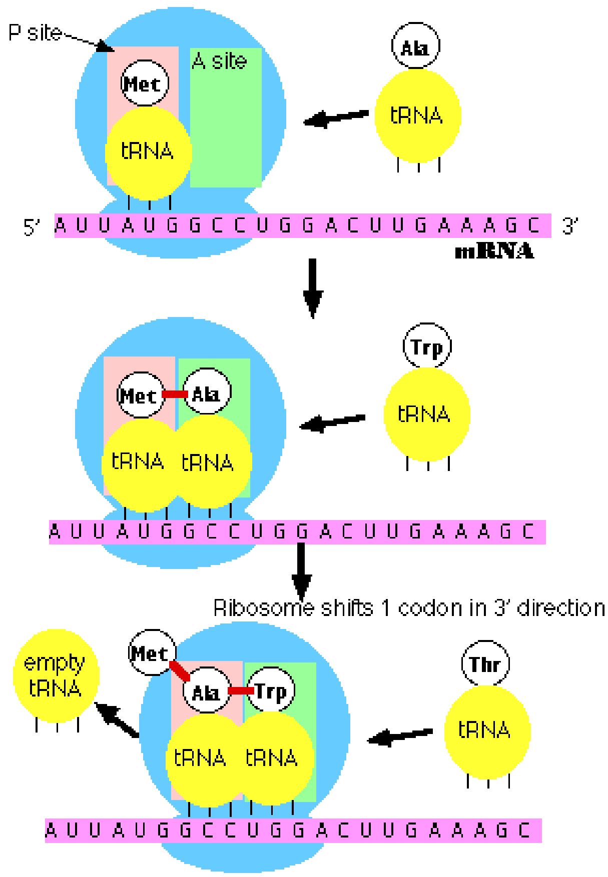
		(Ala)	**acid** (Asp)	(Gly)	
	GUC (Val)	GCC Ala	GAC Asp	GGC Gly	**C**
	GUA Val	GCA Ala	GAA **Glutamic acid** (Glu)	GGA Gly	**A**
	GUG Val	GCG Ala	GAG Glu	GGG Gly	**G**

Note:

- Most of the amino acids are encoded by synonymous codons that differ in the third position of the codon.
- In some cases, a single tRNA can recognize two or more of these synonymous codons.
- Example: phenylalanine tRNA with the anticodon 3' AAG 5' recognizes not only UUC but also UUU.
- The violation of the usual rules of base pairing at the third nucleotide of a codon is called "wobble"
- The codon **AUG** serves two related functions
    - It begins every message; that is, it signals the **start of translation** placing the amino acid **methionine** at the amino terminal of the polypeptide to be synthesized.
    - When it occurs within a message, it guides the incorporation of methionine.
- Three codons, **UAA**, **UAG**, and **UGA**, act as signals to terminate translation. They are called **STOP** codons.

The Steps of Translation

1. Initiation



- The **small subunit** of the ribosome binds to a site "upstream" (on the 5' side) of the start of the message.
- It proceeds downstream (5' -> 3') until it encounters the start codon **AUG**. (The region between the mRNA cap and the AUG is known as the 5'-untranslated region [**5'-UTR**].)
- Here it is joined by the **large subunit** and a special **initiator tRNA**.
- The initiator tRNA binds to the **P site** (shown in pink) on the ribosome.
- In eukaryotes, initiator tRNA carries **methionine** (Met). (Bacteria use a modified methionine designated **fMet**.)

2. Elongation

- An **aminoacyl-tRNA** (a tRNA covalently bound to its amino acid) able to base pair with the next codon on the mRNA arrives at the **A site** (green) associated with:
  - an **elongation factor** (called EF-Tu in bacteria; EF-1 in eukaryotes)
  - **GTP** (the source of the needed energy)
- The preceding amino acid (Met at the start of translation) is covalently linked to the incoming amino acid with a peptide bond (shown in red).
- The initiator tRNA is released from the P site.
- The ribosome moves one codon downstream.

- This shifts the more recently-arrived tRNA, with its attached peptide, to the P site and opens the A site for the arrival of a new aminoacyl-tRNA.
- This last step is promoted by another protein **elongation factor** (called EF-G in bacteria; EF-2 in eukaryotes) and the energy of another molecule of **GTP**.

Note: the initiator tRNA is the only member of the tRNA family that can bind directly to the P site. The P site is so-named because, with the exception of initiator tRNA, it binds only to a **p**eptidyl-tRNA molecule; that is, a tRNA with the growing peptide attached.

The A site is so-named because it binds only to the incoming **a**minoacyl-tRNA; that is the tRNA bringing the next amino acid. So, for example, the tRNA that brings Met into the interior of the polypeptide can bind only to the A site.

3. Termination

- The end of translation occurs when the ribosome reaches one or more **STOP** codons (**UAA**, **UAG**, **UGA**). (The nucleotides from this point to the poly(A) tail make up the 3'-untranslated region [**3'-UTR**] of the mRNA.)
- There are no tRNA molecules with anticodons for STOP codons.
- However, protein **release factors** recognize these codons when they arrive at the A site.
- Binding of these proteins —along with a molecule of **GTP** — releases the polypeptide from the ribosome.

The ribosome splits into its subunits, which can later be reassembled for another round of protein synthesis.