Protein Synthesis

Translation of the Genetic Code

Review of DNA Replication

- DNA is a double stranded molecule that does not leave the nucleus. DNA replication occurs exclusively in the nucleus.
- With several enzymes, 1 double stranded DNA molecule will turn into 2 double stranded molecules that are identical to each other.
- A bonds with T and C bonds with G.

Protein Synthesis

- Sequences of bases in the DNA called genes can code for the production of proteins.
- The process starts in the nucleus and is completed at a ribosome in the cytoplasm.
- Proteins may be further modified in the Golgi Apparatus to be incorporated in the cell membrane or exported from the cell.

Proteins are composed of long chains of amino acids called polypeptides. Proteins can be enzymes, hormones, receptors, structural and catalysts.

- control virtually every reaction
- providing structure
- serving as signals to other cells.

The protein cannot function properly unless it folds in the proper orientation.

Instructions for the sequence of amino acids are encoded in DNA (genes) located in the nucleus.

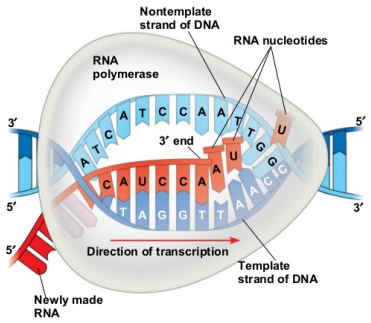
The DNA contains the instructions but several steps must occur before you can build a polypeptide chain and that chain can function.

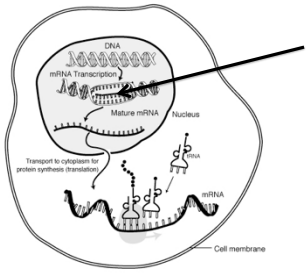
RNA Polymerase II

The DNA is in the nucleus and does not leave. First, the specific gene in the DNA will code for a strand of mRNA that is able to leave the nucleus. The enzyme RNA Polymerase II is needed for this process which is called TRANSCRIPTION.

Transcription

- As you recall, in DNA, the base A will bond with T and the base G will bond with C.
- In transcription to mRNA, A will bond with U, and the base T will bond with A, and the base G will bond with C and C with G.





RNA Polymerase II is the enzyme necessary to form the mRNA molecule from the DNA in the nucleus.

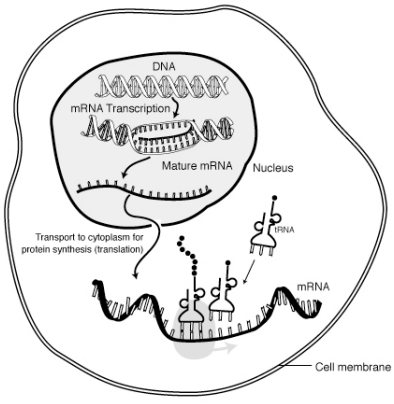
The mRNA will move out of the nucleus into the cytoplasm, then on to a ribosome.

DNA Replication vs Transcription

- DNA
- Transcription

mRNA

- mRNA is a single strand of nucleotides with a phosphate group, a ribose sugar and the bases A, U, G and C.
- The mRNA can leave the nucleus and will join a ribosome in the cytoplasm and begin to build a polypeptide chain.



Let's Practice-TRANSCRIPTION

DNA → mRNA

T A C T T G C C C G G C A T T

_____ _____ _____ _____ _____

How do you know the top strand is DNA and not mRNA?

Codons

Each 3-base sequence of nucleotides transcribed from DNA to mRNA is called a codon. Codons are only found on mRNA. Each codon (3 nucleotides) will code for a 1 specific amino acid. You can determine which specific amino acid is coded for by using the Universal Genetic Code.

Codon U C A

Amino Acid _____

Codon C U C

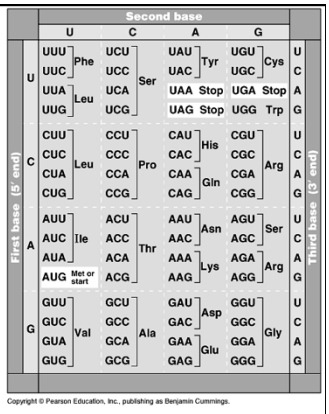
Amino Acid _____

Codon A U G

Amino Acid _____

Codon U G A

Amino Acid _____



Beginning and Ending

Each polypeptide must begin with a START codon and end with one of three STOP codons.

What is the start codon?

What are the three stop codons?

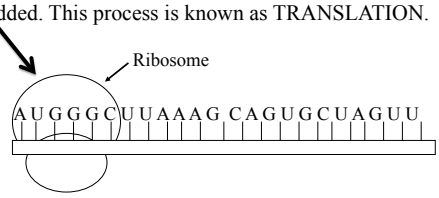
Building the Polypeptide

T A C T T G C C C G G C A T T

A U G A A C G G G C C G U A A

_____ _____ _____ _____ _____

In order to start making a protein from an mRNA strand, the strand must attach to a ribosome in the cytoplasm. This occurs at the START codon (AUG). The ribosome will move with energy provided by ATP. In reality, the ribosome covers two codons and will move down the length of the mRNA strand as soon as an amino acid is added. This process is known as TRANSLATION.



More Practice

mRNA

A U G G G C U U A A A G C A G U G C U A G

____ ____ ____ ____ ____ ____ ____

Polypeptide Chain

Where do the amino acids come from and how are they brought to the ribososme?

Amino acids are in the cytoplasm and come from the food we eat as well as proteins recycled inside the cells.

tRNA brings the amino acids to the ribosome.

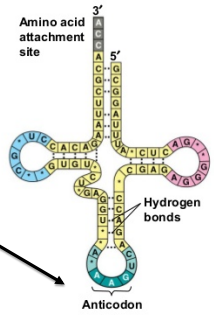
Once the ribosome attaches, tRNA molecules can use the instructions on the mRNA to go and retrieve the proper amino acid. The ribosome will move along until it is instructed to drop off. That will happen at one of three STOP codons. At this point the ribosome will drop off. The resulting amino acid chain will fold and form a functioning protein.

Translation

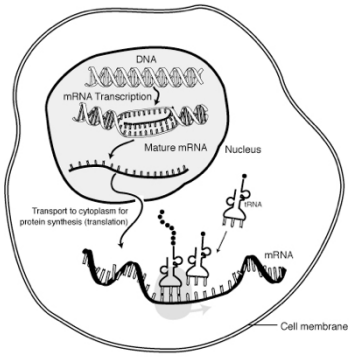
The amino acids in the cytoplasm must be brought to the ribosome. This is done with a molecule of tRNA (transfer RNA). The tRNA has a specific region called the anti-codon that will form a temporary bond with the mRNA. It will then release the amino acid it is carrying and move back to the cytoplasm.

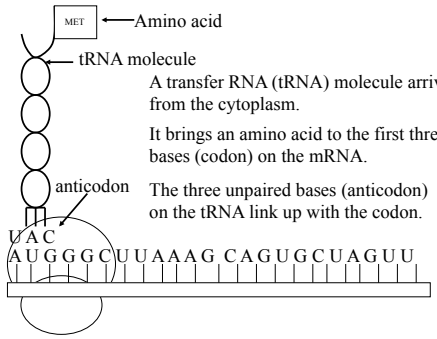
tRNA

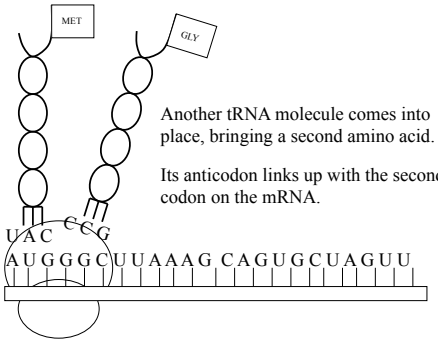
tRNA has an area for the amino acid to bind as well as an area to bond with the mRNA (anticodon)

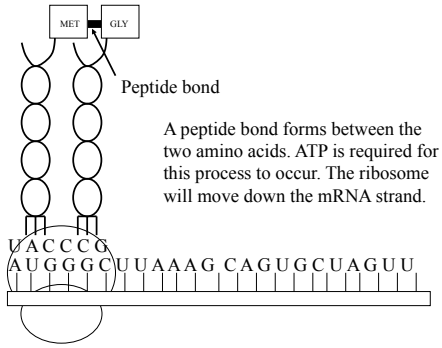


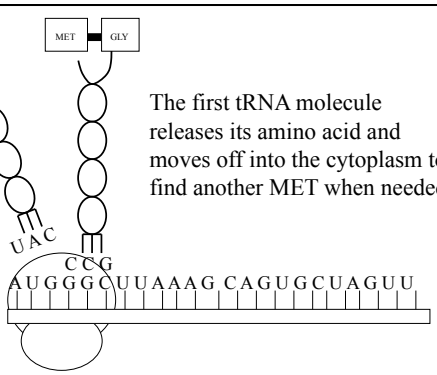
CIRCLE a codon and SQUARE an anticodon.

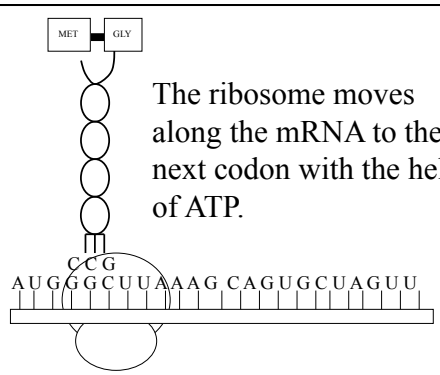


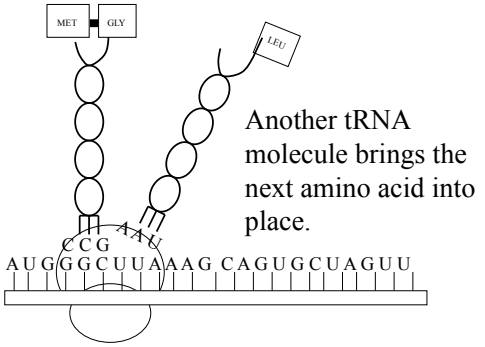


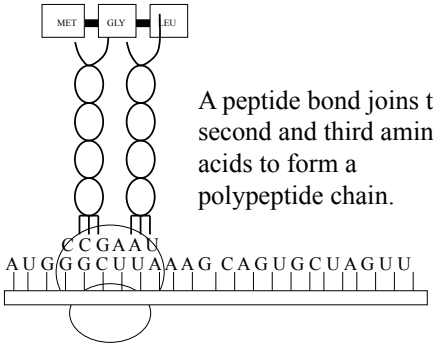


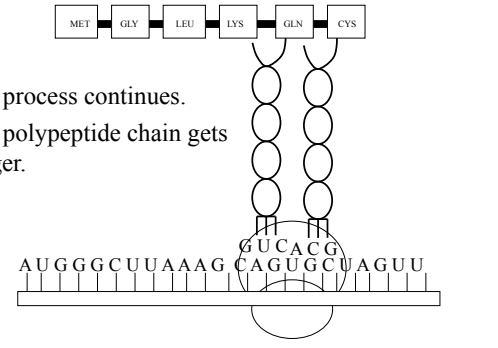


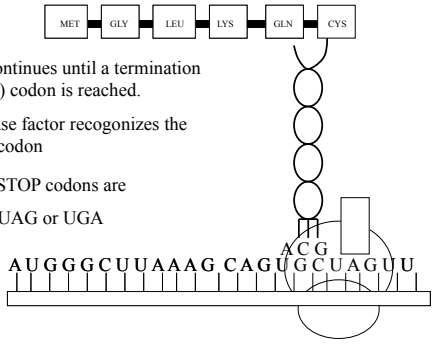


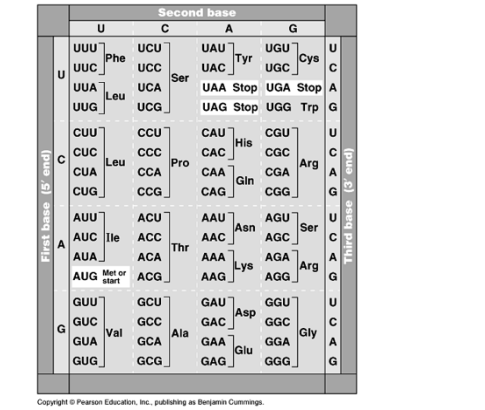



MET
GLY
LEU
Another tRNA molecule brings the next amino acid into place.
C C G
A A U
A U G G G C U U A A A G C A G U G C U A G U U


MET
GLY
LEU
A peptide bond joins the second and third amino acids to form a polypeptide chain.
C C G A A U
A U G G G C U U A A A G C A G U G C U A G U U


MET
GLY
LEU
LYS
GLN
CYS
The process continues.
The polypeptide chain gets longer.
G U C A C G
A U G G G C U U A A A G C A G U G C U A G U U


MET
GLY
LEU
LYS
GLN
CYS
This continues until a termination (STOP) codon is reached.
A release factor recogonizes the STOP codon
Three STOP codons are
UAA, UAG or UGA
A C G
A U G G G C U U A A A G C A G U G C U A G U U


Second base
U
C
A
G
First base (5' end)
Third base (3' end)
UUU Phe
UUC
UUA Leu
UUG
UCU Ser
UCC
UCA
UCG
UAU Tyr
UAC
UAA Stop
UAG Stop
UGU Cys
UGC
UGA Stop
UGG Trp
CUU Leu
CUC
CUA
CUG
CCU Pro
CCC
CCA
CCG
CAU His
CAC
CAA Gln
CAG
CGU Arg
CGC
CGA
CGG
AUU Ile
AUC
AUA
AUG Met or start
ACU Thr
ACC
ACA
ACG
AAU Asn
AAC
AAA Lys
AAG
AGU Ser
AGC
AGA Arg
AGG
GUU Val
GUC
GUA
GUG
GCU Ala
GCC
GCA
GCG
GAU Asp
GAC
GAA Glu
GAG
GGU Gly
GGC
GGA
GGG
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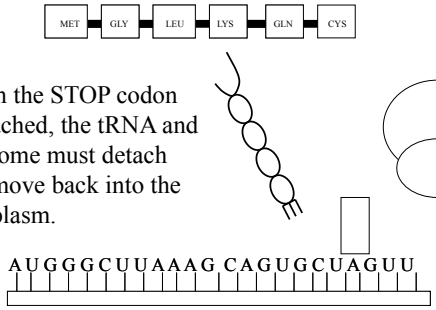
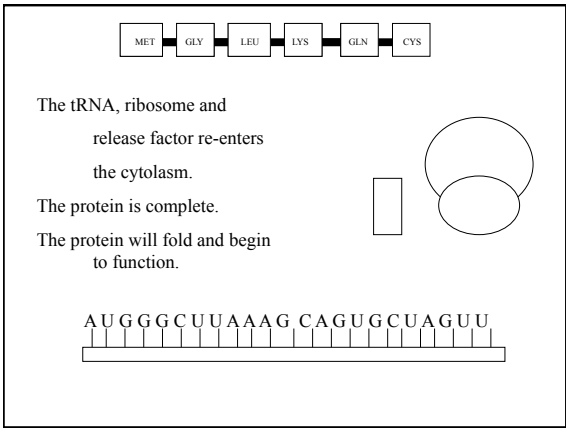
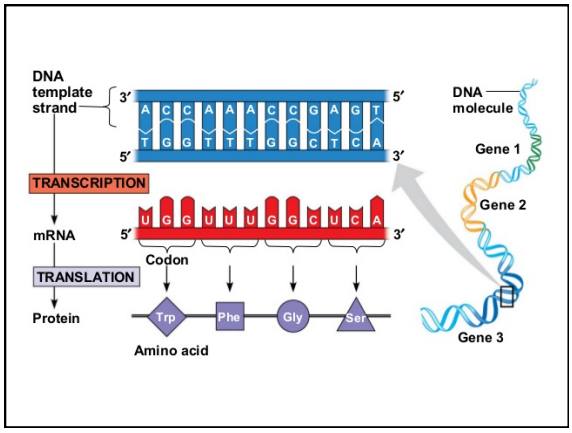

MET
GLY
LEU
LYS
GLN
CYS
When the STOP codon is reached, the tRNA and ribosome must detach and move back into the cytoplasm.
A U G G G C U U A A A G C A G U G C U A G U U

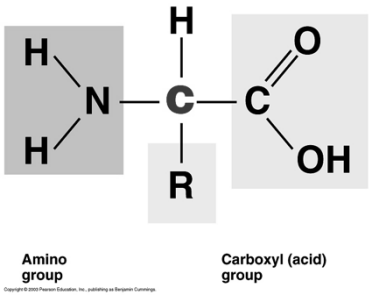


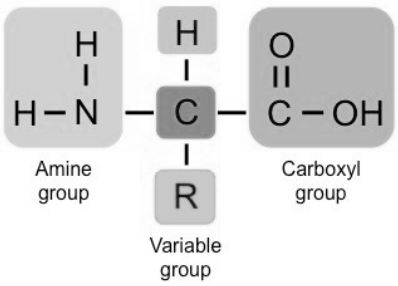


Forming a Peptide Bond

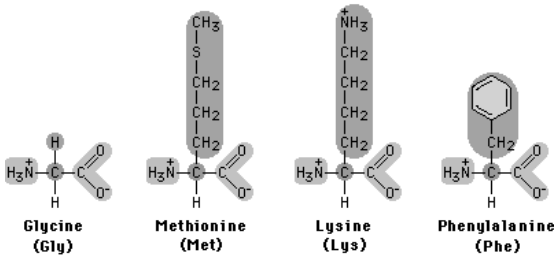
- Amino acids all have the same basic structure. The only difference is the functional R group.
- The amino group of one amino acid will form a bond with the carboxyl group of a different amino acid. This will release a water molecule in a process known as dehydration synthesis.

Basic Amino Acid

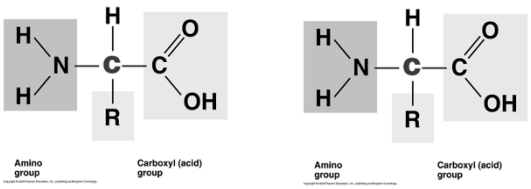




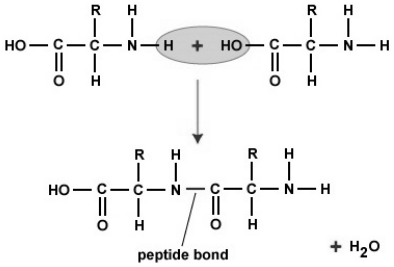
The "R" Group

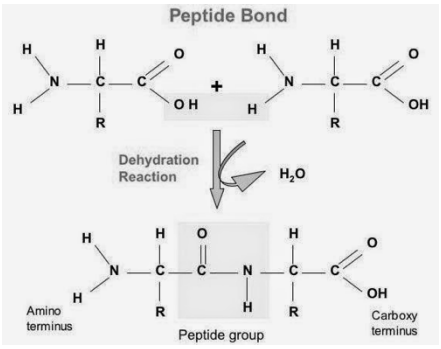


The Peptide Bond



Bye-Bye Water
Dehydration Synthesis





What if there is a problem in the DNA????

Mutations

A mutation is a permanent change in the nuclear DNA sequence of a gene. Mutations in a gene's DNA sequence can alter the amino acid sequence of the protein encoded by the gene.

Causes of Mutations

- Genetic-Inherited the mutation from your parents.
- Caused by radiation such as ultra-violet rays from the sun, X-rays or gamma radiation from nuclear material.
- Random mistake during DNA replication.

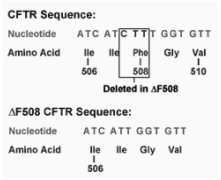
Cystic Fibrosis

Cystic fibrosis is an inherited mutation found on chromosome 7 which affects the lungs and digestive system. It results from mutation in a gene responsible for making a protein which is involved in the transport of ions across cell boundaries.

The effect is to produce a sticky mucus which clogs the lungs and can lead to serious infection. A similar sticky mucus also blocks the pancreas (a part of the digestive system) which provides enzymes for breaking down food. This gets in the way of the processes which convert the food into molecules which can be absorbed by the body.

How it Happens

The phenylalanine (Phe) in red is the amino acid which is missing from the final protein in many sufferers from cystic fibrosis. This occurs at position 508.



Types of Mutations

Mutations can be classified as a deletion, an insertion or a substitution. In each case there can be little to no effect or the effect can be so severe that the protein does not function properly.

Deletion

- Here one base is removed causing all of the remaining bases to shift. This is called a frame shift and the amino acid sequence will be so badly altered that the new protein will not fold correctly and not function.

Insertion

- Here one base is added causing all of the remaining bases to shift. This is called a frame shift and the amino acid sequence will be so badly altered that the new protein will not fold correctly and not function.

Base Substitution-NEUTRAL

- Here, one base is swapped with another base but the order of amino acids does not change. In this case, the protein function will be unaffected.

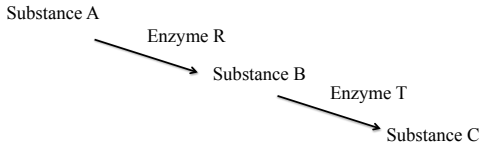
Base Substitution-MISSENSE

- Here, one base is swapped with another base but the number of amino acids does change. In this case, the protein may not function properly or not al all.

Base Substitution-NONSENSE

- Here, one base is swapped with another base and resulting codon is a STOP codon. In this case, the protein will be too short and not function at all.

How Can This Affect The Body's Ability to Produce Certain Substances?



If the DNA is altered/mutated, Enzyme T does not function properly and the cell will be unable to create substance C.

Use the DNA code to make the mRNA strand. With that you can determine the amino acid chain.

DNA code	TAC	GGC	ACC	TTT	GAT	AAA	ATT
mRNA code							
Amino Acid	_____	_____	_____	_____	_____	_____	_____

First Example-Use the original strand below and compare it to the example.

	TAC	GGC	ACC	TTT	GAT	AAA	ATT
DNA code	TAC	GGC	ACC	TTT	GAA	TAA	AAT
mRNA code							
Amino Acid	_____	_____	_____	_____	_____	_____	_____

Insertion Deletion

Substitution NONSENSE MISSENSE NEUTRAL

Affected TOO LONG TOO SHORT

Not Affected

Second Example-Use the original strand below and compare it to the example.

	TAC	GGC	ACC	TTT	GAT	AAA	ATT
DNA code	TAC	GGC	ACC	TTC	GAT	AAA	ATT
mRNA code							
Amino Acid	_____	_____	_____	_____	_____	_____	_____

Insertion Deletion

Substitution NONSENSE MISSENSE NEUTRAL

Affected TOO LONG TOO SHORT

Not Affected

Third Example-Use the original strand below and compare it to the example.

	TAC	GGC	ACC	TTT	GAT	AAA	ATT
DNA code	TAC	GGC	ACT	TTT	GAT	AAA	ATT
mRNA code							
Amino Acid	_____	_____	_____	_____	_____	_____	_____

Insertion Deletion

Substitution NONSENSE MISSENSE NEUTRAL

Affected TOO LONG TOO SHORT

Not Affected

Fourth Example-Use the original strand below and compare it to the example.

	TAC	GGC	ACC	TTT	GAT	AAA	ATT
DNA code	TAC	GGC	ACC	TTA	GAT	AAA	ATT
mRNA code							
Amino Acid	_____	_____	_____	_____	_____	_____	_____

Insertion Deletion

Substitution NONSENSE MISSENSE NEUTRAL

Affected TOO LONG TOO SHORT

Not Affected

Fifth Example-Use the original strand below and compare it to the example.

	TAC	GGC	ACC	TTT	GAT	AAA	ATT
DNA code	TAC	GGA	CC T	TTG	ATA	AAA	TTC
mRNA code							
Amino Acid	_____	_____	_____	_____	_____	_____	_____

Insertion Deletion

Substitution NONSENSE MISSENSE NEUTRAL

Affected TOO LONG TOO SHORT

Not Affected