Unit 3
Genetics

3.3 Protein synthesis

How does a cell 'know' to make a protein?

The code for a protein is specified by DNA and has to be carried to the ribosomes so that they can assemble the amino acids in the correct sequence to form the protein. However, DNA is a huge molecule and remains in the nucleus at all times. The following events occur:

- ✓ The DNA code for the protein is *rewritten* in a molecule of messenger RNA (mRNA); this rewriting of the code is called *transcription*.
- ✓ The mRNA travels from the nucleus through pores in the nuclear envelope to the ribosome.
- ✓ Free amino acids are carried from the cytoplasm to the ribosome by molecules of transfer RNA (tRNA).
- ✓ The ribosome reads the mRNA code and assembles the amino acids carried by tRNA into a protein; this is called *translation*.

Transcription:-is the process that converts genetic information from DNA code into mRNA code.
Translation:-is the process in which the mRNA code is converted into a sequence of amino acids.

What is the genetic code like?

The *genetic code* is held in the DNA molecule. It is the *sequence of bases* in the nucleotides of the DNA that makes up a gene that codes for the protein and that each amino acid in the protein is coded for by a triplet (sequence of three) of bases.

A gene *is a sequence of base triplets in the DNA molecule that carries the code for a protein.*

- ➢ With *four* different bases to work with (*adenine*, *thymine*, *cytosine* and *guanine*), there are 64 possible triplet codes, but only 20 amino acids are used to make all the different proteins. But none of the remaining 44 codes is spare or redundant.

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- ➢ Only one of the strands of the DNA molecule carries the code for proteins. This is called ***the coding strand*** or the ***sense strand.*** The other strand is the *non-coding* or *antisense* strand.

- ➢ ***DNA codes are degenerate*:** Most amino acids have *more than one co*de. Only *methionine* and *tryptophan* have just one triplet that codes for them. *Arginine, serine and leucine* each have six triplets.

- ➢ Three of the triplets **(TAA, TAG and TGA)** do not code for amino acids at all. They are ***'stop' codes*** that signify the end of a coding sequence.

- ***The DNA code is a non-overlapping code:*** This means that each triplet is distinct from all other triplets. The last base in one triplet cannot also be the first base (or second base) in another triplet.
- ***The genetic code is a universal code*:** This means that the triplet TAT is the DNA code for the amino acid *tyrosine* in a human, a giant redwood tree, a bacterium or in any other living organism.

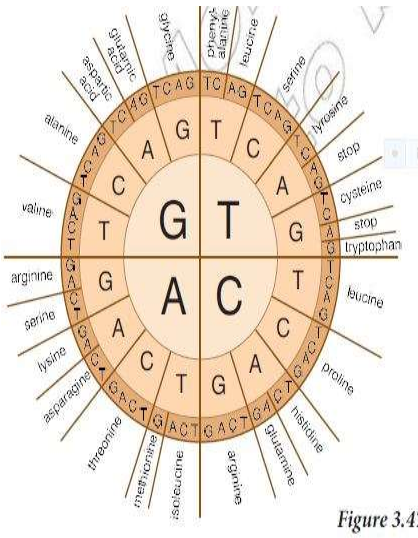


Figure 3.47A The genetic code

second position

first position	T	C	A	G	third position
T	phenylalanine	serine	tyrosine	cysteine	T
			stop	stop	A
	leucine		stop	tryptophan	G
C	leucine	proline	histidine	arginine	T
			glutamine		C
					A
					G
A	isoleucine	threonine	asparagine	serine	T
					C
			lysine	arginine	A
	methionine				G
G	valine	alanine	aspartic acid	glycine	T
			glutamic acid		C
					A
					G

***Figure 3.47B** Another way of representing the genetic code*

In the first method of representing the genetic code (Fig.3. 47A), start with one of the ***'biggest'*** letters in the centre. This represents the *first* base in the triplet. The letters in the next middle layer, ***medium-sized,*** represents the *second* base and the ***smallest*** letters on outer third layer represent the *third* base in the triplet. Outside that is the name of the amino acid for which the triplet codes. For example: ACC codes for *threonine*, GGG codes for *glycine*, etc.

To use the second method (Fig.3.47B), first start with the letters at the left hand side of the table this represents the first base of the triplet. Then read the letters across the top; this represents the second base in the triplet. Finally, read the letter at the right hand side of the table and this represents the third base in the triplet.

How does transcription take place in eukaryotic cells?

- During this process, the coded information in the DNA of one gene is used to synthesize a molecule of *mRNA* that will carry the code to the ribosomes.
- *mRNA* is similar to DNA in that it is built from nucleotides; however, it is different from DNA in a number of ways:
  - ✓ it is a much smaller molecule
  - ✓ it is single stranded
  - ✓ the base thymine is replaced by uracil
  - ✓ the sugar in the nucleotides is ribose, not deoxyribose

- The triplets of bases in mRNA that code for amino acids are called *codons*. The mRNA codons are identical to the DNA triplets that code for specific amino acids, except that U (uracil) is substituted for T (thymine).
- To form the single-stranded *mRNA* when transcription takes place, only the *antisense* strand of DNA is transcribed. This is because the sense strand of this section contains the gene that codes for a protein. However, transcribing this would produce a complementary sequence of bases, similar to those in the antisense strand, which would not code for anything.

 In eukaryotic cells, transcription takes place in the following way:

- ✓ The enzyme *DNA-dependent RNA polymerase (RNA polymerase)* binds with a section of DNA next to the gene to be transcribed.
- ✓ Transcription factors activate the enzyme.
- ✓ The enzyme begins to 'unwind' a section of DNA. *RNA polymerase* moves along the antisense strand, using it as a template for synthesizing the mRNA.
- ✓ The polymerase assembles free RNA nucleotides into a chain in which the base sequence is complementary to the base sequence on the antisense strand of the DNA. This, therefore, carries the same triplet code as the sense strand (except that *uracil* replaces *thymine*).
- ✓ The completed molecule leaves the DNA; the strands of DNA re-join and re-coil.
- ✓ The mRNA molecule now contains the code for the protein that was held in the DNA of the gene.

How does translation take place?

 Translation of the mRNA code into a protein depends on the interaction between *mRNA* and *tRNA* within a ribosome.

 All *tRNA* molecules have the same basic structure. The *'cloverleaf'* configuration of the molecule has, at one end, a triplet of bases called *an anticodon*. This *anticodon* will be complementary to one of the *mRNA codons*.

 The other end of the *tRNA* molecule has an *attachment site* for the amino acid that is specified by the *mRNA codon*.

 Ribosomes are made from *ribosomal RNA (rRNA) and proteins* organized into a large and a small subunit. Within the ribosome, there are *three* sites that can be occupied by a tRNA molecule, called the A, P and E sites. The following events take place:

- ✓ The first two codons of the mRNA enter the ribosome. Transfer RNA molecules (with amino acids attached) that have complementary anticodon to the first two codons of the mRNA bind to those codons.

- ✓ A peptide bond forms between the amino acids carried by these two tRNA molecules and the dipeptide is transferred to the tRNA in the A site.

- ✓ The ribosome moves along the mRNA by one codon, bringing the third codon into the ribosome; at the same time the 'free' tRNA exits the ribosome and the tRNA with the dipeptide moves into the P site.

- ✓ A tRNA with a complementary anticodon binds with the third codon, bringing its amino acid into position next to the second amino acid.

- ✓ A peptide bond forms between the second and third amino acids.

- ✓ The ribosome moves along the mRNA by one codon, bringing the fourth mRNA codon into the ribosome, and the whole process is repeated until a 'stop' codon is in position and translation ceases.

 The translation of the mRNA code into a protein molecule requires energy. However, this does not come from the hydrolysis of ATP as is usual in a cell, but from the hydrolysis of a similar molecule, *GTP– Guanosine Triphosphate*. It is hydrolyzed to GDP and Pi in the same way as ATP, with the release of a small amount of energy.

How is protein synthesis different in prokaryotic cells?

Prokaryotic cells

- ➢ prokaryotic cells *do not have a nucleus*
- ➢ prokaryotic mRNA *does not need post-transcriptional processing*
- ➢ In Prokaryotes transcription and translation are *coupled*; mRNA can be translated by ribosome at one end of its molecule while it is still being transcribed from DNA at the other end.

Eukaryotic cells

- ✓ eukaryotes: transcription and translation are separated
- ✓ transcription occurs in the nucleus
- ✓ translation occurs in the cytoplasm
- ✓ eukaryotic mRNAs are modified before leaving the nucleus

What becomes of the proteins that are synthesized?

 All our proteins are synthesized in the way just described, but all our cells do not synthesize all our proteins. However, we synthesize a vast array of different proteins that we can categories, broadly, into the types shown in table 3.2 below.

Table 3.2 Some of the proteins our body synthesises

Type of protein	Example	Function of example
Structural	Collagen	Building fibres of cartilage
	Keratin	Building nails and feathers
Enzyme	ATP synthase	Producing ATP from ADP and P_i
	DNA helicase	Unwinding the double helix of DNA
Peptide hormone	Insulin	Control of plasma glucose concentration
	Adrenaline (epinephrine)	Fight or flight response
Antigen	A antigen on red cells	Determine blood group
	CD4	Allows binding of HIV to T-lymphocytes
Antibody	Anti-a antibodies	Causes clotting of red cells with A antigen
	HIV antibodies	Destroys some HIV antigens

- To synthesize these proteins continually, our bodies require a constant supply of amino acids. These are obtained from the protein in the foods we eat. The average adult protein requirement per day is about 50 grams.
- The proteins are hydrolyzed to amino acids in our gut and absorbed into the blood plasma by active transport. They are then transported to the cells where they are used to synthesize our proteins.

 20 amino acids are used to make all the different proteins. Some of these can be made in our bodies by a process called *transamination*.

- ***In transamination, the amino group of an amino acid is removed and transferred to a keto acid. The keto acid then becomes a different amino acid.***
- Not all amino acids can be produced by transamination. There are some that we just have to obtain from our food. These amino acids are called ***essential amino acids***.

Meat, fish, poultry, eggs and milk are animal sources of protein that provide a good balance of all eight essential amino acids. The best non animal sources are *quinoa, buckwheat, hempseed and amaranth*, although these contain lower overall amounts of protein than some cereals (wheat, rice, maize) and nuts and pulses.

What controls gene expression?

 The fact that some genes are *sex-limited* tells us that all genes aren't active all the time. There are more examples of this – the genes that control the colour of your iris are present in all your cells, but all your other cells aren't this colour – just the iris.

How are genes switched on?

 Very often, genes are switched on by ***'transcription factors'*** that are present in the cell. These transcription factors are usually proteins that bind to a *regulatory* sequence of DNA near to the gene they influence. They operate in the following way:

- ✓ The *transcription factors* bind to a promoter sequence of DNA near to the gene to be activated.
- ✓ *RNA polymerase* binds to the DNA/ transcription factor complex.
- ✓ The RNA polymerase is 'activated' and moves away from the DNA/transcription factor complex along the gene.
- ✓ The RNA polymerase transcribes the antisense strand of the DNA as it moves along; the gene is now being expressed.

Some cancers are caused by hormones acting as transcription factors.

Oestrogen is steroid hormones that can diffuse through the plasma membrane of a cell.

- It binds with a receptor in the cytoplasm.
- The o*estrogen-receptor complex* moves into the nucleus and binds with and activates specific genes.
- In the breasts, and lining of the uterus, the activated genes *cause cell division*.

 Many breast cancers are said to be *oestrogen-receptor* positive. This means that the cancer cells have oestrogen receptors to which the hormone can bind, causing the same increase in cell division as it does in normal breast tissue.

 The anti-cancer drug *Tamoxifen* can bind with the *oestrogen receptors* and the tamoxifen/receptor complex binds with the DNA. However, Tamoxifen does not allow transcription factors to bind and so expression of the genes is prevented, and cell division in the cancer is slowed.

How are genes switched off?

 Besides transcription factors that promote the expression of genes, other factors can act to *repress gene action*. One group of substances that does this is known as *short interfering RNA* (*siRNA*).

 Short interfering RNA (siRNA) molecules are unusual because:

-they are very short – only about 21 to 23 nucleotides long and
-they are *double stranded*.

 Short interfering RNA (*siRNA*) doesn't act on the gene itself, but they '*interfere with'* or '*silence'* the *mRNA* once it has been transcribed from the DNA. This is called *post-transcriptional interference*.

 If the *mRNA* is prevented from translating its codons into amino acids, then the protein for which the gene codes cannot be built. *The gene has effectively been silenced.*

 Biologists think that the action of siRNA is as follows:

- ✓ Double-stranded RNA (*dsRNA*) is produced in the nucleus from a range of genes.
- ✓ It is then split into the very short lengths that characterize *siRNA* by an enzyme called '*Dicer'*.
- ✓ The *antisense strand* of the *siRNA* then binds with a complex of molecules called *RISC*.
- ✓ The *siRNA* binds with *mRNA* and allows *RISC* to degrade/cleave the *mRNA* into small fragments.

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