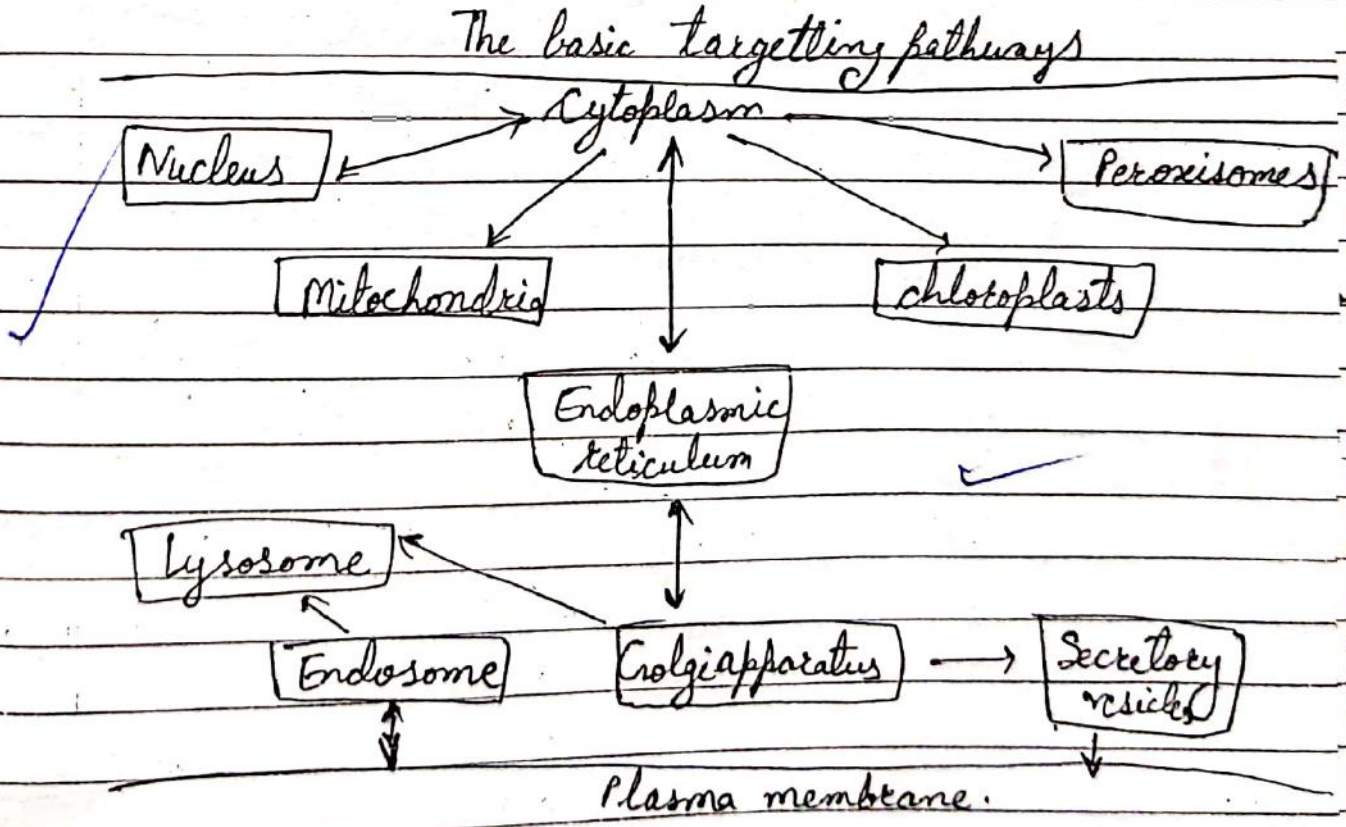
3) Q. Protein trafficking.

→ Proteins are an essential part of life. They are found throughout the body in many different forms, for example as receptors, signalling molecules and enzymes. Proteins are synthesized in the cytoplasm of cells, but this is not always necessarily where they are functionally needed. Mechanisms of protein transport are essential to deliever them to where they are needed. We will discuss the different places where proteins are used, and how they get there.



Protein synthesis :→

Proteins are synthesized using amino acids, from information found encoded in the genome. DNA is copied to mRNA, which then travels out of the nucleus into the cytoplasm

the site of Protein synthesis.

A protein is not coded for directly from mRNA. Another type of RNA, transfer RNAs act as adaptor proteins, to bring the amino acids together. tRNAs recognise the codon on one surface, and attach an amino acid on the other. A tRNA molecule will bind to the appropriate place on the mRNA with an amino acid attached. This amino acid will form a peptide bond with the next amino acid, also brought by a tRNA. This continues and a polypeptide chain forms.

Protein trafficking :→

Protein trafficking, or protein targetting, is the moving of proteins from their site of synthesis to the place where needed. This could be mitochondrial proteins encoded by nuclear DNA, receptor proteins being inserted into plasma membrane, or signalling molecules being secreted from the cell, as well as many other examples.

Most proteins are synthesised in the cytoplasm of cells, where the ribosomes are located, but this is not always their place of function. There are two basic targetting pathways for proteins in eukaryotic cells: Post translational and co-translational. The signals involved are called sorting signals. These are usually short sequences of amino acids, found either at the N-

17

terminus of the protein, or integrated into its structure. They bind to specific receptors either on the target organelle surface or on intermediate carrier proteins.

Post-translational targetting :→ e.g. proteins targeted for nucleus, mitochondria, chloroplasts. The signal is recognised after transcription is complete.

Co-translational targetting :→ e.g. ER, Golgi, lysosomes, plasma membrane and secreted proteins. When the signal sequence is transcribed, the signal recognition particle pauses transcription and redirects the mRNA, ribosome, and partially translated peptide to a membrane.

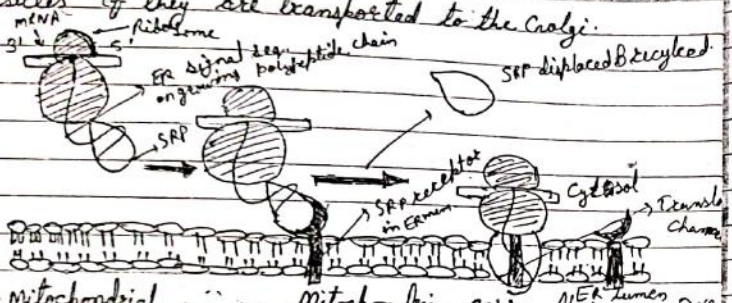
Sorting signals :→ Each sorting signals represents a destination in the cell. For example, those proteins which are destined for the endoplasmic reticulum have a KDEL sequence. These amino acid sequences direct proteins synthesised in the cytoplasm to organelles including the plasma membrane, nucleus, mitochondria and chloroplasts.

Protein trafficking via the secretory pathway :→

The endoplasmic reticulum can bind ribosomes. A protein can be inserted into or through the ER membrane as it is being translated. The ribosomic complex then binds to the ER via a receptor and the signal sequence crosses the ER membrane. Translation then continues, with the peptide chain being pulled into the ER lumen. Whilst in the ER many proteins start to undergo glycosylation.

From the ER, Proteins are dispatched to the

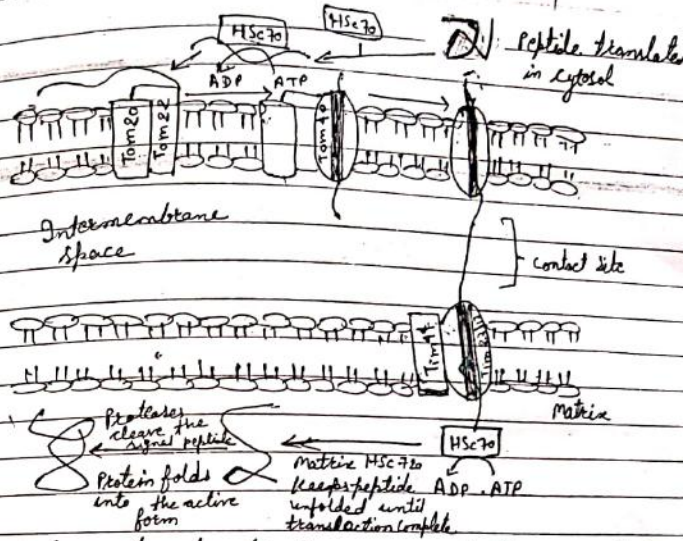
Golgi and on to a range of locations. They may be packaged into vesicles for secretion or fused into the membranes of vesicles which then merge with the plasma membrane. Resident ER proteins contain a KDEL sequence which direct them back to the ER in COPI vesicles if they are transported to the Golgi.



Mitochondrial :- Mitochondria carry their own DNA & some mitochondrial proteins are produced on-site without needing trafficking. Most, however, are encoded by genomic DNA and need to be imported.

As the precursor mitochondrial protein is produced from cytosolic ribosomes : the localization signal is then transported through a transport channel complex including Tom 40 across the outer membrane.

The protein is then transported across the inner mitochondrial membrane by a channel made of Tim proteins (Tim 44, 23, & 17). This process also requires energy in the form of the proton gradient between the intermembrane space & the matrix which is created during respiration.



Nuclear localization :- Some proteins needed need to be transported into the nucleus, as this is their site of action. A nuclear localisation sequence (NLS) is a sequence of amino acids which 'tags' the protein for import into the nucleus, by nuclear transport. The sequence is usually made up of positively charged lysines or arginines which are exposed on the cell surface. Different proteins may have the same NLS.

Trafficked protein degradation :-

In order to remain working efficiently a cell must have mechanisms in place to remove proteins that are no longer needed. This may include : damaged proteins, incorrectly synthesised proteins - for example

during the cell cycle. The degraded proteins amino acids are then recycled by the cell, to make new proteins. Two different mechanisms for protein degradation :- Via lysosome & via ubiquitin labelling.

• Lysosomes :→ Lysosomes are vesicles that contain enzymes needed for the breakdown & digestion of proteins. These enzymes need to be confined to vesicle, as they could cause damage to the insides of the cell.

Ubiquitin labelling :→ Ubiquitin is a small protein, which can be attached to other proteins using an activating enzyme. These ubiquitin tagged proteins are now recognised by proteases which can be found in the cytosol, and degrade the tagged protein.