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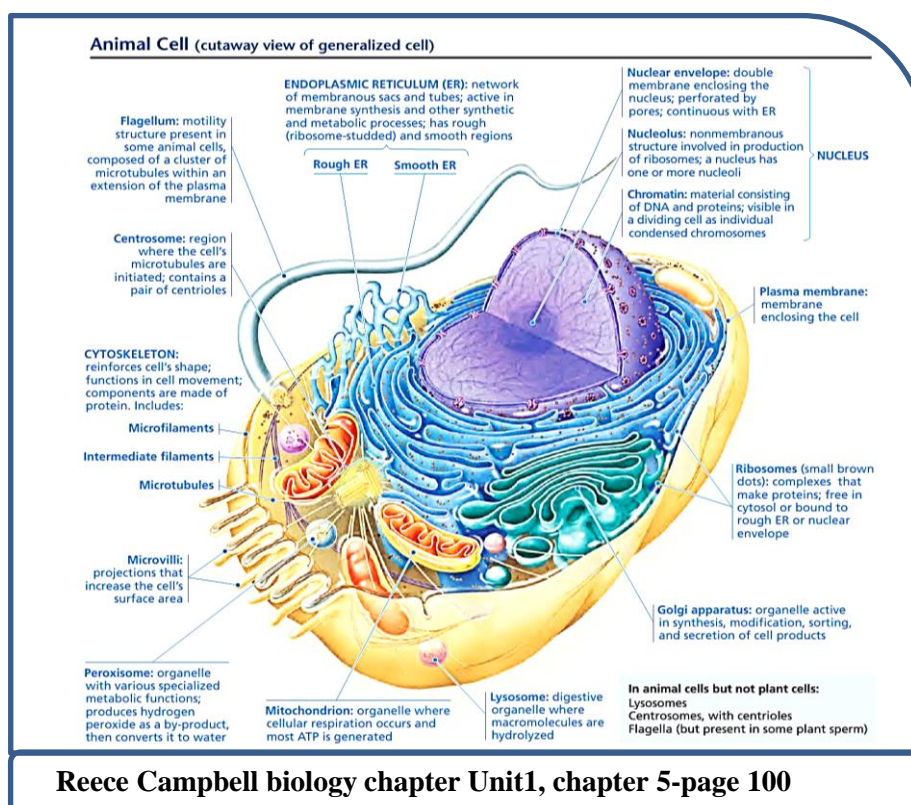
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# Intracellular Compartments and Protein Sorting

Cell is the basic unit of life. Cell exists in either prokaryotic or eukaryotic forms. Both the cells are different from each other in structure and function. A bacterium that generally consists of only intracellular compartment covered by a plasma membrane, is an example of prokaryotic cell whereas on the other side eucaryotic cell have membraned compartments that are functionally distinct and have enzymes of its own. It is necessary to study the structure and dynamics of these compartments of cell and role of protein trafficking in order to understand the cytology. These specific proteins confer upon each compartments their defined structural and functional properties. These protein beside acting as organelle specific surface markers, also catalyses the various reactions inside the cell and transports biomolecule selectively into and out of the cell.



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**Components of Prokaryotic and Eukaryotic Cells and Their Functions**

| <b>Cell Component</b> | <b>Function</b>  | <b>Present in Prokaryotes?</b>                           | <b>Present in Animal Cells?</b> | <b>Present in Plant Cells?</b>   |
|-----------------------|--|--|---------------------------------|----------------------------------|
| Plasma membrane       | Separates cell from external environment; controls passage of organic molecules, ions, water, oxygen, and wastes into and out of the cell  | Yes  | Yes                             | Yes                              |
| Cytoplasm             | Provides structure to cell; site of many metabolic reactions; medium in which organelles are found   | Yes  | Yes                             | Yes                              |
| Nucleoid              | Location of DNA  | Yes  | No                              | No                               |
| Nucleus               | Cell organelle that houses DNA and directs synthesis of ribosomes and proteins   | No   | Yes                             | Yes                              |
| Ribosomes             | Protein synthesis  | Yes  | Yes                             | Yes                              |
| Mitochondria          | ATP production/cellular respiration  | No   | Yes                             | Yes                              |
| Peroxisomes           | Oxidizes and breaks down fatty acids and amino acids, and detoxifies poisons   | No   | Yes                             | Yes                              |
| Vesicles and vacuoles | Storage and transport; digestive function in plant cells   | No   | Yes                             | Yes                              |
| Centrosome            | Unspecified role in cell division in animal cells; source of microtubules in animal cells  | No   | Yes                             | No                               |
| Lysosomes             | Digestion of macromolecules; recycling of worn-out organelles  | No   | Yes                             | No                               |
| Cell wall             | Protection, structural support and maintenance of cell shape   | Yes, primarily peptidoglycan in bacteria but not Archaea | No                              | Yes, primarily cellulose         |
| Chloroplasts          | Photosynthesis   | No   | No                              | Yes                              |
| Endoplasmic reticulum | Modifies proteins and synthesizes lipids   | No   | Yes                             | Yes                              |
| Golgi apparatus       | Modifies, sorts, tags, packages, and distributes lipids and proteins   | No   | Yes                             | Yes                              |
| Cytoskeleton          | Maintains cell's shape, secures organelles in specific positions, allows cytoplasm and vesicles to move within the cell, and enables unicellular organisms to move independently | Yes  | Yes                             | Yes                              |
| Flagella              | Cellular locomotion  | Some   | Some                            | No, except for some plant sperm. |
| Cilia                 | Cellular locomotion, movement of particles along extracellular surface of plasma membrane, and filtration  | No   | Some                            | No                               |

| INTRACELLULAR COMPARTMENT                | PERCENTAGE OF TOTAL CELL VOLUME |
|--|---------------------------------|
| Cytosol                                  | 54                              |
| Mitochondria                             | 22                              |
| Rough ER cisternae                       | 9                               |
| Smooth ER cisternae plus Golgi cisternae | 6                               |
| Nucleus                                  | 6                               |
| Peroxisomes                              | 1                               |
| Lysosomes                                | 1                               |
| Endosomes                                | 1                               |

Table 2. Relative Volumes Occupied by the Major Intracellular Compartments

### Protein Sorting

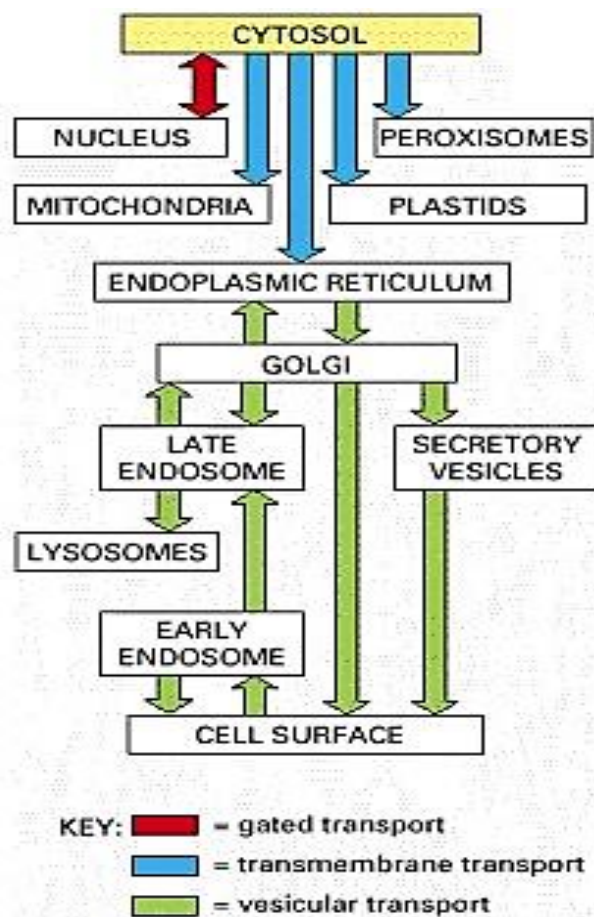
Most of the protein are synthesized in the cytosol by ribosomes except those that are synthesized by ribosome of mitochondria and in case of plant cell, those that are synthesized by ribosome of plastids. The fate of most of the protein are found in the form of sorting signal that guide them to the comparment or location outside the cytosol to nucleus, ER, or any other destination. Those protein that lacks such sorting signals stays behind in the cytosol as permanent residents.

The principle of protein sorting relies on the understanding of the fundamentals of movement of proteins from one portion/ compartment to another. These pathways include gated transport presented by red arrows, transmembrane transport and vesicular transport shown in blue and green color respectively. A signal is always required for either retention or for exit from a compartment.

The various mechanism can be divided into three as describe below:

1. Gated transport
2. Transmembrane transport
3. Vesicular transport

**Gated transport:** It is most notable at the junction between the nucleus and the cytoplasm, where selected macromolecules are actively



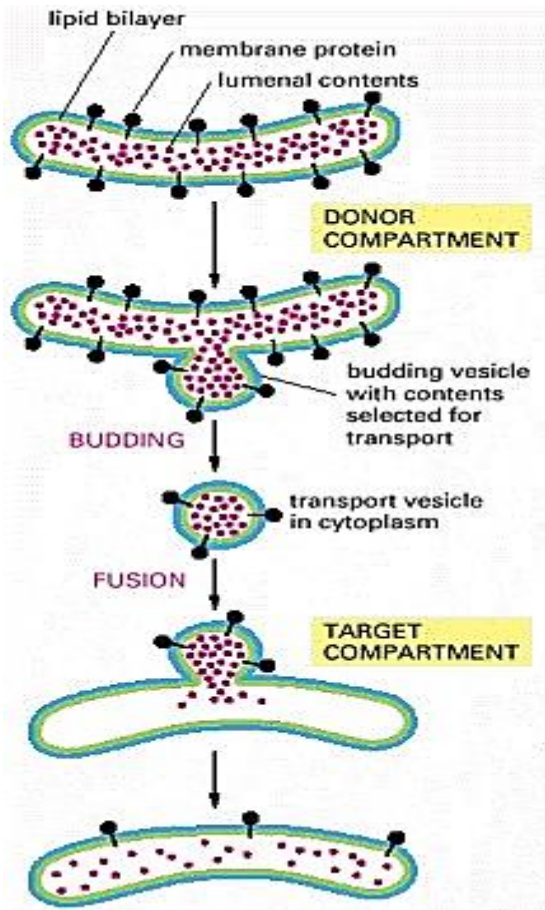
transported while smaller molecules are allowed free passage.

**Transmembrane transport** involves the participation of membrane-bound protein translocators which actively allow migration of proteins from the cytoplasm to other cellular cavities. It is believed that in many cases some degree of protein unfolding is required.

**Vesicular transport** does not require the protein molecules to pass through membranes. Instead, it is the membrane that migrates and fuses with other compartments taking the protein along with it, via a process known as pinocytosis. A transport intermediate enclosed with membrane of variable size and shape loads the cargo of molecule from lumen of a compartment by pinching off from its membrane, unloads their cargo into some other compartment by simply fusing with membrane. Movement between the endoplasmic reticulum and the Golgi apparatus occurs in this manner.

As visible from the diagram, from the donor compartment a transport vesicle buds off and fuses with recipient compartment or target compartment discharging the soluble protein. It can be observed that membrane also gets





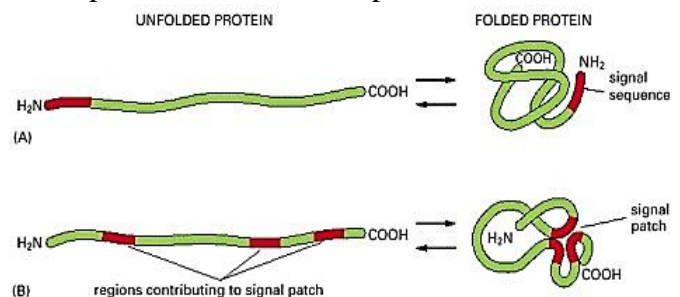
transferred and the original orientation of both proteins and lipids in the donor-compartment membrane is preserved in the target-compartment membrane. Thus, membrane proteins retain their asymmetric orientation, with the same domains always facing the cytosol.

In all three cases of protein transport, the sorting signals in the transported protein guide the protein transfer. This signal sequence is recognised by protein receptors that are complementary with the signal sequence. Thus, every protein's fate is dependent on the sequence they carry. Eg. A protein to be transported to nucleus must be carrying sorting signal that is recognised by receptor proteins that will allow it to pass through the nuclear core complex and if a protein is to be transported directly through the membrane, must be carrying a signal that will allow it to be allowed by translocators present in the membrane to be crossed. Likewise, there are sorting signals also for those proteins that will be loaded in a vesicle or will be retained in the compartment.

## Signal Sequences and Signal Patches Direct Proteins to the Correct Cellular Address

As discussed in above, protein fate relies on the sorting signal. There are at least two sorting signals observable in proteins.

1. First is a continuous amino acid stretch of 15-60 residues, some of which are eliminated at the final stage of sorting process by signal peptidase.
2. The second signal patch consists of 3D arranged atoms on the surface of protein during the folding. The amino acid residues that comprise this signal patch can be distant from one another in the linear amino acid sequence, and they generally persist in the finished protein.



- A) The signal resides in a single discrete stretch of amino acid sequence, called a signal sequence, that is exposed in the folded protein. Signal sequences often occur at the end of the polypeptide chain (as shown), but they can also be located internally. (B) A signal patch can be formed by the juxtaposition of amino acids from regions that are physically separated before the protein folds (as shown). Alternatively, separate patches on the surface of the folded protein that are spaced a fixed distance apart can form the signal.

Each sequence acting as a sorting signal leads to different destination eg. Protein to be sent to ER will have a N- Terminus sequence composed of 5-10 hydrophobic Amino Acids(AA). Out of the proteins that have specific sequence of 4 AA at C terminus will be recognised as ER resident and returned

| FUNCTION OF SIGNAL SEQUENCE   | EXAMPLE OF SIGNAL SEQUENCE   |
|---|--|
| Import into nucleus   | -Pro-Pro-Lys-Lys-Lys-Arg-Lys-Val-  |
| Export from nucleus   | -Leu-Ala-Leu-Lys-Leu-Ala-Gly-Leu-Asp-Ile-  |
| Import into mitochondria  | *H <sub>3</sub> N-Met-Leu-Ser-Leu-Arg-Gln-Ser-Ile-Arg-Phe-Phe-Lys-Pro-Ala-Thr-Arg-Thr-Leu-Cys-Ser-Ser-Arg-Tyr-Leu-Leu-   |
| Import into plastid   | *H <sub>3</sub> N-Met-Val-Ala-Met-Ala-Met-Ala-Ser-Leu-Gln-Ser-Ser-Met-Ser-Ser-Leu-Ser-Leu-Ser-Ser-Asn-Ser-Phe-Leu-Gly-Gln-Pro-Leu-Ser-Pro-Ile-Thr-Leu-Ser-Pro-Phe-Leu-Gln-Gly- |
| Import into peroxisomes   | -Ser-Lys-Leu-COO <sup>-</sup>  |
| Import into ER  | *H <sub>3</sub> N-Met-Met-Ser-Phe-Val-Ser-Leu-Leu-Leu-Val-Gly-Ile-Leu-Phe-Trp-Ala-Thr-Glu-Ala-Glu-Gln-Leu-Thr-Lys-Cys-Glu-Val-Phe-Gln-   |
| Return to ER  | -Lys-Asp-Glu-Leu-COO <sup>-</sup>  |
| Some characteristic features of the different classes of signal sequences are highlighted in color. Where they are known to be important for the function of the signal sequence, positively charged amino acids are shown in <i>red</i> and negatively charged amino acids are shown in <i>green</i> . Similarly, important hydrophobic amino acids are shown in <i>yellow</i> and hydroxylated amino acids are shown in <i>blue</i> . *H <sub>3</sub> N indicates the N-terminus of a protein; COO <sup>-</sup> indicates the C-terminus. |  |

to ER. Similarly, protein that will have +vely charged AA alternating with hydrophobic ones, All sorting signals are recognized by sorting receptors that are complementary to the sorting signals then guide proteins to their appropriate destination, where they unload their cargo. The receptors function catalytically: after completing one round of targeting, they return

to their point of origin to be reused. Most sorting receptors recognize classes of proteins rather than just an individual protein species. They therefore can be viewed as public transportation systems dedicated to delivering groups of components to their correct location in the cell. will be sent to mitochondria. Some of the specific signals are given in the below.