

Protein Sorting

1. Introduction

Protein sorting is the cellular mechanism by which newly synthesized proteins are transported to their correct intracellular or extracellular destinations. Proper sorting is essential for maintaining cell structure and function.

Proteins may be targeted to:

- Nucleus
- Mitochondria
- Chloroplast (in plants)
- Endoplasmic reticulum (ER)
- Golgi apparatus
- Lysosomes
- Plasma membrane
- Secreted outside the cell

3. Types of Protein Sorting

A. Sorting Based on Site of Synthesis

(1) Free Ribosomes

- Synthesize proteins for:
 - Cytosol
 - Nucleus
 - Mitochondria
 - Peroxisomes

(2) Bound Ribosomes (Rough ER)

- Synthesize proteins for:
 - Secretion
 - Lysosomes
 - Plasma membrane
 - Endomembrane system

4. Signal Sequences and Targeting

Protein sorting depends on **signal sequences** (short amino acid sequences).

(A) Signal Peptide (ER Targeting)

- Present at **N-terminal**
- Hydrophobic amino acids
- Recognized by **Signal Recognition Particle (SRP)**
- Directs ribosome to ER membrane
- Protein enters ER lumen through **translocon channel**

This process is called **co-translational translocation**.

(B) Nuclear Localization Signal (NLS)

- Directs proteins to nucleus
- Rich in lysine and arginine
- Transported through nuclear pore complexes
- Import mediated by importin proteins

(C) Mitochondrial Targeting Signal

- Located at N-terminal
- Forms amphipathic helix
- Recognized by mitochondrial receptors
- Transported via TOM and TIM complexes

(D) Lysosomal Targeting Signal

- Mannose-6-phosphate (M6P) tag
- Added in Golgi apparatus
- Directs proteins to lysosome

5. Role of Endoplasmic Reticulum in Protein Sorting

In the **Endoplasmic reticulum**:

- Protein folding occurs
- Chaperone proteins assist folding
- Disulfide bond formation
- Glycosylation begins
- Misfolded proteins are degraded (ERAD pathway)

6. Role of Golgi Apparatus

In the **Golgi apparatus**:

- Proteins are modified (glycosylation, sulfation, phosphorylation)
 - Sorted at Trans-Golgi Network (TGN)
 - Packed into vesicles
 - Directed to final destination
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7. Vesicular Transport

Vesicle transport involves:

1. **Budding** – Coat proteins (COPI, COPII, Clathrin)
2. **Transport** – Movement along cytoskeleton
3. **Docking** – Rab proteins
4. **Fusion** – SNARE proteins

Types:

- ER → Golgi (COPII)
 - Golgi → ER (COPI)
 - Golgi → Lysosome (Clathrin-coated vesicles)
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8. Post-Translational Sorting

Some proteins are fully synthesized in cytosol and later transported:

- Mitochondrial proteins
- Nuclear proteins
- Peroxisomal proteins

Transport occurs through membrane channels using energy (ATP).

9. Quality Control in Protein Sorting

Cells ensure only correctly folded proteins proceed:

- Molecular chaperones
- Unfolded Protein Response (UPR)
- ER-associated degradation (ERAD)

Defects in sorting may lead to diseases such as:

- Cystic fibrosis
- Lysosomal storage disorders