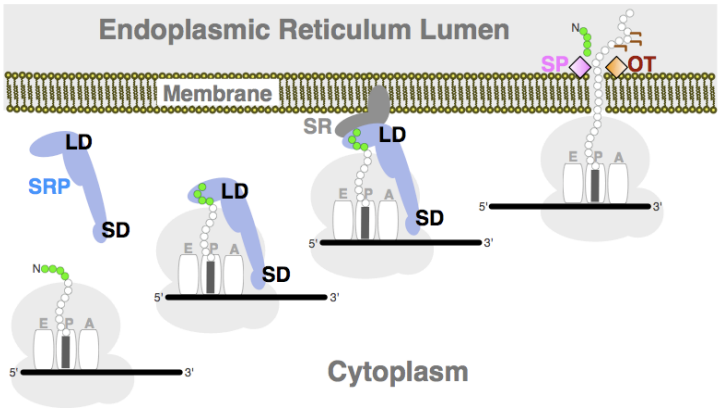
CONCEPT: ER PROCESSING AND TRANSPORT

Two types of ER import

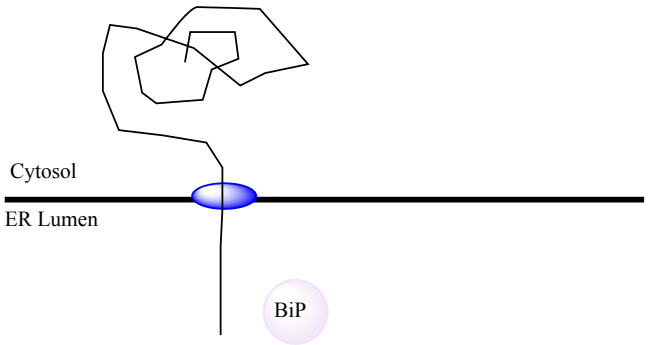
- **Co-translational import** is the process of _____ proteins into the ER as they're being translated
  - □ **ER signal sequence** directs the mRNA and ribosome to the ER during translation (located on N-terminus)
    - **Signal recognition particle (SRP)** recognizes the ER signal sequence
    - **Signal recognition particle receptor (SRPR)** is located on the ER and binds to the SRP
  - □ **Translocon** is a pore in the ER membrane that binds SRP and SRPR to translocate the protein into ER
    - Uses GTP hydrolysis for energy
    - **Signal peptidase** cleaves the ER signal sequence off once it is inside the ER

EXAMPLE: Co-translational import of a protein



- **Post-translational import** is the process of importing proteins into the ER _____ they've been translated
  - □ The chaperone protein **BiP** helps pull the protein across the membrane and fold it once its inside
- **ER-retention signals** are located on the C-terminus and keeps proteins within the ER

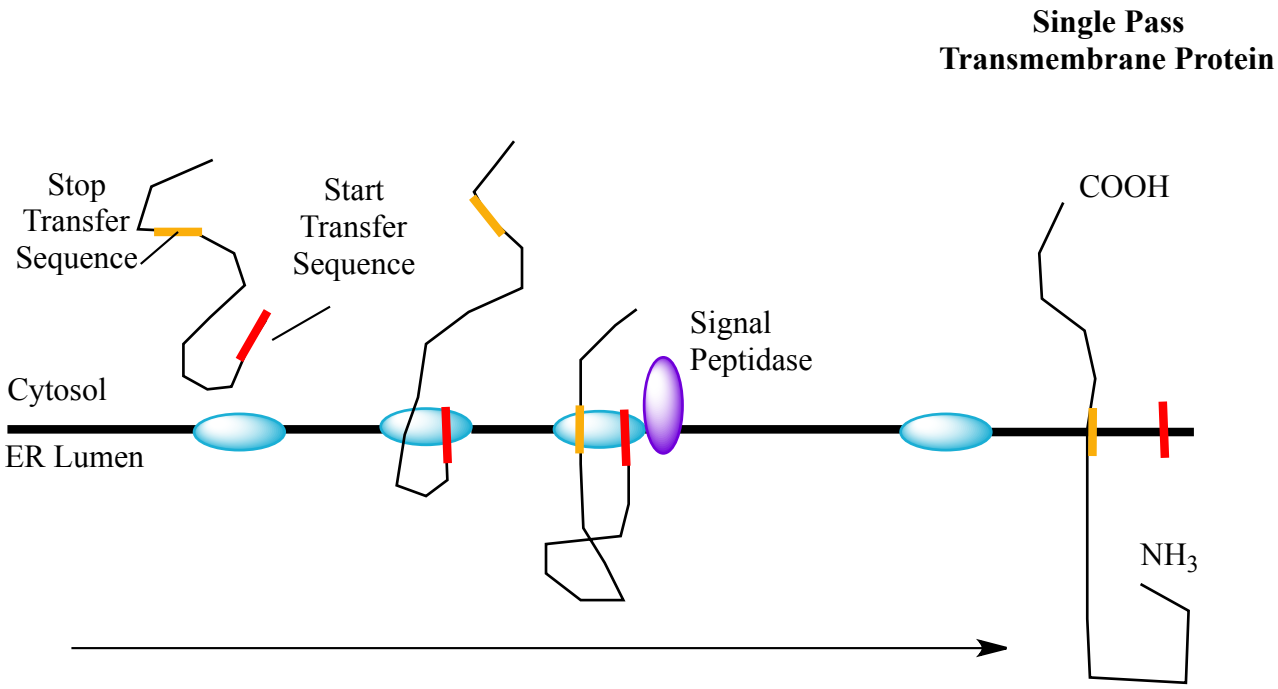
EXAMPLE: Posttranslational import



Inserting Proteins into the Membrane

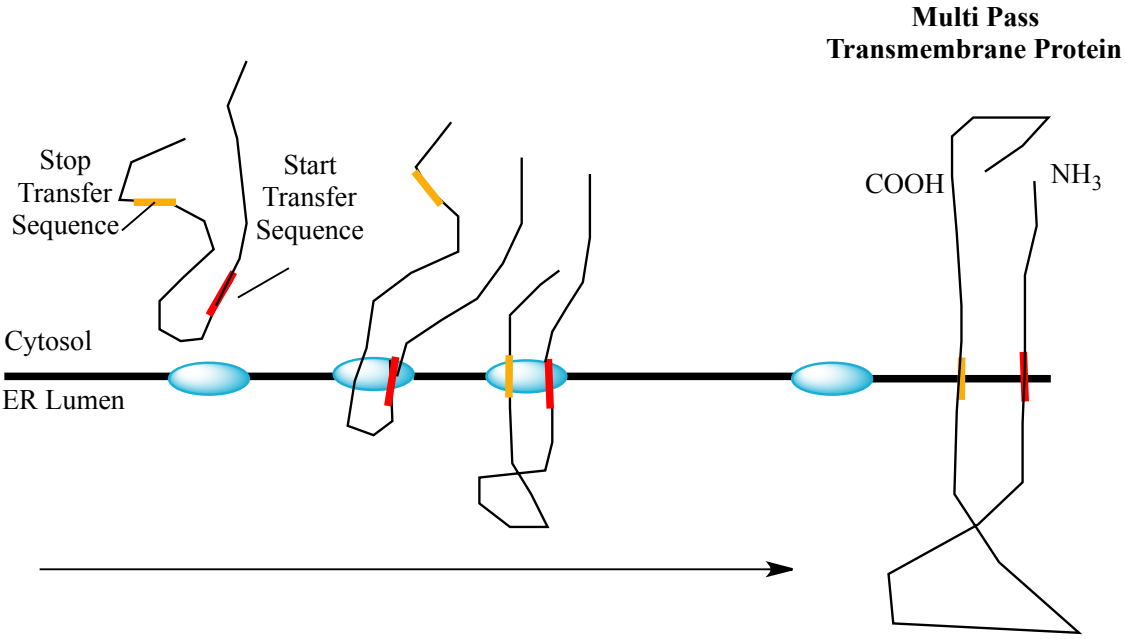
- **Single pass transmembrane proteins** have one insertion in the _____
  - □ **Start transfer signal** is a signal sequence which opens a translocon and the protein is translocated through it
    - **Stop transfer signal** signals to anchor the protein in the membrane
    - The ER signal sequence is then released from the translocon and cleaved off
  - □ Start transfer signal can be on the N-terminus or located within the middle of the polypeptide chain

EXAMPLE: Insertion of single pass transmembrane protein



- **Multi pass transmembrane proteins** have more than one insertion in the membrane
  - □ Polypeptide chains contain multiple start and stop _____ sequences
    - Order of sequence determines whether it is a start or stop sequence (the start sequence is first)
    - Multiple start transfer sequence initiate translocation at different sections along the polypeptide chain

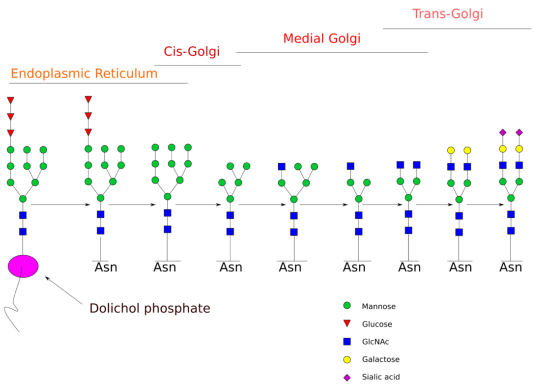
EXAMPLE: Insertion of a multi pass transmembrane protein



ER Protein Modifications

- The ER is a major hub of protein _____
  - □ **Glycosylation** of proteins occurs in the ER
    - **Dolichol** is a precursor oligosaccharide which is added to proteins for N-linked glycosylation
    - Oligosaccharides are important tags to mark the state of protein folding – chaperons bind them
  - □ **Glycosylphosphatidyl-inositol (GPI) anchor** is added to proteins destined for the plasma membrane
    - Can be easily cleaved off in order to release proteins into the extracellular environment

EXAMPLE: Glycosylation in the ER

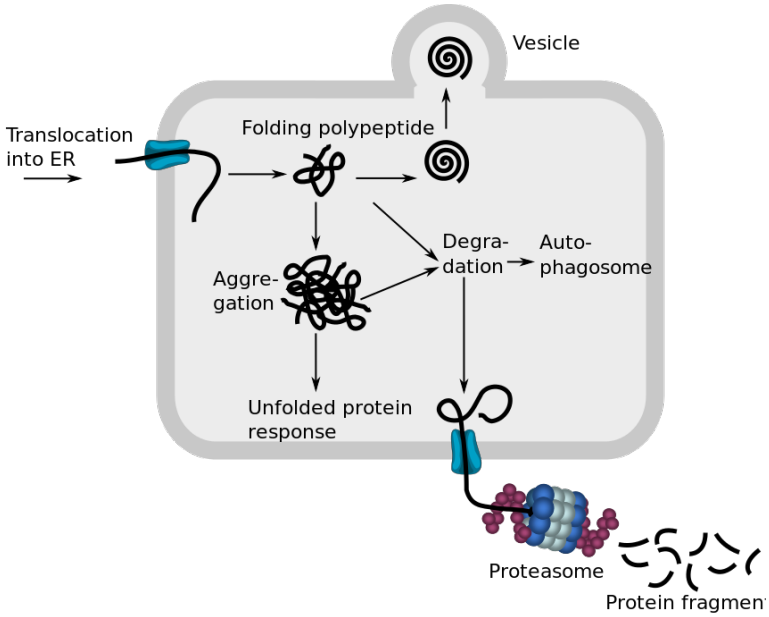


□ **Protein disulfide isomerase** assists with protein disulfide bond formation

□ **Unfolded protein response** detects misfolded proteins

- ER-associated degradation (ERAD) proteins recognize misfolded proteins and transports them to cytosol

EXAMPLE: Unfolded Protein Response in the ER



PRACTICE:

1. Match the following term with its definition
   - I. Co-translational import _____
   - II. Post-translational import _____
   - III. ER retention signal _____
   - IV. Translocon _____

A. Pore in the ER membrane that binds SRP and SRPR to translocate the protein into ER

B. Signal sequence located on the C-terminus and keeps proteins within the ER

C. Process of importing proteins into the ER as they're being translated

D. importing proteins into the ER after they've been translated

2. Which of the following is responsible for recognizing the ER signal sequence?
   a. Signal Recognition Particle
   b. Signal Recognition Particle Receptor
   c. Translocon
   d. Stop Transfer Sequence

3. A protein contains 5 start/stop transfer sequences. How many times will this protein cross the membrane?
    a. 2
    b. 5
    c. 10
    d. 3

4. Glycosylation of proteins in the ER is associated with which of the following molecules or responses?
    a. Unfolded protein response
    b. Protein disulfide isomerase
    c. Glycosylphosphatidyl-inositol (GPI) anchor
    d. Dolichol