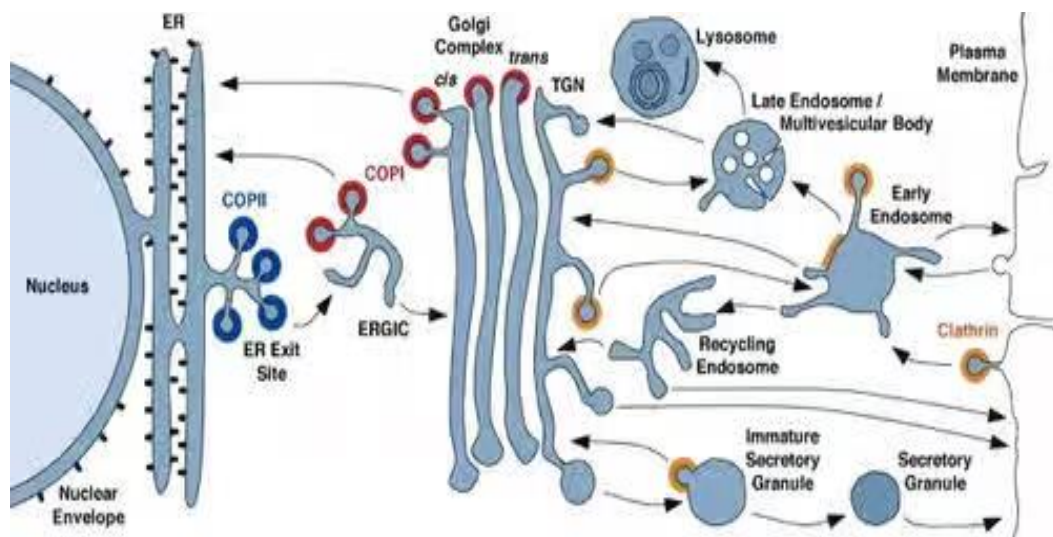


Transport of Protein Across Endoplasmic Reticulum

Proteins synthesized by membrane-bound ribosomes translocate the ER membrane co-translationally.

- Some proteins, however, are translocated into the endoplasmic reticulum and after their synthesis has been completed.
- Synthesis of these protein begins on an unattached ribosome in the cytosol.

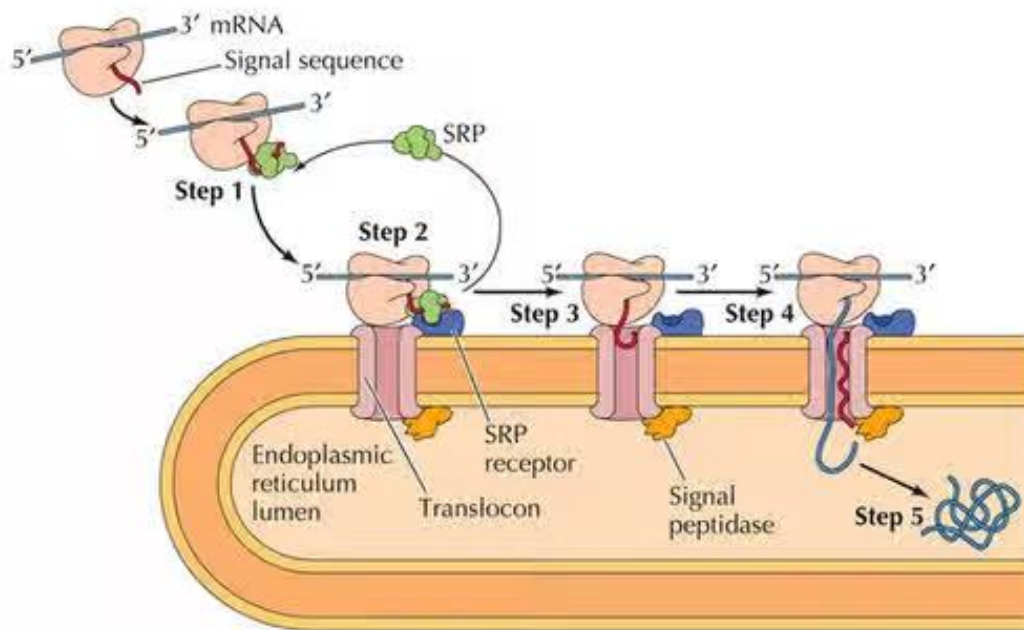


- Ribosome engaged in the synthesis of proteins are targeted to the endoplasmic reticulum by the signal sequence at the N-terminus of the growing polypeptide chain.
- N-terminal signal sequences are cleaved from the polypeptide chain during its transfer to the ER lumen.

Sabatini and Blobel first proposed the hypothesis known as Signal hypothesis in 1971.

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- A signal recognition particle SRP, a cytosolic particle binds to the signal sequence of the nascent polypeptide chain, and the complex of SRP, nascent polypeptide, and a ribosome then binds to the alpha subunit of the SRP receptor in the ER membrane.
- SRP receptor contains two polypeptide subunits: a transmembrane beta subunit and a peripheral alpha subunit.



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- SRP Binding to the signal sequence slows translation, a phenomenon termed as elongation arrest.
- The interaction of SRP and SRP receptors directs the SRP-ribosome complex to the translocon.
- In mammals, translocon is made up of three polypeptides called the Sec61 complex.

The driving force for uni-directional translocation of across the ER membrane is provided by a protein Complex called Sec63 Complex and a member of the hsp70 family of molecular chaperones known as BiP (BiP for binding protein). The ATP-driven cycle of BiP binding and release pulls the protein into the lumen. Cleavage of the signal sequence by signal peptidase releases the polypeptide in the ER lumen.