Protein folding and N linked glycosylation

Post translational modification

- Translation completes the formation of polypeptide chain of proteins
- The sequence of nucleotides in DNA has now been converted to the sequence of amino acids in a polypeptide chain
- The synthesis of a polypeptide, however, is not equivalent to the production of a functional protein.
- To be useful, polypeptides must fold into distinct three-dimensional conformations, and in many cases multiple polypeptide chains must assemble into a functional complex.
- In addition, many proteins undergo further modifications, including cleavage and the covalent attachment of carbohydrates and lipids, that are critical for the function and correct localization of proteins within the cell.

Chaperon

- The three-dimensional conformations of proteins result from interactions between the side chains of their constituent amino acids
- The proper folding of proteins within cells is mediated by the activities of other proteins.
- Proteins that facilitate the folding of other proteins are called molecular chaperones.
- Chaperons helps in stabilizing proteins by folding and keeps a track on misfolding of proteins

Chaperons on ER

- Important chaperon found on the ER: Hsp70-BIP, calnexin, calreticulin
- BIP: binds with the newly form nascent proteins and maintain them in unfolded state
- Calnexin and calreticulin: prevent incorrect folding and premature folding of new protein
- Calnexin is located in the ER membrane
- Calreticulin in the ER lumen

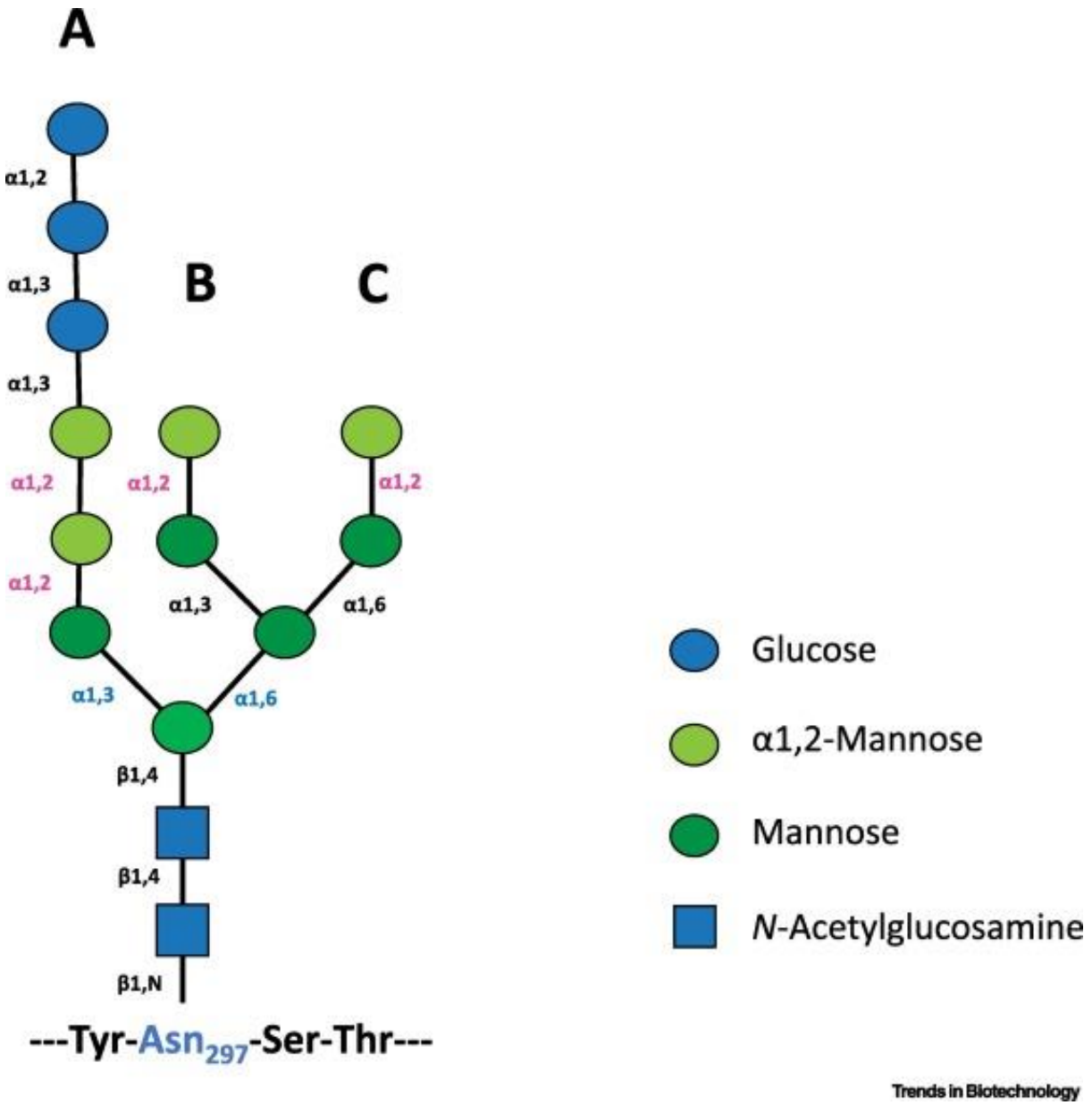
Formation of Di-sulphide bonds in proteins

- Disulfide bonds do not form in the cytosol because cytosol has a reducing environment, due to which cysteine remain its reduced state in the cytosol
- Disulfide bonds are formed in the ER lumen by enzyme protein disulphide isomerase (PDI).
- Cytosolic proteins and organelle proteins lack disulphide bonds
- Thus only secreted proteins and some membrane proteins have disulphide bonds.

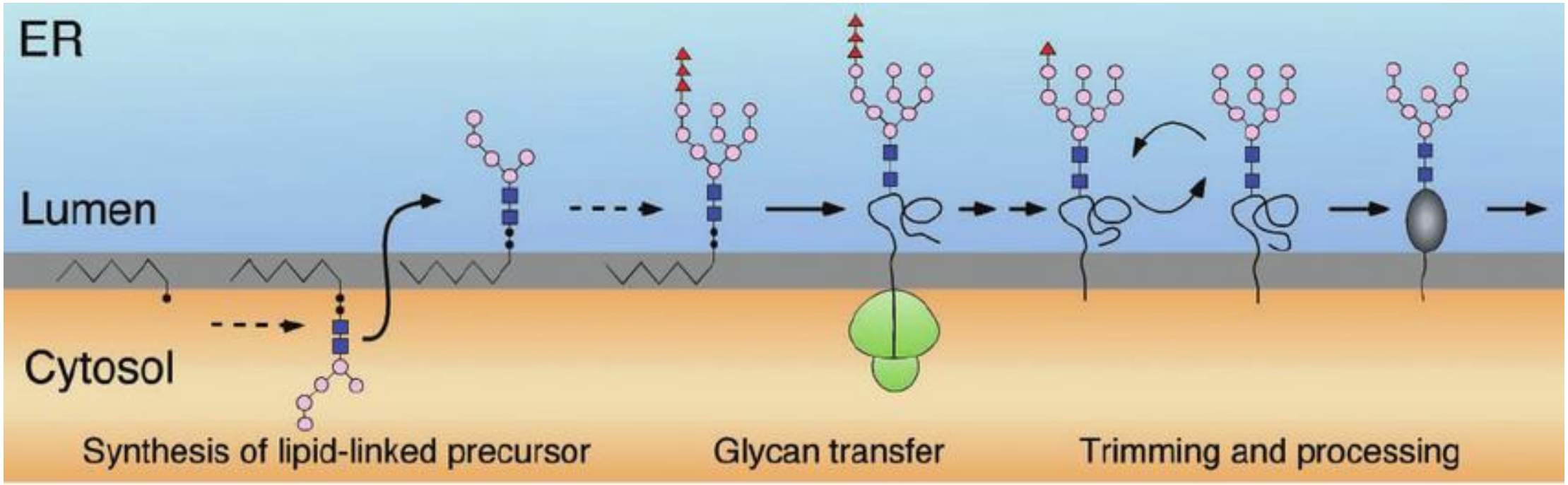
N-linked glycosylation of proteins

- Attachment of sugar to a nitrogen atom in an amino acid residue in a protein
- Sugar-large preformed oligosaccharide
- This oligosaccharide is attached with dolichol (long chain lipid: serve as carrier)

Structure of N-linked oligosaccharide



- Biosynthesis of oligosaccharide starts in the cytosolic part of ER
- N acetyl glucosamine attaches to the dolichol phosphate
- 2, N acetyl glucosamine and 5 mannose added at a time to dolichol phosphate
- After that the molecule flipped to the lumen side



- In the lumen the remaining 4 mannose and 3 glucose added to the molecule
- The whole oligosaccharide is now transferred to the aspargine residue of the new protein
- After that 3 glucose and one mannose are removed by different enzymes.

Function of glycosylation

- Provide proper folding to some proteins in ER
- Provide stability to proteins
- Acts as antigens
- Helps in cell-cell adhesion