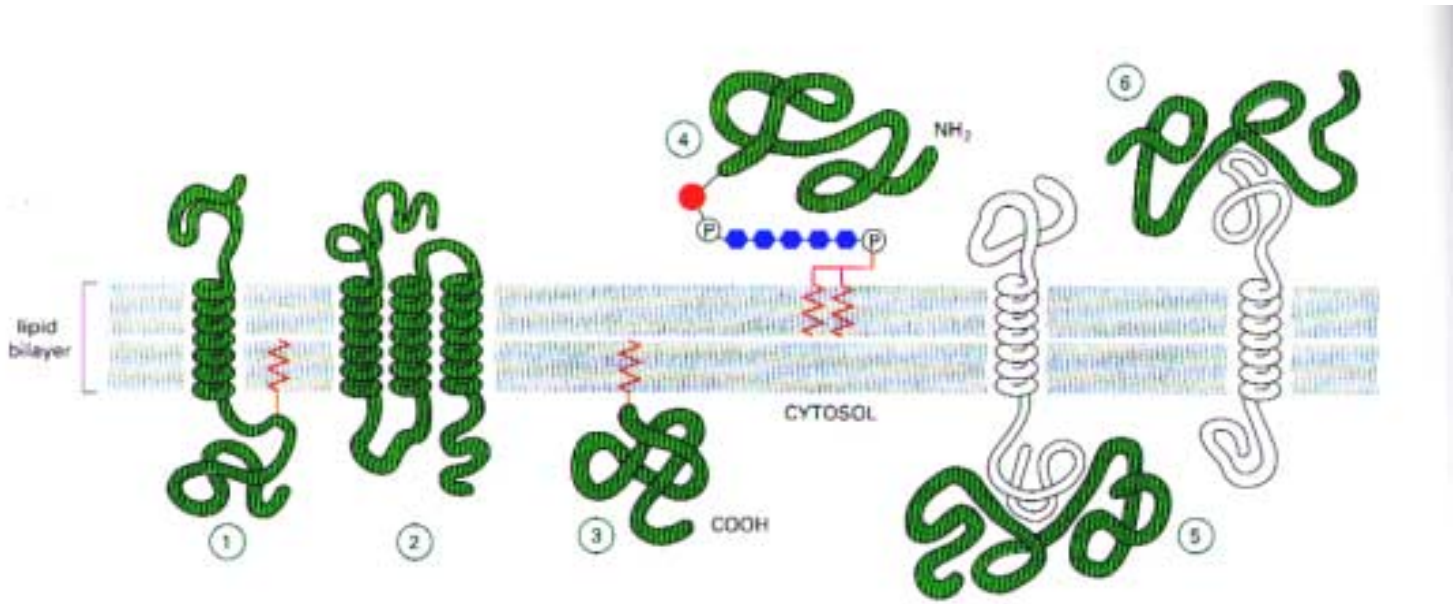
Valkude modifitseerimine endoplasmaatilises võrgustikus.

- 1. Disulfiidsildade moodustumine (ER).
- 2. Valkude õige kokkupakkimine (ER).
- 3. Valkude glükosüleerimine (ER, Golgi).
- 4. Valkude spetsiifiline proteolüütiline töötlemine (ER, Golgi).
- 5. Mitmeahelaliste valkude moodustumine (ER).
- ER-endoplasmaatiline võrgustik

Membraanivalkude seostumine lipiidse kaksikkihiga.



Tüüpiline transmembraanne valk.

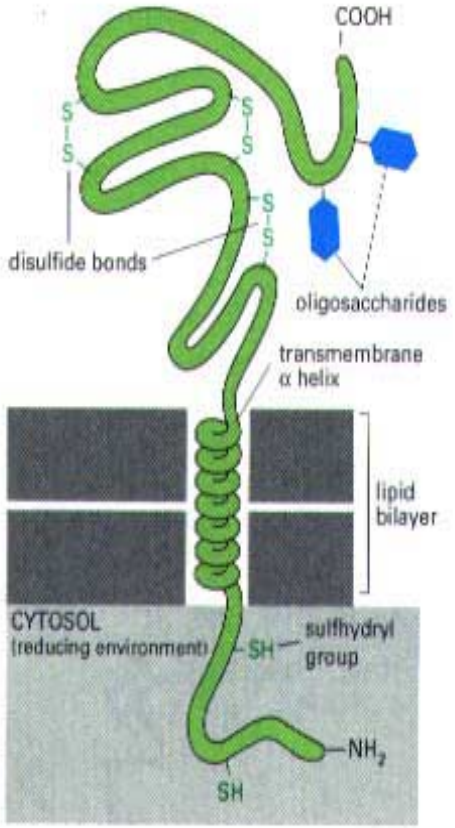


Figure 10–17 A typical single-pass transmembrane protein. Note that the polypeptide chain traverses the lipid bilayer as a right-handed α helix and that the oligosaccharide chains and disulfide bonds are all on the noncytosolic surface of the membrane. Disulfide bonds do not form between the sulfhydryl groups in the cytoplasmic domain of the protein because the reducing environment in the cytosol maintains these groups in their reduced (–SH) form.

Immuunoglobuliini struktuur.

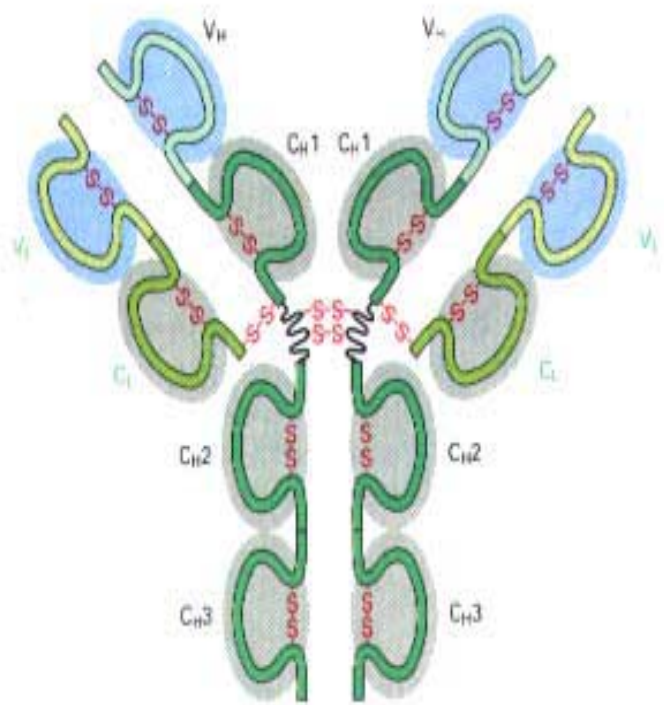
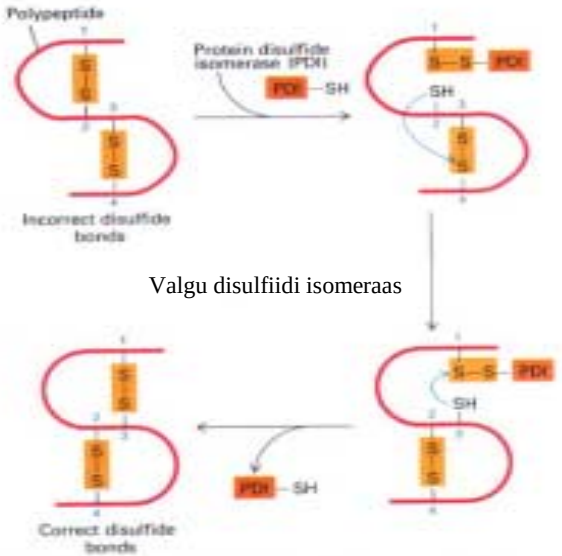


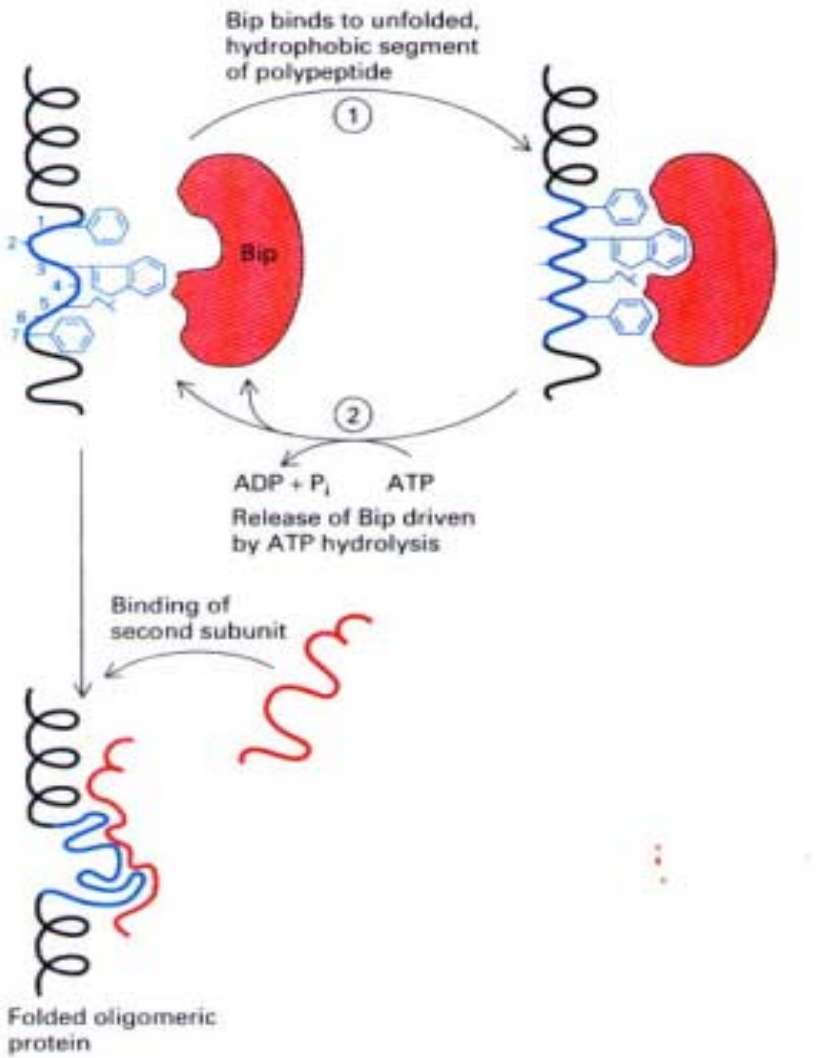
Figure 23-32 **Immunoglobulin domains.** The light and heavy chain in an Ig molecule are each folded in repeating domains that are similar t one another. The variable domains (shaded in *blue*) of the light and heavy chains (V_L and V_H) make up t antigen-binding sites, while the constant domains of the heavy chai (mainly C_H2 and C_H3) determine th other biological properties of the molecule. The heavy chains of IgM and IgE antibodies have an extra constant domain (C_H4). Hydrophob interactions between domains on adjacent Ig chains play an importan part in holding the chains together i the Ig molecule; C_L binds to C_H1, fo example, and the C_H3 domains bind to each other.

Disulfiidsideme ümberkorraldumine.



A FIGURE 16-23 Protein disulfide isomerase (PDI) and the rearrangement of disulfide bonds. PDI catalyzes the breakage and reformation of disulfide bonds and, in so doing, accelerates the folding of proteins containing multiple disulfide bonds. In the oxidizing environment of the ER lumen, disulfide bonds form in newly made secretory proteins, but the bonds are often incorrect. PDI contains an active-site cysteine residue with a free reduced sulfhydryl (SH) group, which reacts with disulfide (S–S) bonds on nascent or newly completed proteins to form an S–S bond between PDI and the protein. This bond, in turn, can react with a free SH on the protein to form a new S–S bond. In this way, the disulfide bonds on a protein can rearrange themselves until the most stable configuration for the protein is achieved. [After R. B. Freedman, 1984, *Trends Biochem. Sci.* **9**:438–441; R. Noiva and W. Lennarz, 1992, *J. Biol. Chem.* **267**:3553–3556.]

Bip valgu seostumine eellasvalgule.



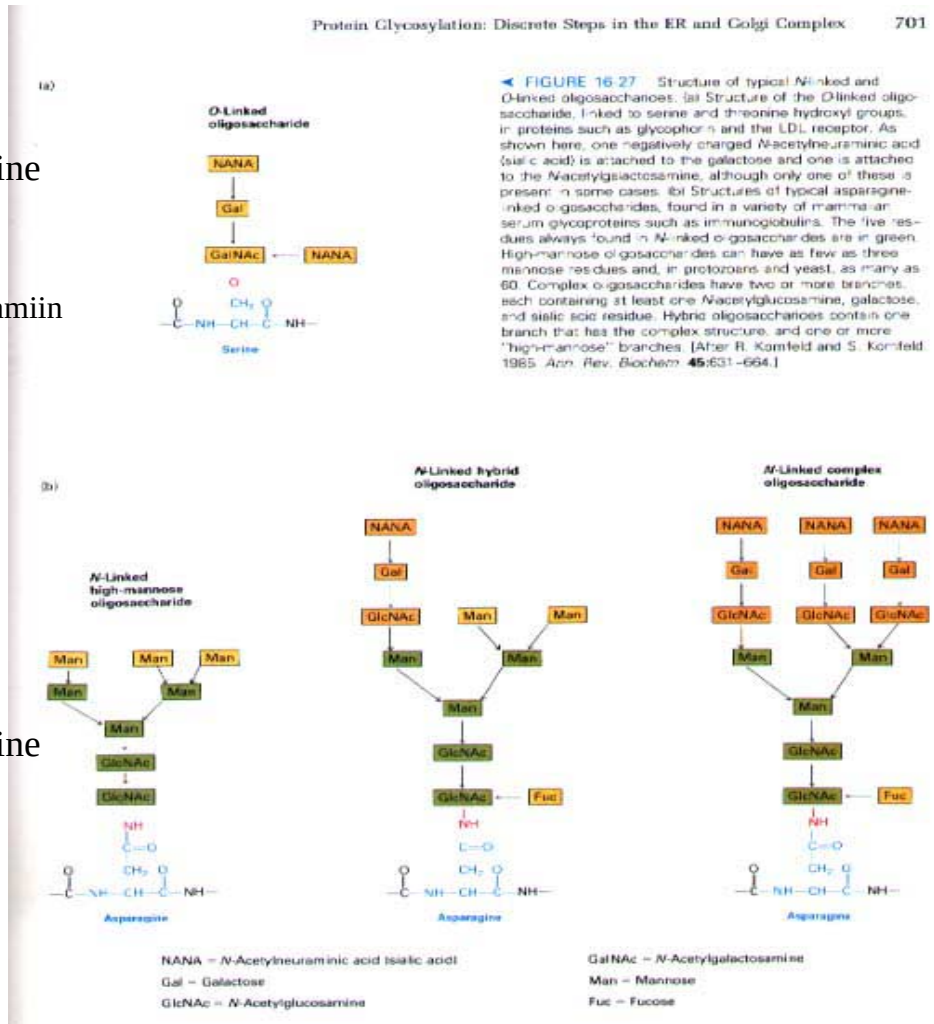
Tüüpilised N- ja O-seoselised oligosahhariidid.

O-seoseline glükosüleerimine (Seriin, Treoniin)

GalNAc=N-atsetüülgalaktoosamiin

Galaktoos, siaalhape e.neuramiinhape, fukoos

N-seoseline glükosüleerimine (Asparagiin)



Golgi kompleksis (glükosüültransferaasid)

Endoplasmaatilises võrgustikus (oligosahhariid-valk transferaas) ja Golgi kompleksis

Valgu glükosüleerimine karedas endoplasmaatilises võrgustikus.

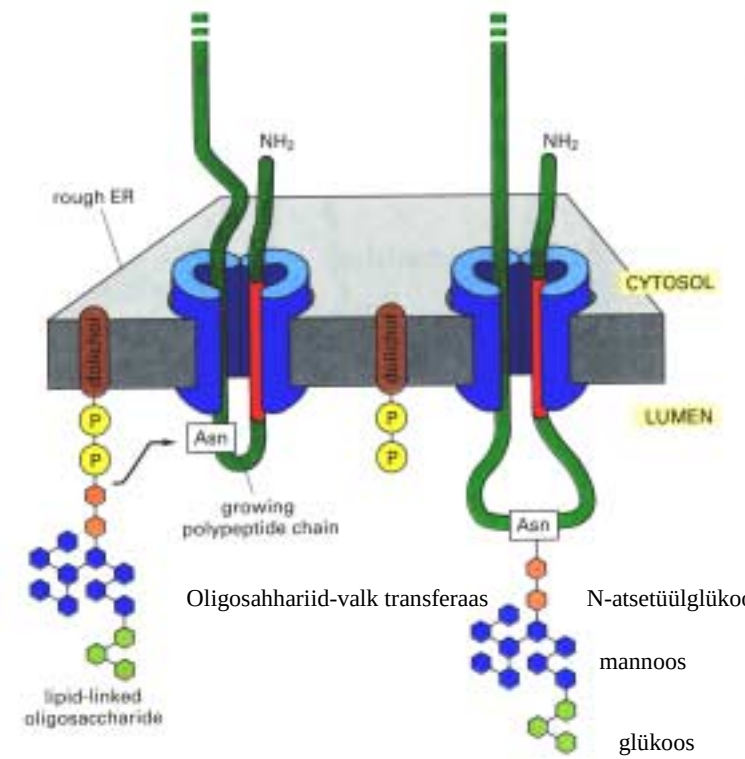


Figure 12–49 **Protein glycosylation in the rough ER.** Almost as soon as a polypeptide chain enters the ER lumen, it is glycosylated on target asparagine amino acids. The oligosaccharide shown in Figure 12–48 is transferred to the asparagine as an intact unit in a reaction catalyzed by a membrane-bound *oligosaccharyl transferase* enzyme. There is one copy of this enzyme associated with each protein translocator in the ER membrane.

Oligosahhariid-valk transferaas

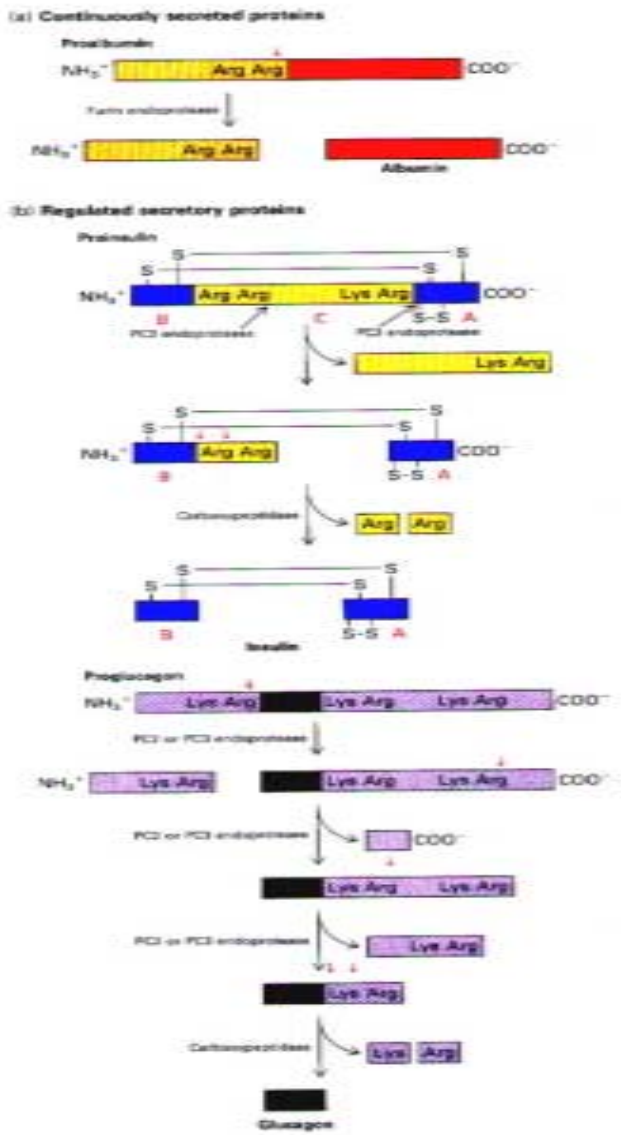
N-atsetüülglükoosamiin

mannoos

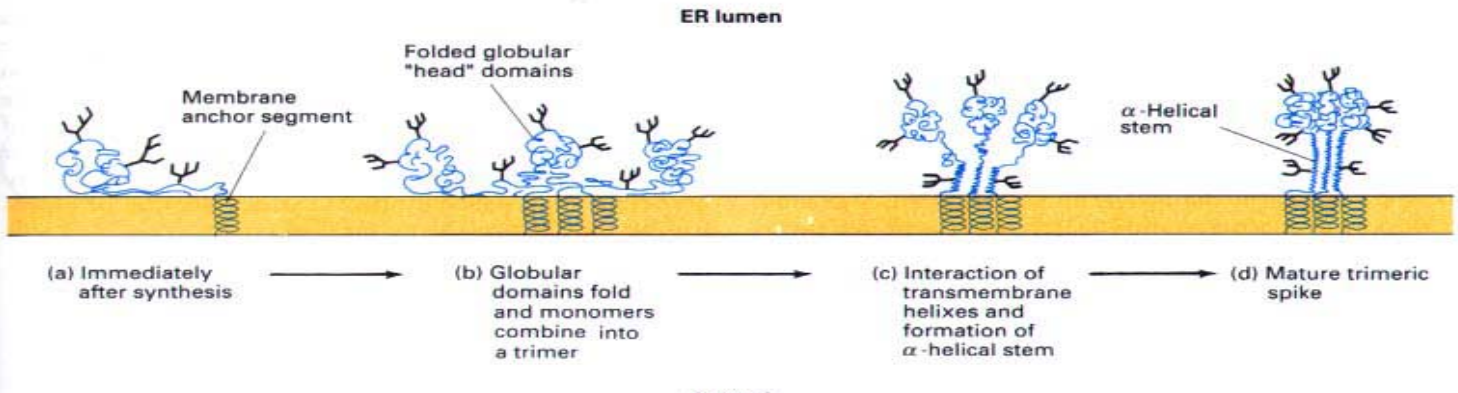
glükoos

Asparagiin peab olema teatud kindalas kontekstis: Asn-X-Ser või Asn-X-Thr; X=ükskõik milline aminohape, v.a. Pro

Eellasvalkude proteolüütiline lõikamine.

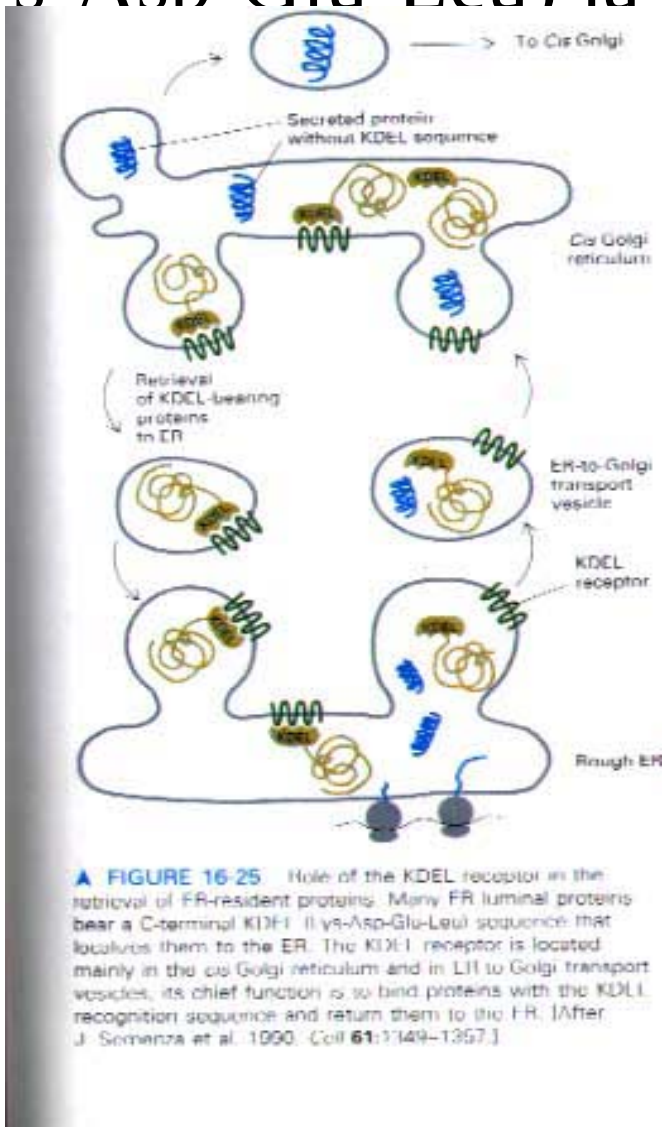


Hemagglutiniini trimeerse molekuli moodustumine endoplasmaatilises võrgustikus.



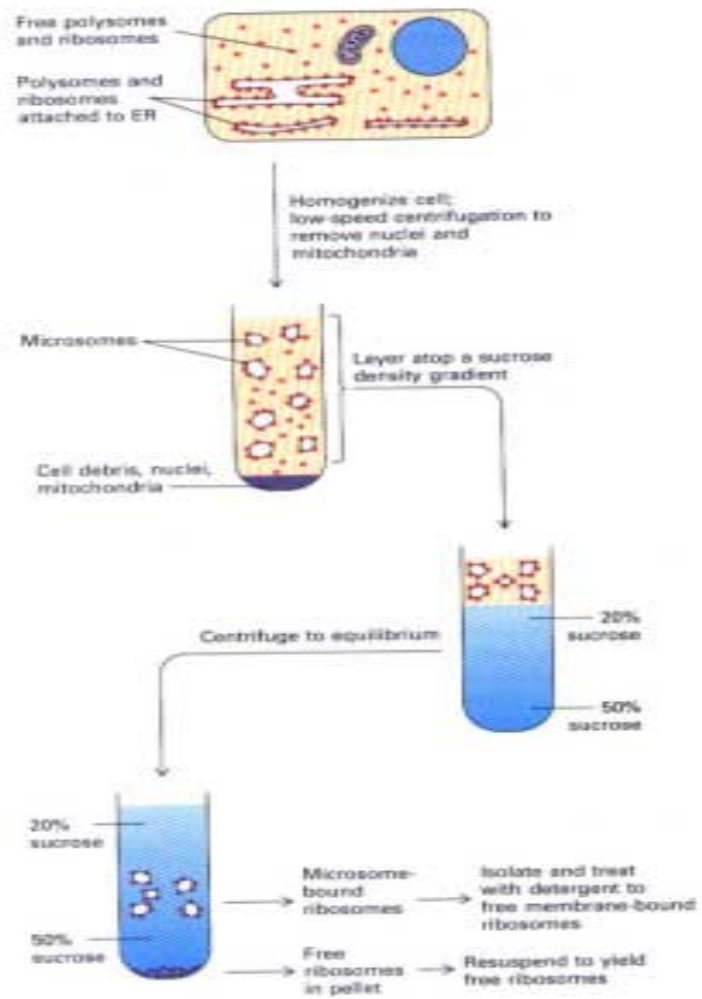
▲ FIGURE 16-24 The folding of the hemagglutinin (HA) precursor polypeptide HA_0 and the formation of a trimer within the ER. (a) Immediately after its synthesis, the bulk of the HA_0 polypeptide is on the luminal side of the ER membrane, anchored by a hydrophobic α helix near its C-terminus. (b) First, the globular domains that will form the head of the spike (see Figure 16-54a) fold, stabilized by disulfide bonds. (c) Then three chains interact with each other, initially via their transmembrane α helices; this activity apparently triggers the formation of a long stem containing one α-helix from the luminal part of each HA_0 polypeptide. (d) Finally, interactions between the three globular heads occur, generating the mature trimeric spike. Not shown here is later proteolytic cleavage of HA_0 to HA_1 and HA_2 in the Golgi complex, well after the trimer has been formed; the molecular structure of the trimer after cleavage to HA_1 and HA_2 is depicted in Figures 16-54 and 3-5. [After M-J. Gething, K. McCammon, and J. Sambrook. 1986. *Cell* **46**:939–950; I. Braakman et al. 1991. *J. Cell Biol.* **114**:401–411.]

Endoplasmaatilise võrgustiku hoidmissignaal KDEL (Lys-Asp-Glu-Leu) ja tema retseptor.



A FIGURE 16-25 Role of the KDEL receptor in the retrieval of ER-resident proteins. Many ER luminal proteins bear a C-terminal KDEL (Lys-Asp-Glu-Leu) sequence that localizes them to the ER. The KDEL receptor is located mainly in the cis Golgi reticulum and in ER to Golgi transport vesicles; its chief function is to bind proteins with the KDEL recognition sequence and return them to the ER. [After J. Semenza et al. 1990. Cell **61**:1349–1357.]

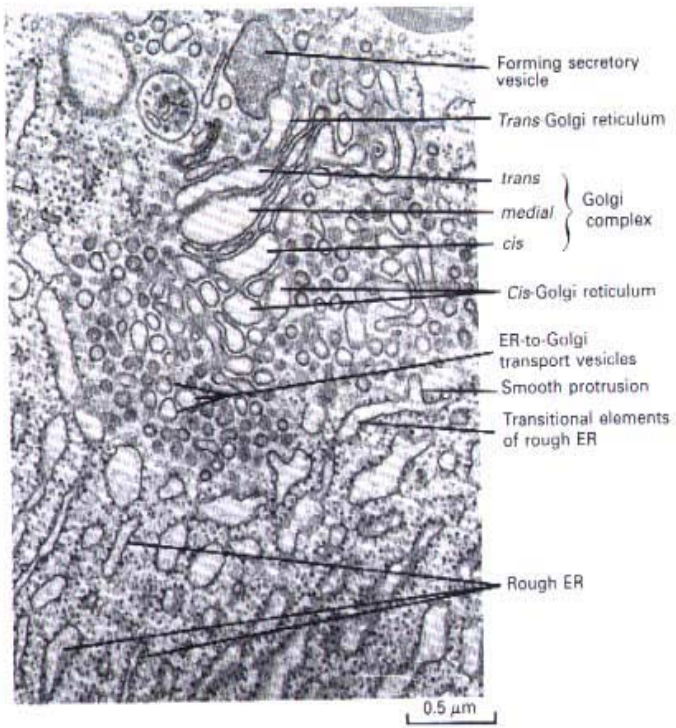
Membaraaniga mitteseostunud ja sellega seotud ribosoomide ning polüsoomide puhastamine.



Sündmused mis toimuvad endoplasmaatilises võrgustikus.

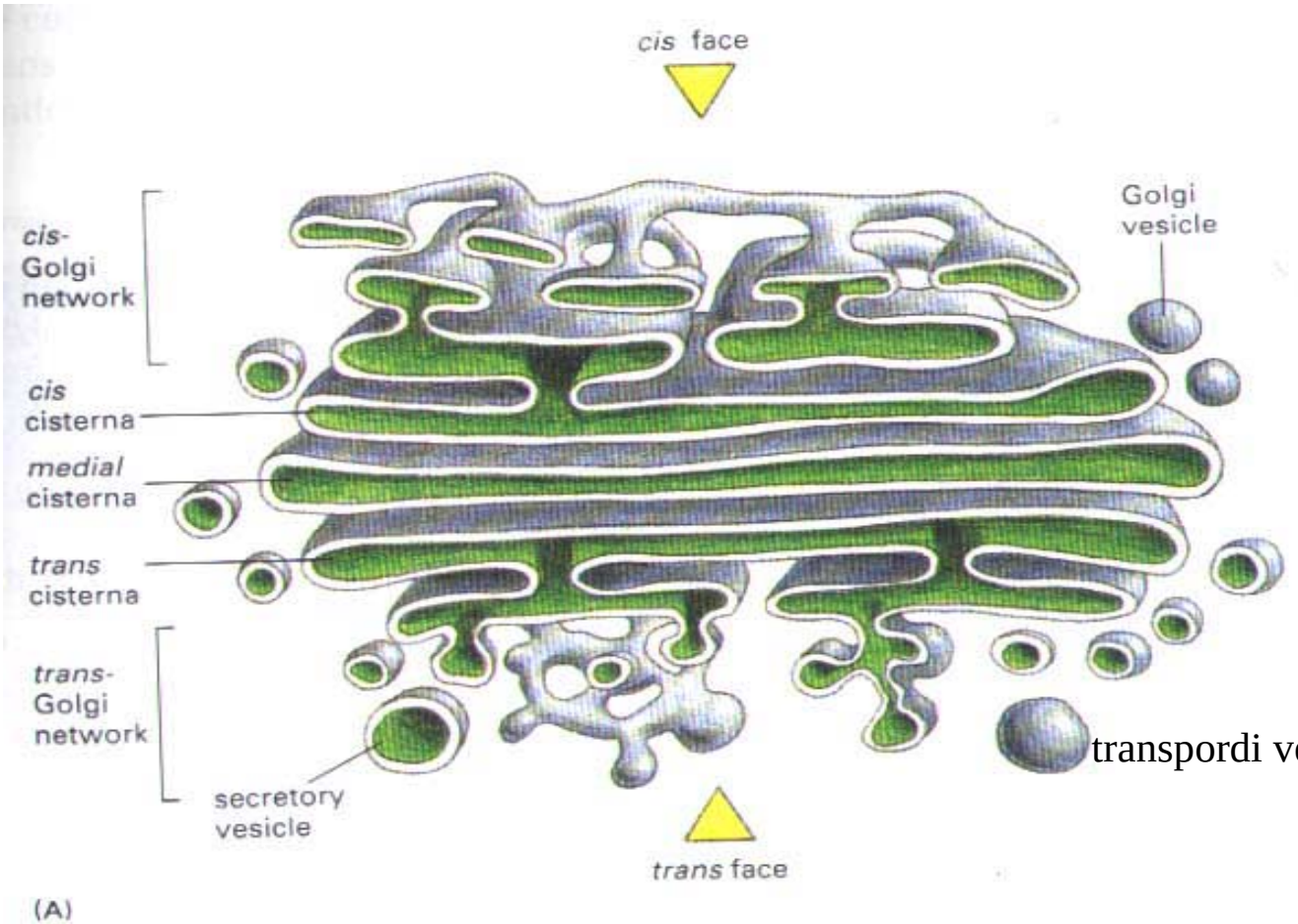
- 1. Seal toimub kogu raku membraanikomponentide süntees (lipiidid, kolesterool).
- 2. Endoplasmaatiline võrgustik ise seob osa sünteesitud valkudest (need on liiderjärjestust omavad valgud).
- 3. Seal toimub valkude kokkupakkimine kõrgema järgu struktuuridesse. Selle eelduseks on õigete disulfiidsildade moodustumine ja N-seoseline glükosüleerimine, mõnedel valkudel ka osaline proteolüütiline töötlemine. Seal toimub ka multimeersete valkude oligomeriseerumine. Korrektselt töödeldud, õige konformatsiooniga valgud saadetakse edasi Golgi kompleksi.
- 4. Siledat endoplasmaatilist võrgustikku leidub rohkem teatud spetsialiseeritud rakkudes, kus toimub lipiidide, steroidhormoonide süntees, kahjulike ainete detoksifikatsioon ja kaltsiumi deponeerimine.

Endoplasmaatiline võrgustik ja Golgi kompleks kõhunäärme rakus.



◀ FIGURE 16-26 Electron micrograph of the Golgi complex and ER in an exocrine pancreatic cell. The stacked vesicles of the Golgi complex and a forming secretory vesicle are evident. The rough ER contains transitional elements from which smooth protrusions appear to be budding. These buds form the vesicles that transport secretory and membrane proteins from the rough ER to the Golgi complex. Other vesicles seen at the periphery of the *cis* side of the Golgi complex form the *cis*-Golgi reticulum, which is an intermediate between the ER and the *cis* Golgi. [Courtesy G. Palade.]

Golgi kompleks.



transpordi vesiikul

Siin toimub valkude ja lipiidide modifitseerimine ja sorteerimine.

Golgi kompleksi ensüümid.

- Oligosahhariidide sünteesi eest vastutavad *glükosidaasid* ja *glükosüültransferaasid*.

- Sulfaatimise (*sulfotransferaasid*), fosforüleerimise (*fosfotransferaasid*), palmitoüleerimise ja valkude proteolüütilise lõikamise eest vastutavad ensüümid.

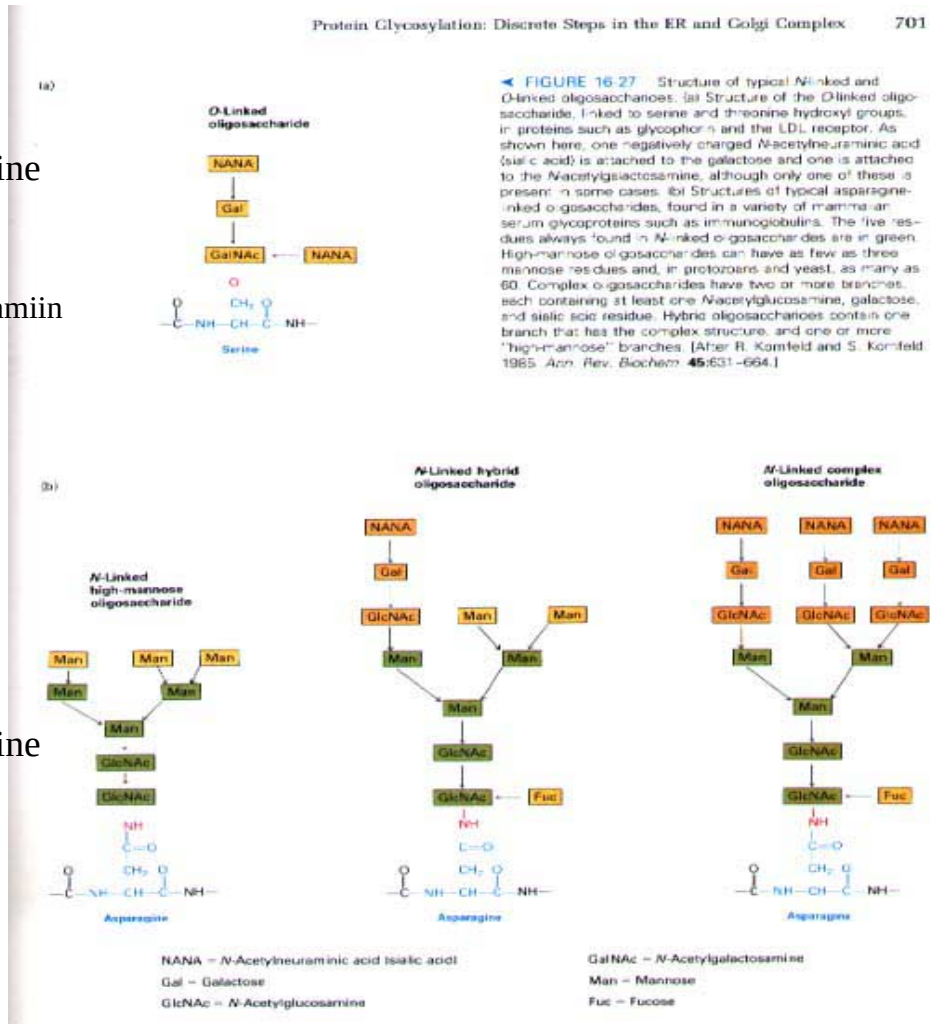
Tüüpilised N- ja O-seoselised oligosahhariidid.

O-seoseline glükosüleerimine (Seriin, Treoniin)

GalNAc=N-atsetüülgalaktoosamiin

Galaktoos, siaalhape e.neuramiinhape, fukoos

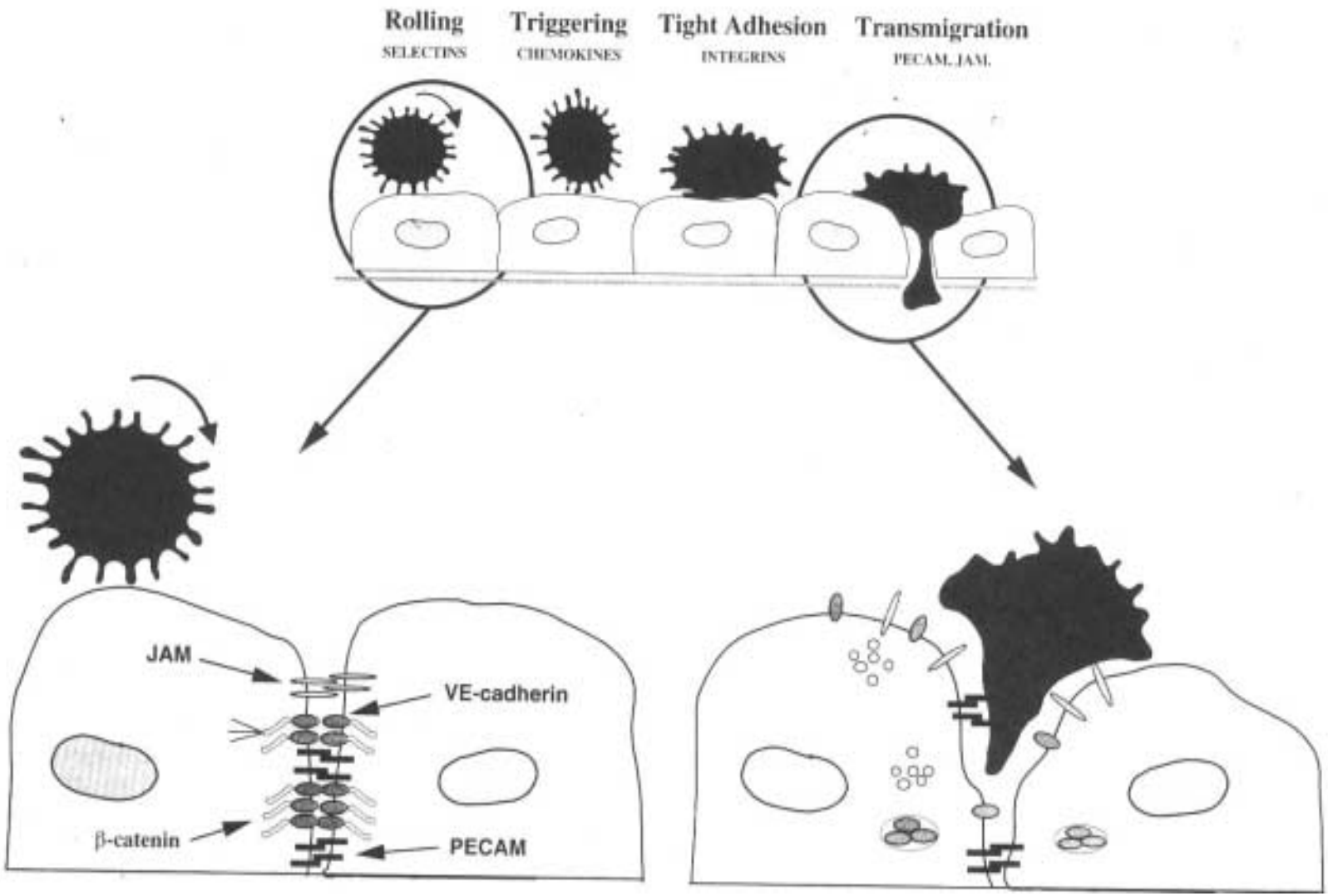
N-seoseline glükosüleerimine (Asparagiin)



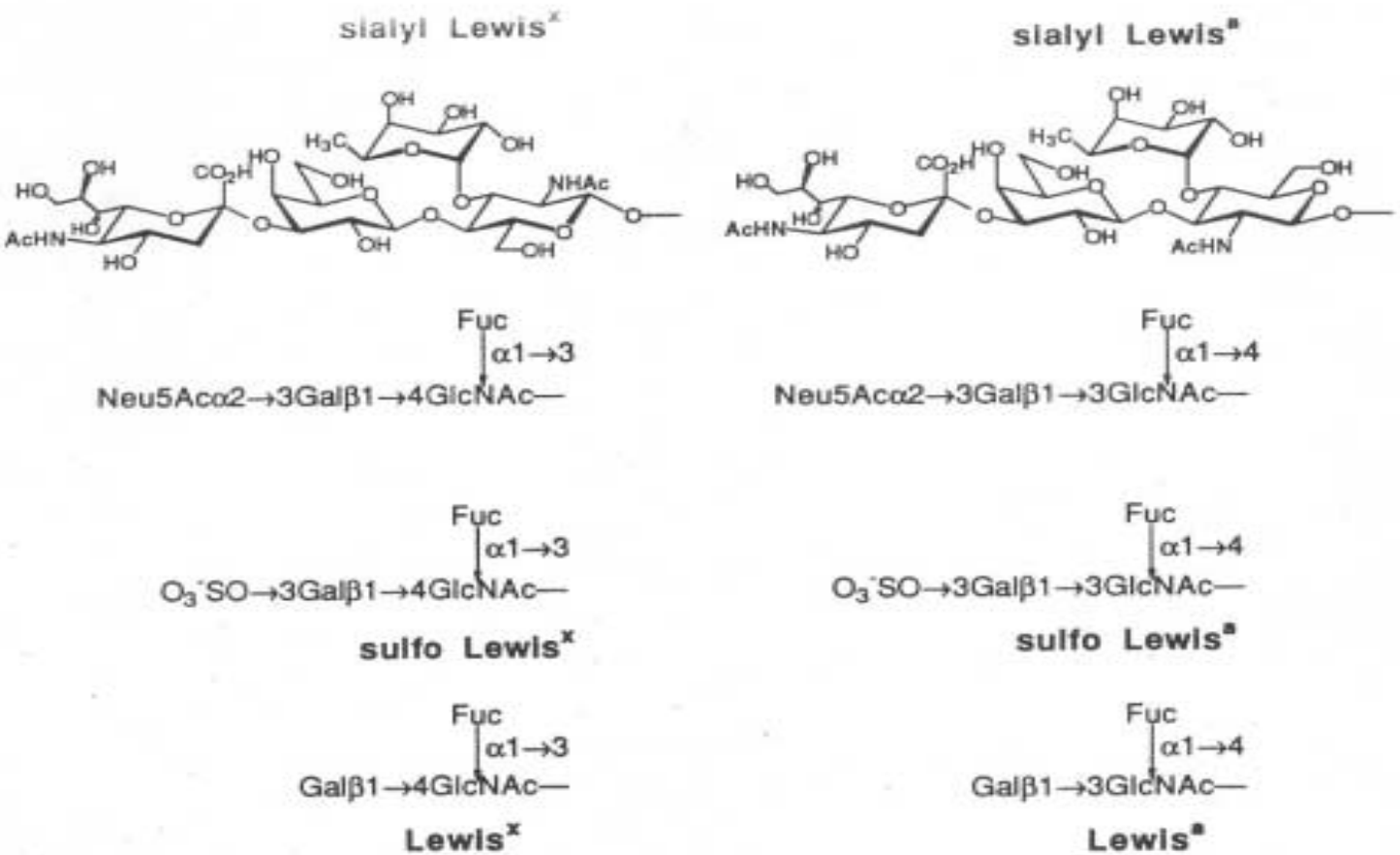
Golgi kompleksis (glükosüültransferaasid)

Endoplasmaatilises võrgustikus (oligosahhariid-valk transferaas) ja Golgi kompleksis

Leukotsüütide rullumine, kinnitumine ning transmigreerumine läbi endoteeli.



Lewis^{x} ja Lewis^{a} ning nendega lähedased karbohüdraatsed struktuurid.



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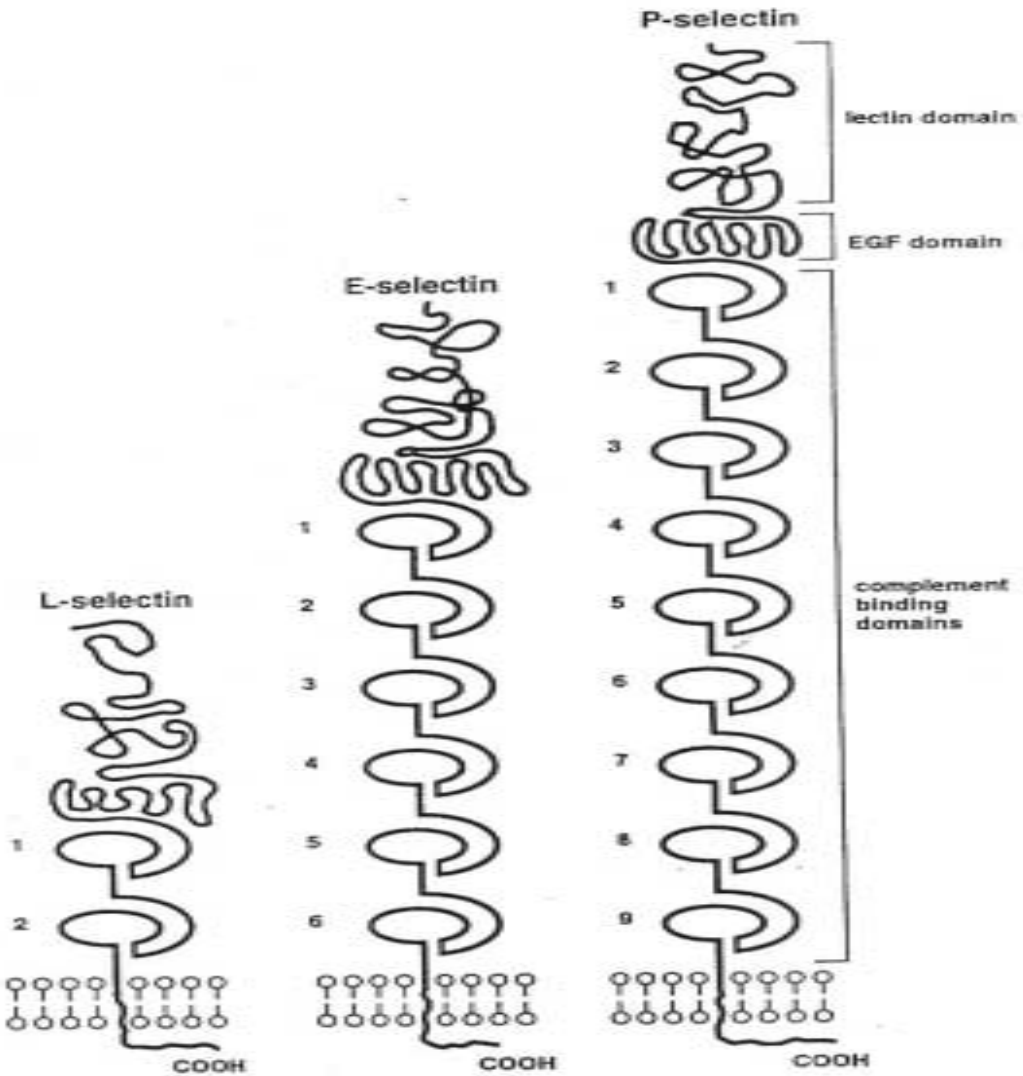

Selektiinide ligandid.