1: Answer: HIAJCDEBFG

2: Answer: 2331
Feedback: Typically, transport vesicles from ER to CGN are COPII-coated, whereas retrograde transport in the Golgi apparatus is mediated by COPI-coated vesicles. Clathrin- coated vesicles are involved in traffic from the plasma membrane as well between the endosomal and Golgi compartments and require dynamin for pinching off efficiently. Clathrin triskelions assemble into a basket-like cage that envelopes these budding vesicles.

3: Answer: TTFF
Feedback: Chains of sugar have limited flexibility and therefore protrude from the protein surface. As a result, the approach of other macromolecules to the protein is limited. At the same time, lectins can recognize the sugar chain and control the proper folding of the protein or send it down a particular sorting pathway.

4: An mRNA molecule is attached to the ER membrane by the ribosomes translating it. his ribosome population, however, is not static. As the mRNA moves through the ribosomes, those ribosomes that have finished translation dissociate from the 3′ end of the mRNA and from the ER membrane. But the mRNA remains attached to the ER by other ribosomes that are still in the process of translating it. As ribosomes move along the mRNA, its 5′ end becomes exposed and new ribosomes, recruited from the cytosolic pool, bind to it, and begin translation. Depending on its length, there are some 10–20 ribosomes attached to each membrane-bound mRNA molecule, forming what is known as a polyribosome.

5: As shown in **Figure 12–26**, elimination of the first transmembrane segment (by making it hydrophilic) would be expected to give rise to a protein with the N-terminal segment in the cytosol (un-glycosylated), but with all other membrane-spanning segments in their original orientation. In the unmodified protein, the first transmembrane segment served as a start-transfer signal, oriented so that it caused the N-terminal segment to pass across the ER membrane. The next transmembrane segment is also a start-transfer signal, but oriented so that it passes C-terminal protein across the membrane until it reaches the next transmembrane segment, which serves as a stop-transfer signal. Two more pairs of similarly orientated start- and stop-transfer signals give rise to the final arrangement. Eliminating the first start-transfer signal would permit the second start-transfer signal to initiate transfer. The arrangement of its flanking charged amino acids would orient it in the membrane so that its positively charged end faces the cytosol, just as it did in the original protein. It would then initiate transfer of C-terminal segments just as it did in the unmodified, original protein.

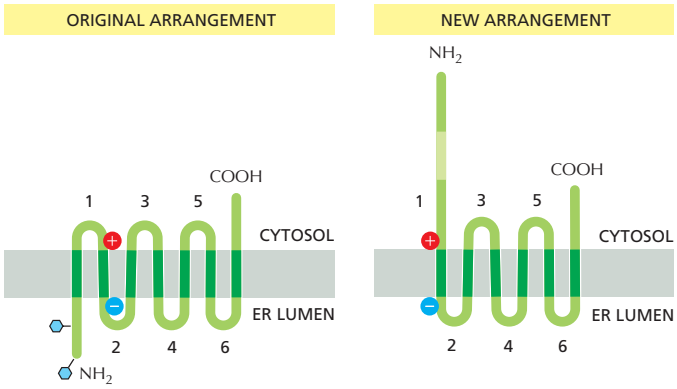

Figure 12–26 Arrangement of the original multipass transmembrane protein and of the new protein after the first hydrophobic segment was converted to a hydrophilic segment (Answer 12–102).

6: The preassembled sugar chain allows for better quality control. The assembled oligosaccharide chains can be checked for accuracy before they are added to the proteins; if a mistake were made in adding sugars individually to the proteins, the whole protein might have to be discarded. Since far more energy is used in building a protein than in building a short oligosaccharide chain, this is a much more economical strategy. Also, once a sugar tree is added to a protein, it is more difficult for enzymes to modify its branches, compared with modifying them on the free sugar tree. his difficulty becomes apparent as the protein moves to the cell surface: although sugar chains are continually modified by enzymes in various compartments of the secretory pathway, these modifications are often incomplete and result in considerable heterogeneity of the glycoproteins that leave the cell. The heterogeneity is largely due to the restricted access that the enzymes have to the sugar trees attached to the surface of proteins. The heterogeneity also explains why glycoproteins are more difficult to study and purify than non-glycosylated proteins.

7: Misfolded proteins in the ER bind to and activate a transmembrane kinase in the ER, which activates its own endoribonuclease domain, causing it to remove an intron from a specific mRNA. his “spliced” mRNA encodes a gene regulatory protein that enters the nucleus and activates the gene for an ER chaperone protein. his chaperone enters the ER and aids in the correct folding of misfolded proteins. his portion of the unfolded protein response is beneficial to the cell because it keeps misfolded proteins from building up in the ER and interfering with the processing of other, correctly folded proteins. Other parts of this response lead to activation of genes for ER protein degradation, which helps to unclog the ER.

8: Symmetry of phospholipids in the two leaflets of the ER membrane is generated by a phospholipid translocator, called a scramblase, that rapidly lips phospholipids of all types back and forth between the monolayers of the bilayer. Because it lips phospholipids indiscriminately, the different types of phospholipids become equally represented in the inner and outer leaflets of the bilayer; that is, they become symmetrically distributed. he plasma membrane contains a different kind of phospholipid translocator, which is specific for phospholipids containing free amino groups (phosphatidylserine and phosphatidylethanolamine). These lipases remove these specific phospholipids from the external leaflet and transfer them to the internal leaflet of the plasma membrane, thereby generating an asymmetrical distribution.

9:

False. When the hydrophobic signal peptide emerges from the ribosome, it is bound by SRP, which causes a pause in protein synthesis. Synthesis resumes when the ribosome with a bound SRP then binds to the SRP receptor on the cytosolic surface of the rough ER.

True. The Sec61 complex is composed of several proteins that assemble into a doughnutlike structure. The central pore in the complex lines up with a tunnel in the large ribosomal subunit through which the growing polypeptide chain exits from the ribosome.

False. The first (most N-terminal) transmembrane segment that exits the ribosome initiates translocation (acts as a start-transfer signal). Its orientation in the ER membrane fixes the reading frame for insertion of sub- sequent transmembrane segments. If the first transmembrane segment is oriented with its N-terminus in the cytosol, even-numbered segments will act as stop-transfer signals, and odd-numbered segments will act as start-transfer signals. If the first segment is oriented with its N-terminus in the lumen, then the second segment and subsequent even-numbered segments will act as start-transfer signals. Subsequent odd-numbered segments will act as stop-transfer signals.

False. The ER lumen does not contain reducing agents (they are in the cytosol) and therefore S–S bonds can form in the ER.

10: The position of one triskelion is shown in **Figure 13–20A**. A triskelion must be flexible at its vertex to be able to accommodate different sizes of coated vesicles (**Figure 13–20B**). As the size of the coat increases, its radius of curvature decreases, requiring individual triskelions to flatten out slightly. To accommodate the different angles required to it into a pentagon and a hexagon, a triskelion needs to be flexible at its “knees” (Figure 13–20B)

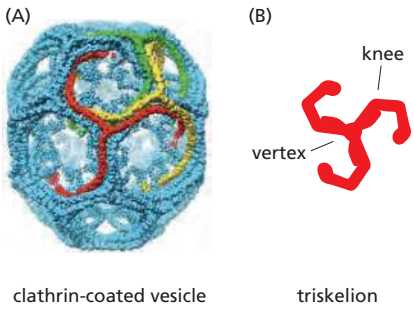

Figure 13–20 Formation of a clathrin coat (Answer 13–18). (A) The location of a single triskelion in a coated vesicle. (B) The sites of maximum flexibility of a triskelion.

11: The specificity for both the transport pathway and the transported cargo comes not from the Clathrin coat, but from the adaptor proteins that link the Clathrin to the transmembrane receptors for specific cargo proteins. he several varieties of adaptor proteins allow different cargo receptors, hence different cargo proteins, to be transported along specific transport pathways. Incidentally, humans are different from most other organisms in that they have two heavy-chain genes. Like other mammals, they also have two light-chain genes. In addition, in the neurons of mammals, the light- chain transcripts are alternatively spliced. Thus, there exists the potential in humans for additional complexity of Clathrin coats; the functional consequences of this potential variability are not clear.

12. GPI anchor comes first, as this takes place in the ER. O-linked glycosylation takes place in the Golgi system. Proteins always will travel first through the ER, before entering the Golgi by vesicular transport