Study Questions for **Lysosomal Recycling and Storage Disorders**

1. The Man-6-P recognition marker assembles mainly on lysosomal enzymes by selective recognition of peptide determinants in the substrate proteins by GlcNAc-P-transferase. Describe other examples of selective modification of glycans on subsets of glycoproteins. How do the recognition determinants differ?
2. How would the number of N-glycans on a lysosomal enzyme affect its affinity for one of the Man-6-P receptors?
3. Provide an alternate route for enzyme replacement therapy in cells carrying a mutation in the cation-independent Man-6-P receptor.
4. Predict which glycans and tissues/organs would be affected most if β-galactosidase was altered.
5. In lysosomal storage disorders, undegraded or partially degraded glycans and glycopeptides are often excreted in the urine. Propose a mechanism for how these partial degradation products escape from lysosomes and cells.
6. Provide possible explanations for the accumulation of glycopeptides with O-glycans in the urine of patients deficient in α-N-acetylgalactosaminidase.
7. How do multivesicular bodies arise and what purpose do they serve?
8. Describe the CLEAR network. How was it discovered?
9. It would seem counterintuitive to use an enzyme inhibitor as a molecular chaperone to restore enzyme activity in a lysosomal storage disorder. Explain the rationale behind this therapeutic approach.