

Biochemistry Cumulative Examination

December 1, 2011, Total 100 points

1. The C2 domain of protein kinase C α binds phosphatidylserine (PS) and phosphatidylinositol-4,5-bisphosphate (PtdIns(4,5)P₂) in a calcium-dependent manner. Predict which cellular membrane this protein will bind in response to the increase in cellular calcium level and explain why (25 points).
2. Sorting nexin 1 (SNX1) has two lipid binding domains, PX and BAR domains. The PX domain is known to bind phosphatidylinositol-3-monophosphate (PtdIns(3)P) whereas the BAR domain binds any anionic lipids, including PS. When the diameter of vesicles (= circular bilayer membranes) containing PS and PtdIns(3)P (97:3) was varied from 50 to 5000 nm, SNX1 binds the vesicles with 200-nm diameter with the highest affinity. Explain a most likely mechanism underlying this finding (25 points).
3. The FENS1 FYVE domain has high affinity for PtdIns(3)P-containing membranes and is thus recruited to PtdIns(3)P-rich early endosomes in the cell. Interestingly, the EEA1 FYVE domain that has much lower affinity for PtdIns(3)P-containing membranes is also recruited to early endosomes in the cell. Describe possible mechanisms that drive early endosome binding of EEA1-FYVE (25 points)
4. ENTH and ANTH domains share common structural elements and bind PtdIns(4,5)P₂. However, the ENTH domain can induce membrane bending and tubulation whereas the ANTH domain simply binds to the membrane without causing any disruption. The main structural difference between the two domains is the presence of the N-terminal helix known as H_0 in the ENTH domain that is known to form an amphiphilic helix. Recently, it was discovered that many plant ANTH domains have the ENTH-like H_0 in their N-termini. Describe a potential role of H_0 in the ENTH domain and predict how plant ANTH domains would behave (25 points).