MCB130 Midterm
September 28, 2007

Name:
SID:
GSI's Name:

Karsten Weis - Part II [90 points total]

Question 1a :

Question 1b :

Question 2 :

Question 3 :

Question 4 :

Question 5 :

Total :

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1. Peroxisomes are small, membrane-enclosed organelles that function in the degradation of fatty acids and in the degradation of H_2O_2. Peroxisomes are not part of the secretory pathway and peroxisomal enzymes are targeted directly from the cytoplasm to the lumen of peroxisomes via a peroxisomal targeting signal (PTS).
   a. Design a *general* experimental strategy to identify the PTS in your favorite peroxisomal protein 1 (FPP1). [15 pts]

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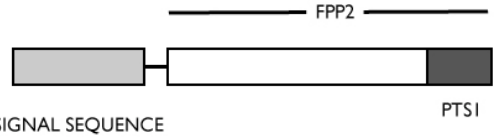
1. b. Previous research has shown that many peroxisomal enzymes contain a PTS at their very carboxy-terminus. This signal, termed PTS1, consists of the three amino acids Ser-Lys-Leu. A researcher fuses the ER signal peptide to his favorite peroxisomal protein 2 (FPP2) and expresses this fusion protein in cells:



Upon expression, in which cellular compartment will he find the fusion protein? Explain your answer. [15 pts]

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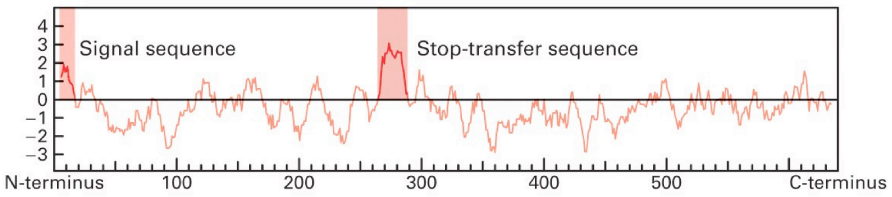
2. The following is a hydrophobicity plot for the human growth hormone receptor:



Use the membrane diagram below to draw your prediction of how this protein is arranged within the ER membrane and the ER lumen. Indicate the amino- and carboxy-terminus of the protein. [6 pts]

CYTOSOL

ER MEMBRANE

ER LUMEN

Design an experiment to test whether your prediction is correct. [9 pts]

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3. Explain how secretory vesicles form at the membrane of the endoplasmic reticulum (ER). [15 pts]

4. VSV-G is a viral protein that travels through the secretory pathway and receives an N-linked complex oligosaccharide. Researchers have identified a temperature-sensitive variant of VSV-G, termed VSV-G^{ts}. At 40°C, VSV-G^{ts} is unable to leave the ER because it is not correctly folded. However, upon temperature shift to 35°C, VSV-G^{ts} folds rapidly and immediately leaves the ER to continue its journey towards the plasma membrane.
   Design an experiment in which you take advantage of the enzyme EndoH to determine the kinetics of the ER to Golgi transport of VSV-G^{ts}. [15 pts]

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5. Statins are a class of widely used hypolipidemic drugs (that include the brands Lipitor and Zocor). Statins function by inhibiting the enzyme HMG-CoA reductase, the rate-limiting enzyme of the mevalonate pathway of cholesterol biosynthesis. Explain why statins lower both the cholesterol and LDL levels in the bloodstream. [15 pts]