

## Exercise 8

### Question 1

Name where the following lipids are produced and which enzymes mentioned in the lecture are required for their transport towards other membranes.

Lipid	Location of synthesis	Transporter proteins
Ceramide		
Cholesterol		
Glycosylceramide		
Phosphoinosited		
Phosphatic acids		
PI4P		
Sphingomyelin		
Triacylglyceride		

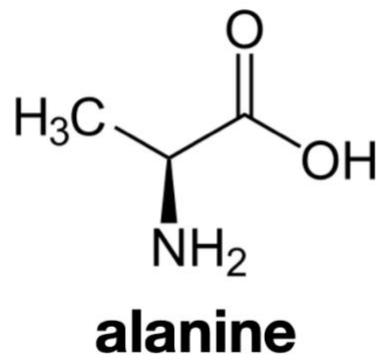
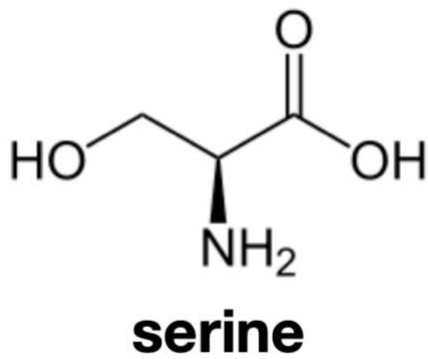
### Question 2

The ceramide transporter CERT is located between the ER and trans golgi membrane and its activity can be inhibited with an inhibitor abbreviated HPA-12.

1. What is the effect on the ceramide levels in the ER and golgi membrane
2. What is the effect of the CERT inhibition on the production of other lipids?
3. Is the lipid composition of other membranes effected by the inhibition of CERT?

### Question 3

In a genetic disease named hereditary sensory and autonomic neuropathy type I SPT subunits are mutated such that they catalyse preferential condensation of palmitoyl-CoA to alanine rather than serine.



1. What is the metabolic outcome of this change in activity?
2. How is this propagated through the sphingolipid synthetic pathway?

### Question 4:

The synthesis of sphingolipids can be blocked with the inhibitors ipoxamycin and fumonsin B1 which bind to the SPT and CerSes respectively.

1. For each inhibitor, which sphingolipid metabolites do you expect to be deprived and accumulated?
2. What treatment will lead to a faster disappearance of the cellular sphingomyelin pool?

Question 5:

OSBP1 is an important cholesterol/ PtdIns(4)*P* transfer protein at the ER-trans Golgi MCS. predict the effects of OSBP1 inhibition on:

1. phosphoinositide levels at the ER and Golgi
2. localisation of CERT1 and FAPP2
3. sphingolipid metabolism

Question 6

The inhibitor L-690.488 is used in research to study the phosphatidylinositol synthase by inhibiting the enzyme.

1. What step of the PI synthesis synthesis will be inhibited?
2. What is the effect of a reduced PI level on
  - a. Membrane composition and recognition
  - b. Cellular signaling