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Phospholipids

Wednesday, January 16, 2008
10:00 AM

23. How is choline incorporated into phosphatidylcholine?
 - a. Choline kinase: $\text{Choline} + \text{ATP} \rightarrow \text{Phosphocholine} + \text{ADP}$
 - b. CTP-Choline Cytidylyl Transferase: $\text{Phosphocholine} + \text{CTP} \rightarrow \text{CDP-Choline} + \text{Ppi}$
 - i. Rate limiting
 - ii. Point of regulation
 - c. $\text{CDP-Choline} + 1,2 \text{ DAG} \rightarrow \text{Phosphatidylcholine}$
24. What is the immediate precursor for diacylglycerol?
 - a. Phosphatidic acid
 - b. See 18 for synthesis of phosphatidate
25. How is phosphatidic acid synthesized from dihydroxyacetone-P and fatty acids?
 - a. $\text{G3P} + 2 \text{ FA-CoA} \rightarrow \text{phosphatidic acid}$
 - b. See 18c for G3P sources
26. What is the methylation pathway? What phospholipids is synthesized by this pathway?
 - a. $\text{Phosphatidylethanolamine} + 3 \text{ adoMet} \rightarrow \text{Phosphatidylcholine} + 3 \text{ adoHomocysteine}$
 - b. adoMet is from S-adenosyl methionine
27. How is phosphatidylethanolamine synthesized from diacylglycerol and from phosphatidylserine?
 - a. From DAG
 - i. CDP-Ethanolamine Pathway
 - ii. Similar to CDP-Choline pathway
 - b. Phosphatidylserine
 - i. PS Decarboxylase
 - ii. $\text{Phosphatidylserine} \rightarrow \text{CO}_2 + \text{Phosphatidylserine}$
28. How is phosphatidylserine synthesized?
 - a. From phosphatidylethanolamine
 - b. $\text{Phosphatidylethanolamine} + \text{serine transferase} : \text{Phosphatidylethanolamine} + \text{Ser} \rightarrow \text{Phosphatidylserine} + \text{Ethanolamine}$
 - c. W/ PS decarboxylase, forms cycle that can change charge distribution on plasma membranes (ethanolamine is positive, serine is negative)
29. How are phosphatidylinositol and phosphatidyl glycerol synthesized?
 - a. From Phosphatidic Acid + CTP \rightarrow CDP-DAG + Ppi
 - b. $\text{CDP-DAG} + \text{G3P} \rightarrow \text{CMP} + \text{Phosphatidylglycerol-P} \rightarrow \text{Phosphatidylglycerol} + \text{Pi}$
 - c. $\text{CDP-DAG} + \text{Inositol} \rightarrow \text{CMP} + \text{Phosphatidylinositol}$
 - i. Phosphatidylinositol is a major molecule in signal transduction
 - ii. Phosphatidylcholine and phosphatidylethanolamine are the major constituents of plasma membranes
30. What are the actions of phospholipases A₁, A₂, C and D?
 - a. PL-A₁: splits FA₁ off of phospholipid
 - b. PL-A₂: splits FA₂ off of phospholipid
 - c. PL-C
 - i. G-protein coupled (learned it before)
 - ii. Produces diglyceride and phosphoX
 - d. PL-D: splits off phosphatidic acid and X
31. What are the functional significance of these phospholipases?
 - a. PL-A₂
 - i. Adjusts FA composition
 - ii. Can be used to switch groups from unsaturated to saturated (surfactant)
 - b. PL-C: signal transduction
 - i. G-protein coupled receptor activation
 - ii. Takes phosphatidylinositol and makes IP₃ and DAG

- c. PL-D: signal transduction
32. What is the overall composition of pulmonary surfactant? What is the major surface active component? How is it synthesized?
- a. Role of Surfactant
 - i. Produced by type II pneumocytes
 - ii. Alveolar spaces have enormous air/liquid interface
 - iii. Surfactant forms layer at surface and reduces surface tension to prevent alveolar collapse
 - iv. Also allows for larger alveolar spaces
 - v. Contributes to defense mechanism
 - 1) Supports non-specific host defense mechanisms by forming barrier to microorganisms
 - 2) Suppresses activation and proliferation of lymphocytes
 - 3) Augments alveolar macrophage activities
 - b. Surfactant deficiency
 - i. Neonatal RDS: premature birth, babies haven't began to secrete surfactant
 - ii. ARDS: lung injury
 - iii. Can lead to respiratory failure
 - c. Composition
 - i. Isolated from bronchoalveolar lavage fluid
 - ii. Nearly half saturated (dipalmitoyl phosphatidylcholine) fatty acids
 - iii. Number of proteins and other phosphatidylcholine make up rest
 - d. Synthesis of dipalmitoyl phosphatidylcholine
 - i. CDP-choline pathway: dipalmitoyl diglyceride + CDP-choline
 - ii. Using PL-A2 to replace unsaturated FA on C2 w/ palmitate