LIPOPROTEIN METABOLISM

Problem

What are lipids?

If so, how are these water insoluble molecules transported from one tissue to other through an aqueous environment?

Mark the hydrophobic and hydrophilic parts on these molecules

Phospholipid

Proteins have both hydrophobic and hydrophilic regions

Composition of aminoacids

Proteins are absolutely essential for forming the LP particles

Lipoproteins

Core of TG and CE
Surface of phospholipids and some cholesterol
Apolipoproteins (regulators of LP metabolism)
CM, VLDL, IDL, LDL, HDL

Lipid metabolism occurs in three major areas

Intestine

Liver

Extrahepatic tissues (Muscle and adipose tissue)

Enzymatic hydrolysis of TAG yields fatty acids and diacylglycerol, monoacylglycerol and free glycerol

Chylomicron assembly

Chylomicron assembly

Assembled in enterocyte Golgi/ER

Apolipoprotein (Apo) B organizes assembly

B48

Requires

Phospholipids

for surface

Chylomicron Assembly

2 forms of apo B

- B100, large- liver
- B48, smaller – intestine

Picks up apo A,C and E in plasma

TG composition closely resembles dietary intake

Chylomicrons are released from the intestine into the *lymphatics*, bypassing the liver

Questions

What are the lipids carried by CM?

Where is CM formed?

What is the source for lipids in CM?

How does the CM release FFA?

What is the fate of the FFA and Glycerol?

Where is the LPL found?

What are the components of Remnant CM?

VLDL Assembly

Endogenous Lipid Transport

This animation shows how VLDL are metabolised once they enter the circulation from the liver

LPL "Metabolic Gatekeeper"?

LPL deficiency (chylomicronaemia)

Massive accumulation of chylomicron -TG in plasma

Cannot clear TG normally

Normal fat storage and body weight

???!?!?

Regulation of Lipoprotein Lipase

QUESTIONS

Where is VLDL formed?

What are the lipids Carried by VLDL?

Which lipid is delivered by VLDL?

What is the mechanism of FFA release from VLDL?

What is the fate of Remnant VLDL?

What are the lipids present in excess when VLDL becomes VLDLR?

Nobel Prize 1985
Endogenous Lipid Transport

Function of LDL receptor

Endocytosis of LDL and other LP
Release free cholesterol into liver

- Incorporate into plasma membrane
- Inhibit new LDL receptors
- Inhibit cholesterol synthesis
- Promote ACAT activity (FC -> CE)
- Regulated by SREBP
  monitors free cholesterol

Cholesterol uptake down regulates the cells own

production of cholesterol and down regulates LDL receptor synthesis

Questions

How is LDL formed?
What is IDL?
What is HTGL?
How is CE transferred from HDL to IDL?

What is CETP?

HYPERLIPIDEMIA

Effect of Exercise

Increases LPL activity in muscle.

Reduces TGL from the particle.

Reduction in weight

Increases HDL

Effect of diet
Vegetarian diet – Cholesterol intake less
Reduced Carbohydrate – VLDL TG Reduced
Reduced Fat – Reduces CM TG
Unsaturated fats (Mono and Poly)- Reduction in Plasma cholesterol

Fiber – decreases cholesterol absorption

Postprandial Changes in Plasma Lipid Metabolism