

## Lipid and Cholesterol Transport

- I. Fatty Acids: from adipose tissue to other tissues
  - A. Fatty Acids released from adipose tissue (hormone sensitive lipase)
  - B. Travel in the plasma bound to albumin
  - C. Liver
    1. Oxidation for energy
    2. ketone body formation
  - D. skeletal Muscle
    1. Oxidation for energy
  
- II. Lipoproteins
  - A. Chylomicrons
  - B. Very Low Density Lipoproteins (VLDL)
  - C. Intermediate Density Lipoproteins (IDL)
  - D. Low Density Lipoproteins (LDL)
  - E. High Density Lipoproteins (HDL)
  - F. Remnants

### III. Dietary lipids: from intestine to other tissues

#### A. Chylomicron Metabolism

##### 1. Chylomicron Formation

###### a. Nascent chylomicron apoproteins

###### i. Apo B-48

(i) Necessary for secretion

###### ii. Apo A-IV

(i) Amount secreted increases with the amount of fat in the diet

(ii) Circulating signal for anorectic response to fat meal?

(iii) May inhibit gastric acid secretion and gastric emptying

##### 2. Chylomicron catabolism

###### a. Lipoprotein Lipase

###### i. Adipose

(i) Insulin dependent

(ii) Down regulated during fasting

###### ii. Muscle (Cardiac and Skeletal)

(i) Insulin independent

(ii) Activity maintained during fasting

(iii) Lower  $K_m$  (higher affinity) for substrate than  
adipose LPL

b. Apo C-II

- i. Required by Lipoprotein Lipase
- ii. Preferentially moves to new chylomicrons and VLDL
- iii. As hydrolysis of triacylglycerols occurs, apo C-II  
migrates from the surface
- iv. After about 80 % hydrolysis, there is not enough apo  
C-II present to sustain the reaction with LPL

c. Remnant Uptake

- i. Apo B/E Receptor
  - (i) apo B-100
  - (ii) Apo E

IV. Endogenously synthesized lipids: from liver to other tissues

A. VLDL metabolism

1. Formation

- a. Liver
- b. Apo B-100

2. Hydrolysis by LPL

3. IDL Uptake

#### 4. LDL formation

- a. Hepatic lipase

#### B. LDL metabolism

##### 1. Receptor mediated uptake

- a. HMG CoA Reductase

- b. ACAT

##### 2. Scavenger receptor

#### V. Reverse transport of cholesterol from extrahepatic tissues to the liver - HDL metabolism

##### A. Receptors

1. SRB1: cholesterol ester
2. Apo B/E: apo E containing HDL

##### B. Enzymes

##### 1. LCAT (PCAT):

- a. phosphatidyl choline + Cholesterol → Esterified Cholesterol

##### 2. Hepatic Lipase: Hydrolysis of triacylglycerol

##### 3. CETP: Exchanges esterified cholesterol for triacylglycerol

##### 4. PLTP: Transfer of phospholipids to and from HDL

##### C. Apoproteins

1. AI

a. Promotes the desorption of free cholesterol from membranes

b. Activates LCAT

2. Reservoir for apo CII and apo E

VI. Fate of Cholesterol

VII. Problem 1

A. Type IIa

B. Familial hypercholesterolemia

C. Elevated cholesterol levels

D. Usually normal triglyceride levels

E. LDL is elevated

F. Most commonly a defect in LDL receptor

VIII. Problem 2

A. Type I and Type V

B. Triglyceride levels elevated

C. Type I: chylomicrons elevated

D. Type V: chylomicrons and VLDL elevated

E. Inherited deficiency of LPL or Apo C-II

IX. Problem 3

A. Type III

B. Dysbetalipoproteinemia

- C. Elevation of chylomicron and VLDL remnants
- D. Defect in, or lack of apo E results in inhibition of remnant removal  
from plasma

X. Problem 4

- A. Type IV
- B. Increased flux of apo B-100
- C. Increased numbers of VLDL particles
- D. Presentation depends on the ability to catabolize VLDL
  - 1. results in high LDL levels
  - 2. results in high VLDL levels