

# Metabolic basis for dyslipidaemia in Type 2 Diabetes

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# Summary

- Overview of lipid metabolism
- Diabetic dyslipidaemia and insulin action
- Aspects of diabetic dyslipidaemia independent of insulin action

# Lipid abnormalities in Type 2 diabetes

- High triglyceride concentrations, particularly postprandially (postprandial lipaemia)

↑ TG

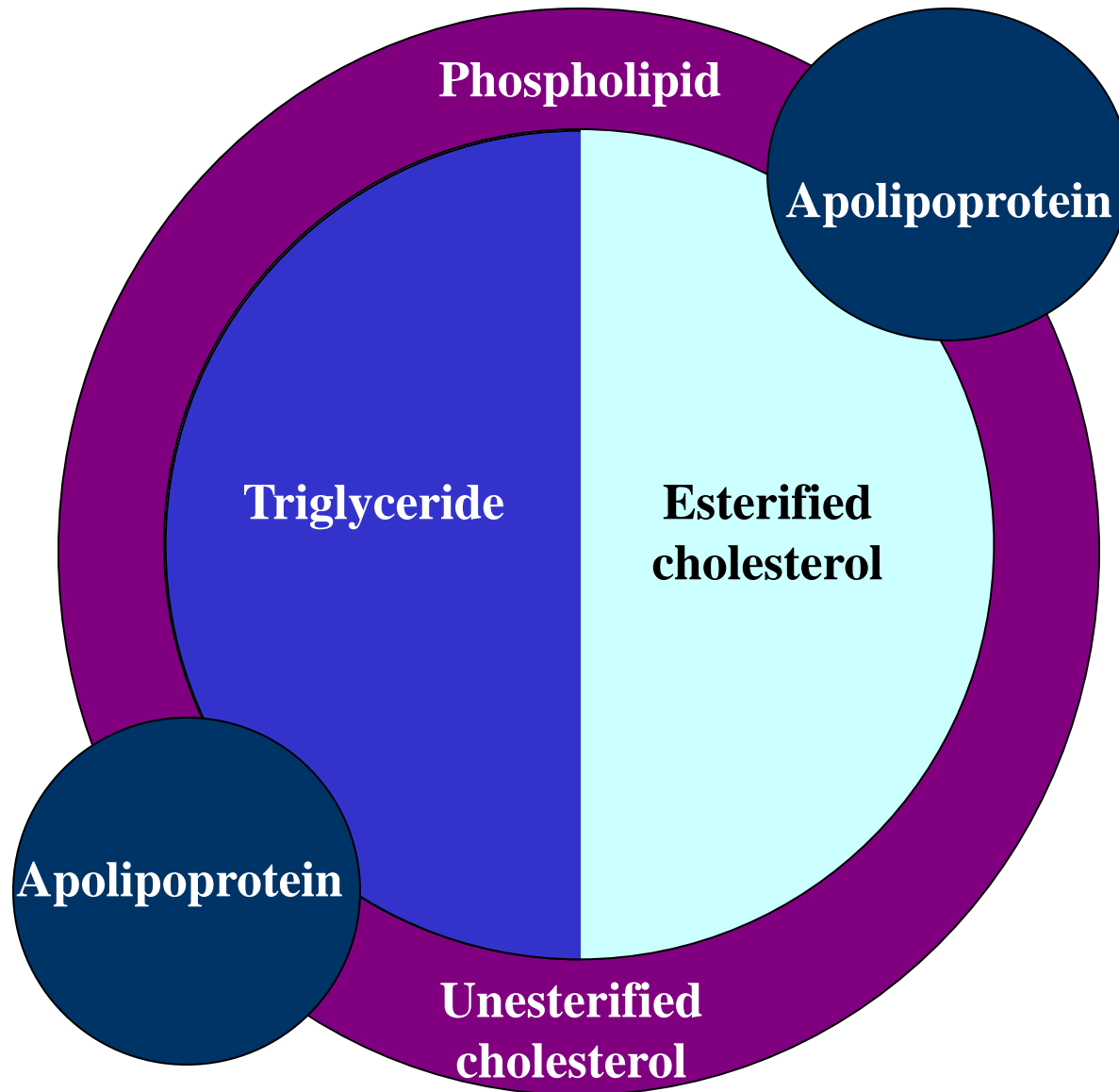
- Low HDL cholesterol concentrations

↓ HDL chol

- Normal total and LDL cholesterol concentrations, but small dense LDL particles

→ Total + LDL chol





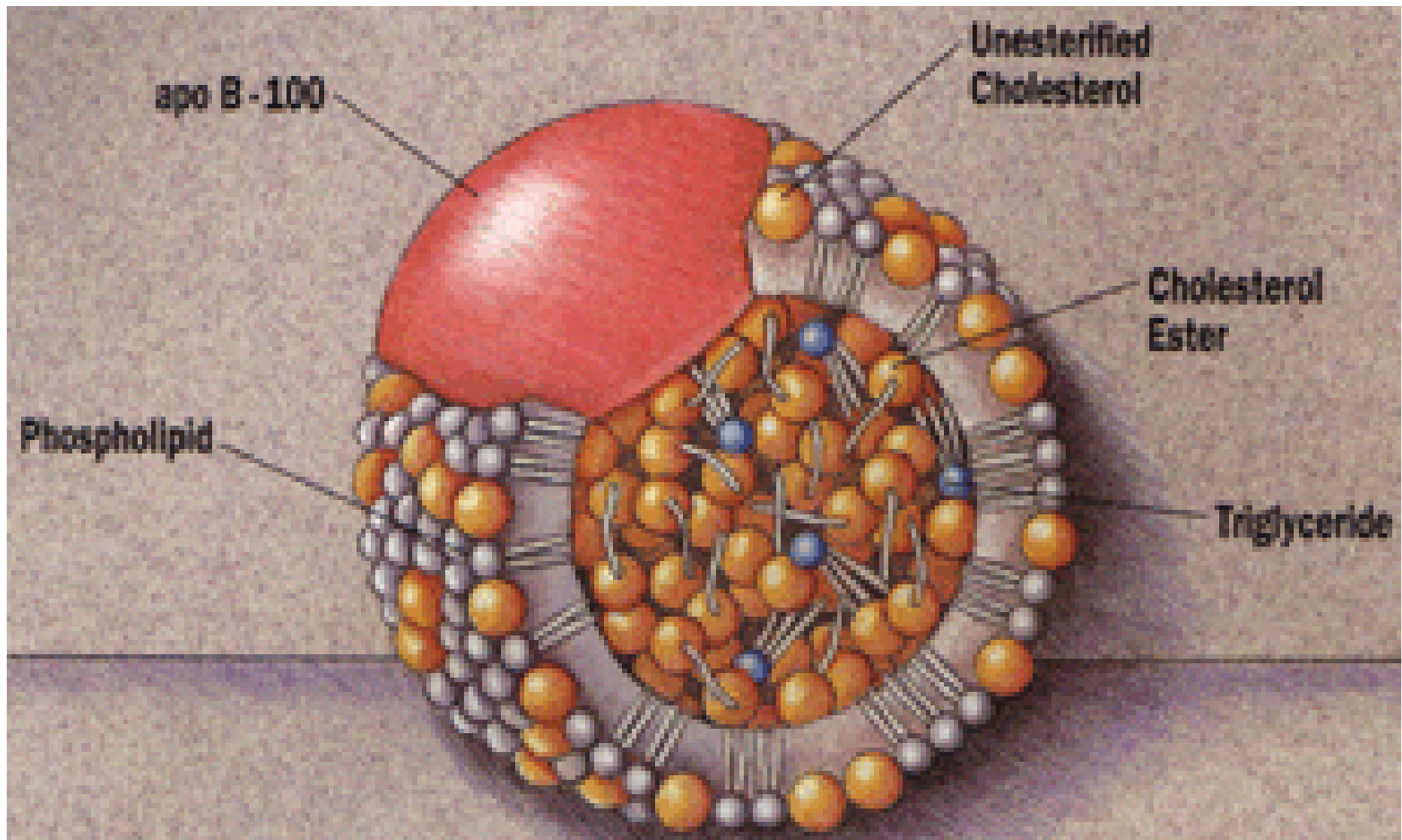
apo B - 100

Unesterified  
Cholesterol

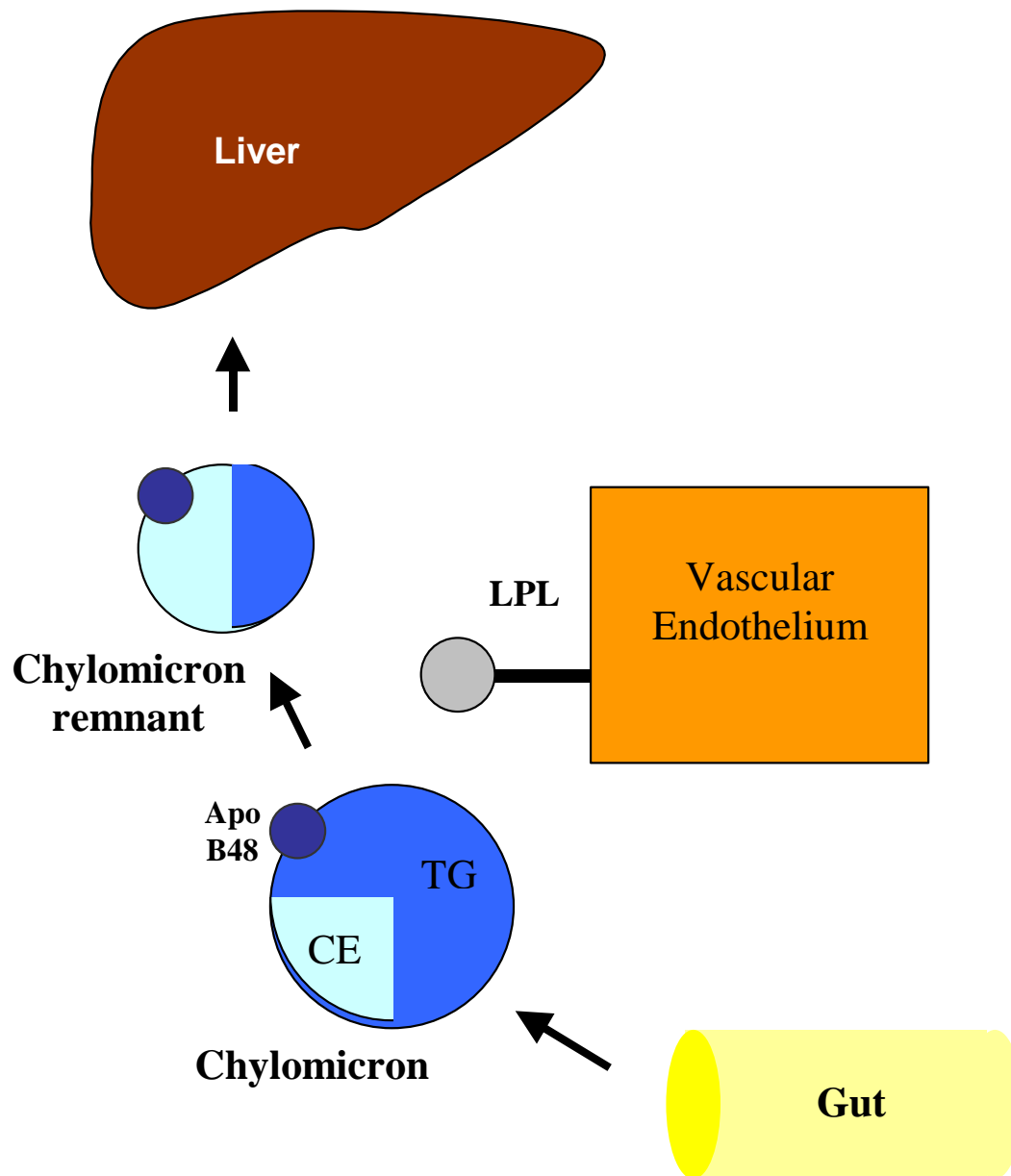
Cholesterol  
Ester

Phospholipid

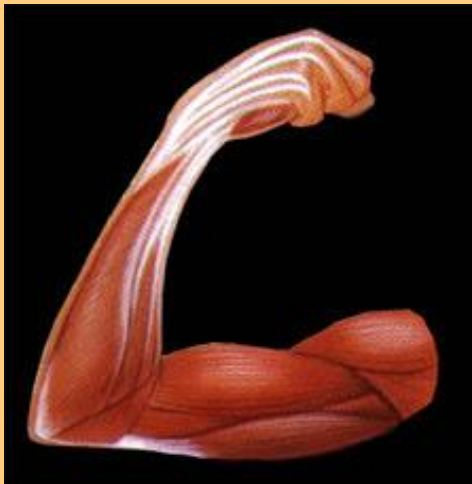
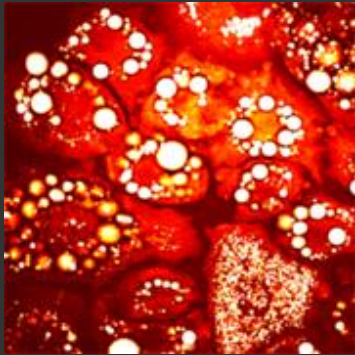
Triglyceride

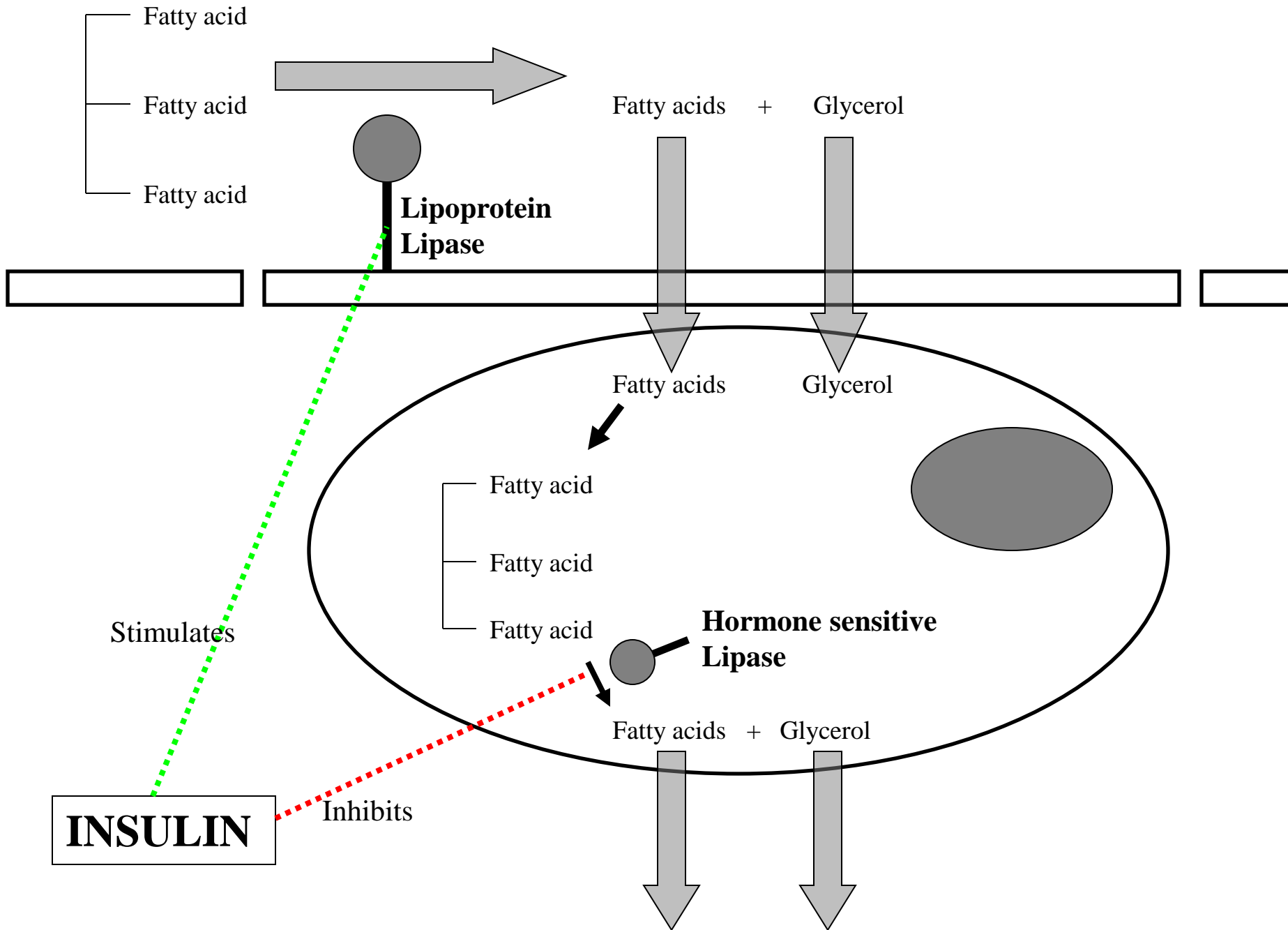


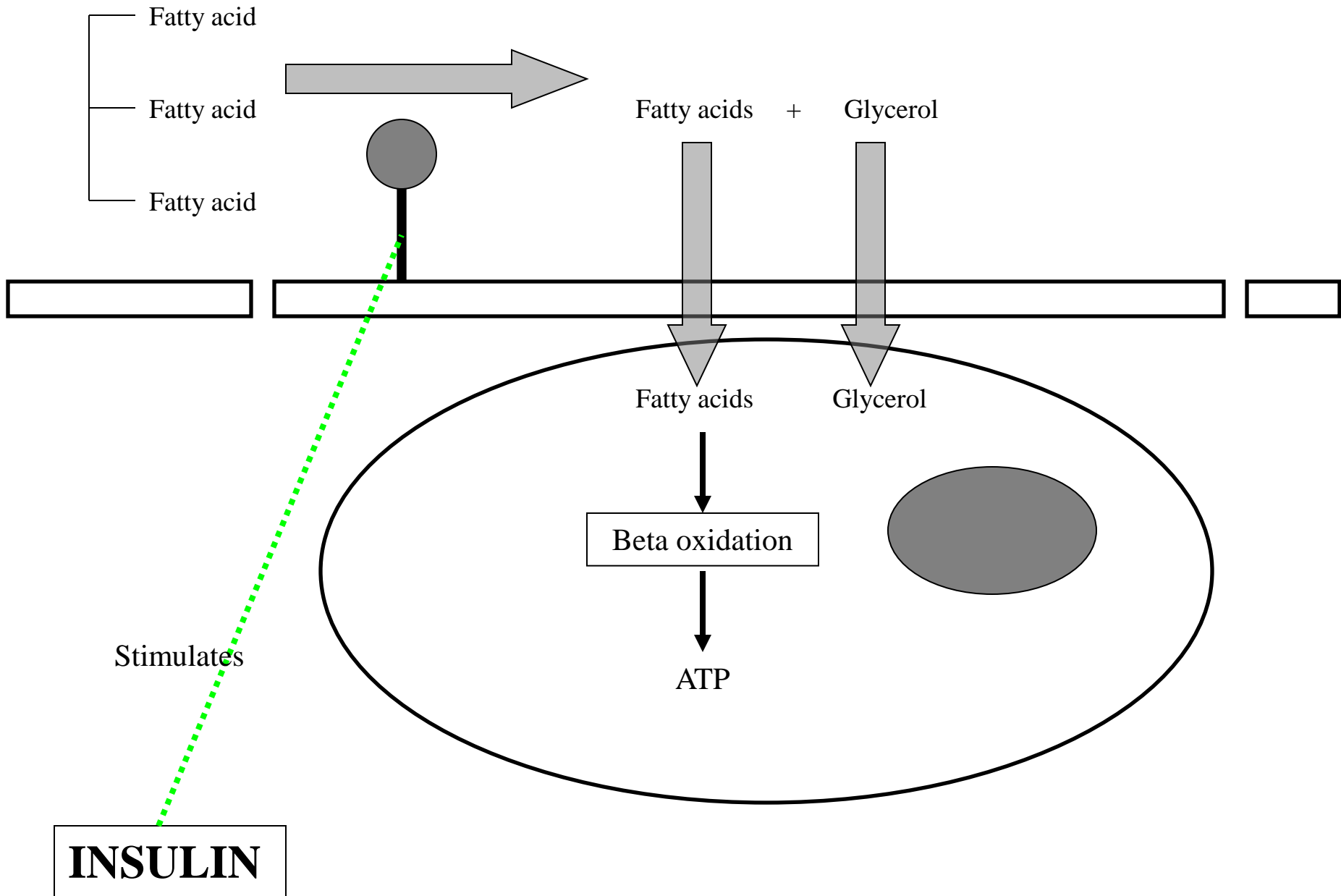
# **Triglyceride metabolism in the post-prandial state**

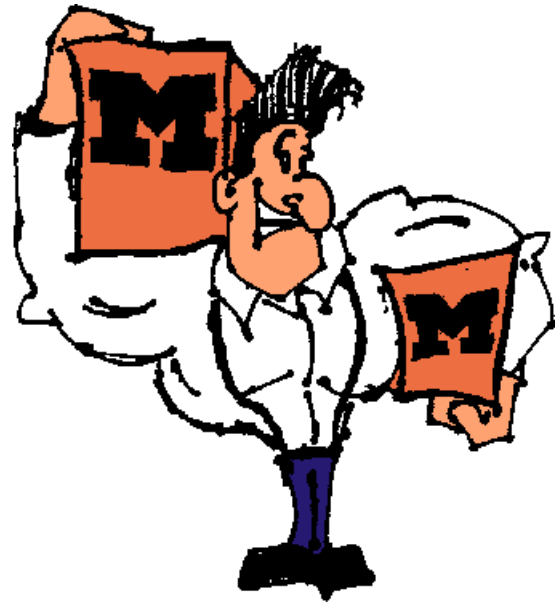
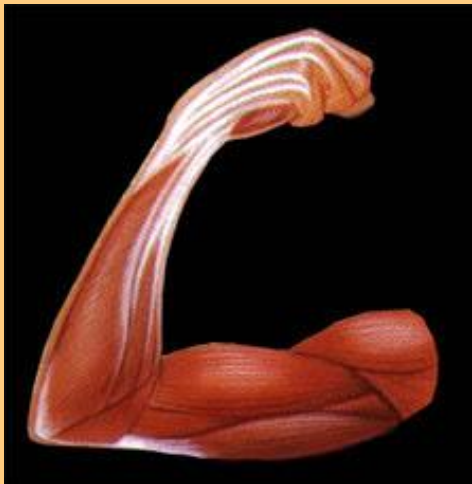
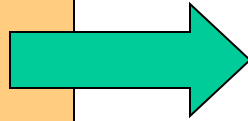
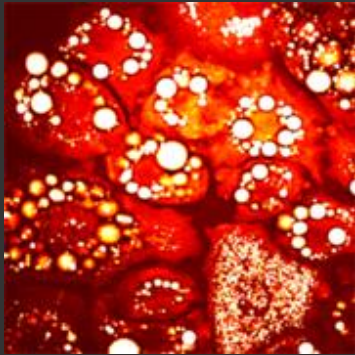


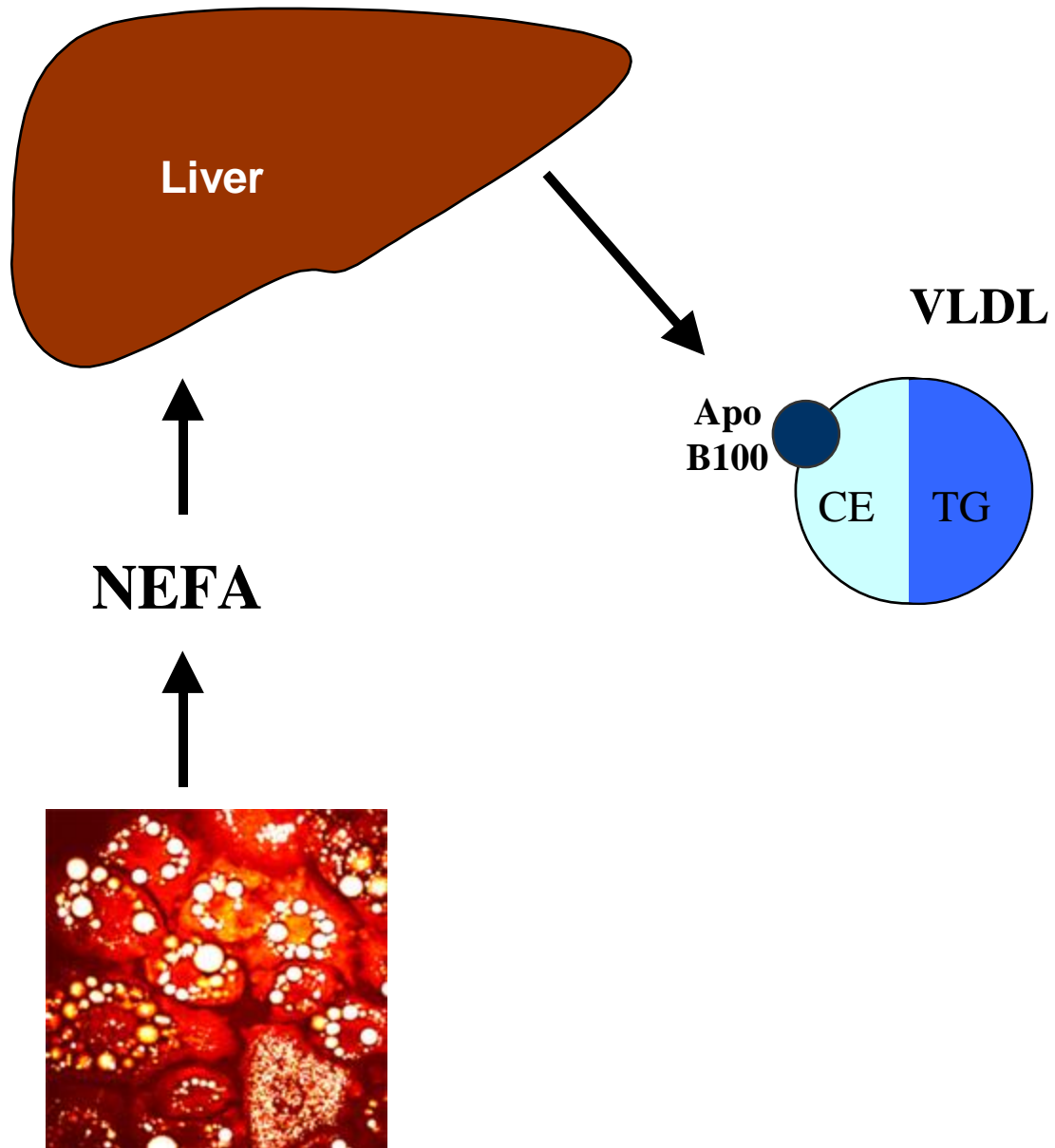


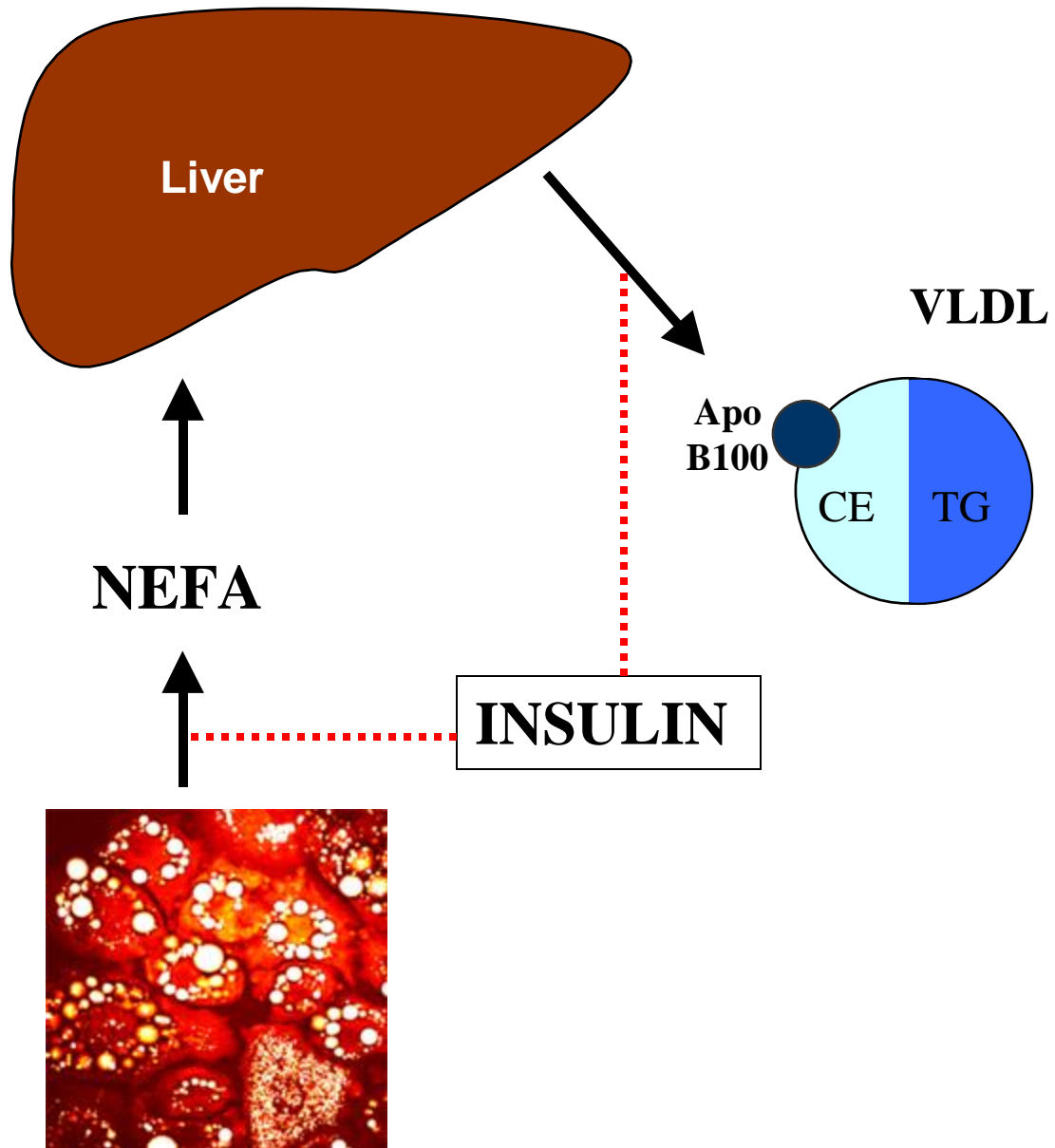








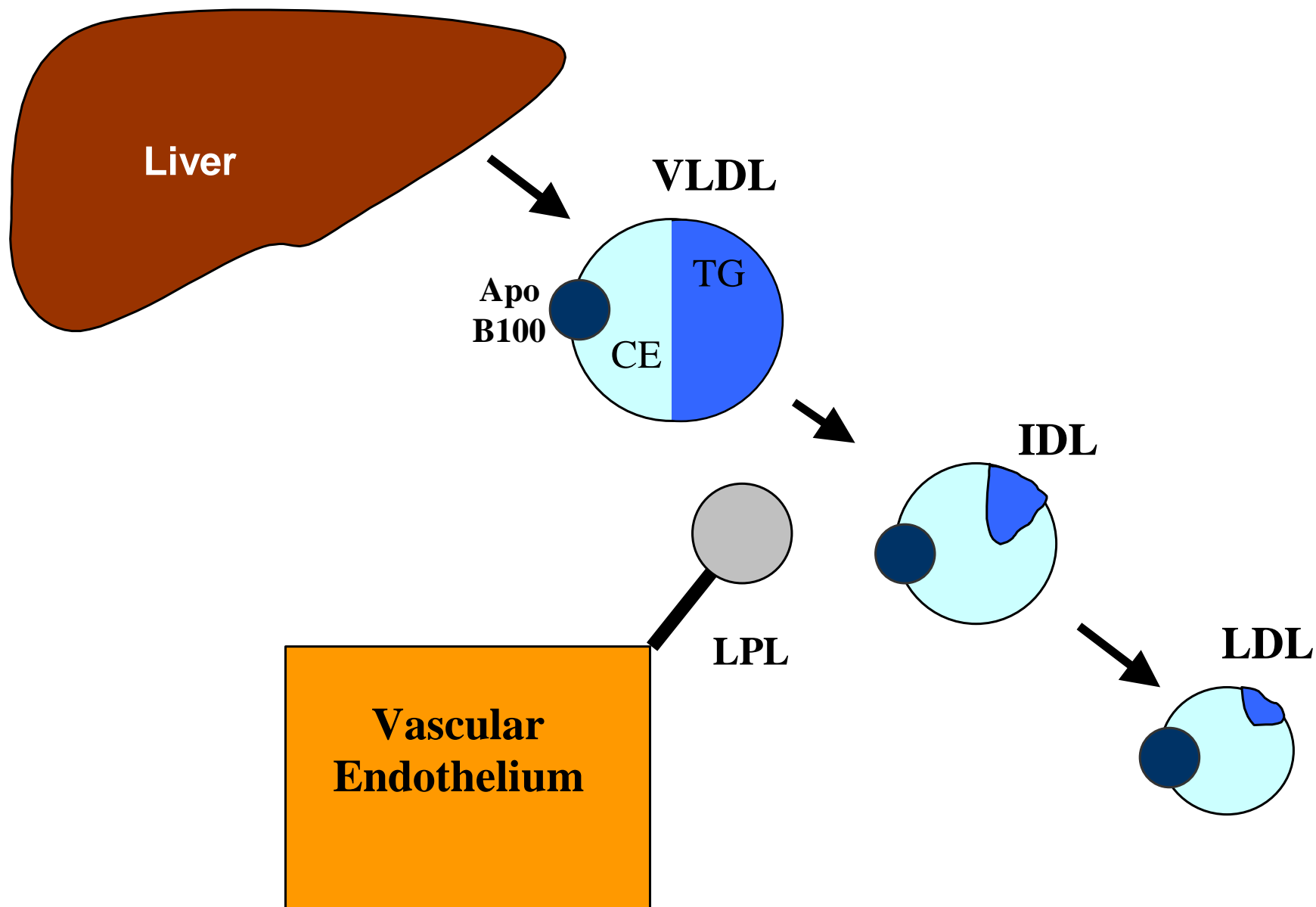




**Triglyceride metabolism in  
the fasting state**

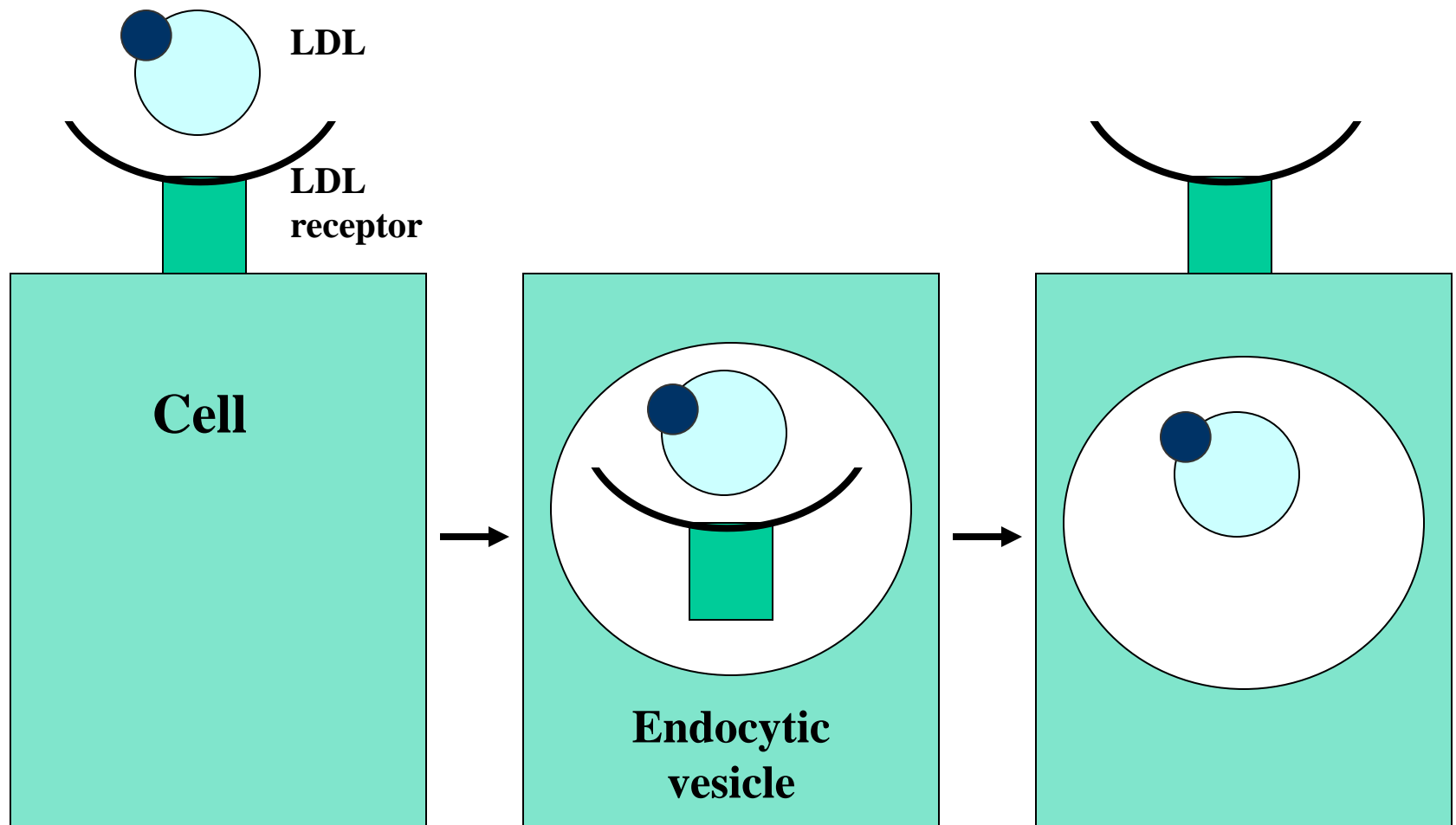
**and**

**Forward cholesterol  
transport**

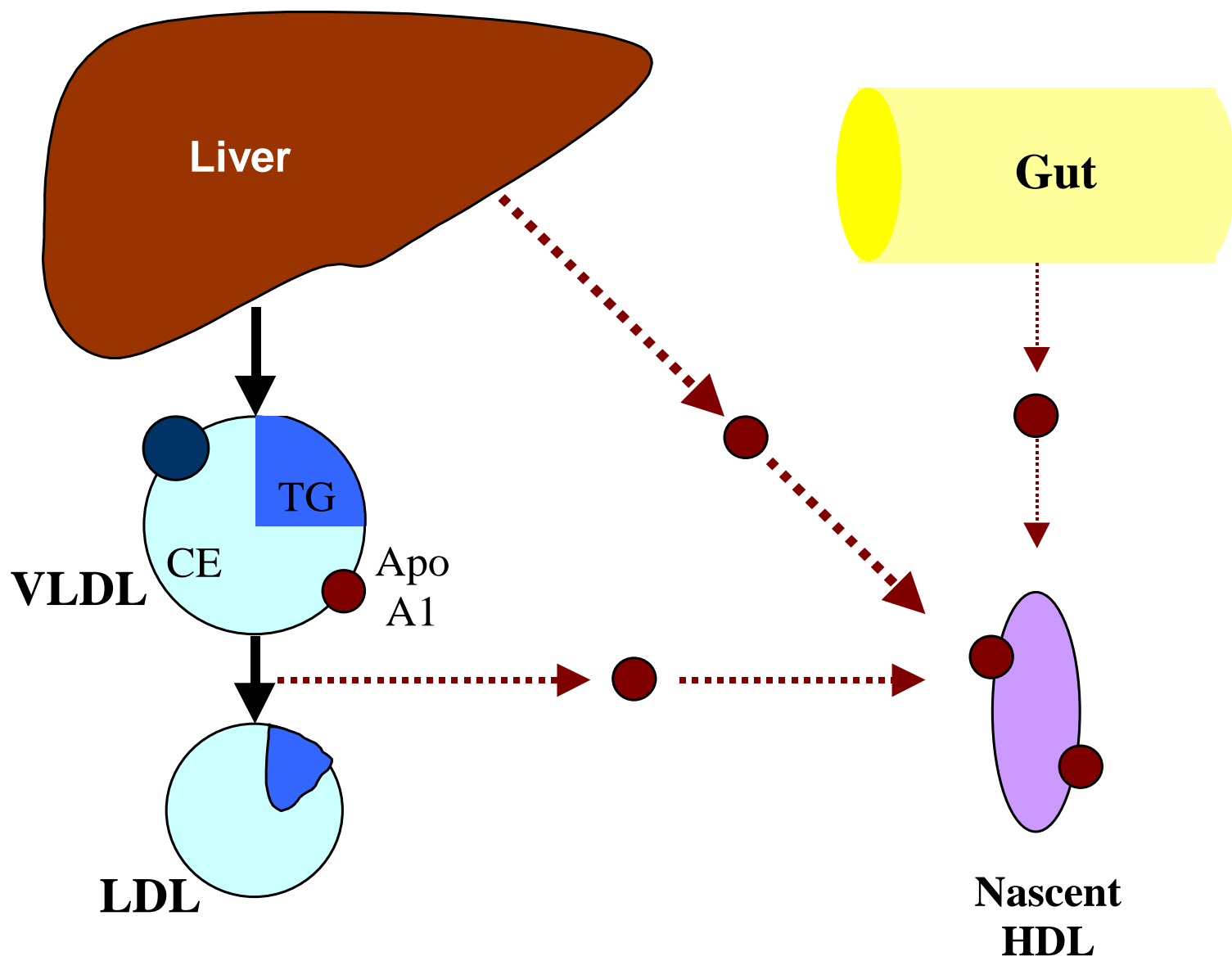


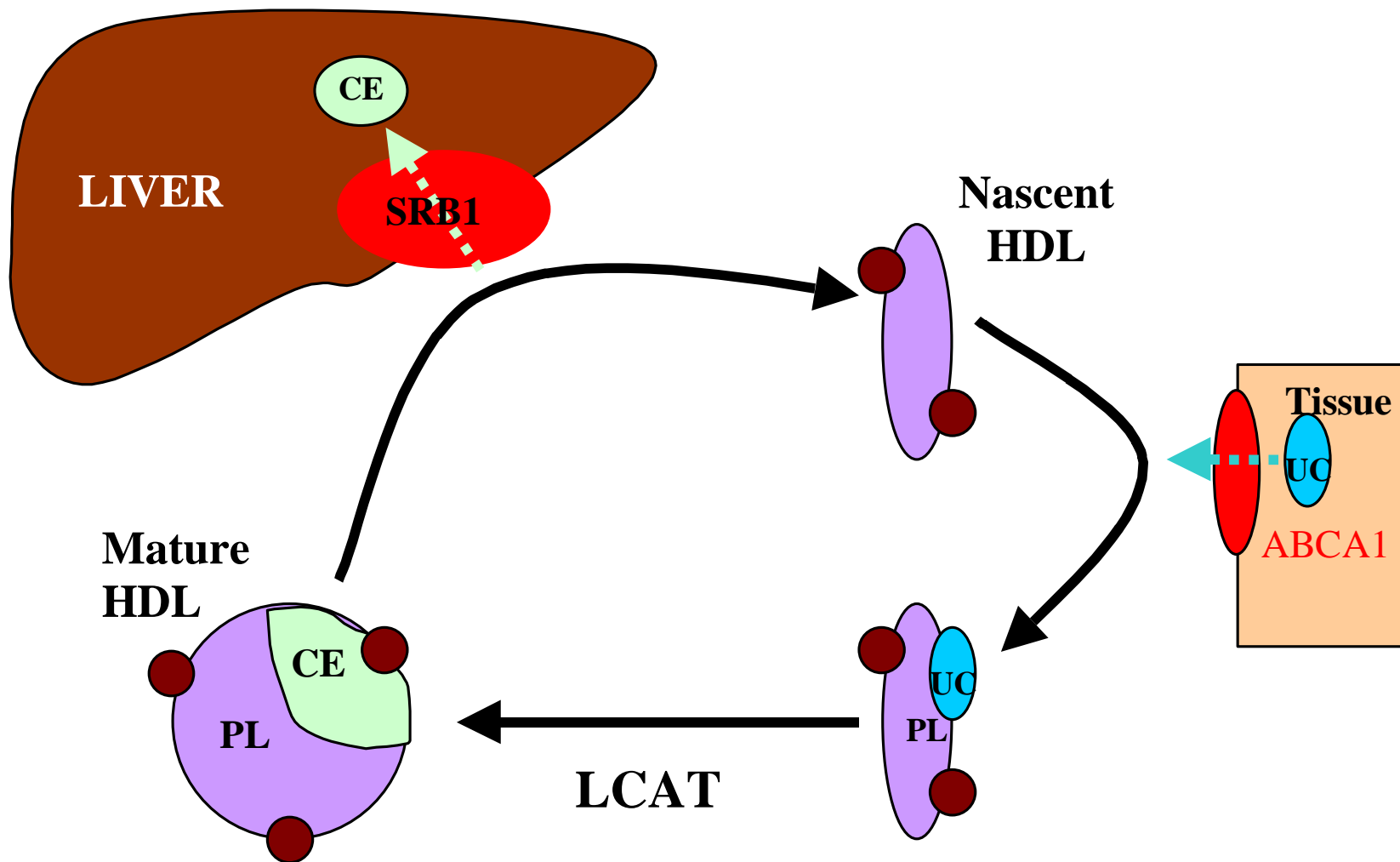


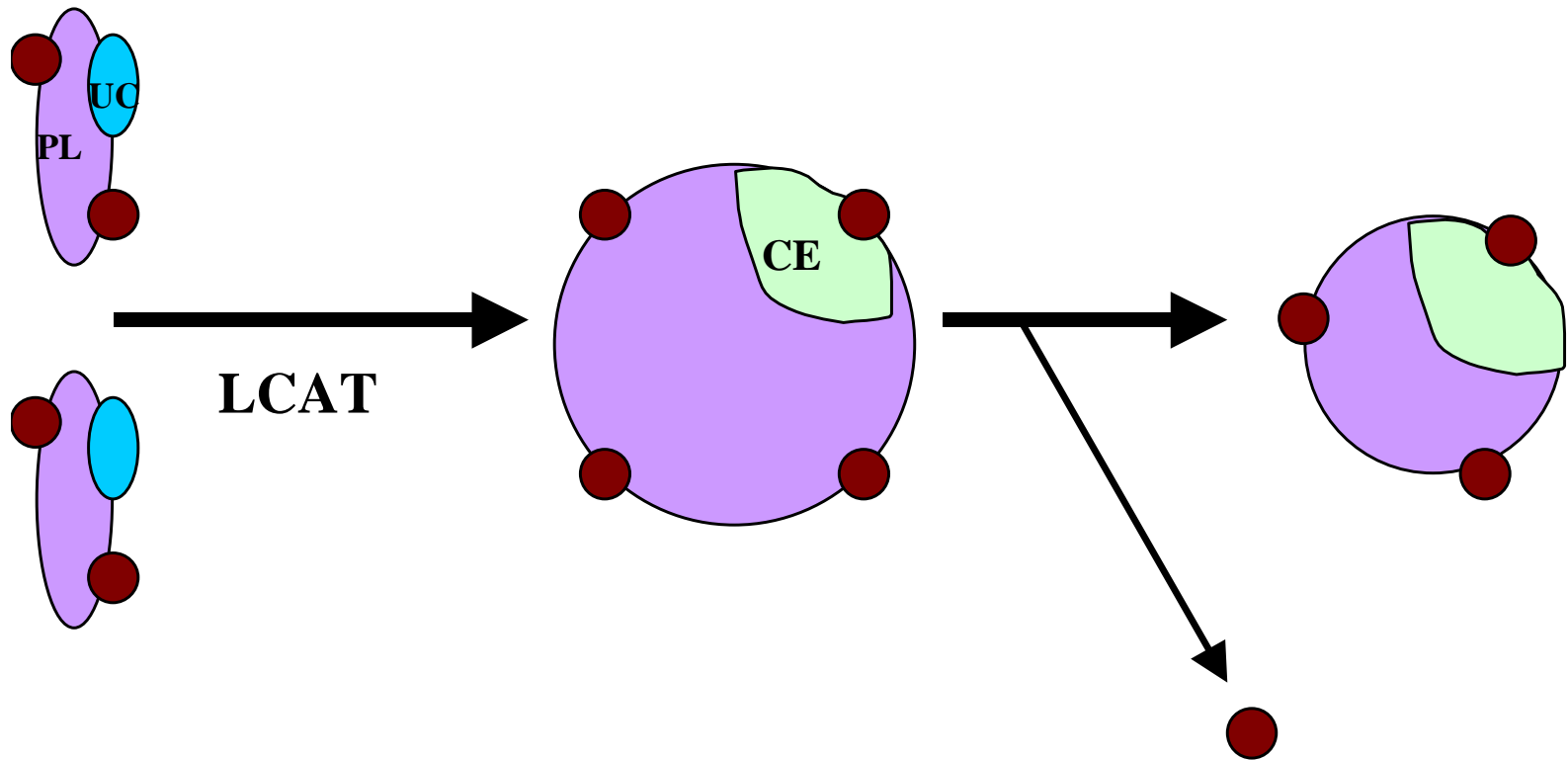
# The LDL receptor and LDL uptake



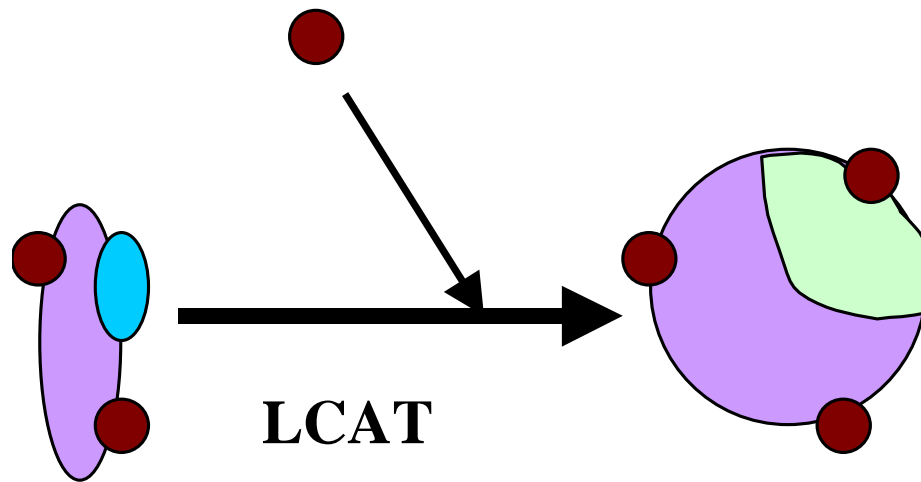
# **Reverse cholesterol transport**



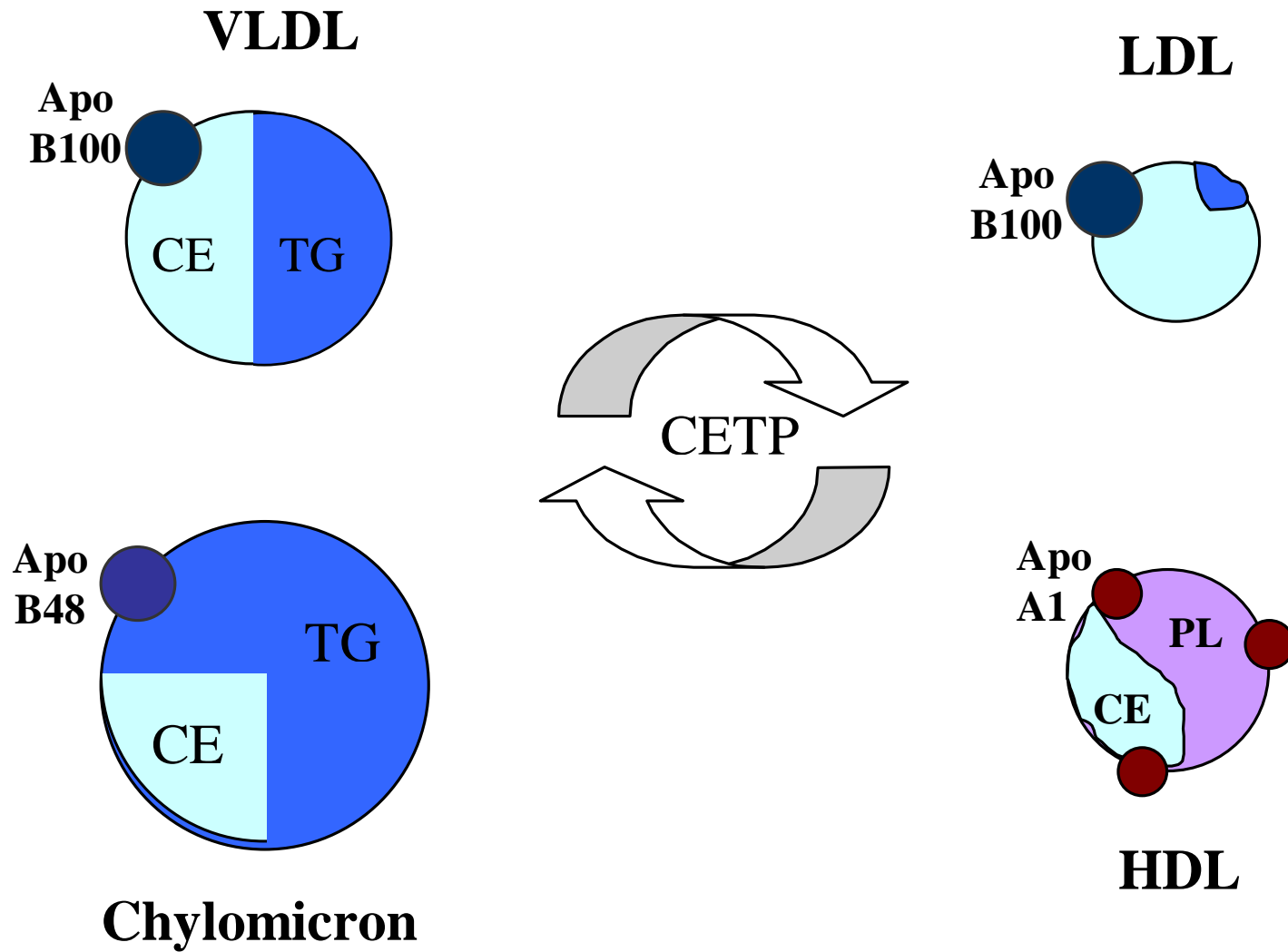




**Lecithin:cholesterol acyltransferase**



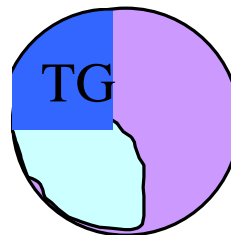
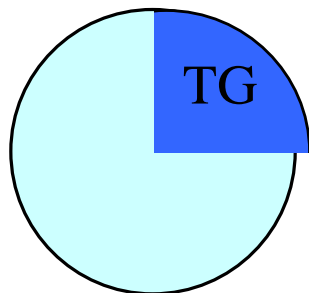
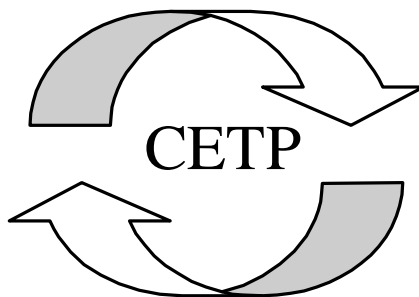
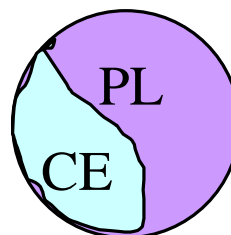
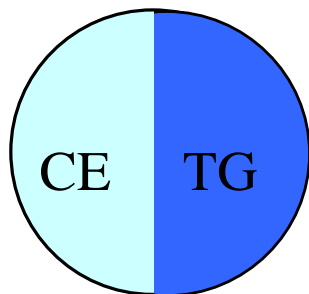
**Lecithin:cholesterol acyltransferase**



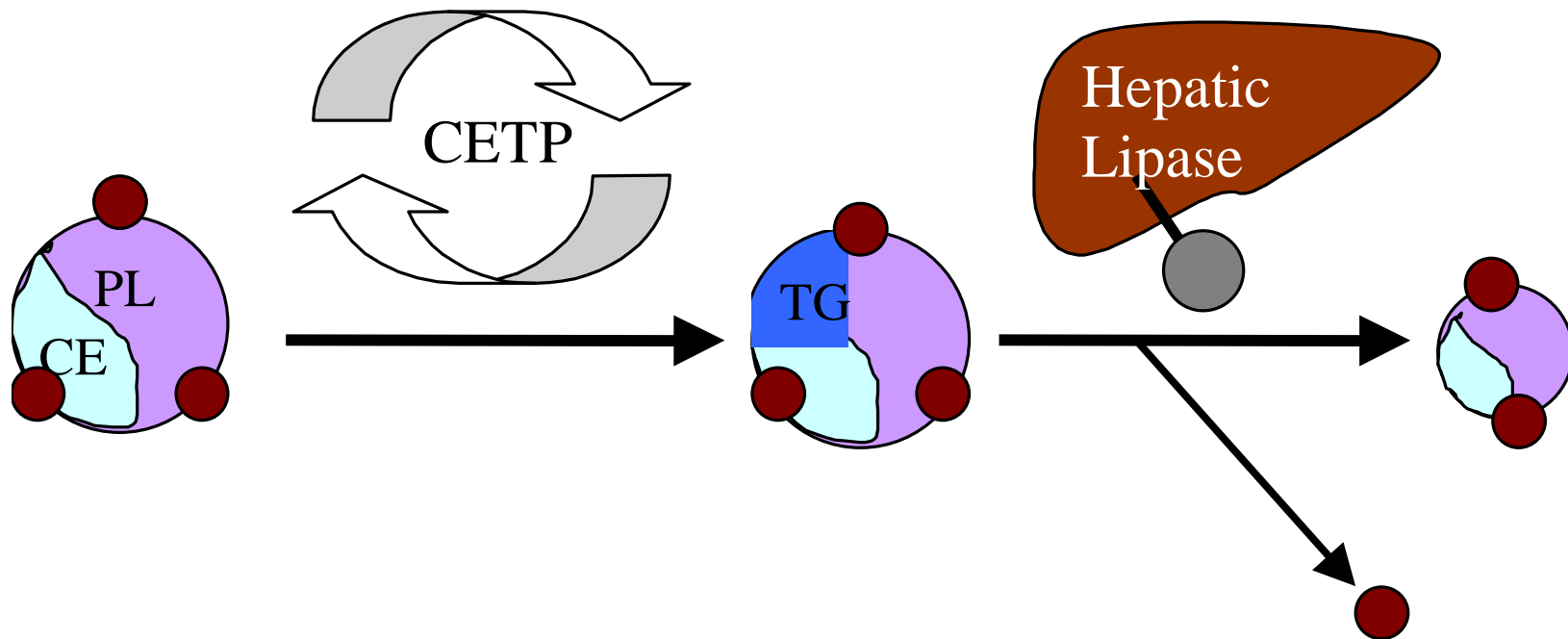
# Cholesterol ester transfer protein

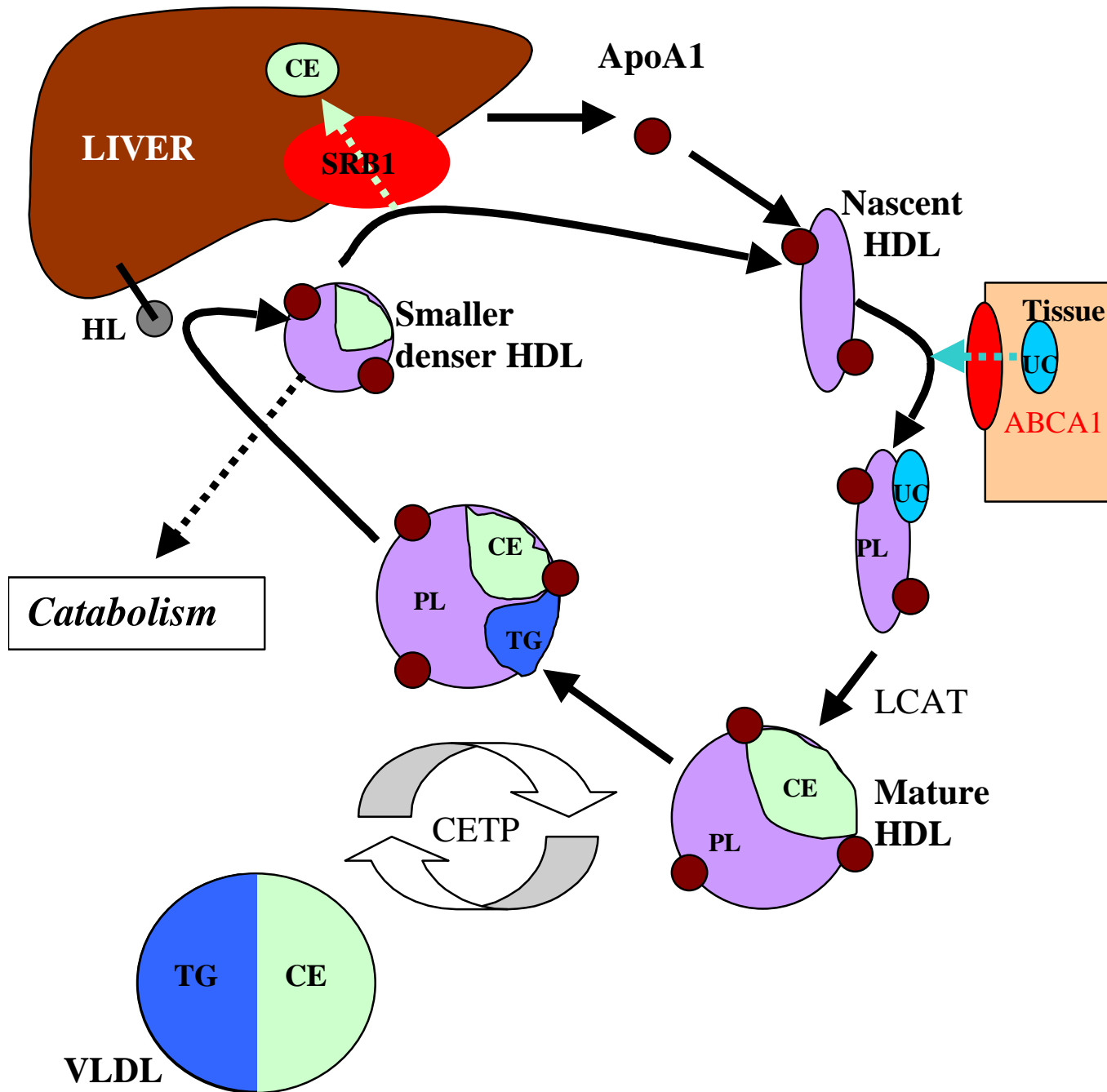
**VLDL**

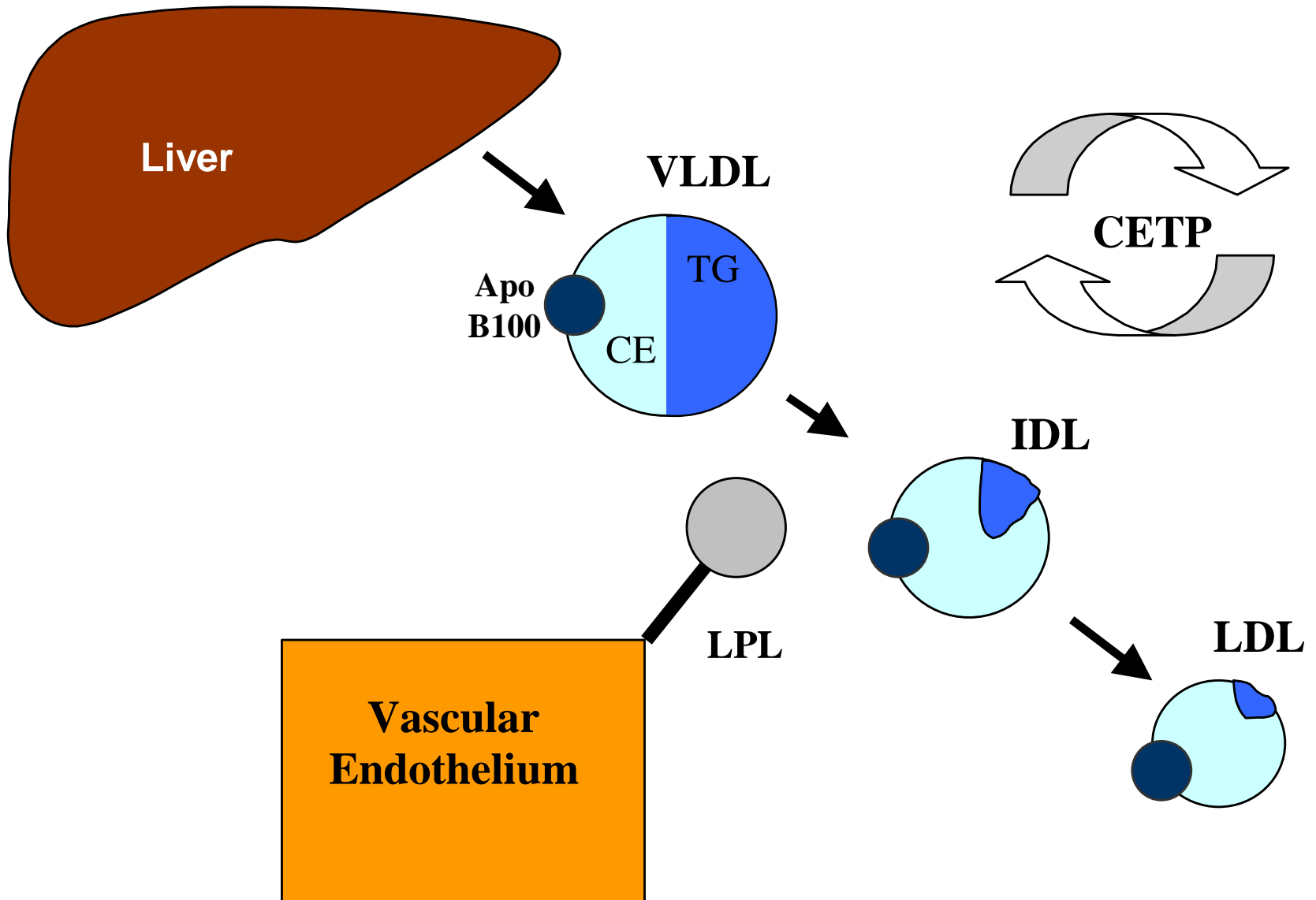
**HDL**

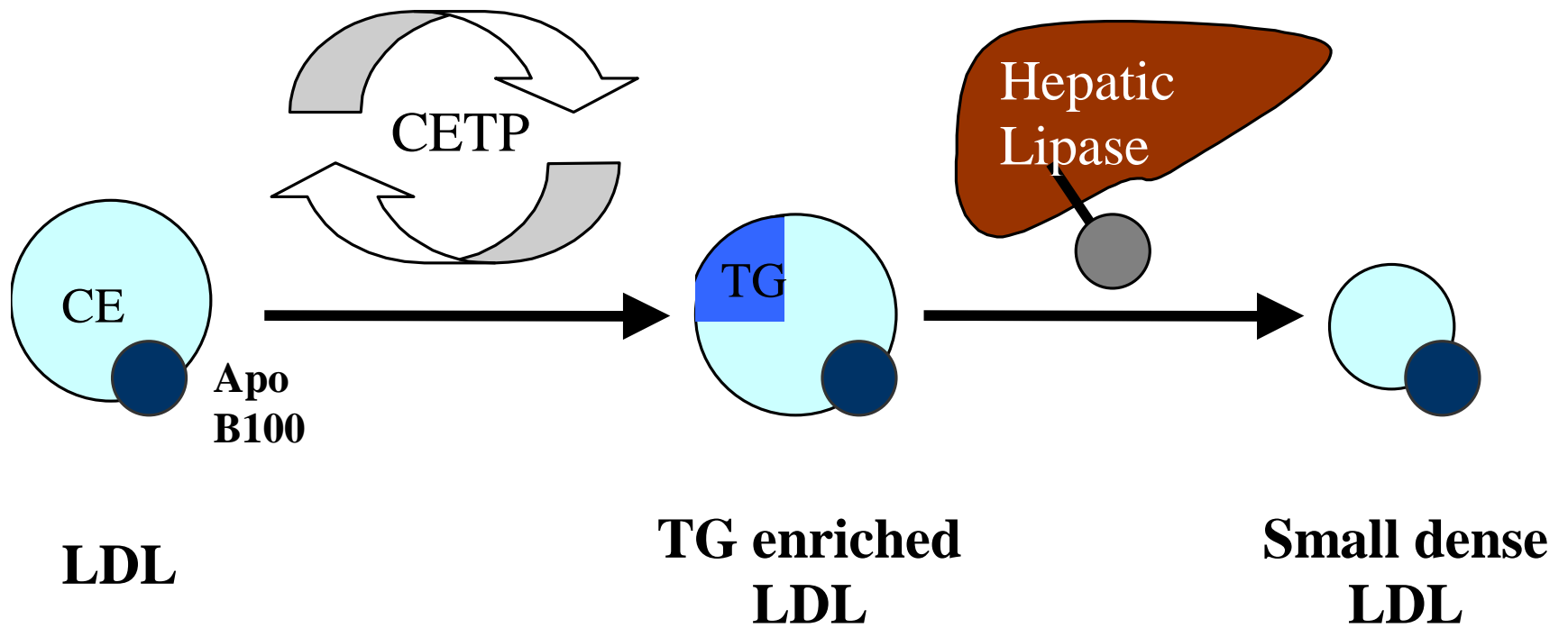












# Lipid abnormalities in Type 2 diabetes

- High triglyceride concentrations, particularly postprandially (postprandial lipaemia)

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# Reduced insulin action

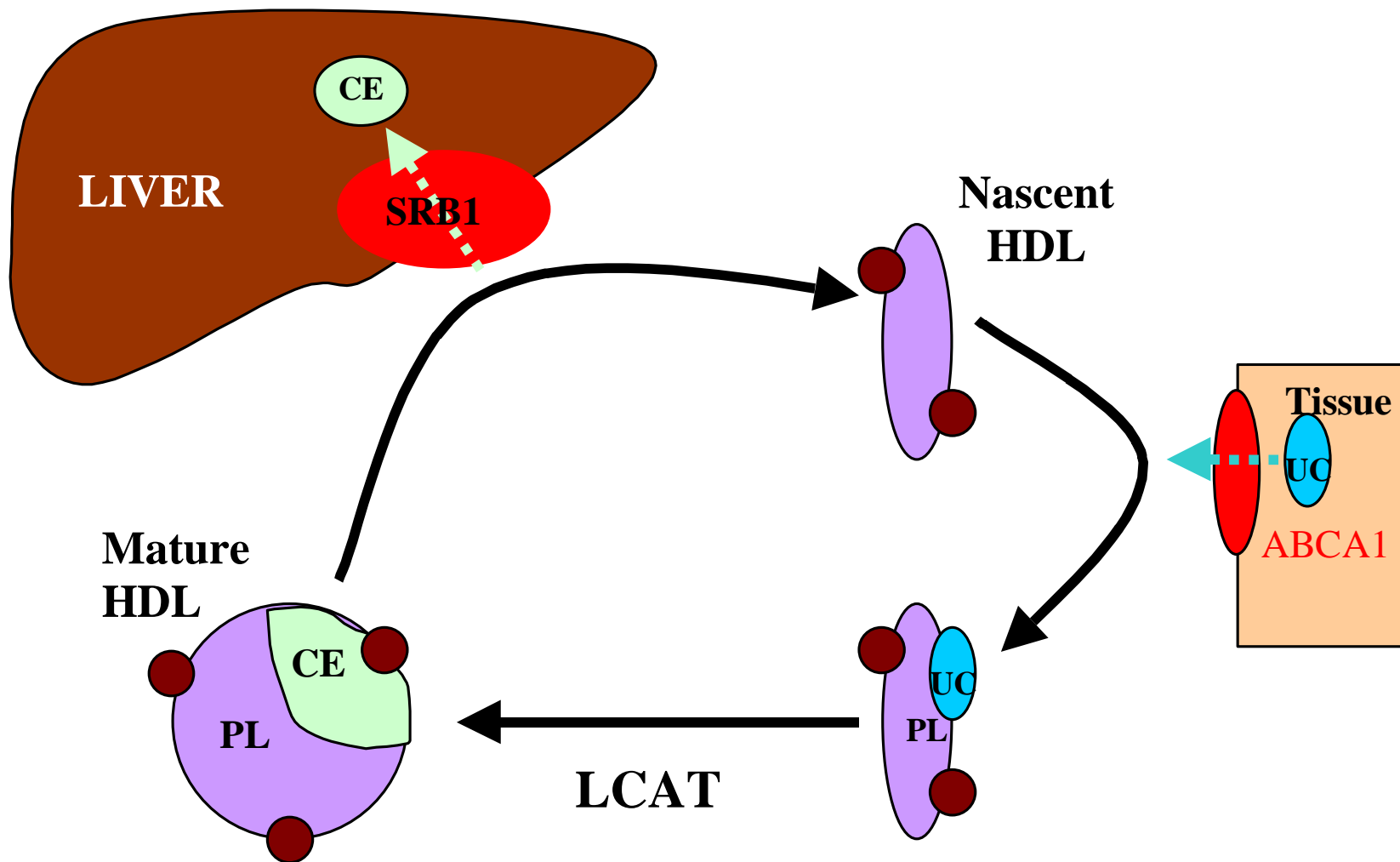
## Insulin and lipid metabolism

- Hormone sensitive lipase - *inhibitory*
- Hepatic VLDL production - *inhibitory*
- Lipoprotein lipase - *stimulatory*

## Insulin resistance results in hypertriglyceridaemia

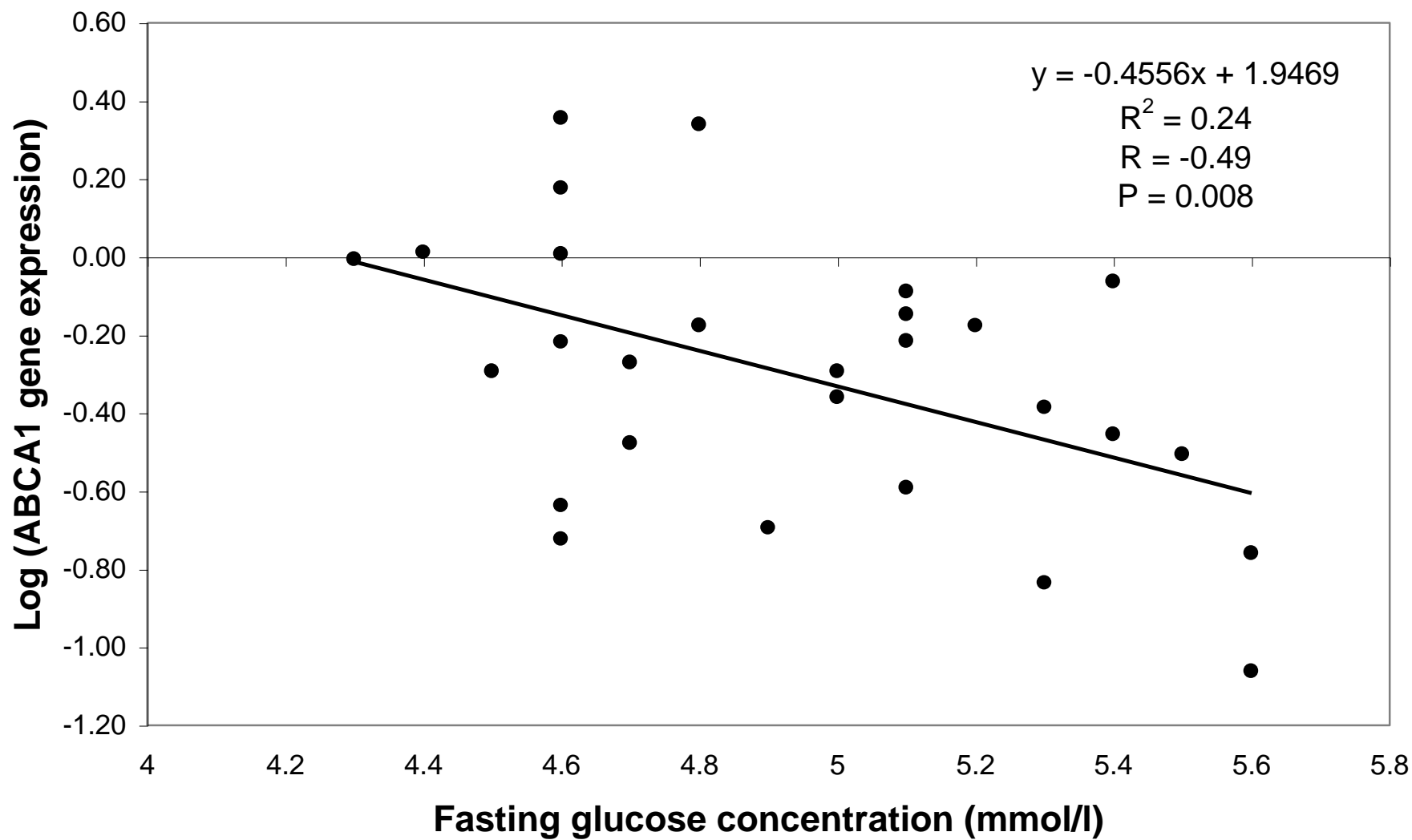
- CETP - *stimulatory*
- Hepatic lipase - *stimulatory*

**Lipid abnormalities possibly not  
associated with reduced insulin  
action**



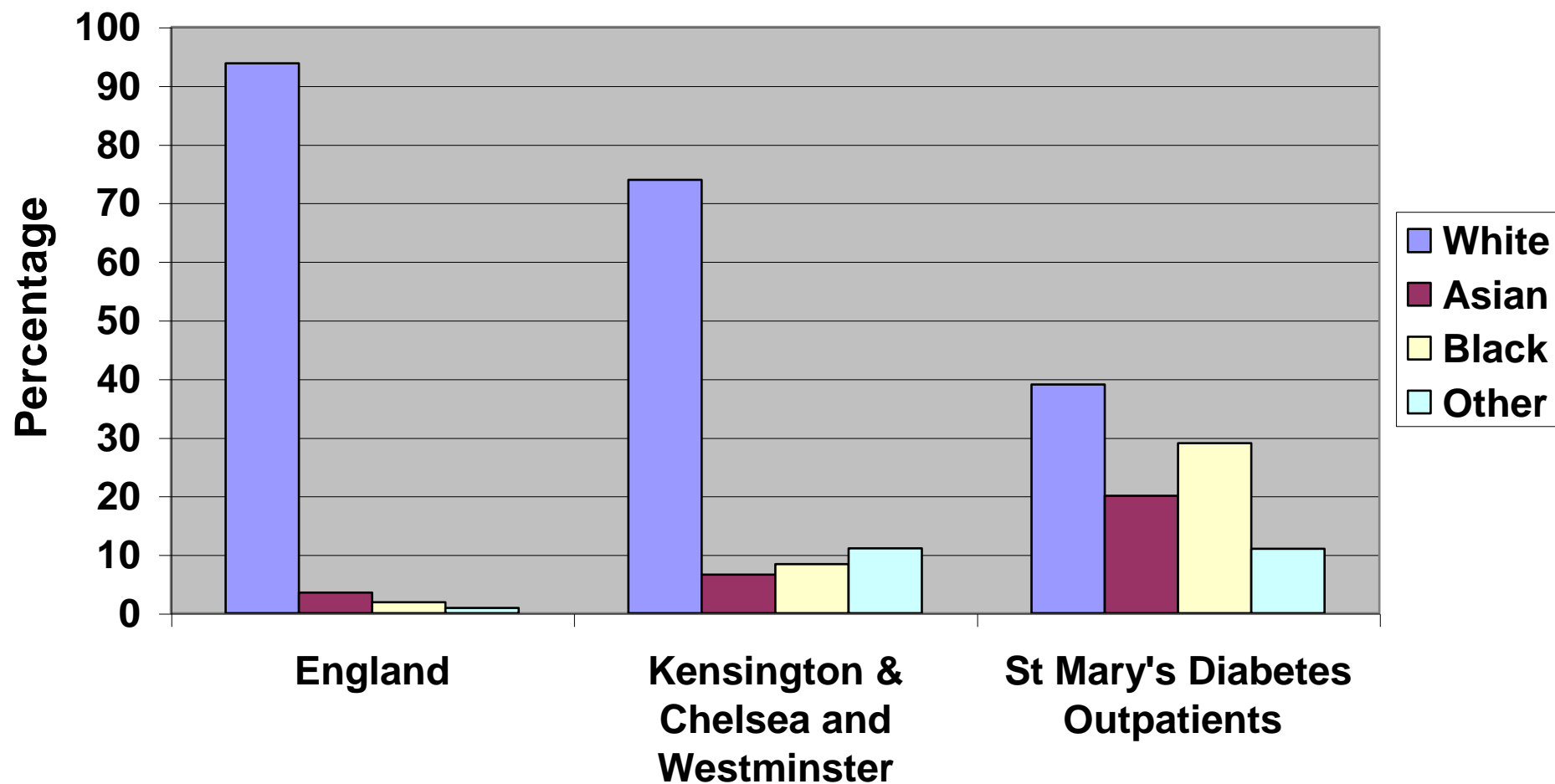


<b>Parameter</b>	<b>Mean (or Median)</b>	<b>Standard deviation (or Interquartile range)</b>	<b>Range</b>
<b>Age (years)</b>	30	27 – 34	23 - 46
<b>Body mass index (kg/m<sup>2</sup>)</b>	25.6	3.1	20.3 – 33.3
<b>Systolic blood pressure (mm Hg)</b>	121	10	90 - 143
<b>Diastolic blood pressure (mm Hg)</b>	82	8	60 - 97
<b>Fasting glucose (mmol/l)</b>	4.9	0.4	4.2 - 5.6
<b>HbA1c (%)</b>	4.8	0.4	4.1 - 5.7
<b>Creatinine (umol/l)</b>	105	8	93 - 128
<b>Total cholesterol (mmol/l)</b>	4.94	0.94	2.86 - 7.54
<b>Triglyceride (mmol/l)</b>	0.89	0.69 – 1.53	0.41 - 4.27
<b>HDL cholesterol (mmol/l)</b>	1.32	0.29	0.88 – 2.02
<b>Apolipoprotein B100 (mg/dl)</b>	99	28	47 – 176
<b>Apolipoprotein A1 (mg/dl)</b>	129	15	104 - 156

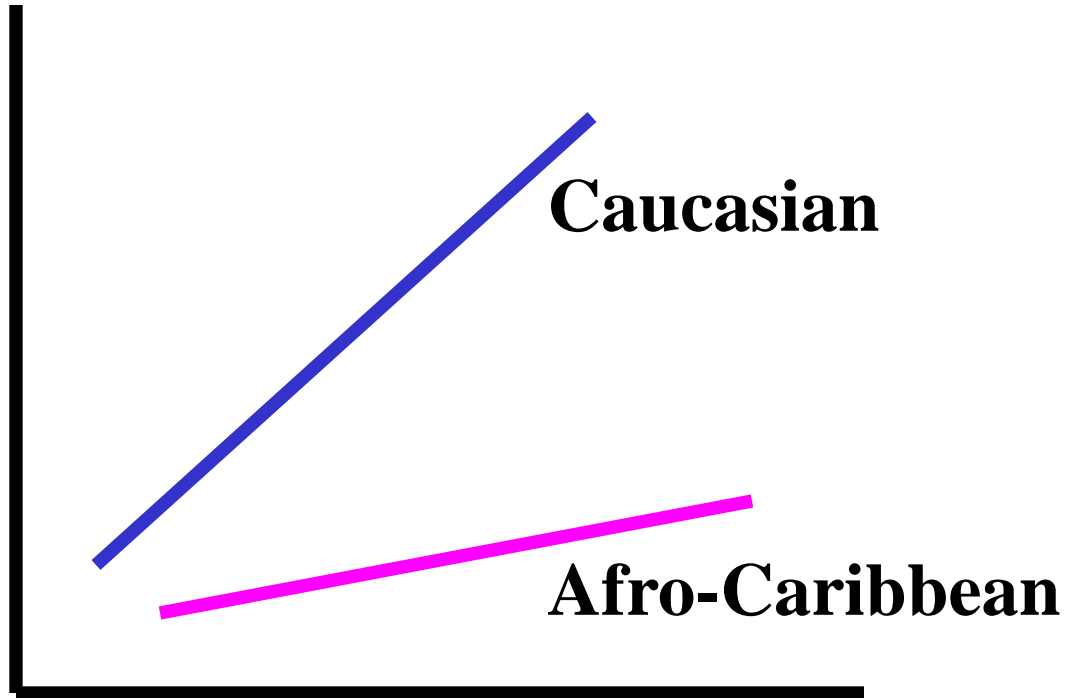
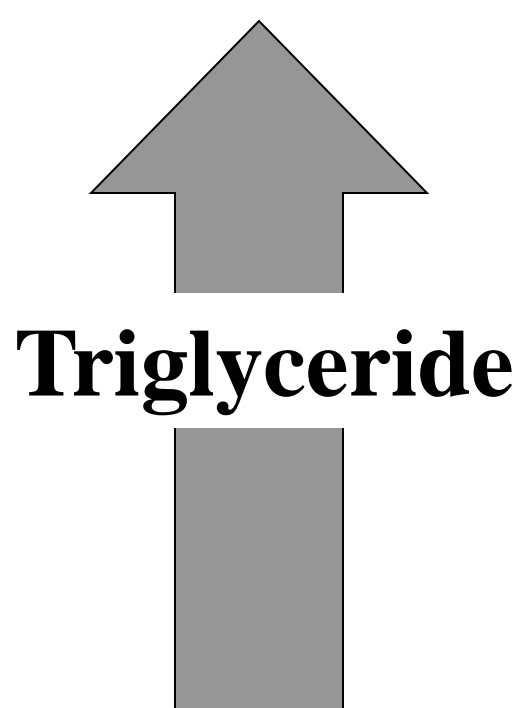


# **Effects of ethnicity**

# Population Ethnicity



	Afro-Caribbean subjects	Caucasian subjects	P-value
Number	23	47	
Age (yrs)	62 (56-65)	63 (57-66)	NS
Body-mass index (kg/m <sup>2</sup> )	28.9 (27.0-32.3)	29.1 (27.9-30.9)	NS
HbA1c (%)	8.1 (6.7-8.9)	7.2 (6.3-8.0)	0.10
Fasting glucose (mmol/l)	11.4 (8.4-15.2)	10.6 (8.4-12.6)	NS
Specific insulin conc. (pmol/l)	42 (20-92)	22 (6-35)	< 0.01
Total cholesterol (mmol/l)	4.80 (4.03-5.32)	5.17 (4.70-5.89)	0.057
Triglyceride (mmol/l)	1.03 (0.77-1.49)	1.77 (1.37-2.71)	< 0.001
HDL cholesterol (mmol/l)	1.11 (0.98-1.64)	1.09 (0.94-1.25)	NS



# Summary

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# Acknowledgements

Christiane Albrecht

Chris Higgins

Ian Godsland

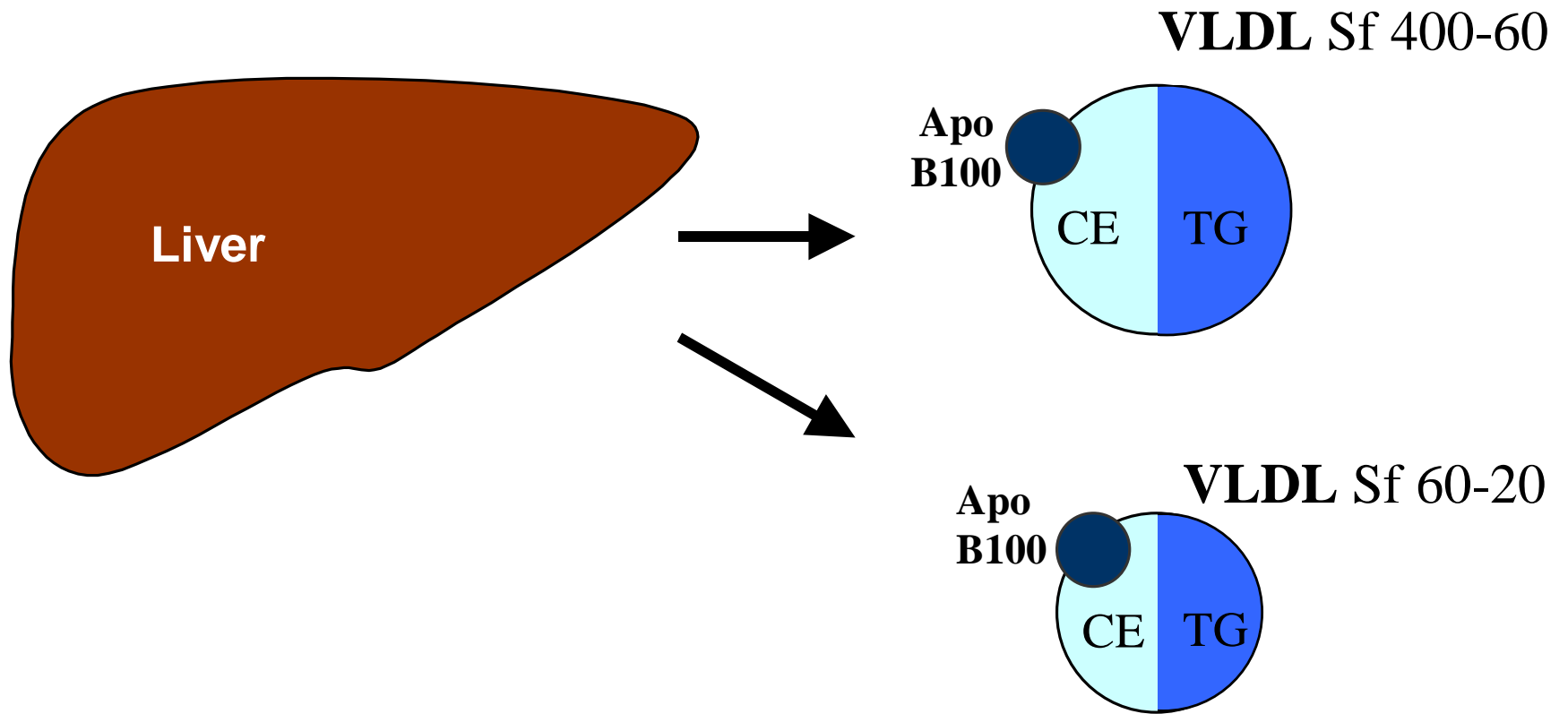
Nish Chattervedi

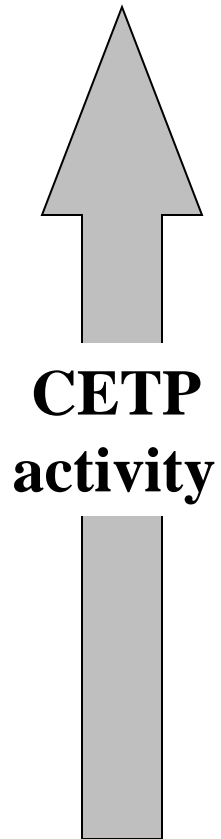
Des Johnston

Bill Richmond

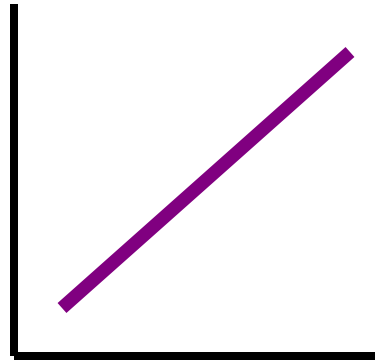
Robert Elkeles







**Triglyceride  
< 2 mmol/l**

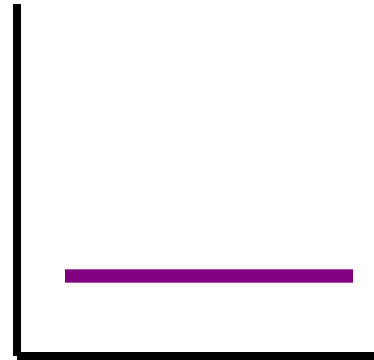


**Triglyceride**

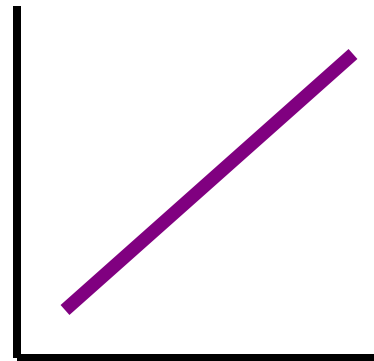


**CETP mass**

**Triglyceride  
> 2 mmol/l**



**Triglyceride**



**CETP mass**

