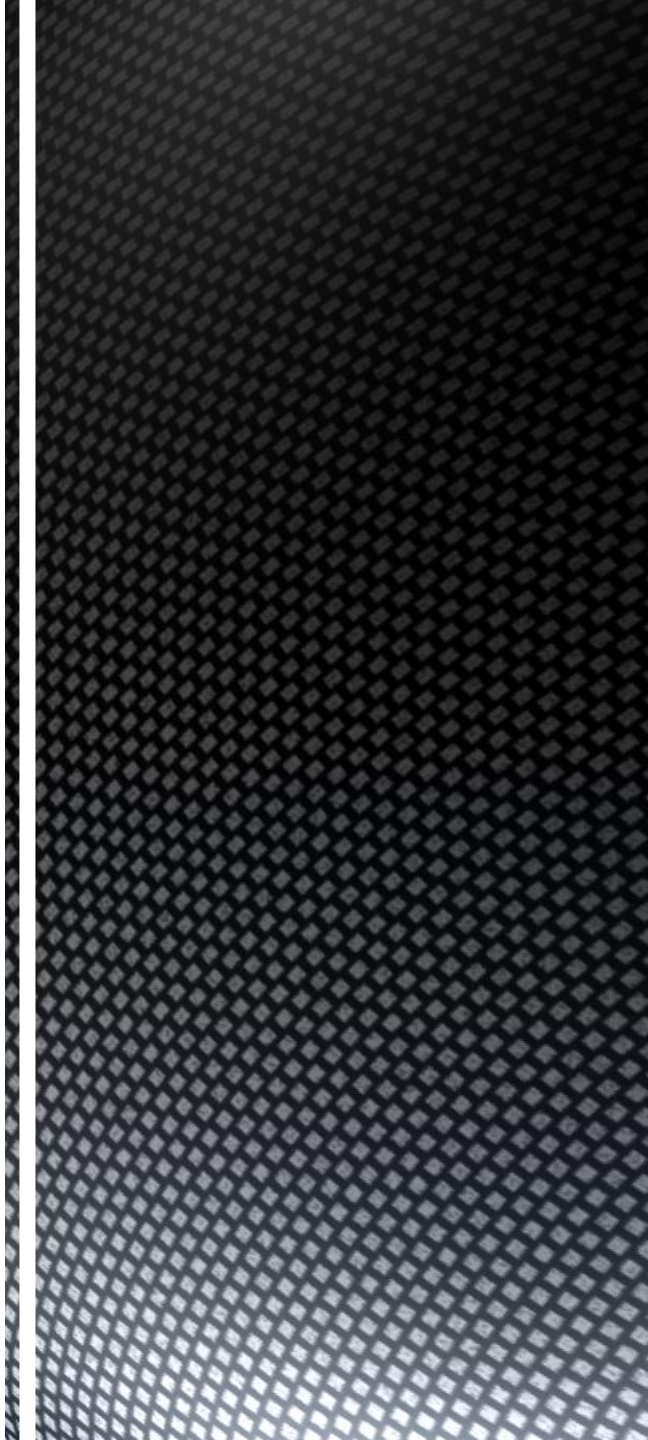
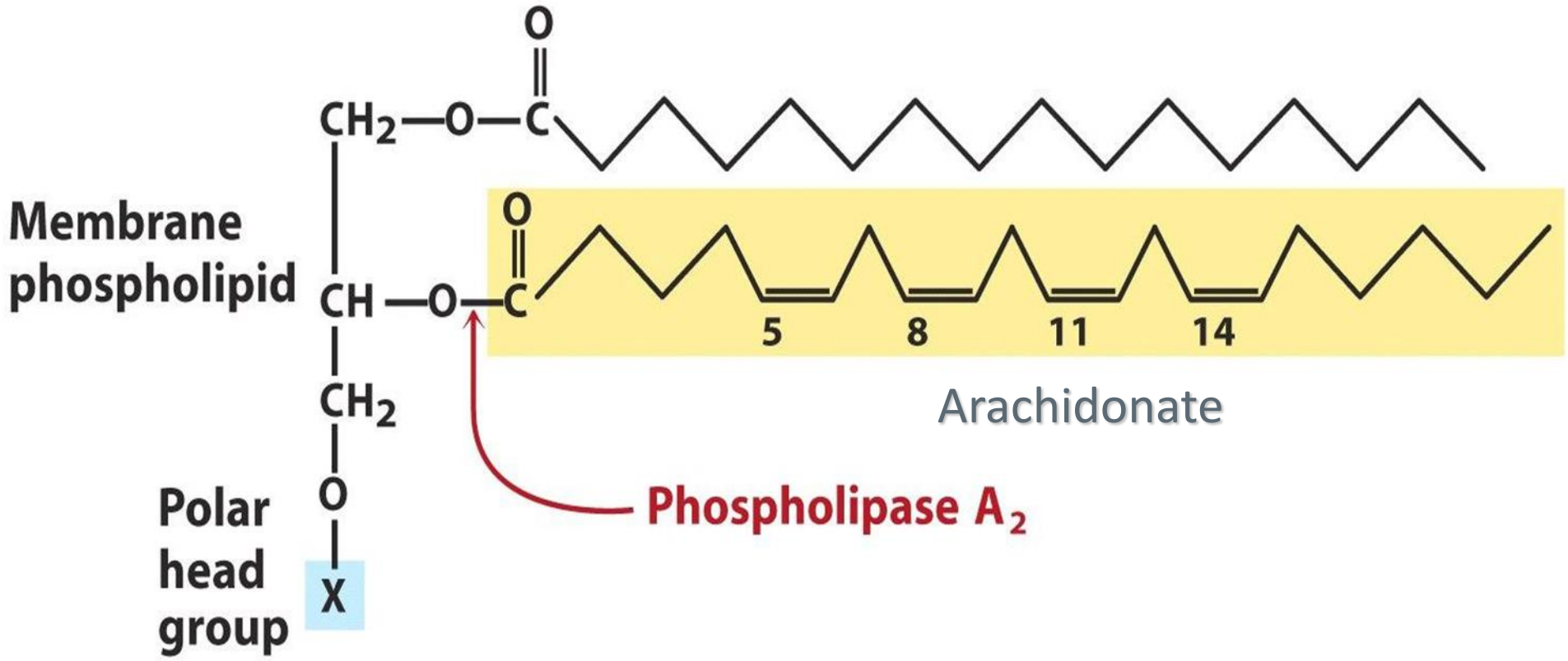
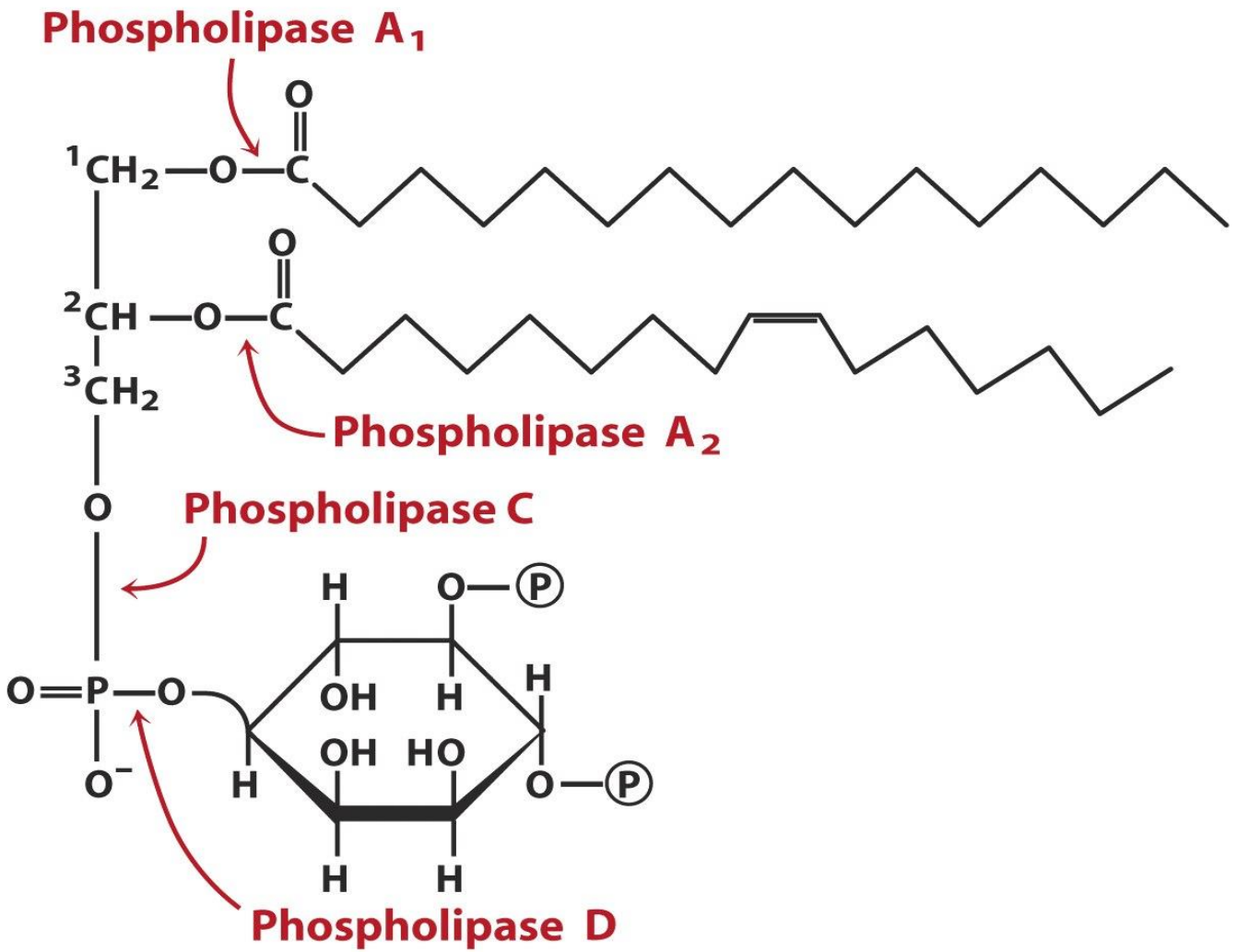
Lipid metabolism II.

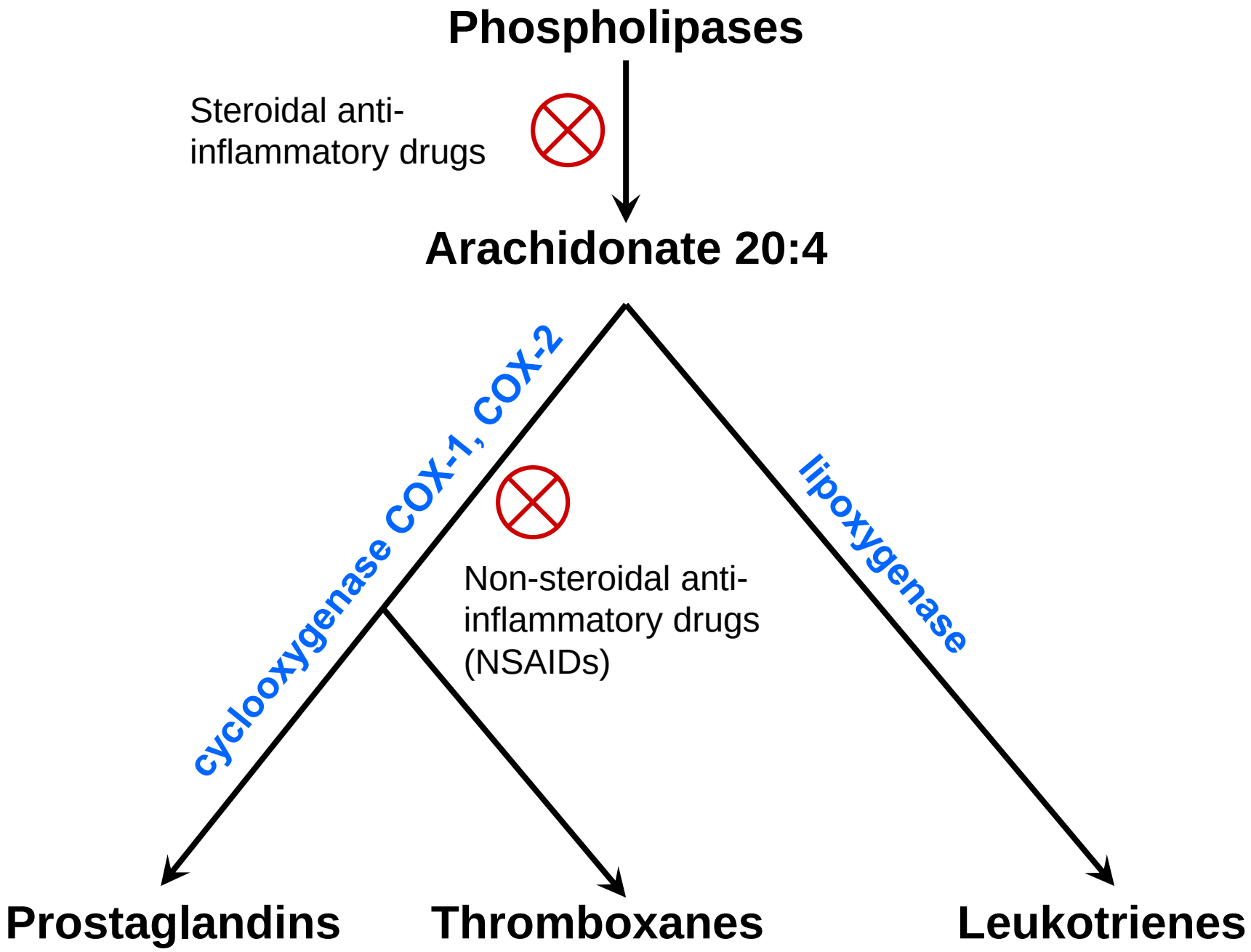


Eicosanoids

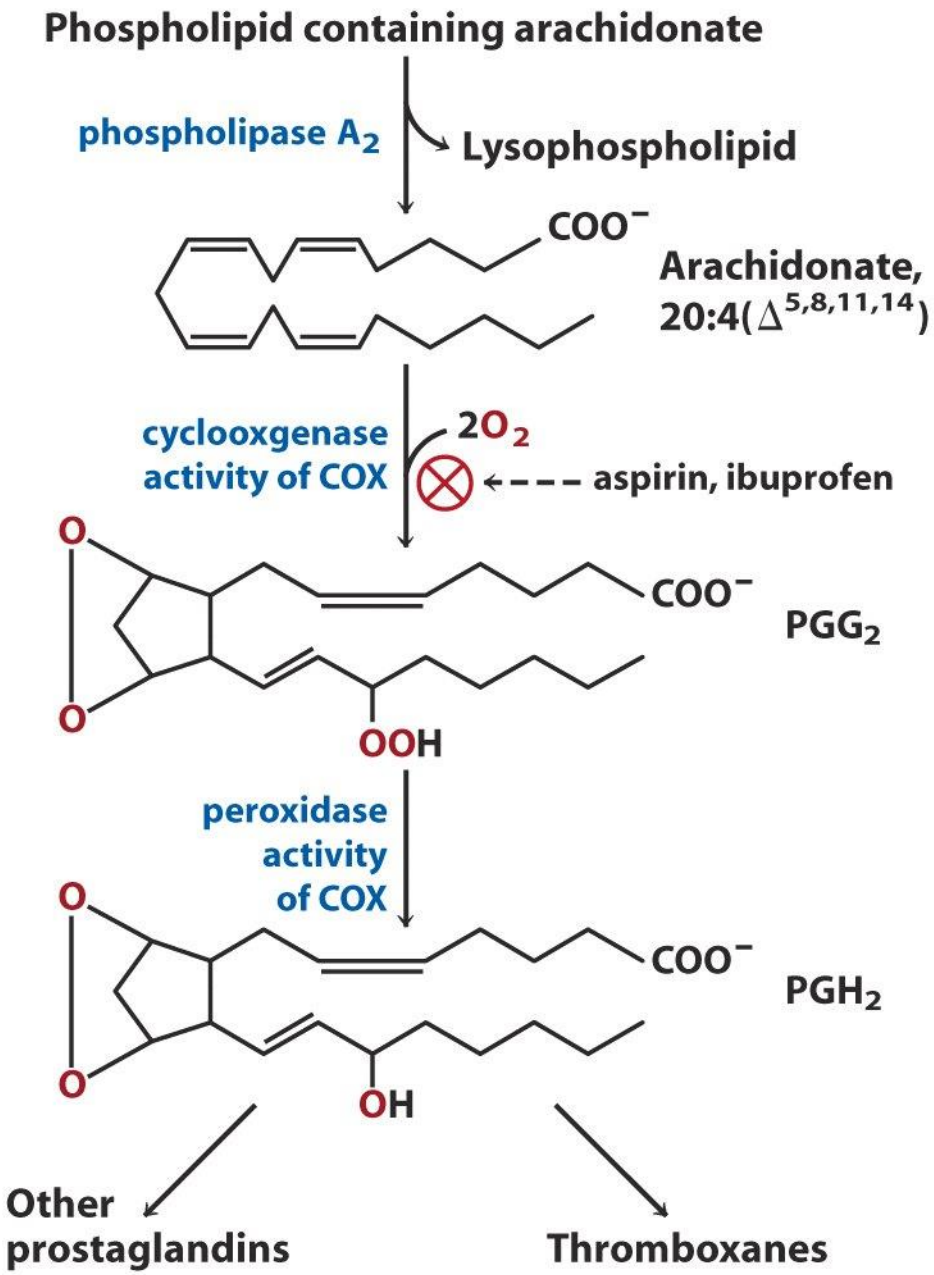


Cleavage sites of phospholipases

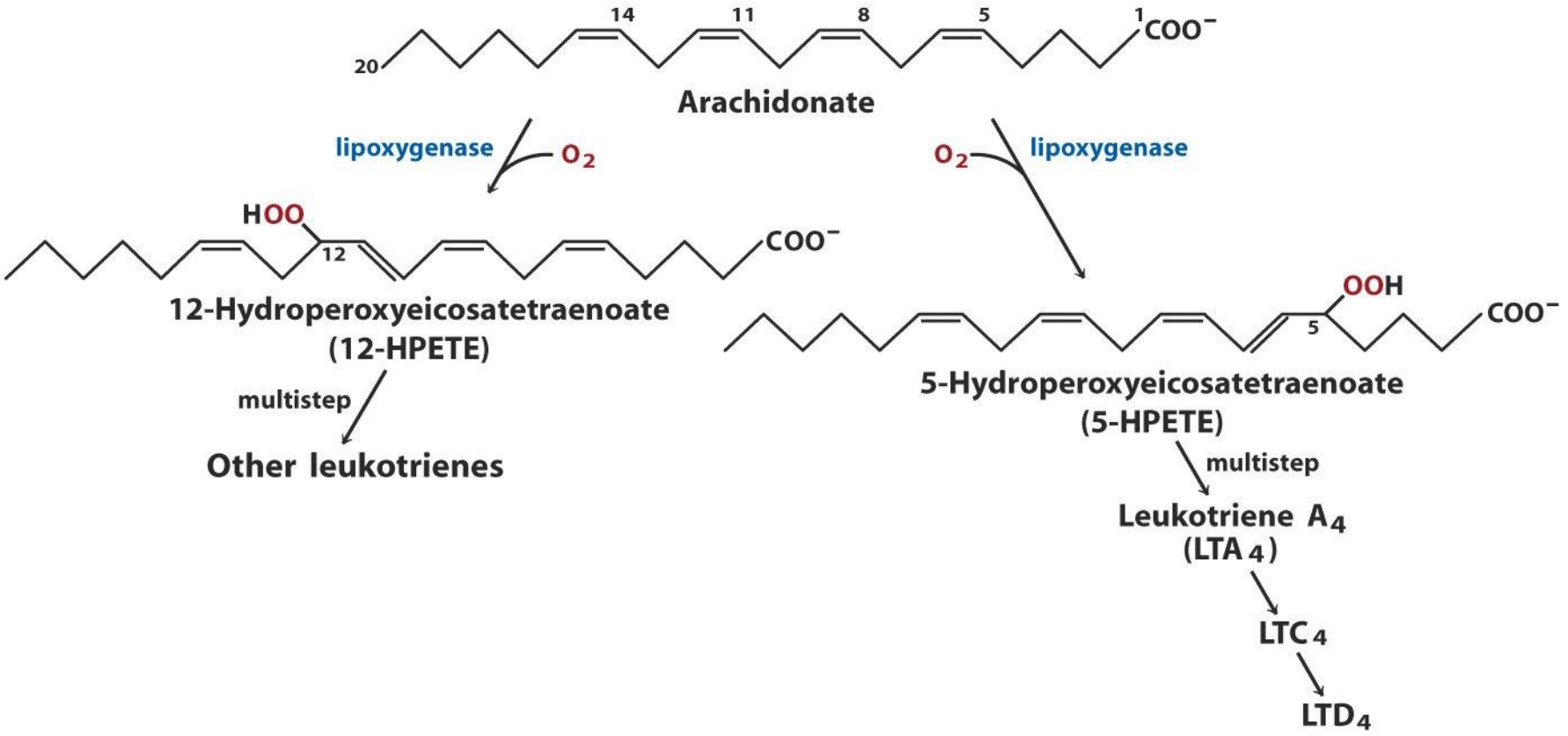



Phospholipases
Steroidal anti-inflammatory drugs
Arachidonate 20:4
cyclooxygenase COX-1, COX-2
lipoxygenase
Non-steroidal anti-inflammatory drugs (NSAIDs)
Prostaglandins
Thromboxanes
Leukotrienes

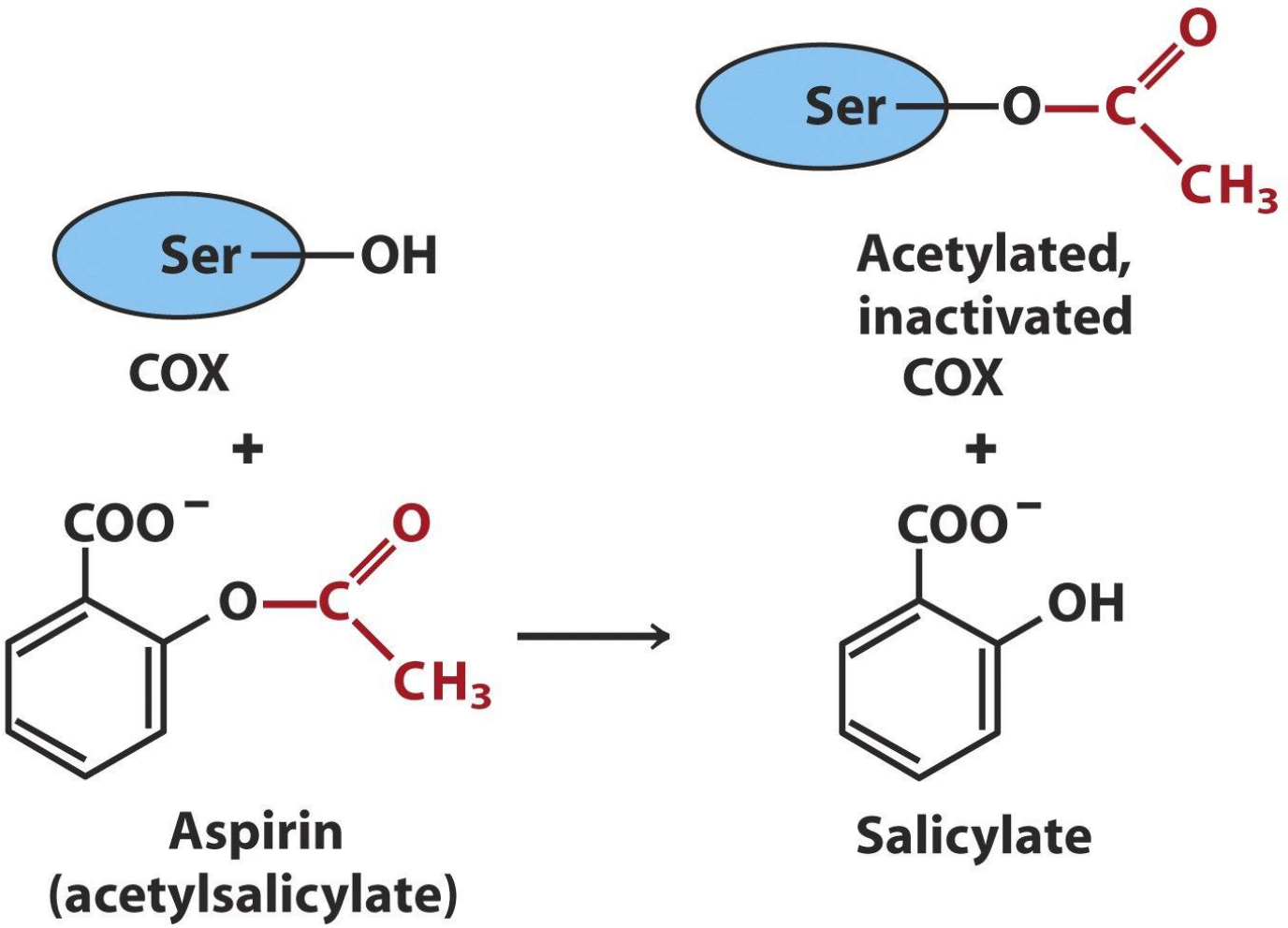
Cyclooxygenase pathway



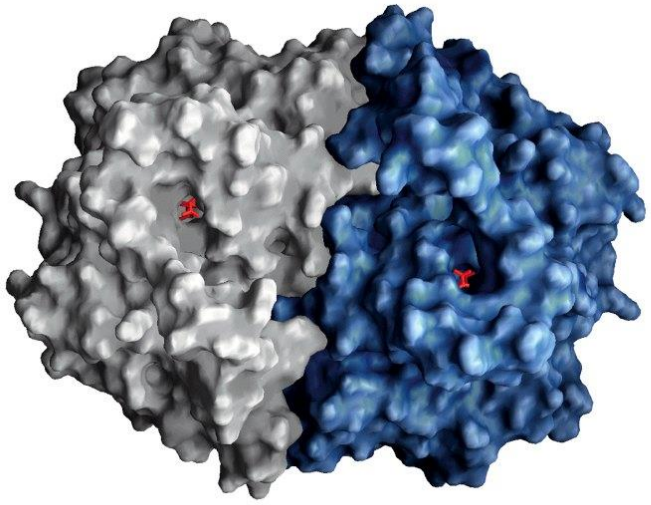
Lipoxygenase pathway



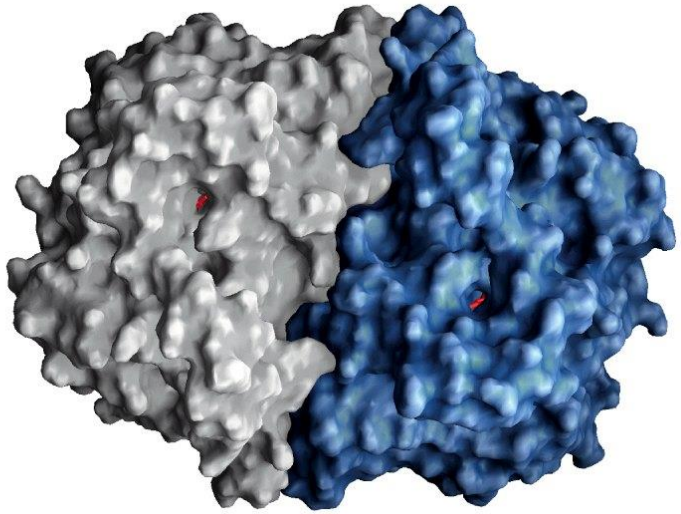
Specific inhibition of cyclooxygenase pathway



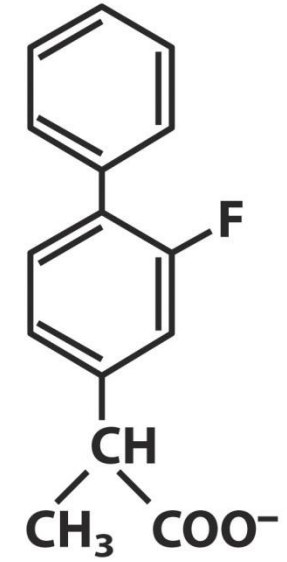
Isotype specific inhibition of cyclooxygenase pathway



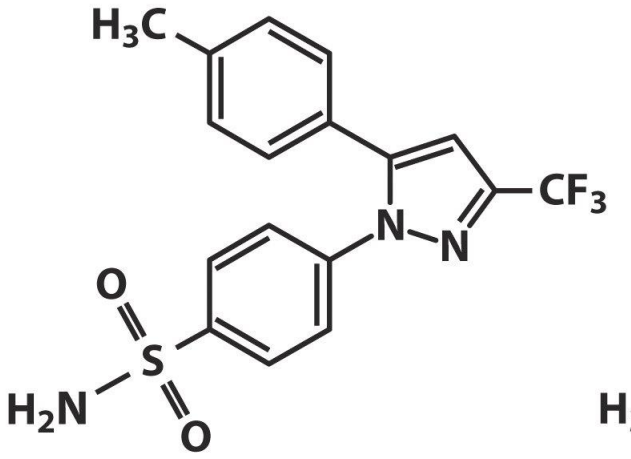
COX-1
synthesis of PGs that regulate the secretion of gastric mucin



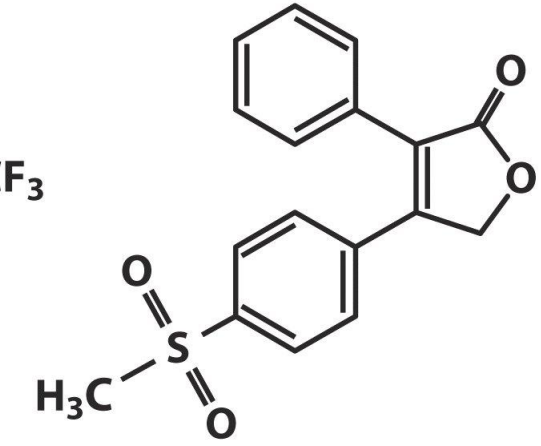
COX-2
synthesis of PGs that mediate inflammation, pain, and fever



Flurbiprofen

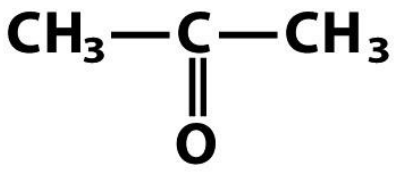


Celecoxib
(Celebrex)

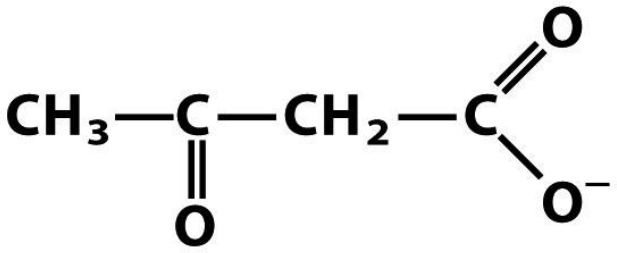


Rofecoxib
(Vioxx)

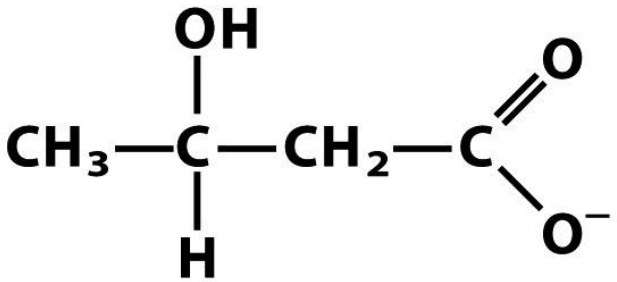
Ketone bodies



Acetone



Acetoacetate



D-β-Hydroxybutyrate

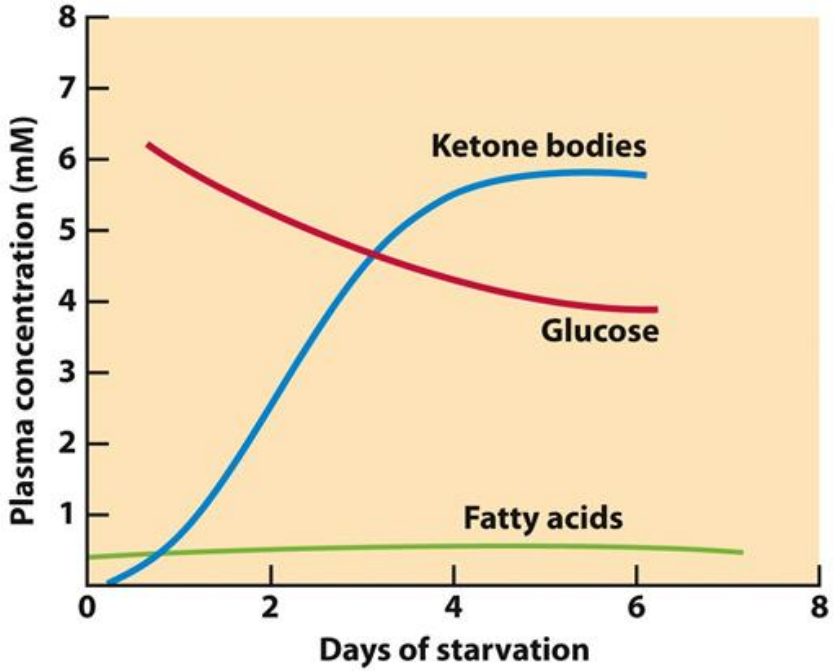


Figure 23-32
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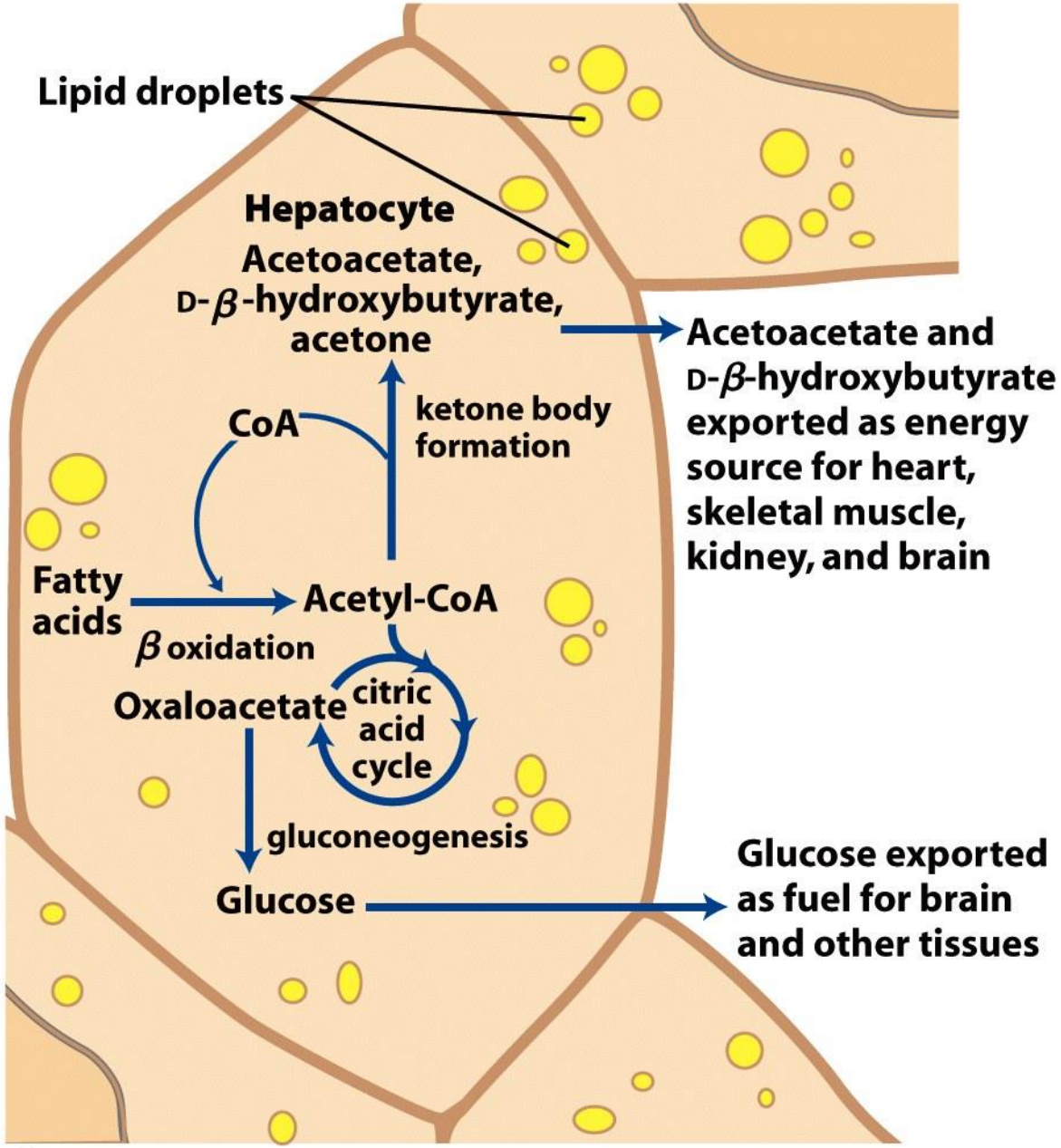

Figure 17-20

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Formation of ketone bodies

mitochondrial!

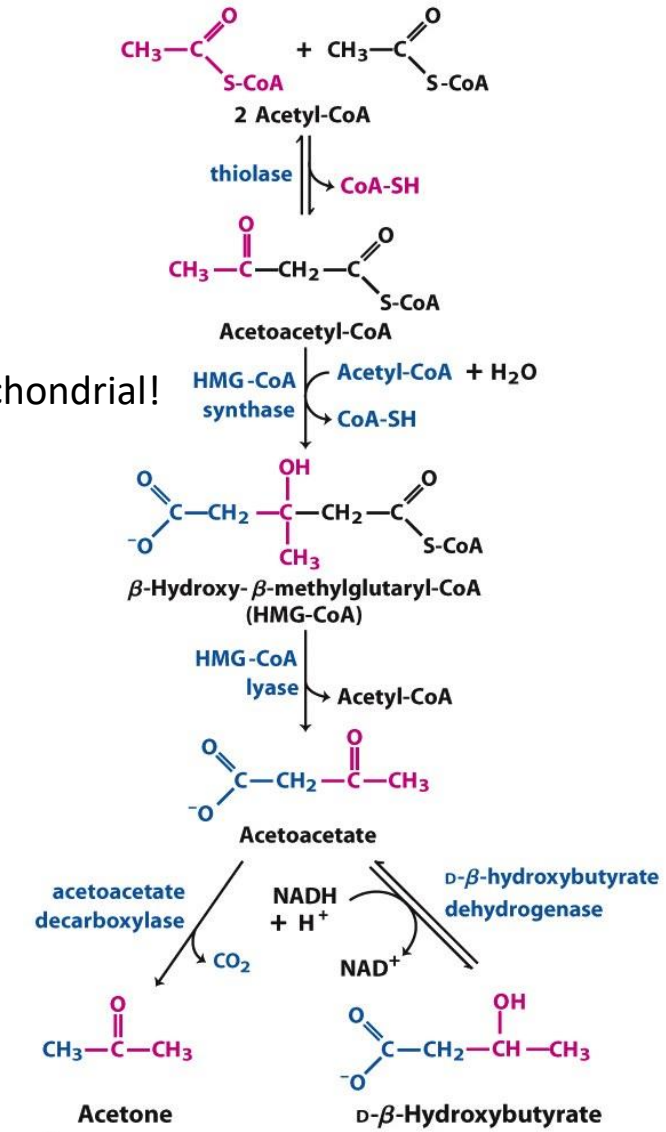

Figure 17-18

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The use of ketone bodies as fuel

Ketone bodies are used as fuels in all tissues except liver, which lacks this enzyme.

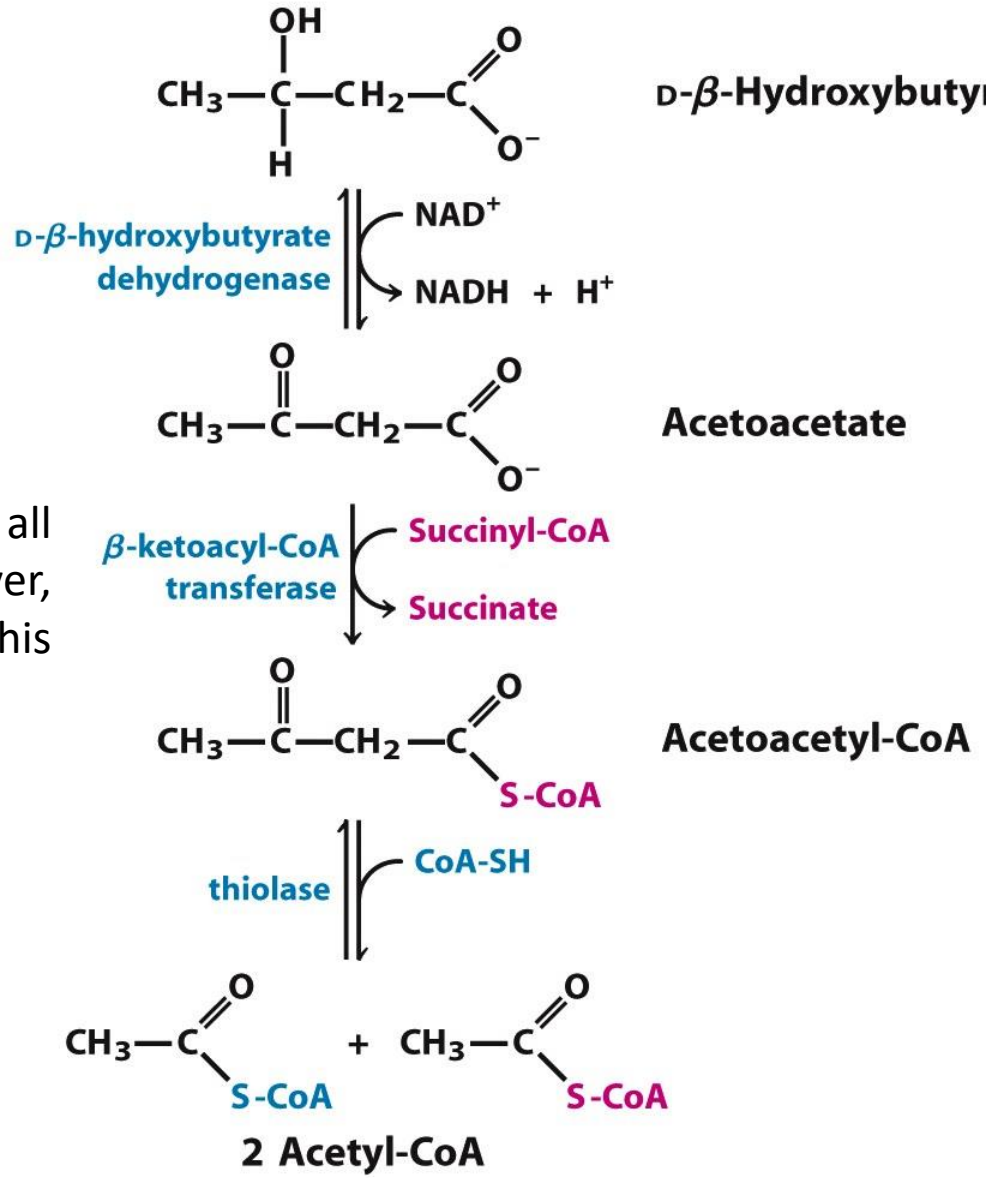

Figure 17-19
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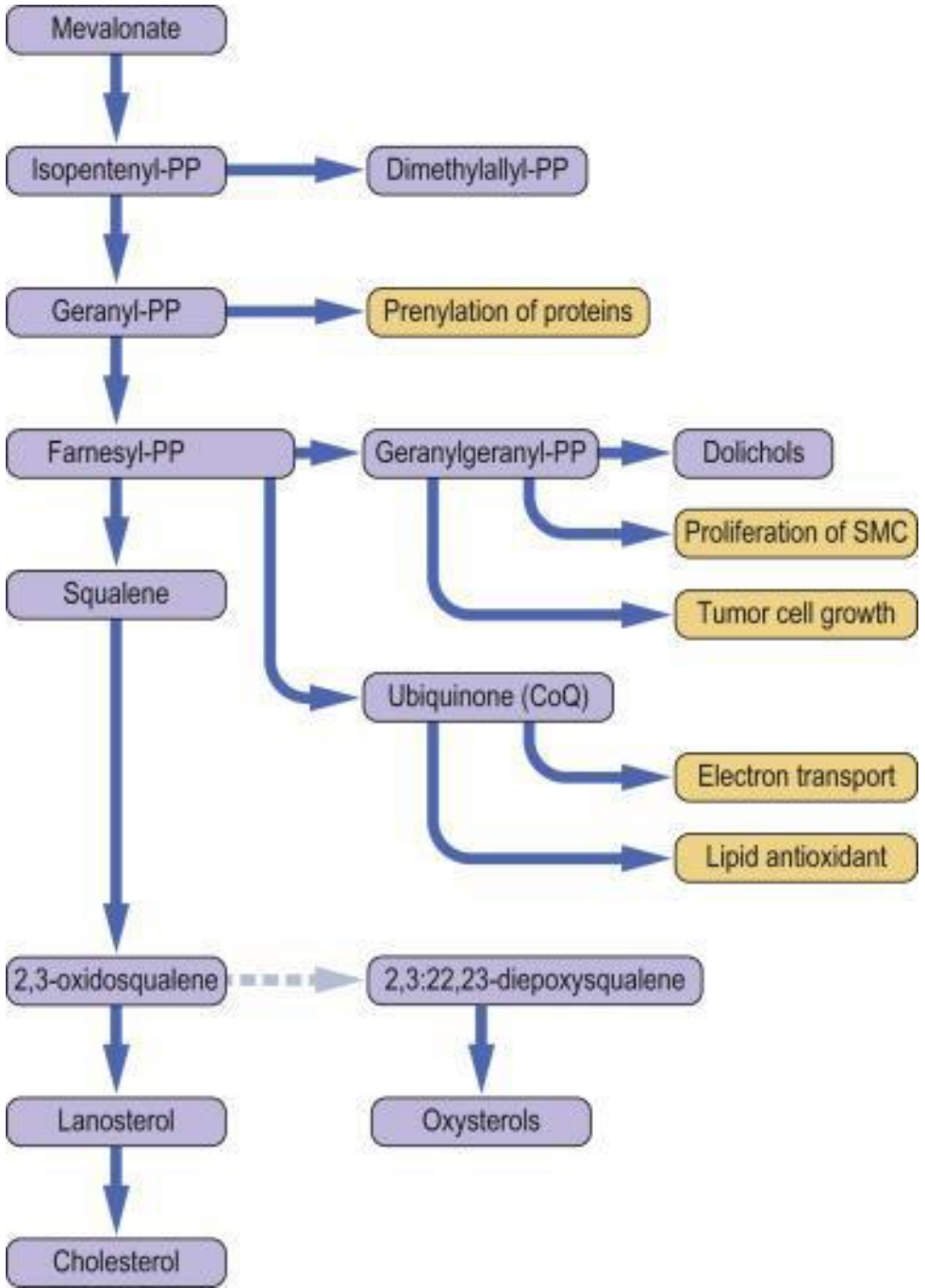
Biosynthesis of cholesterol



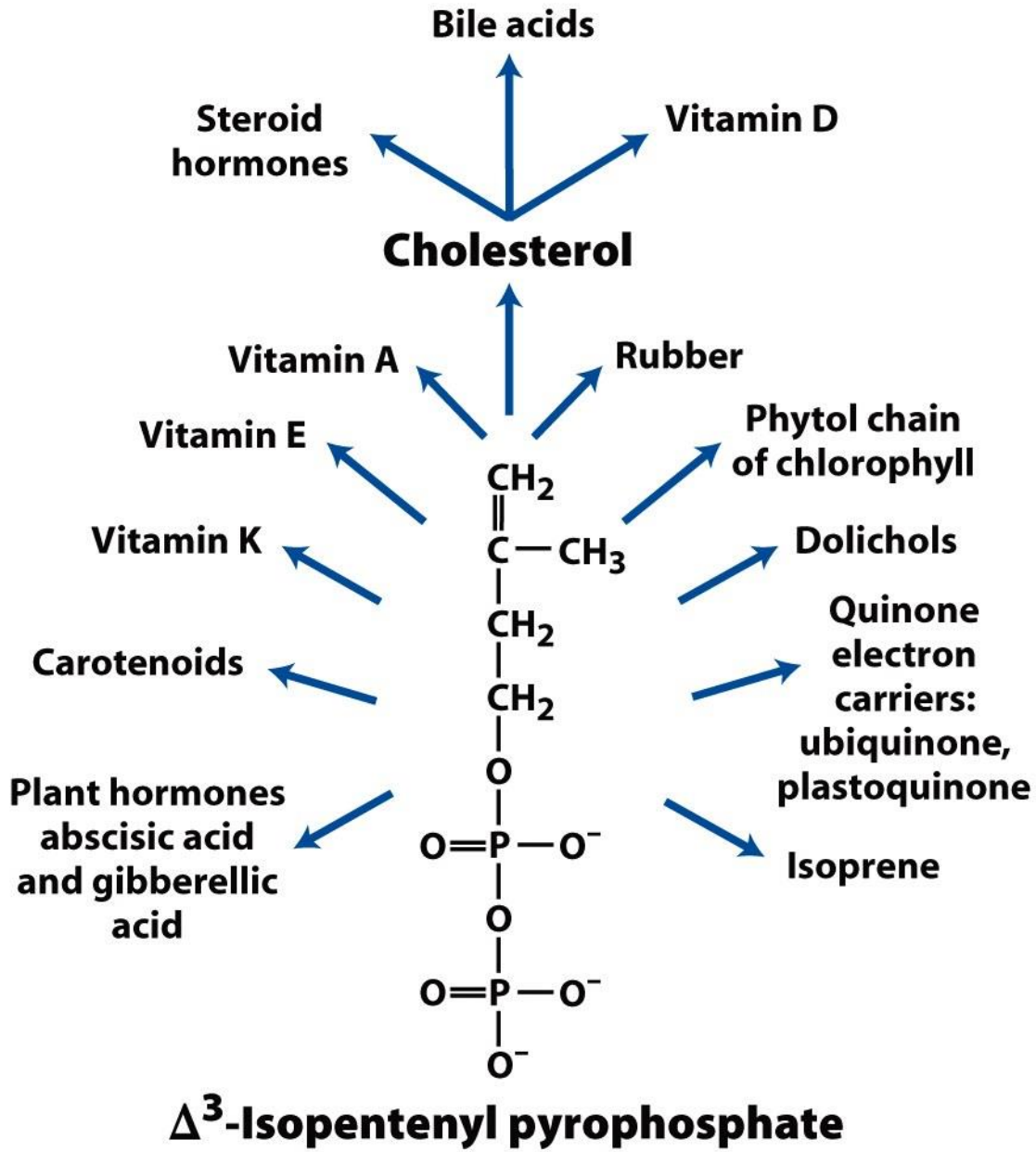


Figure 21-47
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Summary of cholesterol biosynthesis

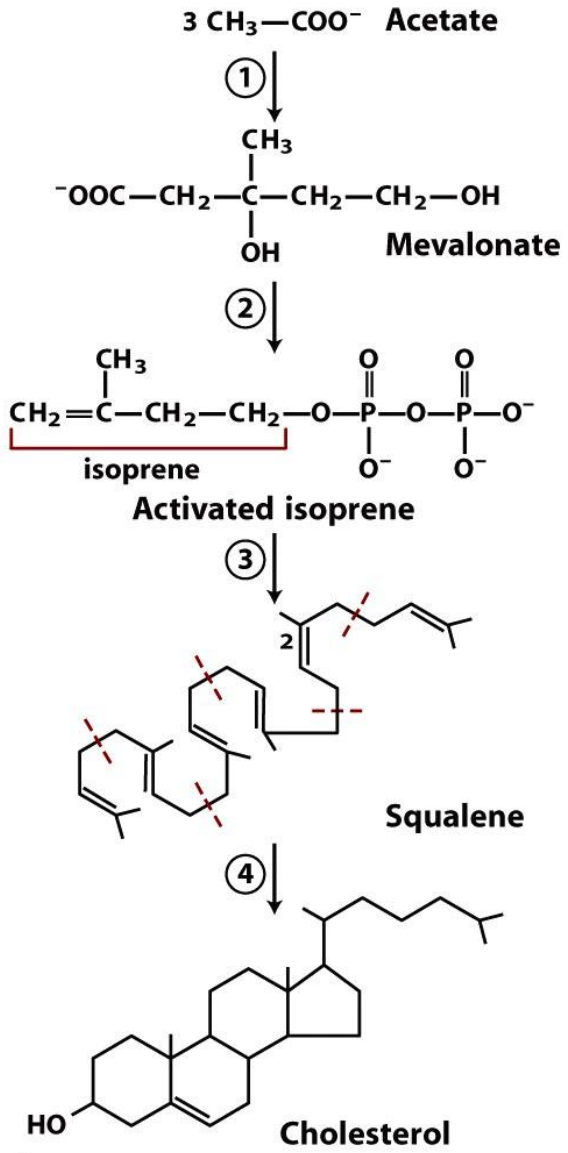

Figure 21-33
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Synthesis of mevalonate

cytosolic!

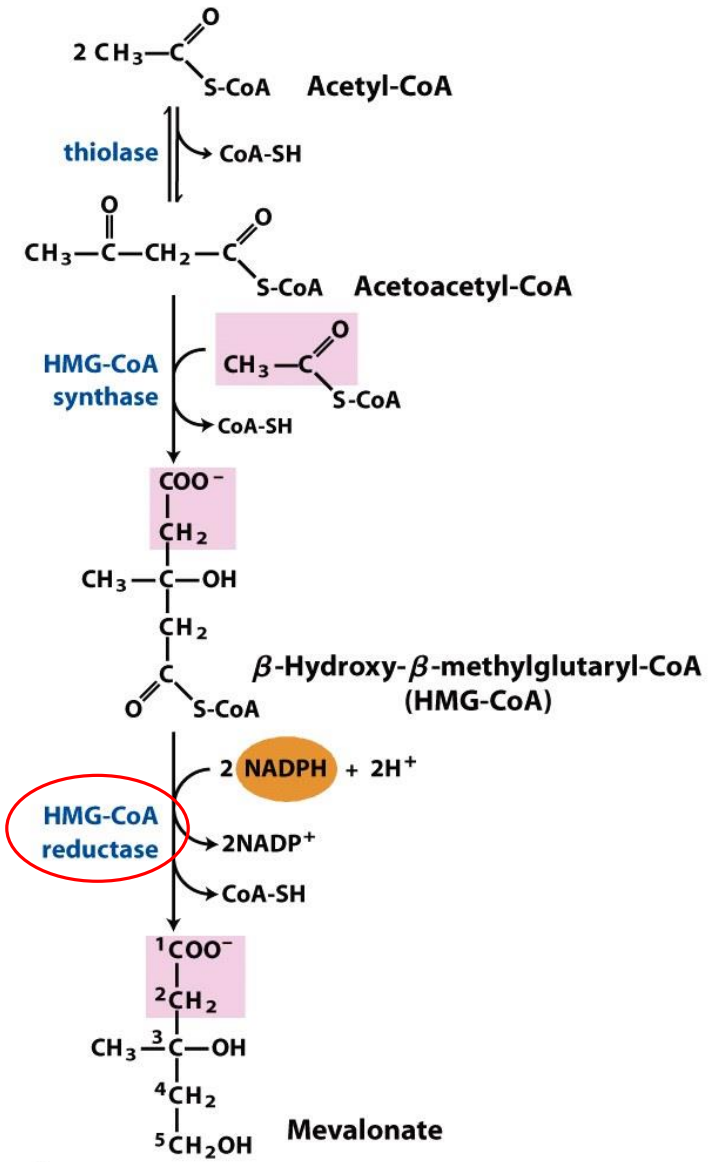

Figure 21-34

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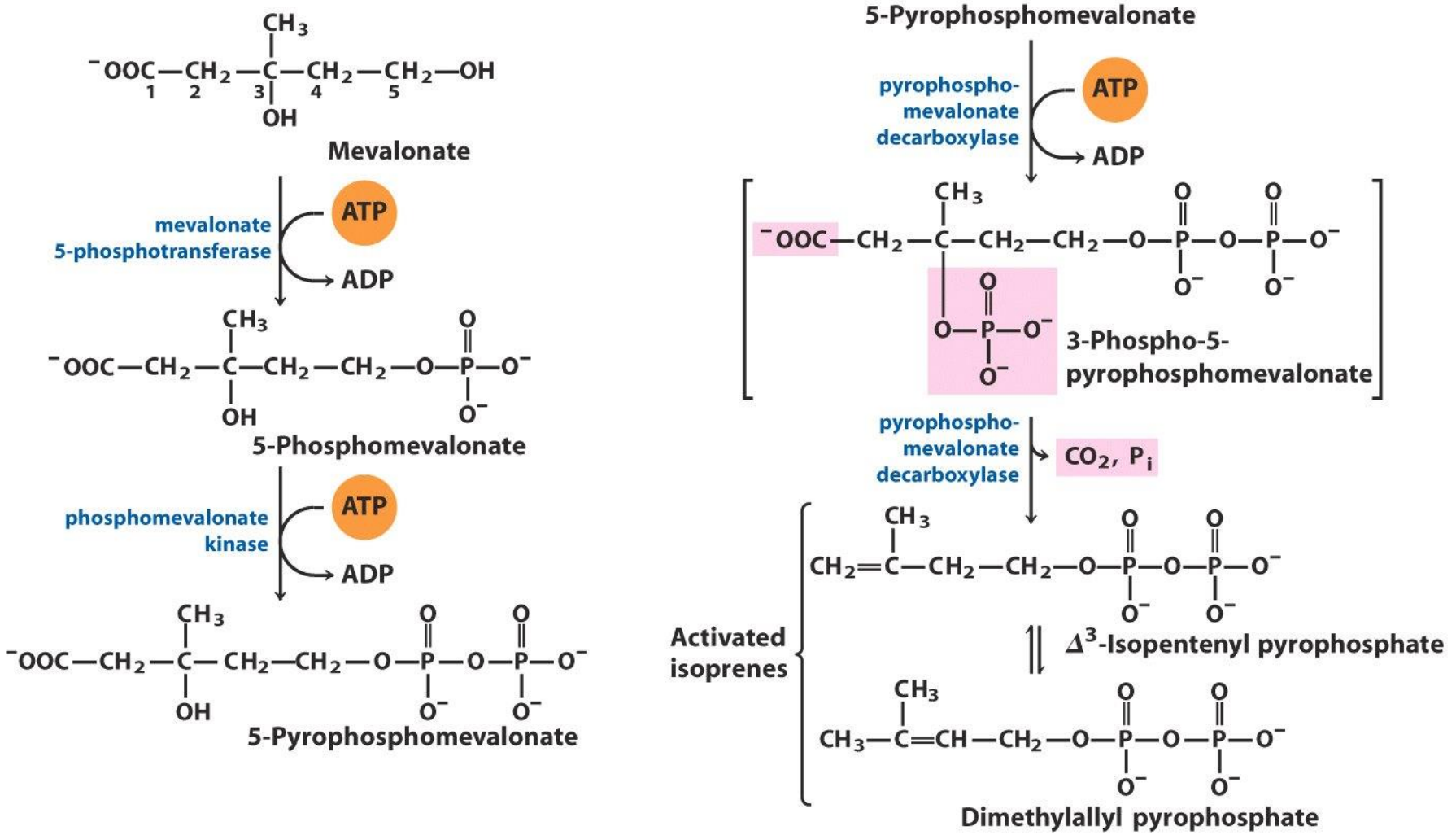
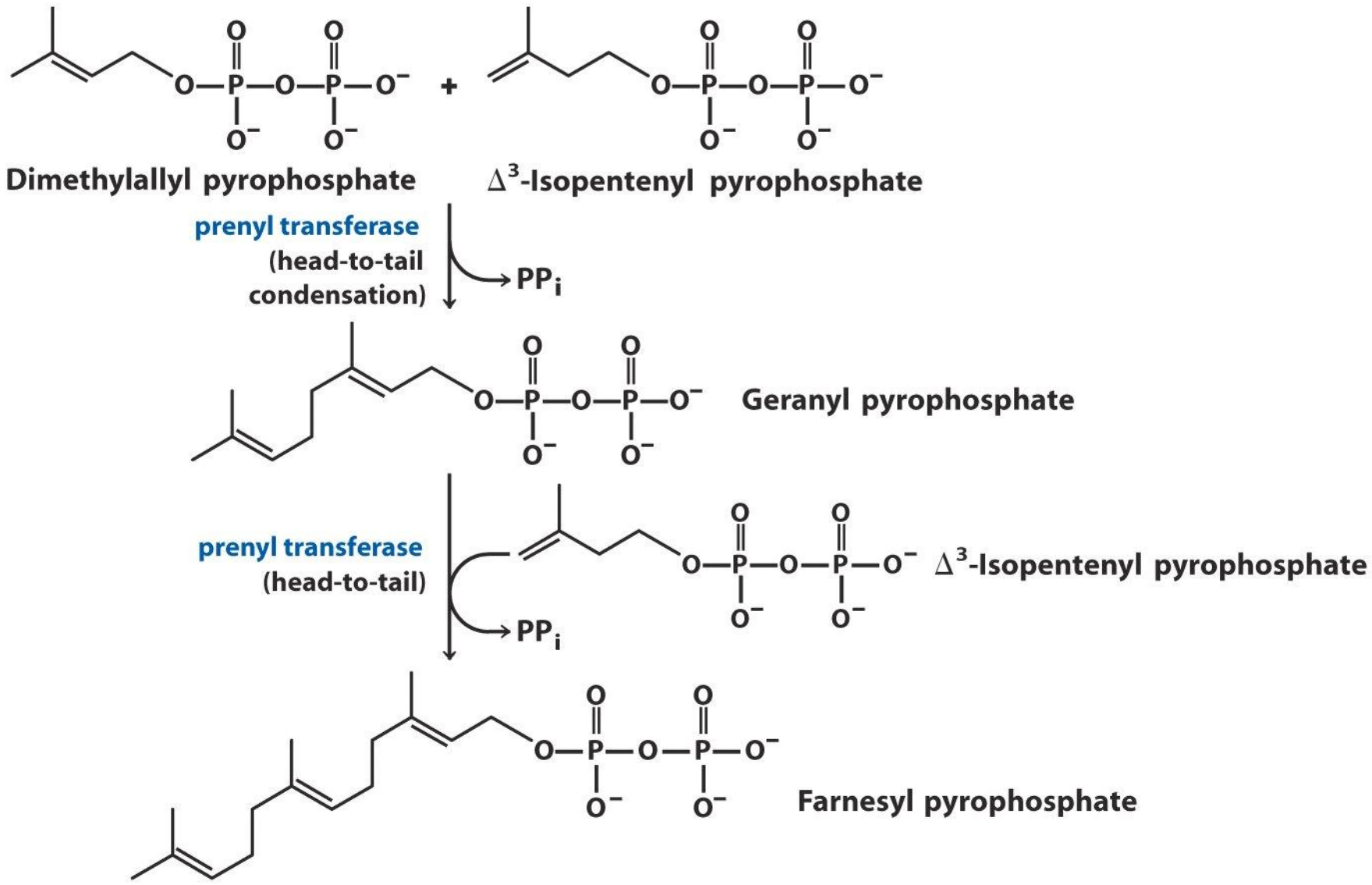
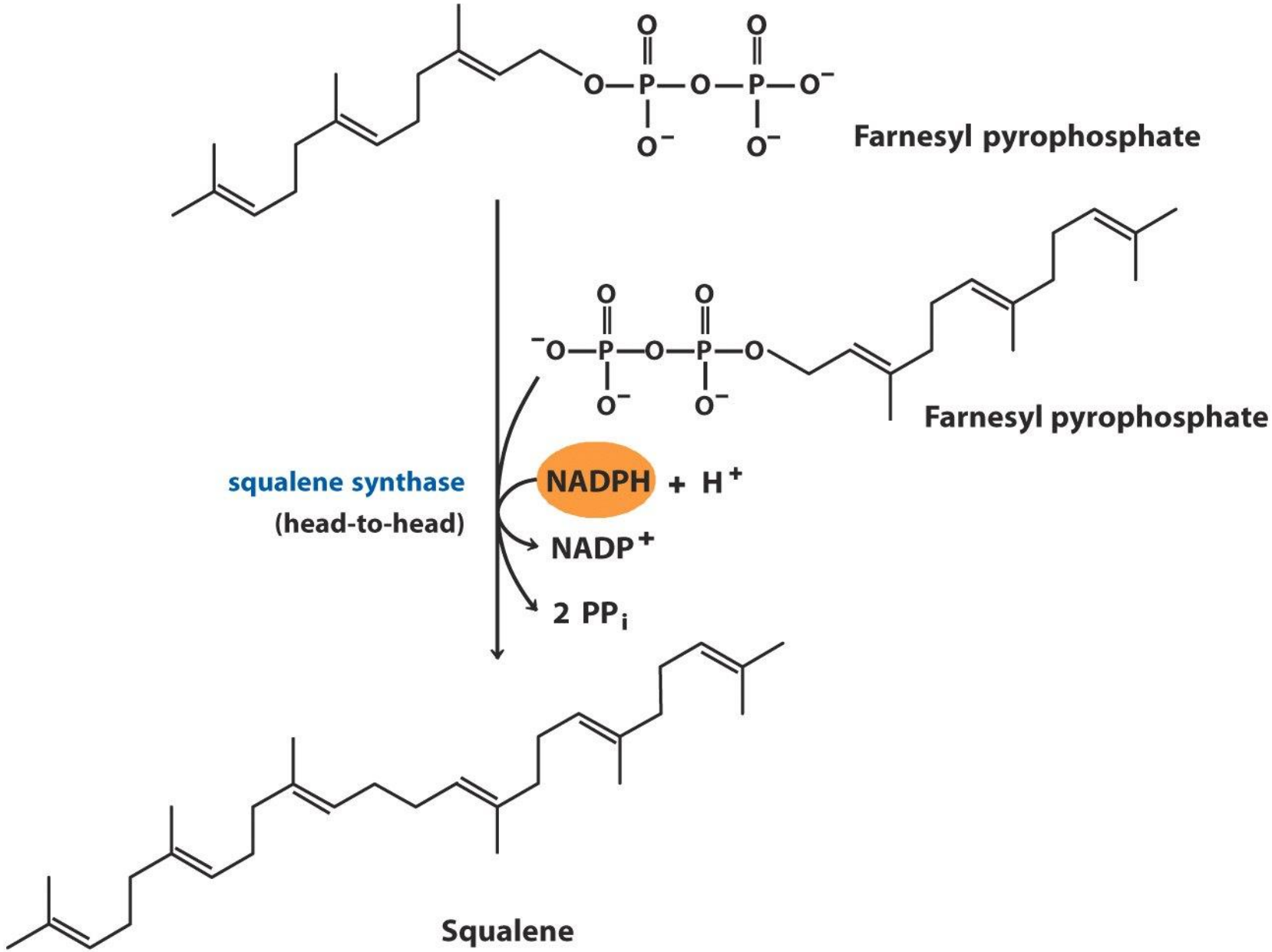
Synthesis of activated isoprenes



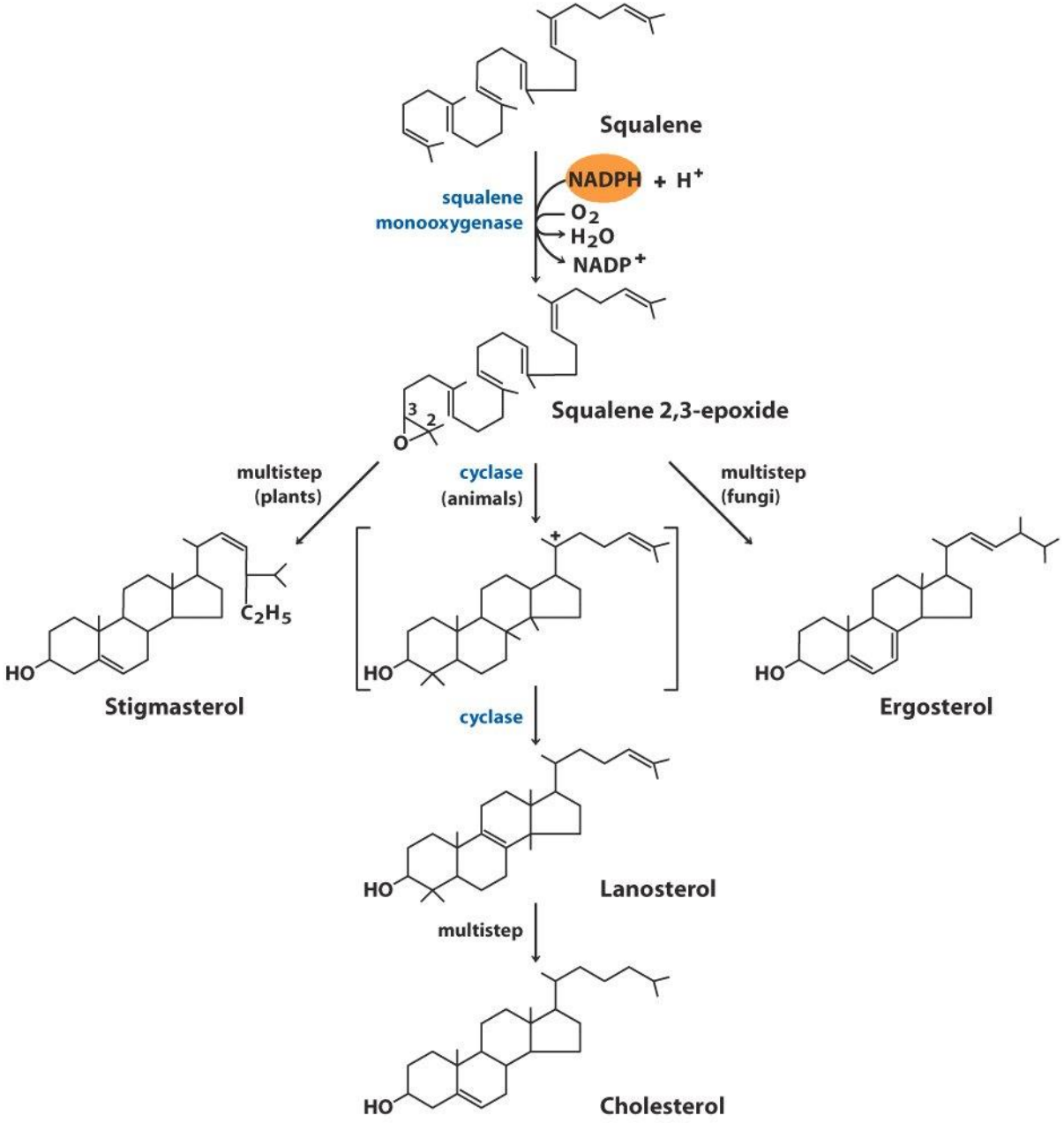
Synthesis of squalene I



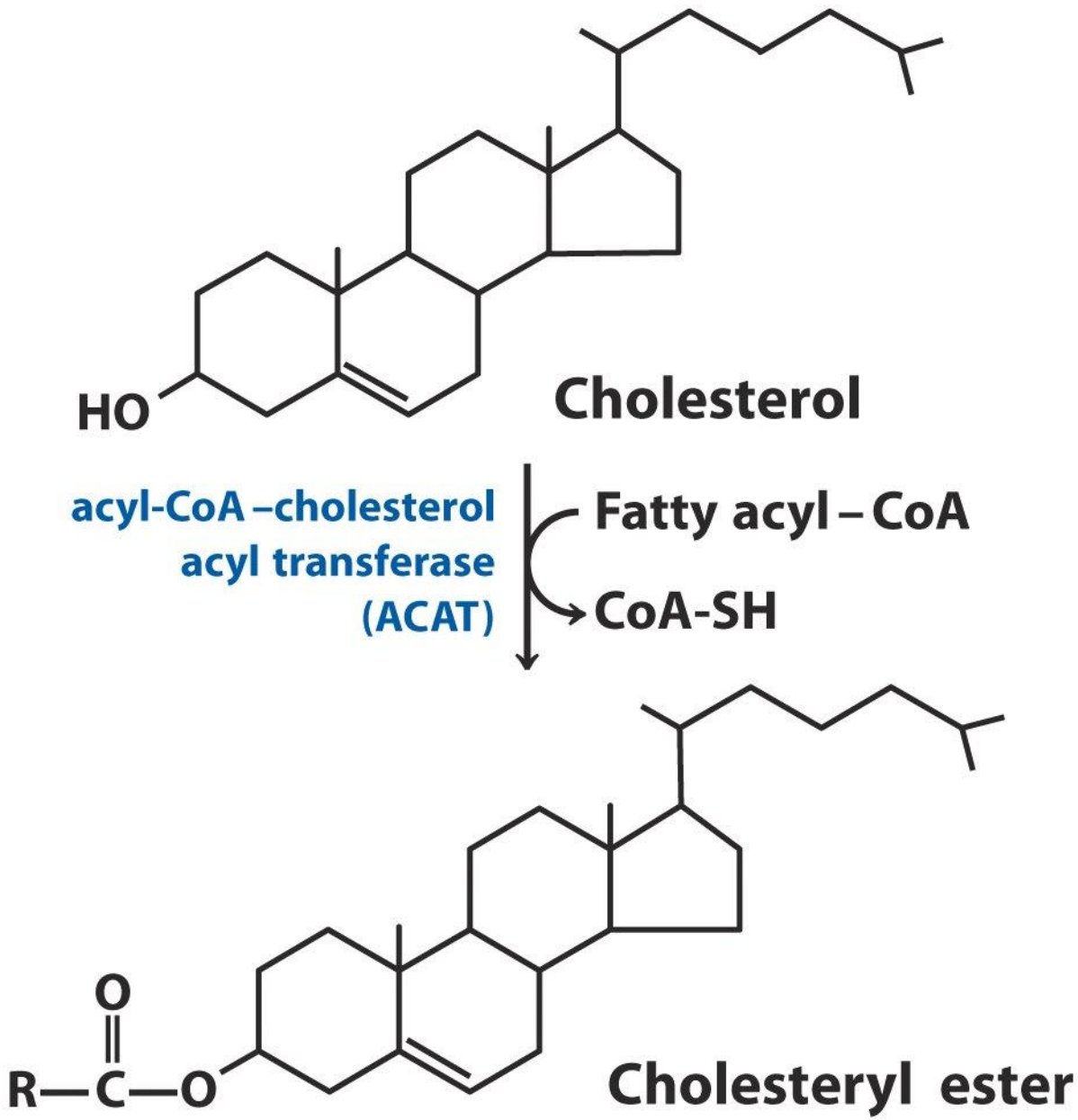
Synthesis of squalene II



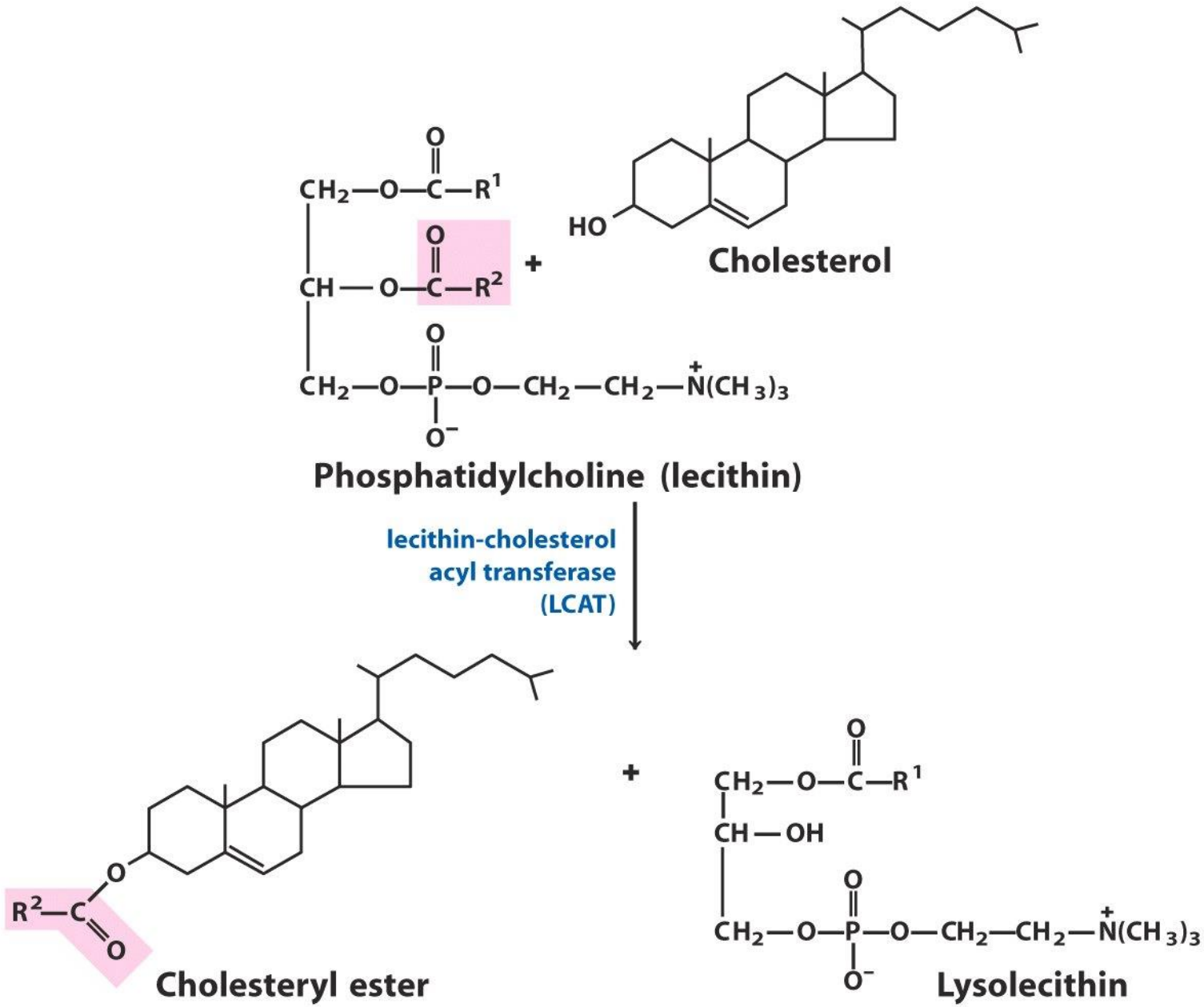
Production of cholesterol from squalene



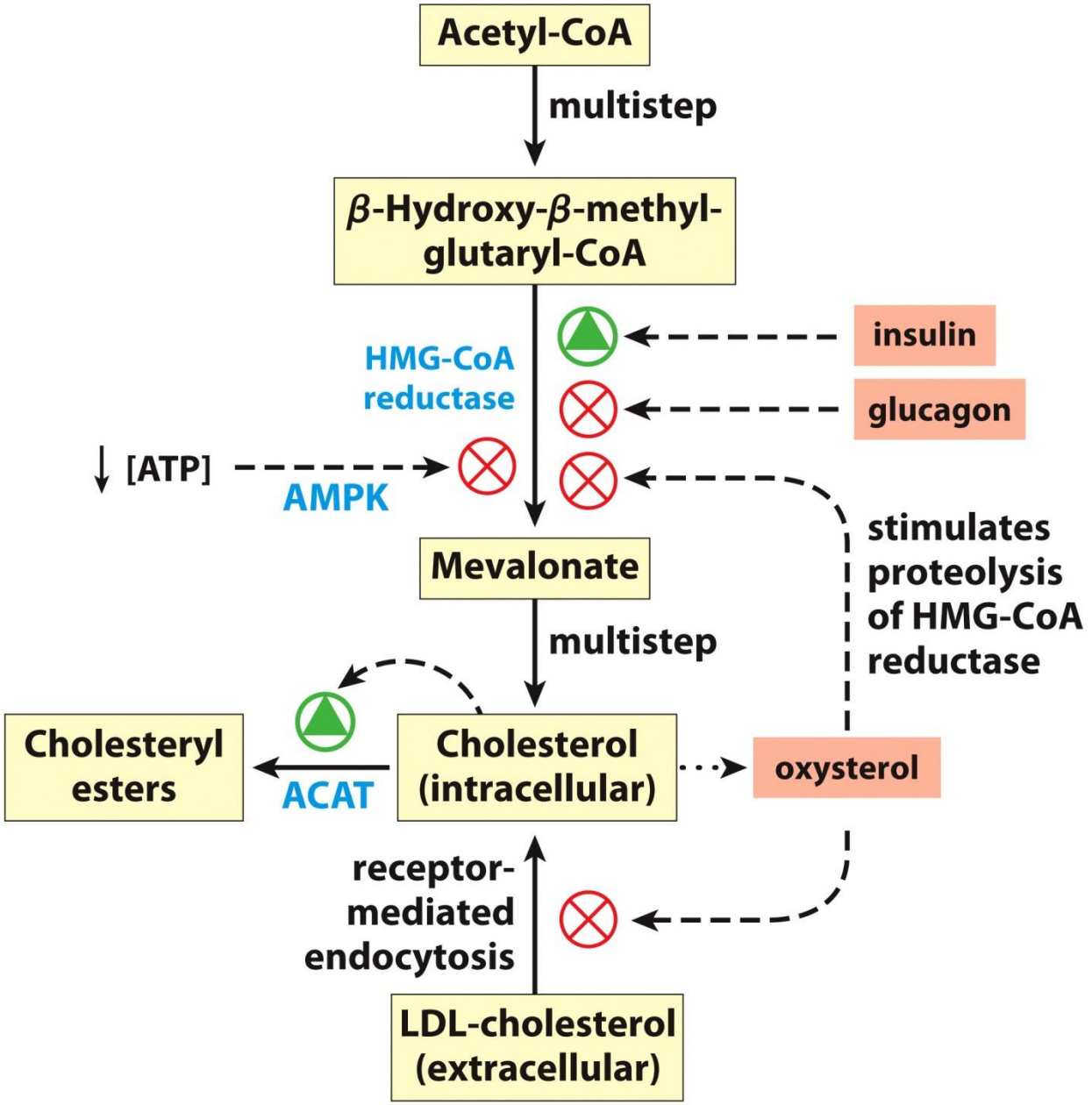
Esterification of cholesterol I.



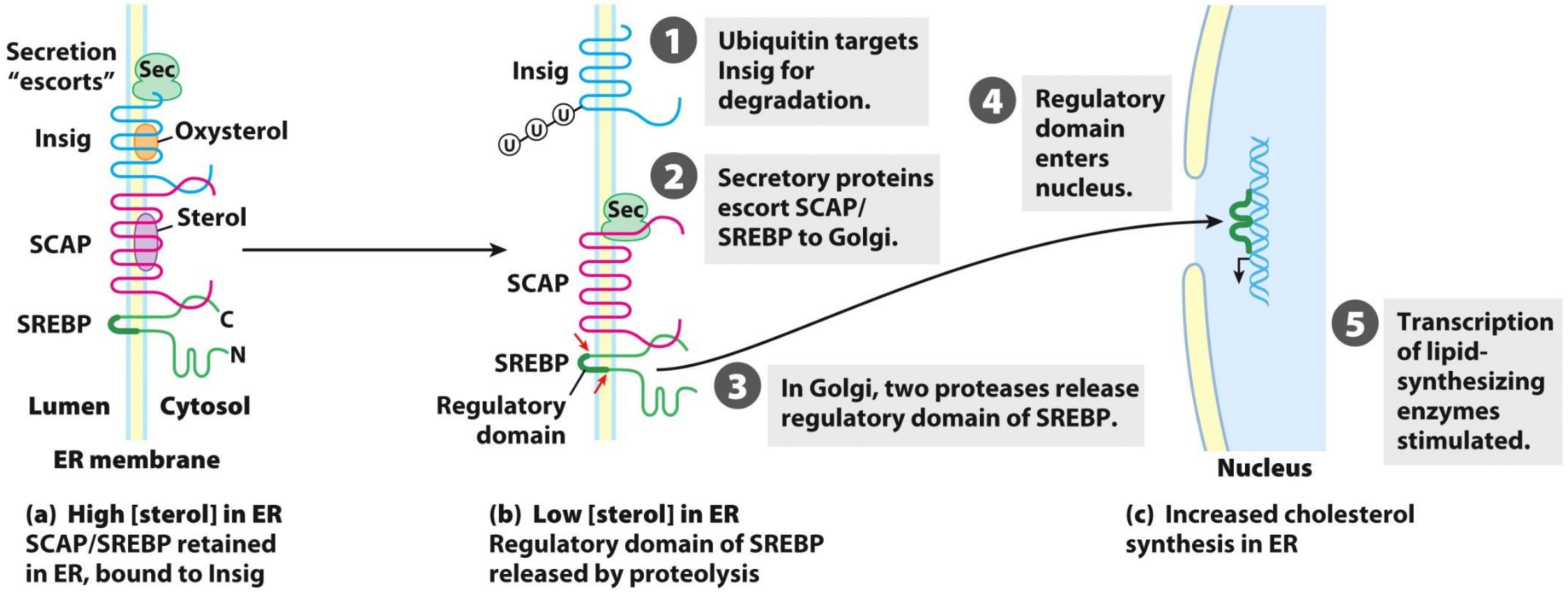
Esterification of cholesterol II.



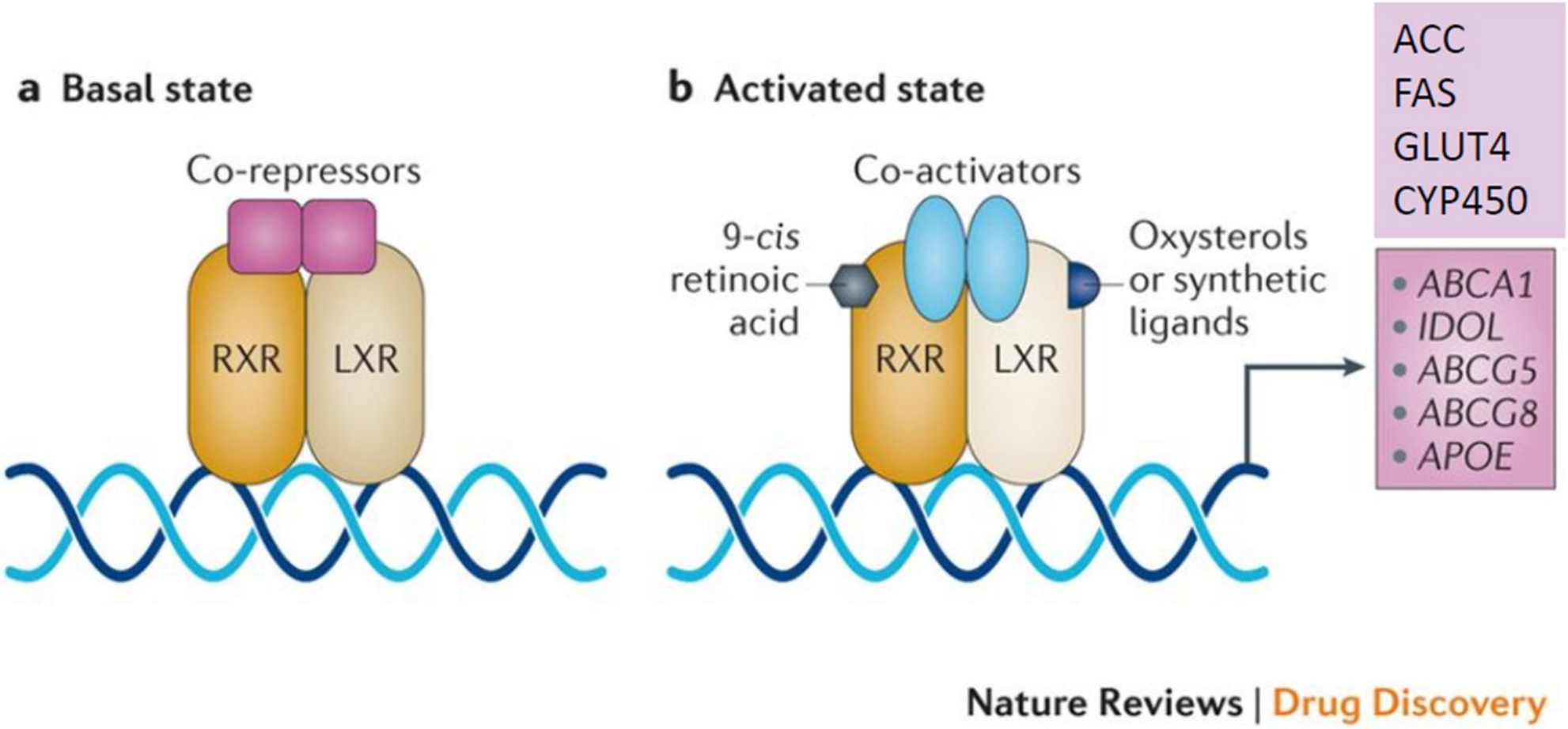
Regulation of cholesterol synthesis



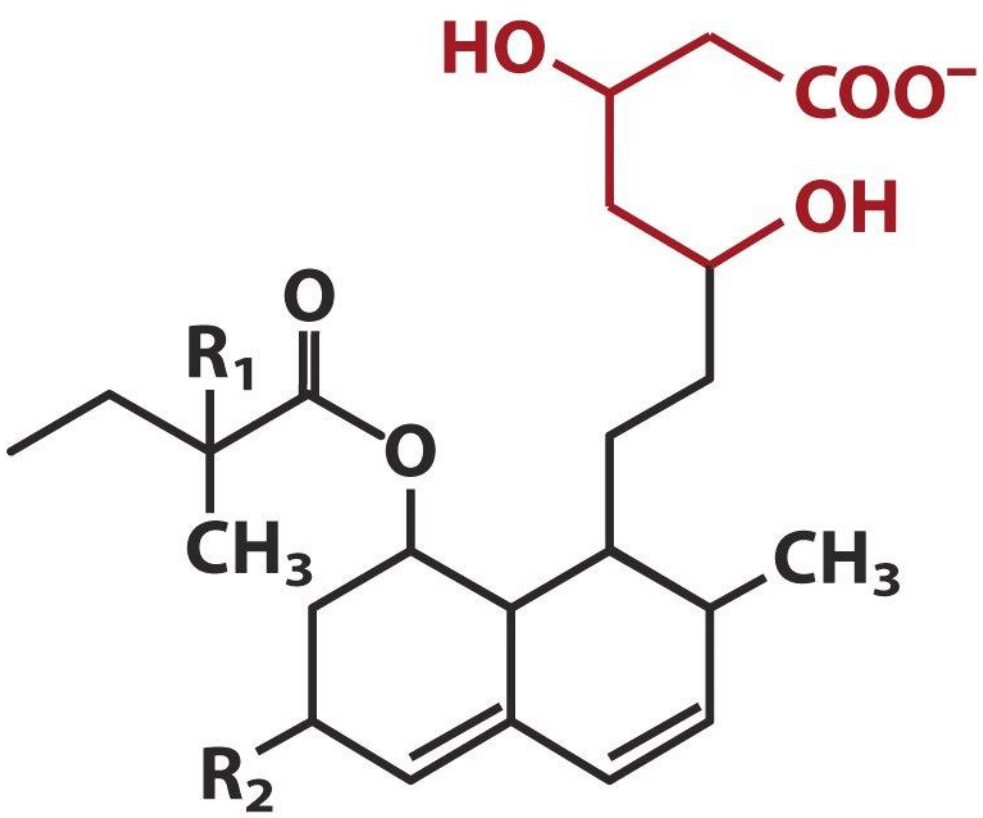
Transcriptional regulation

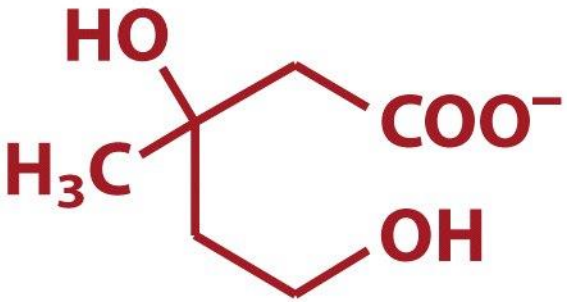


Transcriptional regulation



Statins

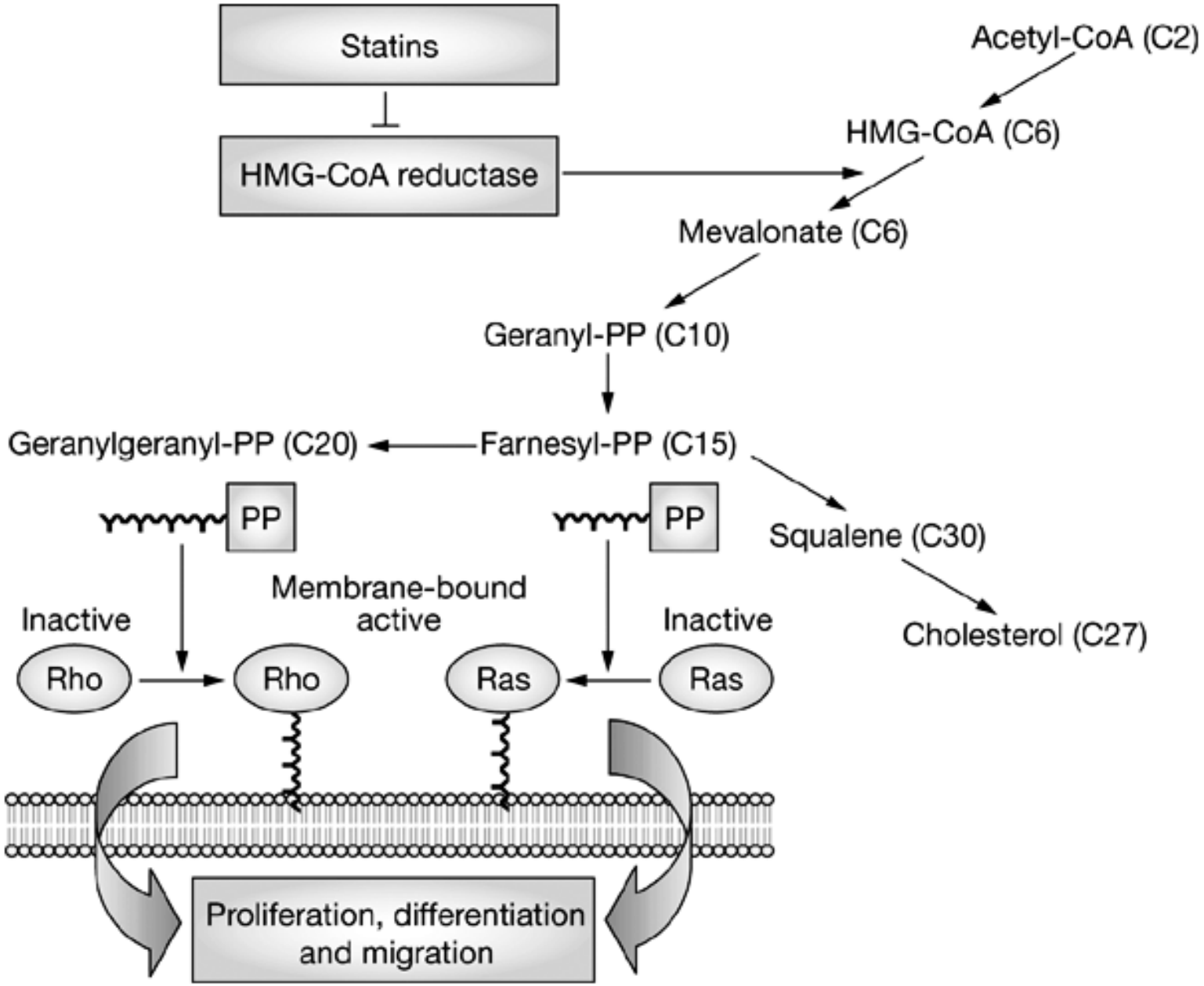




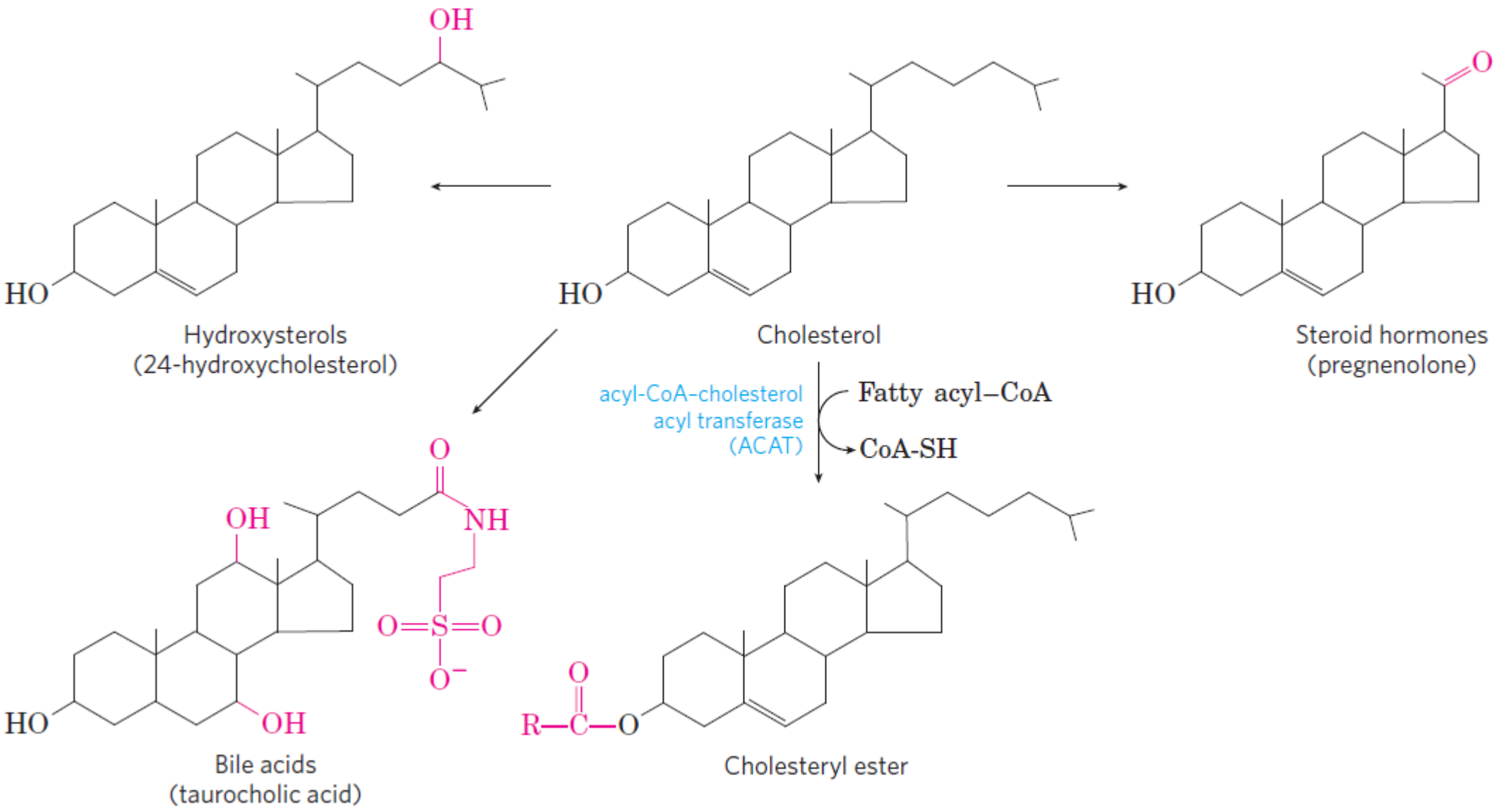
Mevalonate

$R_1 = H$	$R_2 = H$	Compactin
$R_1 = CH_3$	$R_2 = CH_3$	Simvastatin (Zocor)
$R_1 = H$	$R_2 = OH$	Pravastatin (Pravachol)
$R_1 = H$	$R_2 = CH_3$	Lovastatin (Mevacor)

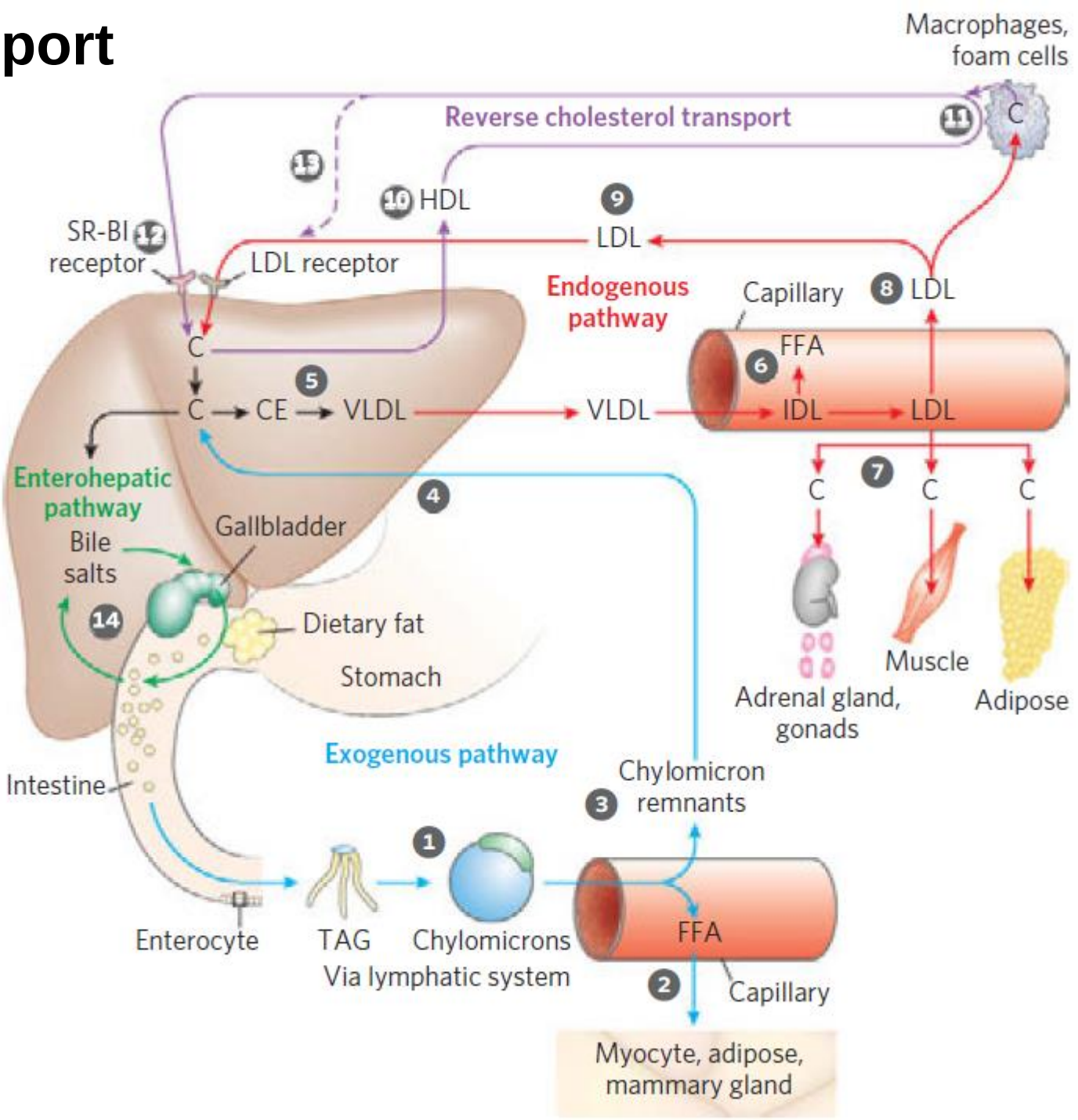
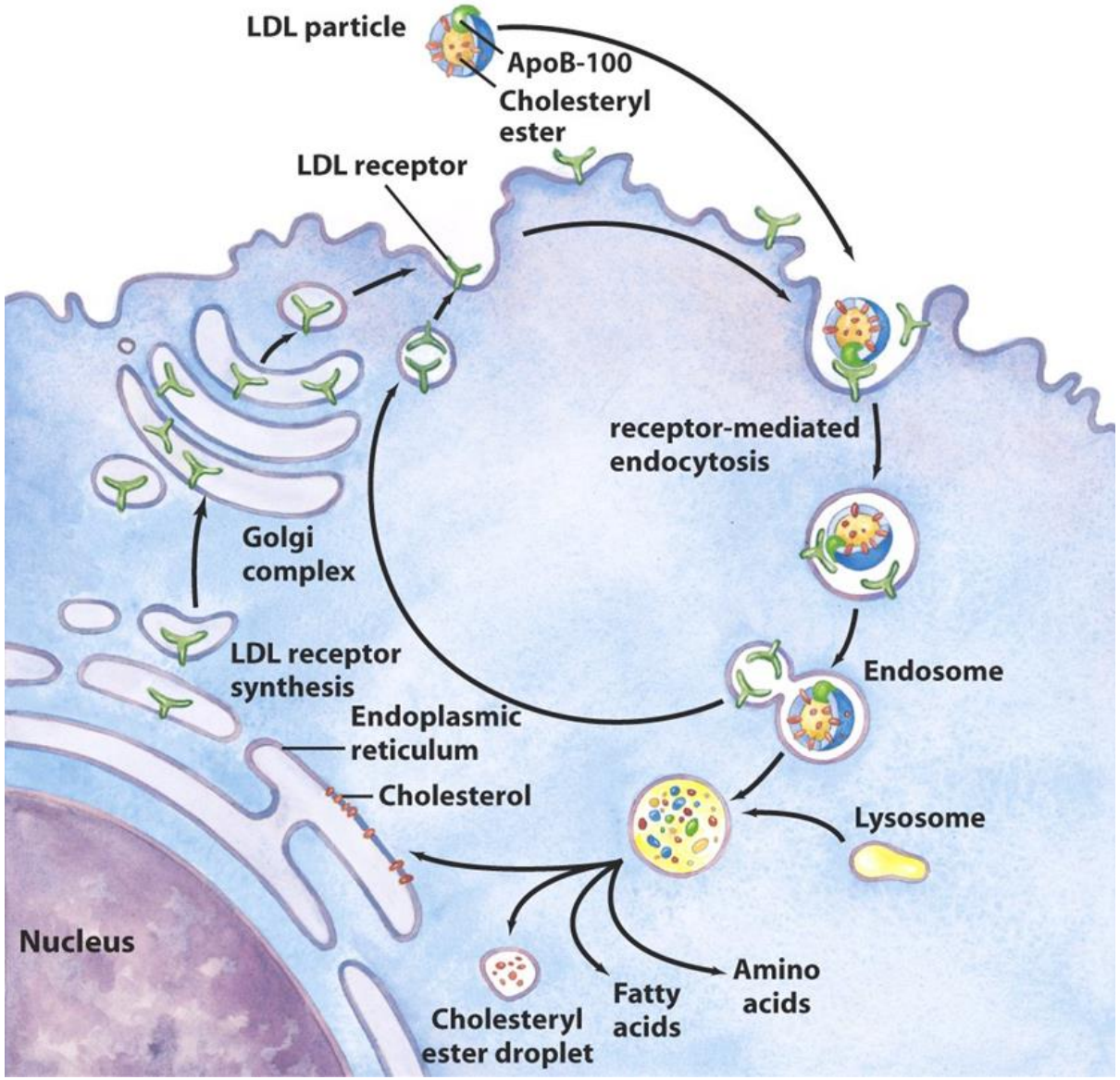
Statins


Statins
HMG-CoA reductase
Acetyl-CoA (C2)
HMG-CoA (C6)
Mevalonate (C6)
Geranyl-PP (C10)
Farnesyl-PP (C15)
Geranylgeranyl-PP (C20)
Squalene (C30)
Cholesterol (C27)
PP
PP
Membrane-bound
active
Inactive
Inactive
Rho
Rho
Ras
Ras
Proliferation, differentiation
and migration

Possible metabolic fates of cholesterol



Cholesterol transport



Cholesterol transport - LDL