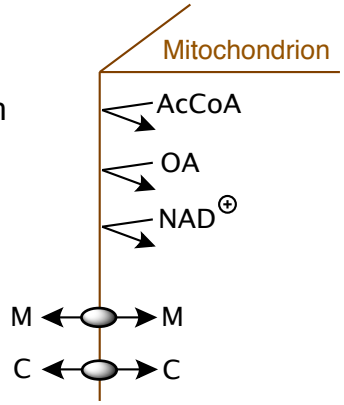
Session 17
5.07

So far: CATABOLISM | Next: ANABOLISM

Fatty Acid and Lipid Biosynthesis

Some Rules

Cytoplasm ||| Site of FA Biosyn



Stages of FA Biosynthesis

1.) FA biosynthesis = cytoplasmic reaction, but precursor (AcCoA "packaged" as citrate) is in mitochondrion; must get citrate to cytoplasm.)

2.) Must maintain OA mass balance between cytoplasm and mitoplasm.

3.) Activation of Acetyl CoA → MalCoA

4.) Formation of ACP (acyl carrier protein) derivatives

5.) FAS (Fatty Acid Synthase) reactions to make palmitate (16:0)

Post FAS Reactions

1) Elongation, Desaturation, Branching

2) 2 FA + $G_{ol}3P$ → Phospholipid (PL)

Constituent of biological membrane

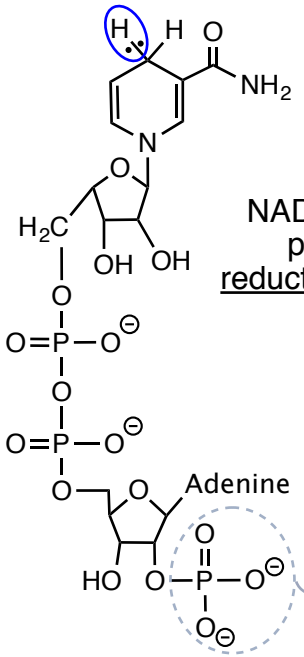
P_i FA

TAG

Energy storage

3) Polyketide biosynthesis

Introducing NADPH (Biosynthesis is reductive)



NADPH is our principal reductive cofactor

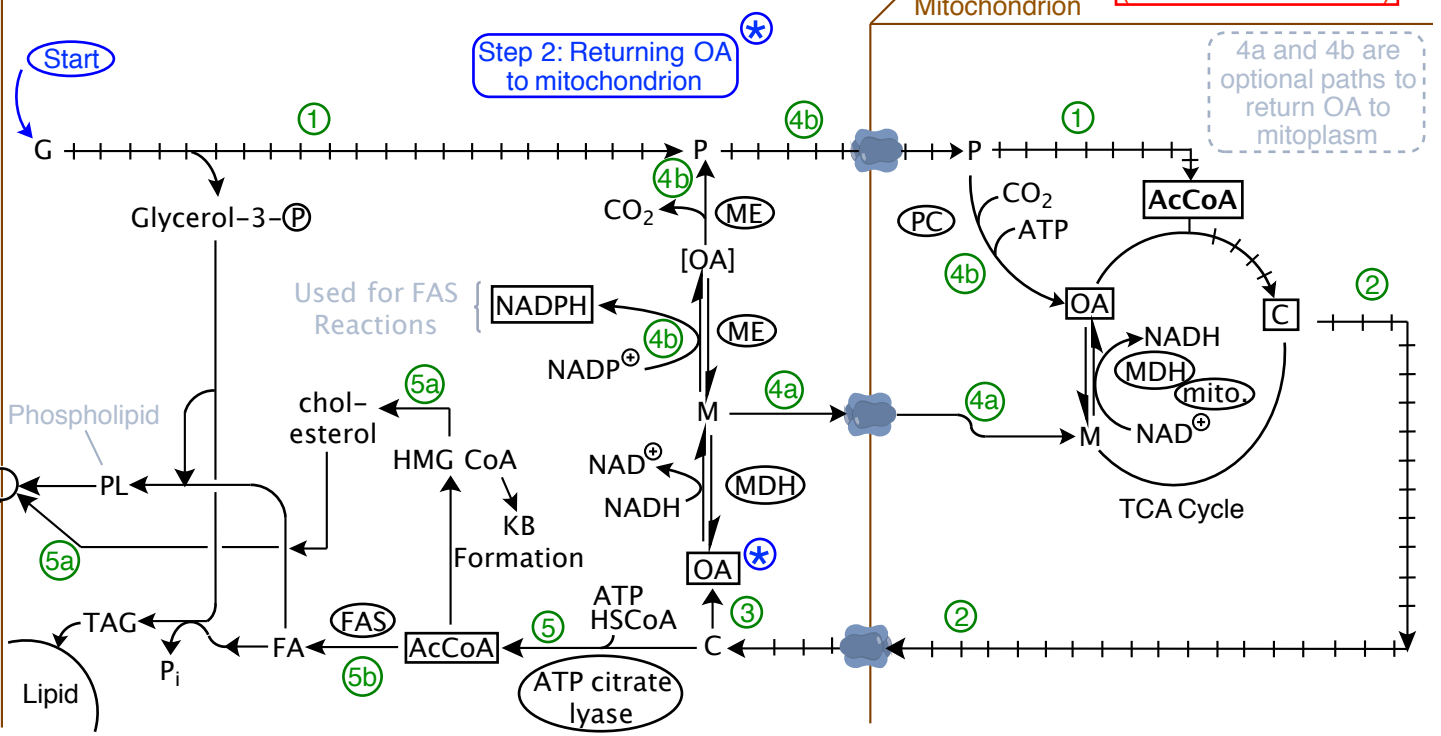
Differentiates NADPH from NADH

Step 1: Getting Acetyl CoA (as citrate) into Cytoplasm (location of FAS)

Physiological Scenario: eat sugar → get fat

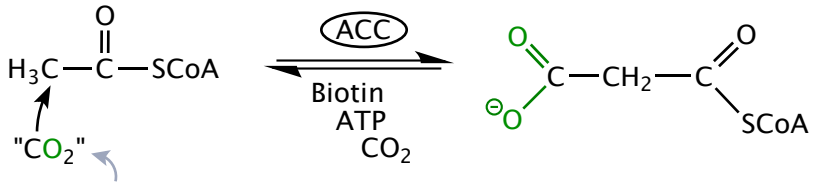
ME = Malic enzyme (uses NADP+/NADPH)

4a and 4b are optional paths to return OA to mitoplasm



A

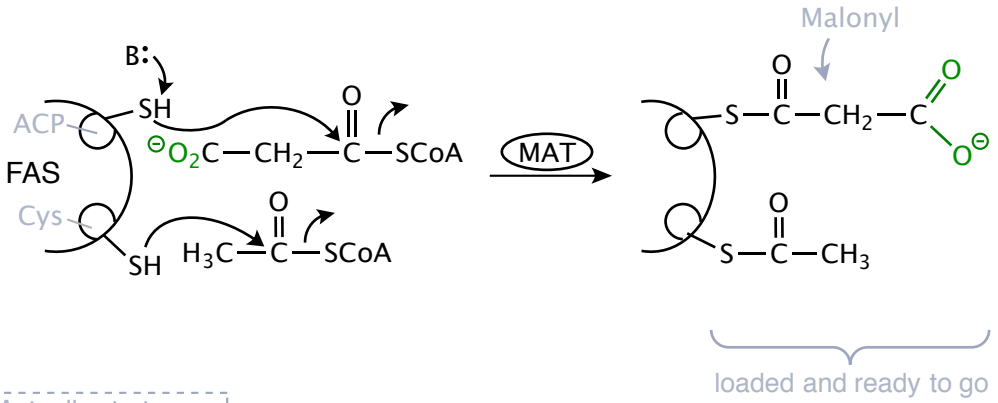
Step 3 Synthesis of Malonyl CoA (the precursor to all but (2) carbons of the FA)



Acetyl CoA Carboxylase

B

Step 4 Synthesis of ACP derivatives

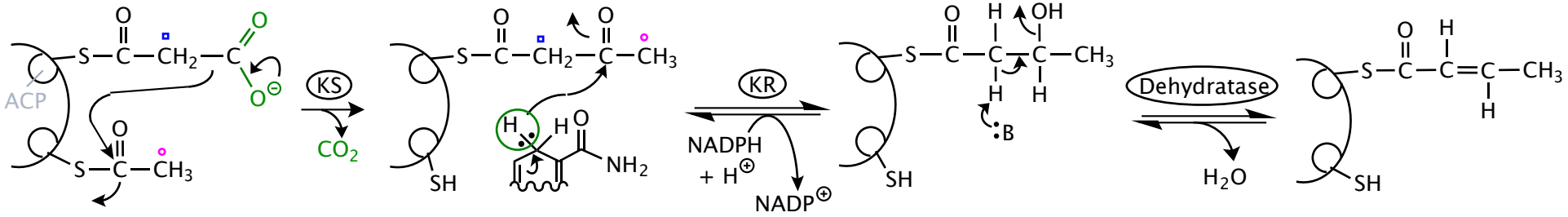


Actually starts on ACP and is transferred to Cys

Malonyl/Acyl Transferase

C

Step 5 FAS Reactions



ACP = Acyl Carrier Protein

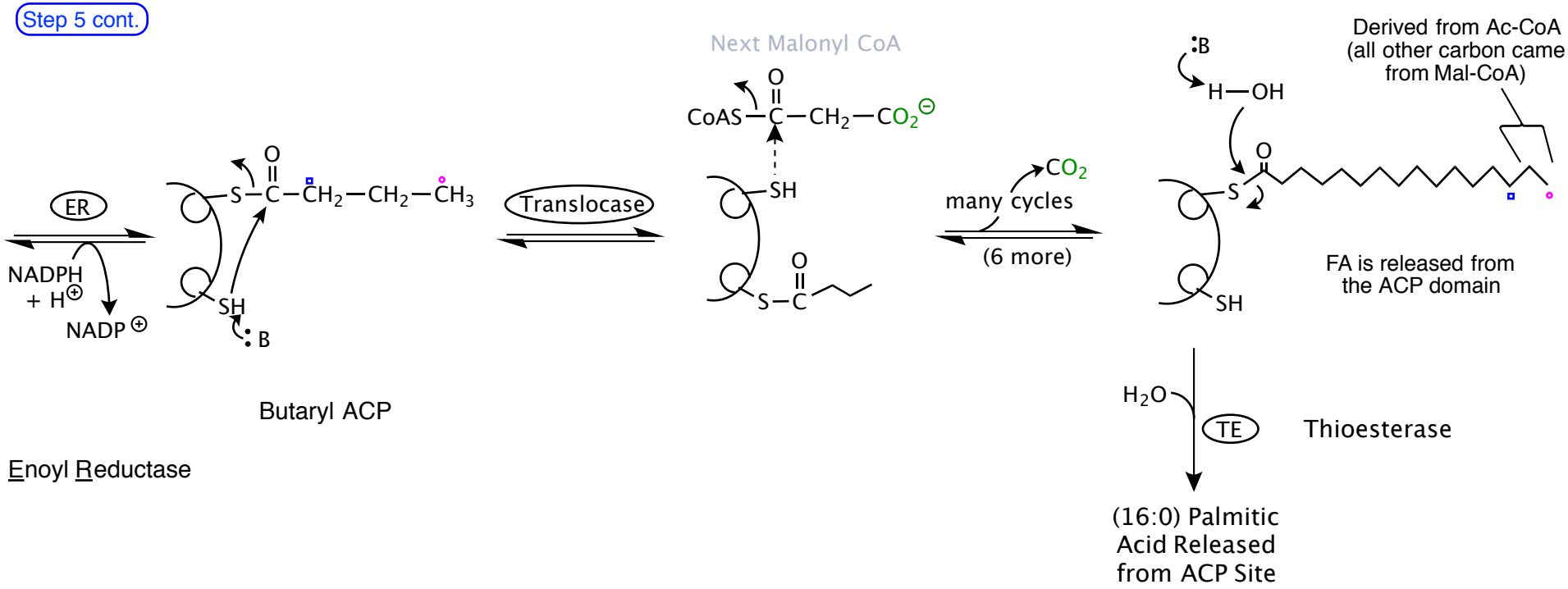
= long arm transports substrate among different catalytic domains

β-ketoacyl ACP

β-Hydroxy-Acyl ACP

Δ^2 enoyl ACP

Step 5 cont.

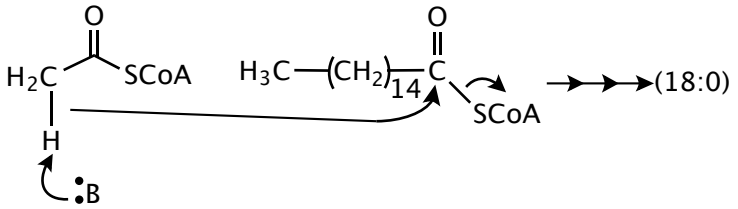


Elongation

-- FA released from FAS in cytoplasm

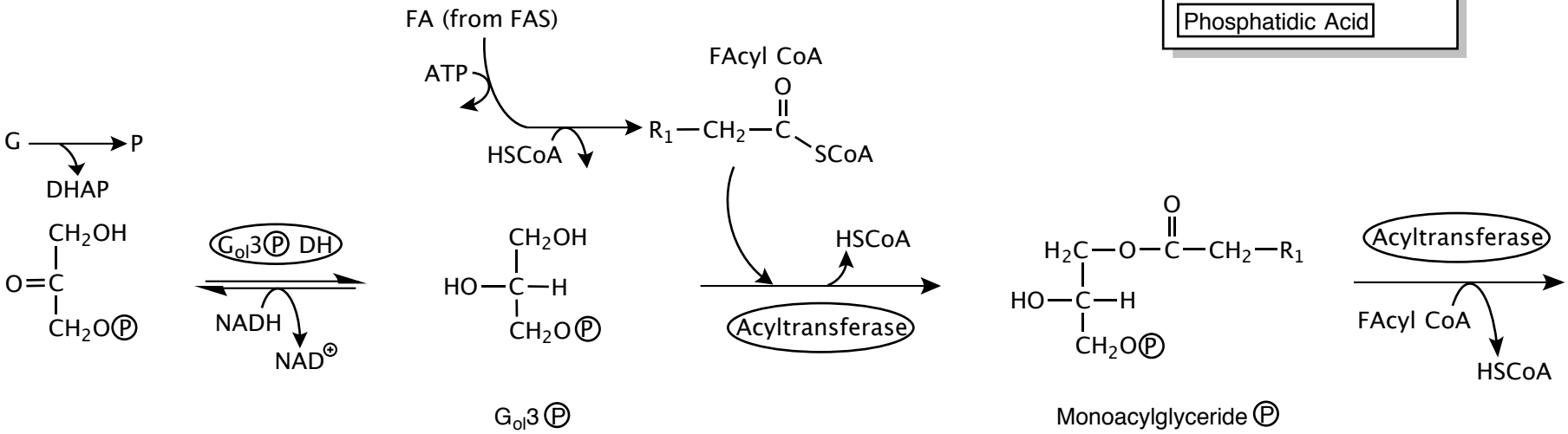
-- If it needs to be elongated - it is transported (as HSCoA ester) to mitochondrion or endoplasmic reticulum

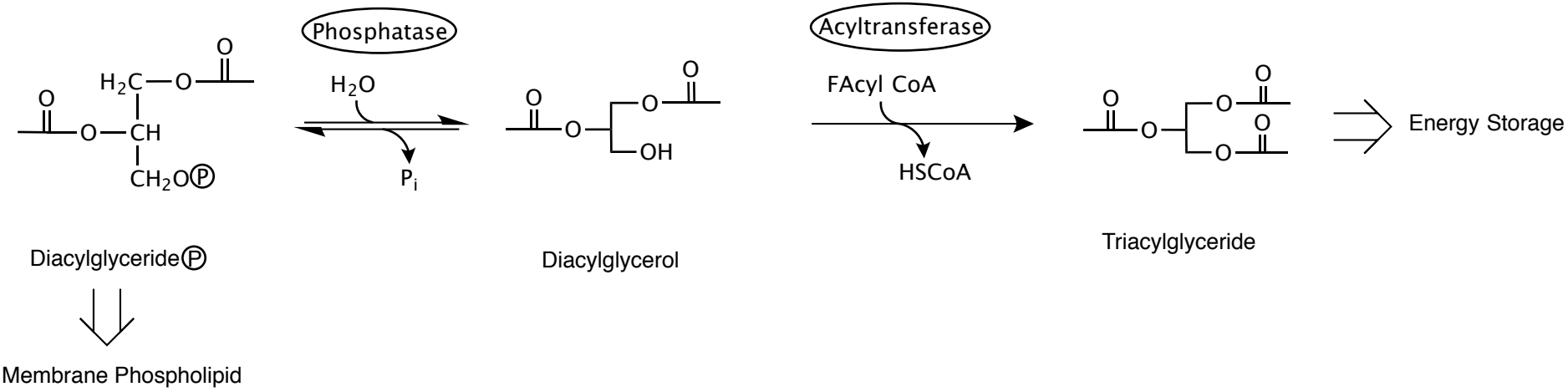
-- See book for mechanisms of elongation



Converting FA to Phospholipid and TAG

Membrane lipid
Phospholipid
Phosphatidic Acid





5.07SC Biological Chemistry I
Fall 2013