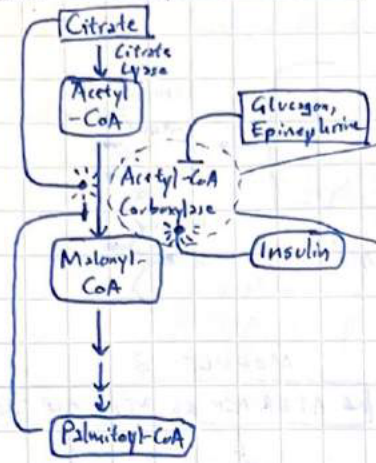
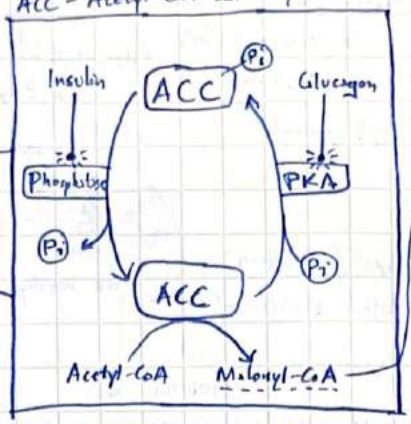
Regulation of Fatty Acid Metabolism

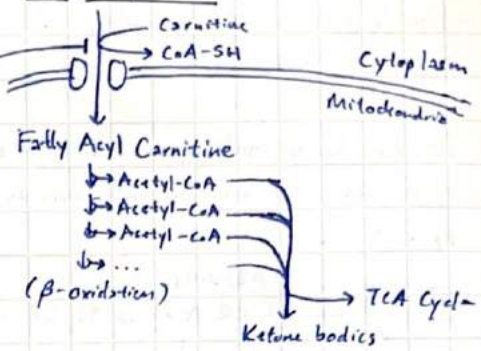


ACC - Acetyl-CoA Carboxylase



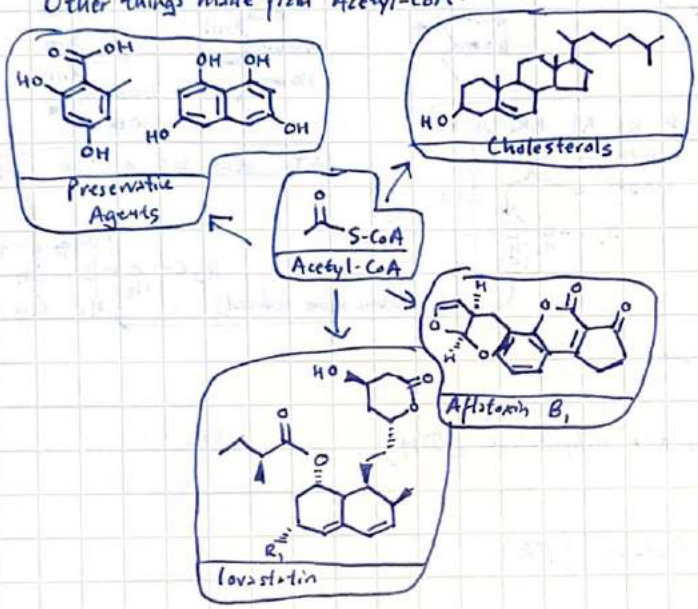
- Malonyl-CoA acts as an inhibitor for the TCA cycle and ketogenesis as it prevents fatty acyl CoA membrane transport; during well-fed state (high insulin concentration) → Less TCA cycle & Ketone body metabolite generation.

Effect on fatty acyl transport:

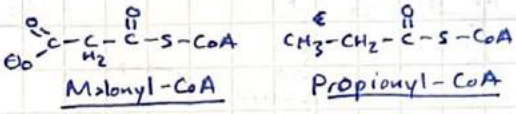


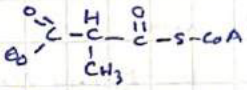
POLYKETIDE BIOSYNTHESIS

Other things made from Acetyl-CoA:

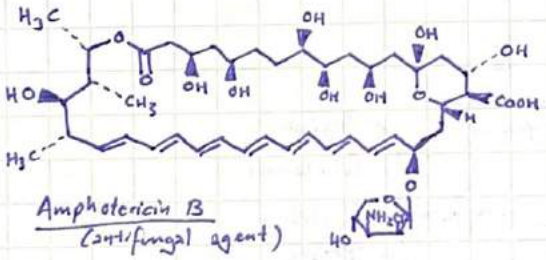


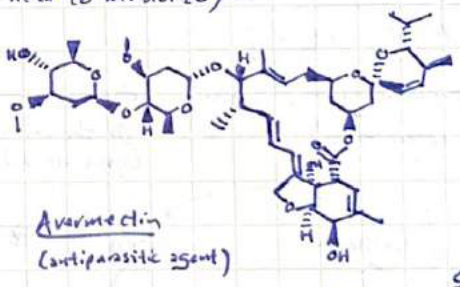
Acetyl-CoA is not the only molecule required for polyketide synthesis, however. Other molecules include:



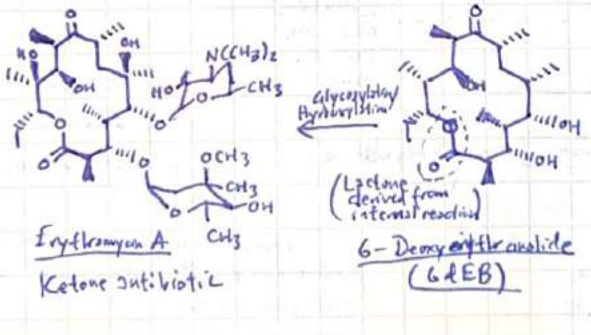


Medically important polyketides include: (Absolutely no need to memorize) –





Structure formed from "assembly line" synthesis of erythromycin.

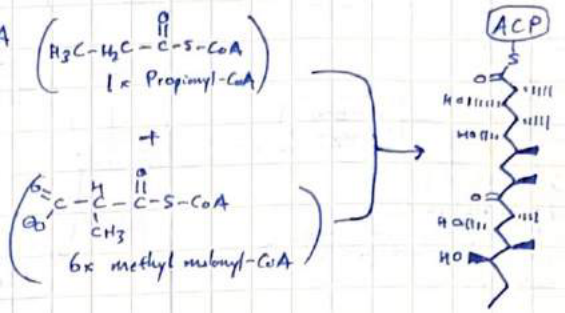


Assembly-line synthesis of erythromycin (modular assembly line)

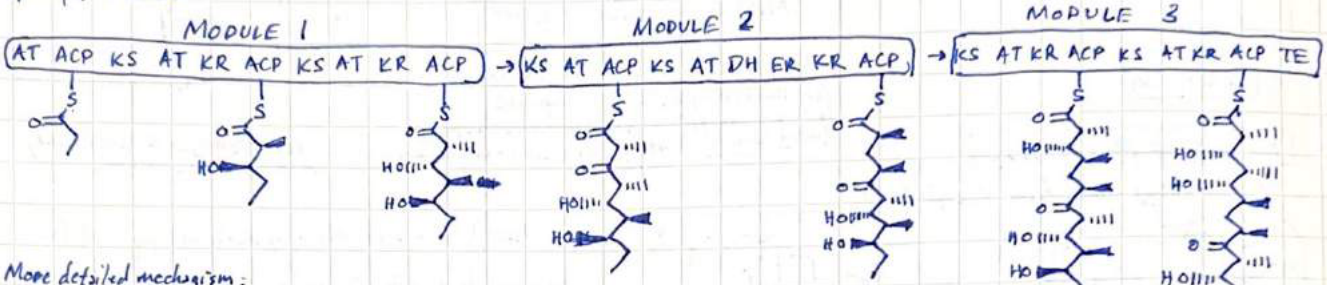
Materials required: 6x Methyl-malonyl-CoA, 1x Propionyl-CoA

Recall that a combination of (AT) and (ACP) = condensation.

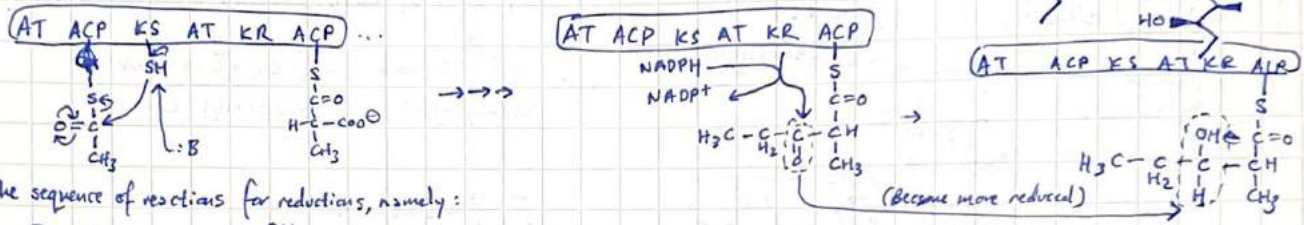
- How is the exact order of carbonyls and hydroxyls formed on the erythromycin chain?



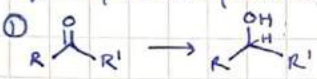
The assembly of erythromycin follows a very specific pattern of subunits, contributing to differences in oxidation state of specific carbons:

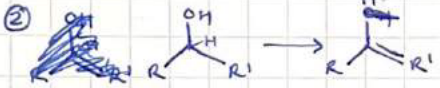


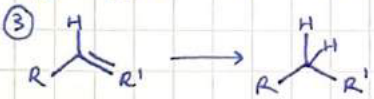
More detailed mechanism:



The sequence of reactions for reductions, namely:

①  by Ketoacyl ACP reductase (KR)

②  by Hydroxyacyl ACP dehydratase (DH)

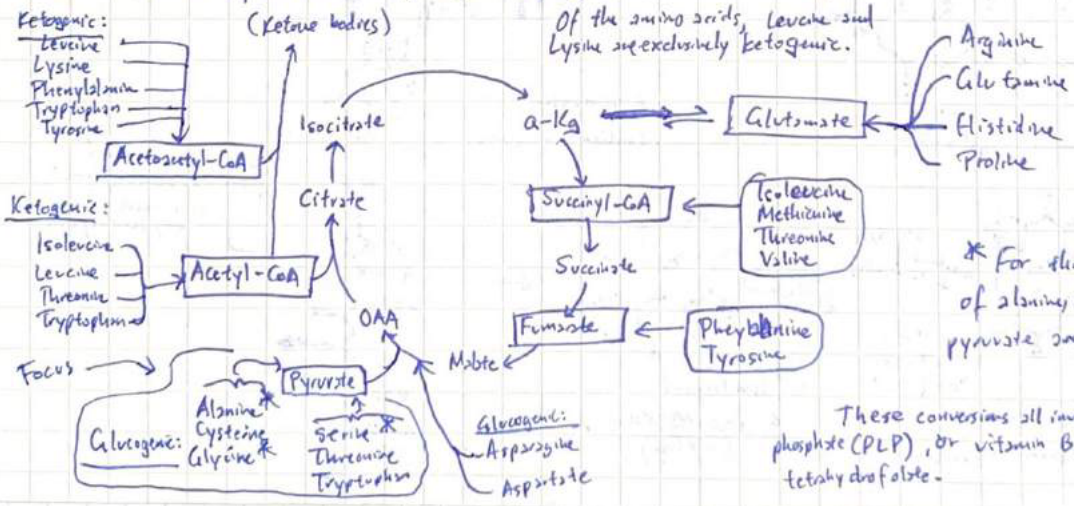
③  by Enol-ACP reductase (ER)

is the process by which specific carbons have specific oxidation/reduction states.

AMINO ACID CATABOLISM

Amino acids are separated into either glucogenic or ketogenic:

Of the amino acids, Leucine and Lysine are exclusively ketogenic.



* For this class, the mechanisms of alanine, serine, and glycine to pyruvate are of main concern

These conversions all involve either pyridoxal phosphate (PLP), or vitamin B6: and H4-folate, tetrahydrofolate.