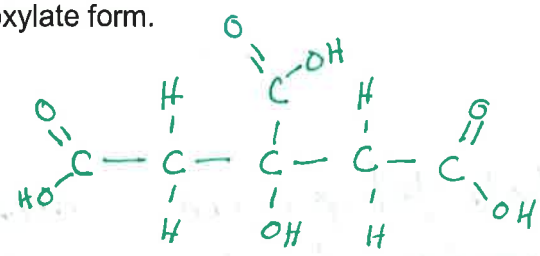
Name: Key Exam 2

All references to data or authors on this exam are from:

Kim CW; Addy C; Kusunoki J; Anderson NN; Deja S; Fu X; Burgess SC; Li C; Ruddy M; Chakravarthy M; Previs S; Milstein S; Fitzgerald K; Kelley DE; and Horton JD. (2018). Acetyl CoA Carboxylase Inhibition Reduces Hepatic Steatosis but Elevates Plasma Triglycerides in Mice and Humans: A Bedside to Bench Investigation. *Cell Metabolism* **26:** 394-406.

1. In order to assay for acetyl CoA carboxylase function, the authors prepared a solution that contained 20 mM citrate.
   a. (5 pts) Draw citric acid, the protonated or acid form not the deprotonated conjugate-base carboxylate form.



   b. (5 pts) Determine the mass of dry citric acid powder required to make 1 L of 20 mM citric acid. The following are atomic masses: C→12.01 g mole^{-1}; H→1.008 g mole^{-1}; O→16.00 g mole^{-1}.

$C_6H_8O_7$

$72.06 + 8.064 + 112 = 192.124\ g/mole$

$\left(\frac{0.02\ mole}{L}\right)(1\ L)\left(192.124\ \frac{g}{mole}\right) = 3.8425\ g$

2. (10 pts) The authors found that inhibiting acetyl-CoA carboxylase resulted in decreased new fatty acid synthesis within hepatocytes. Explain why this occurs. [Only the first two sentences will be read and graded. Write legibly; I will not guess.]

Acetyl-CoA carboxylase synthesizes the production of Malonyl-CoA. Malonyl-CoA is required for fatty acid synthesis.

3. (10 pts) The authors found that inhibiting acetyl-CoA carboxylase resulted in increased concentrations of acetoacetate and β-hydroxybutyrate within hepatocytes. Explain why this occurs. [Only the first two sentences will be read and graded. Write legibly; I will not guess.]

The malonyl-CoA produced by acetyl-CoA carboxylase usually inhibits fatty acid transport into the mitochondrial lumen. Without malonyl-CoA, more fatty acids will enter the lumen and be converted to ketone bodies via acetyl-CoA.

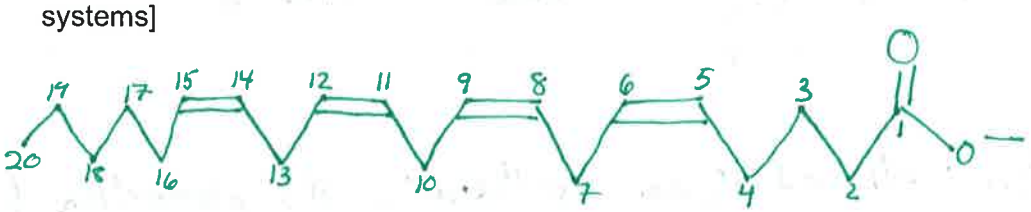
4. (10 pts) If the fasting triacylglycerol concentration in human plasma increases, which lipoprotein complex do you predict to find elevated? Explain your reasoning. [Only the first two sentences will be read and graded. Write legibly; I will not guess.]

VLDL will be elevated because it is primarily composed of triacylglycerols.

5. (10 pts) The authors found that SREBP-1 located in the nucleus of mouse hepatocytes increased the expression of ATP-citrate lyase; fatty acid synthase; fatty acid elongase; fatty acid desaturase; acyl transferase; lipase; and phospholipid transfer protein. All of these proteins are directly linked to lipid metabolism. Interestingly, glucose-6-phosphate dehydrogenase expression was also increased. Why is this carbohydrate metabolic enzyme regulated here? [Only the first two sentences will be read and graded. Write legibly; I will not guess.]

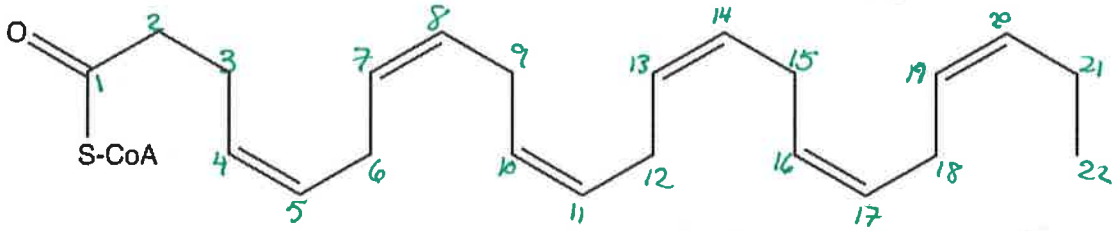
Glucose-6-phosphate dehydrogenase catalyzes the first step of the pentose phosphate pathway. The pentose phosphate pathway is the source of NADPH for fatty acid synthesis.

6. (10 pts) The authors substituted mouse diet with arachidonic acid. Arachidonic acid was presented as 20:4n6 in Figure 6. The "n" is a substitute for ω which means that the first double bond starts six carbons from the terminal methyl group (not the carboxylate). Draw arachidonic acid. [Hints: Human fatty acids usually contain all *cis* carbon double bonds and no conjugated π systems]



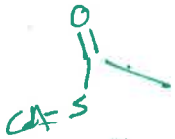
20 : 4 $\Delta^{5,8,11,14}$

7. The authors substituted mouse diet with docosahexaenoic acid (shown in the acyl-CoA form below).



Make 11 acetyl-CoA

10 round of β-ox.



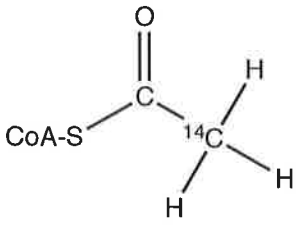
11
x 4
44

a. (4 pts) How many redox reactions occur for the conversion of this acyl-CoA to acetyl-CoA via β-oxidation? C-C 27 C-H 31 = 58 - 44 = (14)

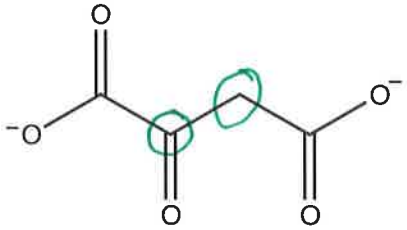
b. (3 pts) How many NADH would be generated from the conversion of this acyl-CoA to acetyl-CoA via β-oxidation? 10 - 3 = (7)

c. (3 pts) How many $FADH_2$ would be generated from the conversion of this acyl-CoA to acetyl-CoA via β-oxidation? 10 - 3 = (7)

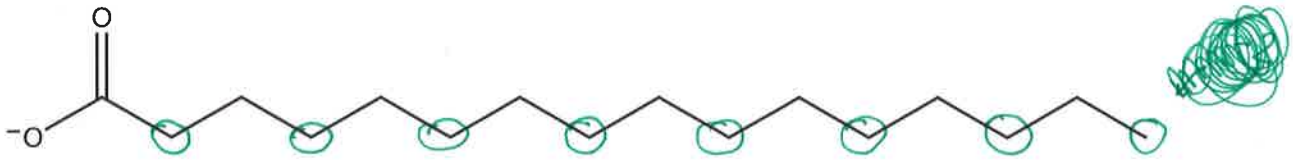
8. The authors use ^{14}C containing acetyl-CoA to trace metabolic pathways. Imagine the following molecule was used by a hepatocyte:



a. (10 pts) Circle any carbons that may be the ^{14}C isotope in oxaloacetate after one around of the TCA cycle.



b. (10 pts) Circle any carbons that may be the ^{14}C isotope in newly synthesized palmate.



c. (10 pts) Circle any carbons that may be the ^{14}C isotope in newly synthesized β-hydroxybutyrate.