Name: _____ Exam 1

This exam is inspired by the following paper and is where any reference to authors or data originates:

Chaodong Wu, Salmaan Khan, Li-Jen Peng, Honggui Li, Steven Carmella, and Alex Lange. (2006) Perturbation of glucose flux in the liver by decreasing $F26P_2$ levels causes hepatic insulin resistance and hyperglycemia. **Am. J. Physiol endocrinol Metab 291:** E536-E543.

1. (14 pts.) Imagine that you create a stock solution of the dye tartrazine. You need to know the absorbance of the stock solution, but it is too concentrated to read in the spectrophotometer. The following dilution scheme allows you to determine the needed absorbance value. Fill in all the blank cells in the table below:

Tube	Tartrazine	dH_2O	Total Volume	Dilution Factor	Absorbance
1	stock	0 uL	1 mL	1	
2	250 uL of tube #1	750 uL	1 mL	1:4	
3	500 uL of tube #2		1 mL	1:2	
4	100 uL of tube #3	900 uL	1 mL		
5	62.5 uL of tube #4		1 mL	1:16	0.20

2. (27 pts.) The authors fed hepatocytes lactate that was uniformly labeled at each position with ^{14}C. Later, they measured the concentration of UDP-glucose that contained ^{14}C. Write out the pathway by which ^{14}C from lactate is incorporated into UDP-glucose. Include (*i*) chemical structures starting with lactate and ending with UDP-glucose and (*ii*) enzyme names for each catalyzed step.

3. (20 pts.) Consider **a normal-state hepatocyte after a meal**.

	High	Low	Unchanged	N/A
Blood [glucose]				
Blood [Insulin]				
Insulin Receptor Signal				
Blood [Glucagon]				
Glucagon Receptor Signal				
[cAMP]				
Inflow through GLUT2	X			
Outflow through GLUT2		X		
PFK-2/F-2,6-BPase Phosphorylation				
Flux through hexokinase				
Flux through glucokinase				
Flux through glucose-6-phosphatase				
PFK-1 activity				
PFK-2 activity				
F-1,6-BPase activity				
F-2,6-BPase activity				
[F-2,6-BP]				
Glycogen synthase phosphorylation				
Glycogen synthase activity				
Glycogen phosphorylase phosphorylation				
Glycogen phosphorylase activity				
Flux through glycolysis				
Flux through gluconeogenesis				
Flux through glycogenesis				
Flux through glycogenolysis				

What is the metabolic fate of glucose flowing into the hepatocyte?

4. (19 pts.) The authors expressed a mutant form of phosphofructokinase-2 in mouse hepatocytes. This mutant PFK-2 was not active regardless of its phosphorylation state. The fructose-2,6-bisphosphatase was unaltered. This lead to a significantly lower [fructose-2,6-bisphosphate]. Consider **the mutant mouse hepatocytes after a meal.**

	High	Low	Unchanged	N/A
Blood [glucose]				
Blood [Insulin]				
Insulin Receptor Signal				
Blood [Glucagon]				
Glucagon Receptor Signal				
[cAMP]				
Inflow through GLUT2	X			
Outflow through GLUT2		X		
PFK-2/F-2,6-BPase Phosphorylation				
Flux through hexokinase				
Flux through glucokinase				
Flux through glucose-6-phosphatase				
PFK-1 activity				
PFK-2 activity				X
F-1,6-BPase activity				
F-2,6-BPase activity		X		
[F-2,6-BP]		X		
Glycogen synthase phosphorylation				
Glycogen synthase activity				
Glycogen phosphorylase phosphorylation				
Glycogen phosphorylase activity				
Flux through glycolysis				
Flux through gluconeogenesis				
Flux through glycogenesis				
Flux through glycogenolysis				

What is the metabolic fate of glucose flowing into the hepatocyte under reduced [fructose-2,6-bisphosphate]?

5. (20 pts.) Interestingly over time, the reduction in [fructose-2,6-bisphosphate] lead the mutant hepatocytes to develop insulin resistance. This means that even though insulin is present in the blood and bound to the extracellular side of the hepatic insulin receptor, the signaling cascade is not initiated (e.g., the phosphorylation of regulated enzymes does not decrease). Consider **the insulin-resistant, mutant hepatocytes after a meal. Before the meal, the mice were in a fasting state.**

	High	Low	Unchanged	N/A
Blood [glucose]	X			
Blood [Insulin]	X			
Insulin Receptor Signal			X	
Blood [Glucagon]		X		
Glucagon Receptor Signal		X		
[cAMP]		X		
Inflow through GLUT2		X		
Outflow through GLUT2	X			
PFK-2/F-2,6-BPase Phosphorylation			X	
Flux through hexokinase				
Flux through glucokinase				
Flux through glucose-6-phosphatase				
PFK-1 activity				
PFK-2 activity				X
F-1,6-BPase activity				
F-2,6-BPase activity			X	
[F-2,6-BP]		X		
Glycogen synthase phosphorylation			X	
Glycogen synthase activity				
Glycogen phosphorylase phosphorylation			X	
Glycogen phosphorylase activity				
Flux through glycolysis				
Flux through gluconeogenesis				
Flux through glycogenesis				
Flux through glycogenolysis				

Insulin resistance is the hallmark of the pathogenic state of Type II diabetes. Hepatocytes have reduced influx of glucose and even begin to release (outflow) glucose while blood glucose levels remain higher than normal (hyperglycemia). What is the metabolic source of glucose from hepatocytes with insulin resistance?