

STEP 1 - NAME (*Print clearly*) _____*(first)**(last)*

Circle your college and campus: 301 --- CHM-EL
 302 --- CHM-GR
 303 --- COM-EL
 304 --- COM-DMC
 305 --- COM-MUC

STEP 2 – Fill in your answer sheet with a #2 scoring pencil, as follows:

- Print your first and last name on the line provided
- Code in your Student Number (PID)
- Code in your section as corresponds to the above list
- Code in the correct FORM **This is Form A**
- Sign your name in the signature box. By signing the answer sheet for this exam, the student certifies that he/she has adhered to the policies of academic honesty in the performance of this exam.

STEP 3 - Read these instructions:

- Turn off cell phones; keep them out of sight.
- The proctors have the authority/responsibility to assign any student a different seat at any time, without implication and without explanation, before or during the examination, as they deem necessary. Accomplish any relocation quietly and without discussion.
- Make sure your exam has 32 questions.
- We will not answer questions of clarification. However, if you think there is an error on your exam, summon an exam proctor.
- Read each question very carefully. Choose the single, best answer and mark this answer on your answer sheet. No points will be added for correct answers which appear on the exam page but not on the answer sheet.
- When you finish, carefully follow the instructions at the end of the exam. When you leave the exam room, please turn in your answer sheet AND your exam to the proctors standing by the doors INSIDE the auditorium. Once you exit the auditorium, please leave the building. Hallway conversations disturb those still taking the exam.
- There will be answer keys to this exam posted on the course website by 5:00 p.m. the day of the exam. You may wish to copy your responses from your answer sheet onto the answer grid on the LAST page of this exam so that you can check your results. You can tear off the last page and take it with you.
- You have 70 minutes to complete this exam. No additional time will be allowed for transfer of answers from the exam to the answer sheet. We will close the exam promptly at 9:10 a.m. Once we withdraw the boxes for the answer sheets from the doors, no additional answer sheets will be accepted.

STEP 4 – Wait until instructed to proceed with the exam!

Dr. Otto Warburg proposed that cancer cells have an altered metabolism, one that is much more reliant on glycolysis for ATP production, which explains their ability to grow and metastasize. In the 80 years since the "Warburg Hypothesis" was presented, we have learned a lot about the biochemistry of cancer. **The following 6 questions are focused on these findings.**

1) Cancer cells have a higher rate of glycolysis than their neighboring normal cells. One reason for this increased rate is the over-expression of hexokinase (HK). Given that most tumors have a limited supply of glucose because of their inadequate vasculature, which statement below correctly describes a characteristic of hexokinase that would explain why this increased HK concentration would be an advantage to the cancer?

- A) Its low K_m would allow it to bind and phosphorylate any available glucose
- B) Its high V_{max} would allow it to phosphorylate a large number of glucose molecules in a short time
- C) The fact that glucose 6-phosphate has no effect on HK activity means it will not turn off in the presence of high glucose concentrations
- D) Its high K_m means that it needs high glucose concentrations to become active
- E) Its activity does not require ATP, making it better suited for tumor development

2) The cancer cell's increased dependence on glycolysis for its energy needs also implies that which of the following statements must also be true in a cancer cell?

- A) Fructose 2,6-bisphosphate will be low in the cancer cell
- B) Phosphoenolpyruvate carboxykinase will be active
- C) Glucose 6-phosphatase will be active
- D) Phosphofructokinase 2 will be active
- E) Pyruvate will be turned into oxaloacetate in the matrix of the mitochondria

3) Another phenotype of many cancer cells is the overexpression of pyruvate dehydrogenase kinase 1 (PDK1), the enzyme responsible for phosphorylating the pyruvate dehydrogenase complex. This increase in PDK1 activity would result in which of the following?

- A) Trafficking of pyruvate into the mitochondria will increase
- B) The level of lactate in the cell will increase
- C) Citrate synthase activity will increase
- D) The PDH complex will be responsive to direct activation by acetyl-CoA
- E) The electron transport chain activity will be unaffected

4) Interestingly, inheriting a deleterious mutation in the succinate dehydrogenase (SDH) complex makes a person prone to getting pheochromocytomas, a cancer of the adrenal gland. Which of the following would **NOT** be an effect of SDH deficiency?

- A) Decreased levels of fumarate
- B) Increased levels of ubiquinol (QH_2)
- C) Increased levels α -ketoglutarate
- D) Decreased levels of malate
- E) Decreased efficiency of complex III of the electron transport chain

5) As a cancer cell grows into a tumor, it needs a lot of nucleic acids (i.e. Ribose 5-P) and synthesis power (i.e. NADPH). Which of the following enzymes are not required to meet these needs?

- A) Hexokinase
- B) Glucose 6-phosphate dehydrogenase
- C) Ribulose 5-phosphate isomerase
- D) 6-phosphogluconate dehydrogenase
- E) Transketolase

6) One of the main reasons tumors become more dependent upon glycolysis is because they are hypoxic in nature. This means they have a deficiency of oxygen. In fact, central portions of the tumor are almost anoxic, completely lacking oxygen. Anoxia is capable of impacting the electron transport chain in the same manner as cyanide. Which of the following statements would describe the mitochondria of cancer cells if they could be isolated and tested under anoxic conditions?

- A) The addition of 2,4-dinitrophenol would restart the electron transport chain
- B) Complex I would remain active
- C) The potential across the inner mitochondrial membrane would be low
- D) ATP production would be unaffected
- E) Cytochrome c would be completely oxidized

7) A patient comes into clinic suffering from lack of energy and very low hemoglobin levels. You run some tests and determine his red blood cells have a high level of phosphoenolpyruvate with little pyruvate produced and decreased ATP levels. You quickly deduce that he has a mutation in which glycolytic enzymes?

- A) Glyceraldehyde 3-phosphate dehydrogenase
- B) Glucokinase
- C) Phosphofructokinase
- D) Enolase
- E) Pyruvate kinase

8) A patient suffering from glucose 6-phosphate dehydrogenase deficiency would be expected to have which of the following phenotypes?

- A) Decreased risk of having Wernicke-Korsakoff syndrome
- B) Increased cellular concentrations of 6-phosphogluconolactone
- C) Normal levels of reduced glutathione
- D) Experience hemolysis following exposure to antimalarial drugs
- E) Normal NADPH-dependent cytochrome P450 enzyme activity

9) Fructose intolerance and galactose intolerance are similar in that they both:

- A) fail to trap the sugar inside the cell
- B) deplete the cell of reducing power
- C) fail to split a 6-carbon sugar into 3-carbon units
- D) effectively sequester inorganic phosphate
- E) only affect infants

10) Lactate dehydrogenase (LDH) plays an essential role in an exercising muscle, especially when the level of excursion surpasses the ability of circulatory systems ability to supply adequate oxygen. What is the main reason LDH is so important to the muscle under these conditions?

- A) It produces one mole of ATP via substrate level phosphorylation.
- B) It decreases pH thus decreasing the dissociation rate of oxygen from hemoglobin
- C) It removes excess lactic acid from the muscle to create pyruvate
- D) It produces NADH for energy while converting pyruvate into lactate
- E) It resupplies NAD^+ to glyceraldehyde 3-phosphate dehydrogenase

11) A 3 month infant is brought into the ER with an abnormally large liver and spleen. The infant is very small for her age and her liver is already showing signs of progressive scarring. You quickly deduce that the little girl has a glycogen storage disease. You analyze her glycogen enzymes and determine she has a branching enzyme deficiency (Anderson's Disease). If you were to analyze the structure and content of her glycogen stores what is most likely what you would find:

- A) Normal amount, normal structure
- B) Normal amount, fewer branches that are much longer than normal
- C) Less than normal amount, fewer branches that are much longer than normal
- D) Higher than normal amount, normal structure
- E) Higher than normal amount, normal number of branches but they appear shorter

12) A patient suffering from an isocitrate dehydrogenase deficiency is most likely to exhibit which of the following?

- A) Increased level of α -ketoglutarate
- B) Decreased electron transport chain activity
- C) Increased levels of glutamate
- D) Normal NADH levels within the matrix
- E) Decreased levels of isocitrate

13) You isolate mitochondria from a patient suffering from muscle weakness and lactic acidosis. You determine that the patient is UNABLE to oxidize ubiquinol, pump protons across the inner membrane if given succinate as a carbon source, nor reduce cytochrome c. This patient most likely suffers from a defect in which of the following protein complexes?

- A) Complex I
- B) Complex II
- C) Complex III
- D) Complex IV
- E) Complex V, ATP synthase

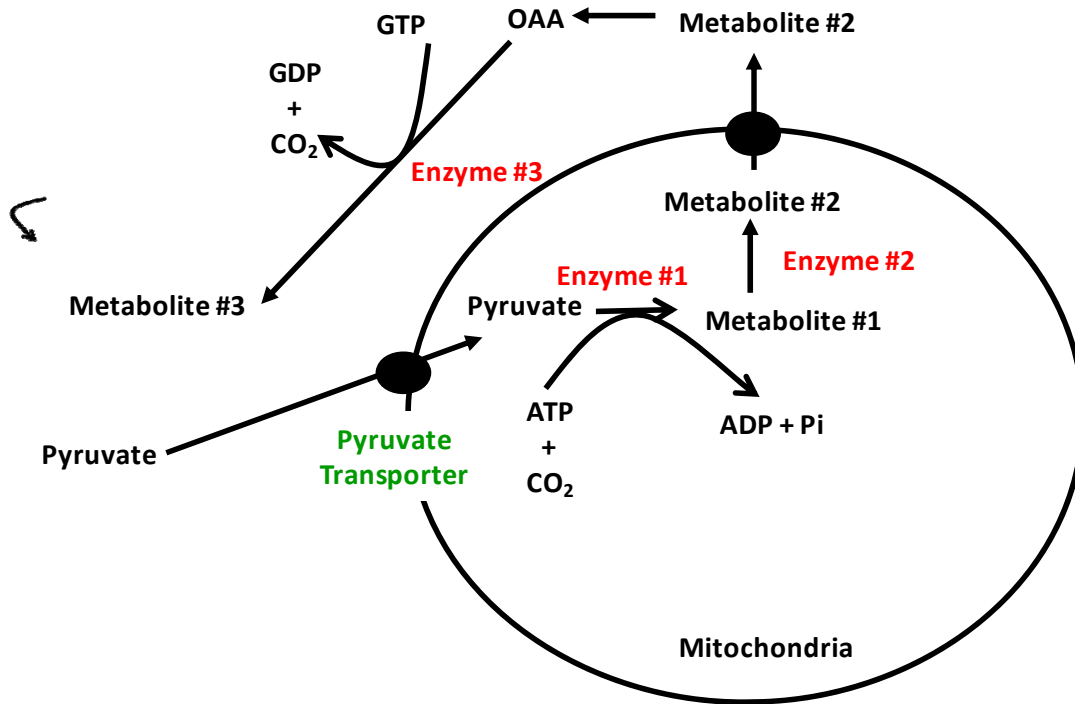
14) In a coupled mitochondria which of the following would you expect to observe?

- A) Oxygen consumption should stop when ADP is low
- B) The addition of oligomycin will not affect oxygen consumption
- C) The ratio ATP/O₂ consumed (i.e. P/O ratio) is the same for FADH₂ and NADH
- D) The membrane potential will be unaffected by 2,4-DNP
- E) Increased membrane potential upon exposure to rotenone

15) If the concentration of ATP is low, the availability of glucose and acetyl-CoA is high, and no other metabolic demands are made on the cell, what is the most likely fate of oxaloacetate?

- A) It is converted to phosphoenolpyruvate for gluconeogenesis to continue.
- B) It is polymerized in glycogenesis.
- C) It is converted to pyruvate.
- D) It is combined with acetyl-CoA and enters the TCA cycle.
- E) It is converted to malate through the reversal of a reaction in the TCA cycle.

Question 16 – 18 refer to the following diagram:



16) Enzyme #1 is:

- A) Pyruvate carboxylase
- B) Pyruvate Kinase
- C) Lactate Dehydrogenase
- D) Phosphoglycerate kinase
- E) Pyruvate dehydrogenase

17) Metabolite #2 is:

- A) Lactate
- B) Isocitrate
- C) 2-phosphoglycerate
- D) Malate
- E) Fumarate

18) Enzyme #3 is

- A) Pyruvate kinase
- B) Phosphoglycerate kinase
- C) Enolase
- D) Malate dehydrogenase
- E) Phosphoenolpyruvate carboxykinase

19) Glycogen metabolism relies on reciprocal regulation to ensure that your cells are not trying to make and breakdown glycogen at the same time. Which of the following is NOT involved in this reciprocal regulation?

- A) Biological amplification
- B) Cyclic AMP
- C) Protein phosphorylation
- D) Pyrophosphatase
- E) Hormones

20) You have been hired as a consultant on the hit show “Royal Pains” and are asked to check the plausibility of a storyline centered on antimycin toxicity. While reading the script you notice that the writers have Hank, the lead character, ordering a mitochondrial functional test that shows the exposed patient’s mitochondria are not consuming oxygen, but that it can be restored upon 2,4-dinitrophenol (2,4-DNP) treatment and the mitochondria have a higher than normal level of ubiquinol. What would you tell the writer’s about their storyline?

- A) Antimycin toxicity would not affect oxygen consumption.
- B) This is a great storyline and I would not change a thing.
- C) Antimycin would cause a buildup of reduced cytochrome C, not ubiquinol.
- D) 2,4-DNP would not restore oxygen consumption since antimycin inhibits complex III.
- E) This whole storyline is unbelievable because Hank is not a smart enough doctor to order mitochondrial testing.

21) What are the products of beta-oxidation of a C₂₀ fatty acid?

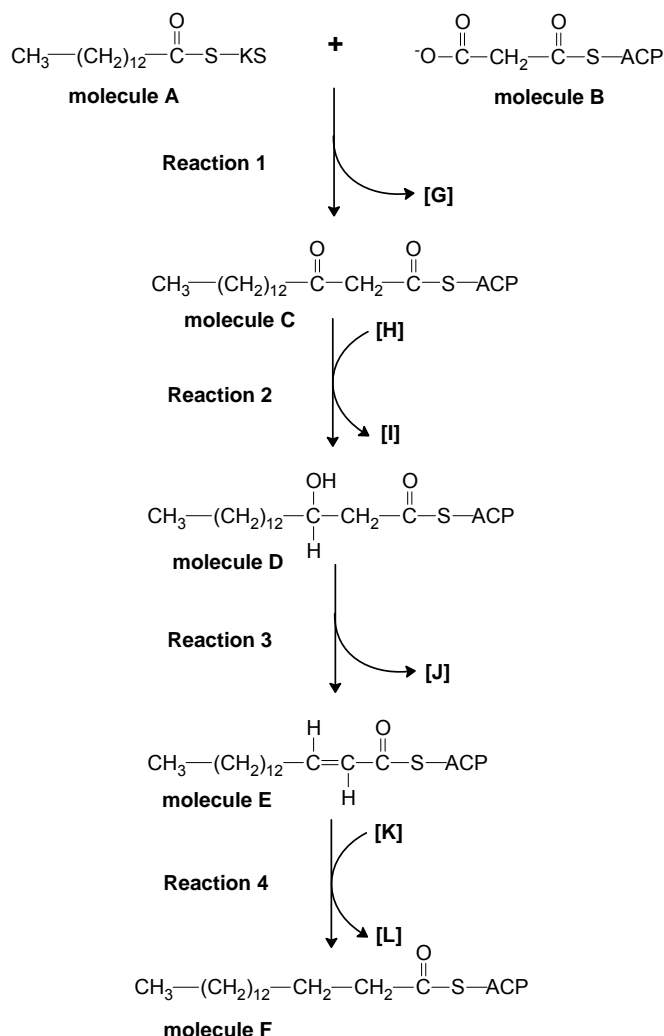
- A) 1 propionyl CoA, 9 acetyl CoA, 9 FADH₂, and 9 (NADH + H⁺)
- B) 9 acetyl CoA, 8 FADH₂, 8 (NADH + H⁺)
- C) 9 acetyl CoA, 9 FADH₂, 9 (NADH + H⁺)
- D) 10 acetyl CoA, 9 FADH₂, 9 (NADH + H⁺)
- E) 10 acetyl CoA, 10 FADH₂, 10 (NADH + H⁺)

22) A patient has a defective cytosolic beta-ketothiolase enzyme. In this person’s liver cells, which of the following pathways would be immediately affected?

- A) ketone body synthesis
- B) cholesterol synthesis
- C) beta-oxidation of fatty acids
- D) ketone body synthesis and beta-oxidation of fatty acids
- E) ketone body synthesis, cholesterol synthesis, and beta-oxidation of fatty acids

23) Which of the following statements regarding the reciprocal regulation of fatty acid synthesis and beta-oxidation is **incorrect**?

- A) acetyl CoA carboxylase is activated by insulin.
- B) Carnitine acyl transferase II (CAT II) is inhibited by malonyl CoA.
- C) Leptin inhibits fatty acid synthesis.
- D) Glucagon stimulates beta-oxidation of fatty acids.
- E) Palmitoyl CoA is an inhibitor of fatty acid synthesis.



The following 2 questions refer to the pathway drawn above. The letters in brackets [] represent additional substrates and products for the reactions indicated.

24) Which of the following statements regarding the above pathway is **correct**?

- A) Reactions 1 through 4 are oxidation, hydration, oxidation, and cleavage respectively.
- B) Molecule F undergoes two more rounds of these four reactions to produce the normal final product of this pathway.
- C) Coenzyme A carries the intermediates to each of the enzymes in this pathway.
- D) The enzymes that carry out reactions 2 and 4 are both reductases.
- E) The fatty acid synthetase complex includes the enzymes of reactions 1 through 4.

25) Which of the following statements regarding the production of molecule B in the above pathway is **correct**?

- A) Acetyl CoA carboxylase catalyzes the reaction that produces molecule B.
- B) The enzymatic reaction that produces molecule B is readily reversible.
- C) The enzymatic reaction that produces molecule B requires biotin and ATP.
- D) Both A and C are correct.
- E) All of the above are correct.

26) Malonyl CoA, which was ^{14}C labeled (a radioactive isotope of carbon) at **both** carbons #1 and #2, and unlabeled acetyl CoA were mixed together with the fatty acid synthase complex in a test tube. Which of the carbons of the final product, palmitate, will be ^{14}C labeled?

- A) All of the carbons will be labeled
- B) Only carbons #15 and #16 will be labeled
- C) All of the even numbered carbons will be labeled, except for carbon #16
- D) All of the odd numbered carbons will be labeled, except for carbon #15
- E) Carbons #1 through #14 will all be labeled.

27) A patient has a low insulin/glucagon ratio. You need to determine her levels of ketone bodies in the blood and urine using the nitroprusside test, which detects molecules with ketone groups. Which of the following molecules will be detected?

- A) acetone
- B) β -hydroxybutyrate
- C) acetoacetate
- D) acetoacetate and acetone
- E) β -hydroxybutyrate, acetoacetate, and acetone

28) Which of the following statements is **correct**?

- A) Triacylglycerols (TAG) and phospholipids are synthesized by branches from a common intermediate.
- B) ATP is used for activation in the salvage pathway of phospholipid synthesis.
- C) Serine is a source used to create the backbone of phospholipids and triacylglycerols (TAG).
- D) Breakdown of phospholipids yields important first messengers for signaling pathways.
- E) Insulin inhibits triacylglycerol (TAG) synthesis.

29) Sphingomyelin is

- A) a lipid which functions mainly as a storage form of energy.
- B) synthesized using phosphatidate as the key intermediate of the pathway.
- C) a major glycolipid of nerve cell membranes.
- D) the major component of lung surfactant, and indicates fetal lung maturity.
- E) a membrane lipid containing a sphingosine backbone, an amide linked fatty acid, and phosphoryl-choline as the headgroup.

30) A 28-year-old white male complains of severe retrosternal pain radiating to his left arm and jaw. He has not had a physical exam as an adult. His father died at a young age of a myocardial infarction. Physical exam revealed that he is anguished and dyspneic (shortness of breath). There were elevated plaques on eyelids (xanthelasmas), as well as xanthomas (pinkish nodules) of Achilles tendons and patellae (knee joint). Although serum triglycerides and HDL (high density lipoprotein) were within the normal range, LDL (low density lipoprotein) cholesterol was 650 mg/dL (normal ~130 mg/dL).

You suspect the following **genetic defect** and prescribe a **drug**.

<u>genetic defect</u>	<u>drug</u>
A) pyruvate dehydrogenase	thiamine
B) glucose 6-phosphate dehydrogenase	primaquine
C) lactase	lactose
D) apoB-100	statin
E) lipoprotein lipase	lecithin

31) A mother awakes after sleeping soundly for 8 hours for the first time since bringing her newborn daughter home from the hospital. She goes to check on her infant and finds her covered with vomit, soaked in sweat, and barely able to be aroused. The child is rushed to the emergency room. Initial tests rule out bacterial and viral infection. The intern on duty suspects that she may have a metabolic disorder involving a defect in medium-chain fatty acid oxidation, and orders a series of blood tests. Which set of laboratory findings would confirm this hypothesis (normal serum values are in parentheses)?

	Glucose (3.6 – 6.0 mM)	Fatty Acids (0.2 – 0.6 mM)	Beta-hydroxybutyrate (0.2 – 0.25 mM)
A)	2.6	6.1	0.1
B)	5.1	6.1	0.1
C)	2.6	0.1	0.1
D)	23	0.5	13
E)	2.6	0.5	13

32) A 33-year old man with a BMI of 38 was prescribed orlistat (Xenical) as part of his treatment to reduce obesity. Orlistat works in the small intestine to block the absorption of dietary fat. When taking orlistat he may need to supplement his diet with several compounds, including:

- A) linoleic acid
- B) cholesterol
- C) fat soluble vitamins
- D) linoleic acid and fat soluble vitamins
- E) linoleic acid, cholesterol, and fat soluble vitamins

END OF EXAMINATION

Tear off this sheet and save to check your answers.

Please remember to:

- Write the letter corresponding to your **FORM** in the appropriate place on the **answer sheet**.
- SIGN AND RETURN YOUR EXAMINATION** to an instructor **before leaving the exam room.**

FORM: A

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| 1. _____ | 11. _____ | 21. _____ | 31. _____ |
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