Biochemistry 507-311A **Print Name_____**
Signature_____ **Student Number _____**

STUDENT NAME:_____ **STUDENT NUMBER:_____**
(Last name, first name)

VERSION 1 (ONE)

BIOCHEMISTRY 507-311A

FACULTY OF SCIENCE
FINAL EXAMINATION

Examiner: Dr. W. Mushynski
Associate
Examiners: Dr. J. Bergeron

Dr. R. MacKenzie
Dr. A. Storer

Instructions: Put your name, student number (and signature) on each page where requested. Fill out the identification portion of the multiple choice answer sheet. Multiple choice questions (Sections I-III) are to be answered on the answer sheet. Answer written questions (Section IV) on the exam.

This exam comprises 13 pages

60% multiple choice (49 Questions)
40% short answers (9 Questions)

NO CALCULATORS ALLOWED

PLEASE INDICATE YOUR STUDENT NUMBER, NAME AND SIGNATURE ON EACH PAGE WHERE REQUIRED

EXAM PAPERS ARE TO BE RETURNED

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SECTION I

Each of the questions or statements below is followed by five suggested answers or completions. Select the one which is best in each case, and then on the answer card blacken the appropriate brackets with the corresponding number.

1. How many ATP equivalents are formed during a turn of the citric acid cycle itself?

    1. One
    2. Two
    3. Three
    4. Four
    5. Five

2. If pyruvate labelled with 14C in the carboxyl carbon is oxidized by mitochondria, all the radioactive 14C will appear as CO2 after how many turns of the cycle?

    1. One
    2. Two
    3. Three
    4. Four
    5. More than 4.

3. Which of the following is likely to inhibit oxidative phosphorylation without affecting respiration?

    1. Oligomycin
    2. A proton channel blocker
    3. A long chain fatty acid
    4. Cyanide
    5. Rotenone

4. In the mitochondrial electron transport chain, the reducing equivalents from NADH are transferred via NADH dehydrogenase directly to

    1. The FAD of succinate dehydrogenase
    2. Cytochrome b
    3. Cytochrome c
    4. Coenzyme Q
    5. Cytochrome a/a3

5. The pentose phosphate pathway:

    1. produces 1 NADH per glucose-6-P
    2. produces 2 NADH per glucose-6-P
    3. activity in liver is increased by a high carbohydrate diet
    4. sedoheptulose-7-P is the product of the oxidative portion
    5. is absent from erythrocytes

6. Which one of the following statements about cholesterol is true?

    1. cholesterol is degraded to CO2 only in liver.
    2. high levels of cholesterol-containing HDL are atherogenic.
    3. cholesterol down-regulates the synthesis of LDL receptors.
    4. cholesterol can be synthesized only in liver.
    5. none of these statements are true.

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SECTION 1 - CONTINUED

Each of the questions or statements below is followed by five suggested answers or completions. Select the one which is best in each case, and then on the answer card blacken the appropriate brackets with the corresponding number.

7. An absence of glycogen phosphorylase in muscle would result in:

    1. hypoglycemia (low blood sugar)
    2. lack of glycogen stores in muscle
    3. reduced ability to do short intense exercise
    4. elevated VLDL during fasting
    5. enhanced ketogenesis

8. Which of the following is **NOT** found in adipose tissue?

    1. glucose -6- phosphate dehydrogenase
    2. glycerol kinase
    3. HMG CoA reductase
    4. hexokinase
    5. fatty acyl CoA synthetase

9. Which of the following is true.

    1. IDL is produced from chylomicrons
    2. cholesterol esters are found on the surface of lipoprotein particles.
    3. VLDL is a larger particle than chylomicrons.
    4. the LDL receptor binds lipoproteins containing the Apo B protein.
    5. chylomicrons enter the circulation via the portal blood.

10. Which one of these provides the most net ATP upon degradation to C02 + H20?

    1. fatty acid 16:0
    2. fatty acid 18:1 (Œ9)
    3. three glucose molecules
    4. fatty acid 18:1 (Œ12)
    5. fatty acid 18:2 (Œ9,12)

11. The thermodynamics of the triose phosphate isomerase catalyzed reaction is best described by:

    1. ΔG° . -20 kjoules
    2. ΔG° . 0 kjoules
    3. ΔG . 0 kjoules
    4. ΔG . -20 kjoules
    5. ΔG . +20 kjoules

12. You are given several unknown samples, only **one** of which represents an extract of mitochondria. Which **single** component would best identify it? The presence of:

    1. lipoic acid
    2. pyridoxal phosphate
    3. thiamine pyrophosphate
    4. NAD
    5. Co-enzyme A (CoA-SH)

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SECTION I - CONTINUED

Each of the questions or statements below is followed by five suggested answers or completions. Select the one which is best in each case, and then on the answer card blacken the appropriate brackets with the corresponding number.

13. The shortest path for net conversion of 100 molecules of " - ketoglutarate to CO2 is by:

    1. Direct oxidation of alpha-ketoglutarate by the TCA cycle.
    2. conversion of alpha-ketoglutarate to acetylCoA
    3. conversion of alpha-ketoglutarate to citrate and export from mitochondria
    4. conversion of alpha-ketoglutarate to glucose
    5. None of these

14. Which of the following citric acid cycle components is not an amphibolic intermediate formed from the carbon skeleton of amino acids.

    1. Fumarate
    2. Succinyl CoA
    3. alpha-Ketoglutarate
    4. Malate
    5. Oxaloacetate

(Questions 15-25 are worth 2 points each).

15. All statements pertaining to phosphatidyl inositol 3,4,5 trisphosphate are correct except:

    1. Regulates intercellular Ca2+ stores.
    2. Is produced from phosphatidyl inositol 4,5 bisphosphate.
    3. Is a product of the signal transduction cascade from the activated insulin receptor.
    4. Is a membrane phospholipid.
    5. None of the above.

16. All statements pertaining to down-regulation are correct except:

    1. Refers to the phenomenon whereby insulin receptors decrease from the cell surface of target cells.
    2. Is a consequence of insulin receptor internalization.
    3. Causes decreased sensitivity to insulin in fat cells from type II (non-insulin dependent) diabetic obese patients.
    4. Leads to increased degradation of the insulin receptor.
    5. None of the above.

17. All statements pertaining to the Scatchard plot are correct except:

    1. Defines the kinetic parameters of ligand-receptor associations.
    2. Is curvilinear for the particular case of insulin binding to the insulin receptor.
    3. The intercept on the abscissa indicates the total number of receptors.
    4. Explains the decreased sensitivity to insulin in fat cells from type II (non-insulin dependent) diabetic obese patients.
    5. None of the above.

18. All statements pertaining to protein kinase C are correct except:

    1. Phosphorylates the alpha-1-adrenergic receptor as an example of a homologous feedback mechanism.
    2. Phosphorylates the insulin receptor as an example of a heterologous feedback mechanism.
    3. Phosphorylates the beta-2-adrenergic receptor as an example of a heterologous feedback mechanism.
    4. Phosphorylates glycogen synthase.
    5. Hydrolyzes phosphatidyl inositaol 4,5 bisphosphate for Ca2+ release via inositol 1,4,5 trisphosphate.

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SECTION I - CONTINUED

Each of the questions or statements below is followed by five suggested answers or completions. Select the one which is best in each case, and then on the answer card blacken the appropriate brackets with the corresponding number.

19. All statements pertaining to the following sentence are correct except:

Insulin stimulates glucose transport and utilization in fat cells:

1. At insulin doses of 10-11 - 10-10 M.
2. This stimulation is mimicked by anti-receptor antibody.
3. Insulin causes an increase in glucose transport which is seen in Lineweaver-Burke plots as a decrease in km.
4. Insulin binding to the receptor in fat cells shows negative cooperativity.
5. None of the above.

20. All statements pertaining to phosphotyrosine are correct except:

1. Is a rare amino acid in proteins.
2. Serves as part of a docking signal in the context of adjacent amino acids in cytosolic domains of proteins.
3. When present in the catalytic domain of the activated insulin receptor can maintain activation in the absence of insulin.
4. In cytosolic oriented proteins is dephosphorylated by phosphotyrosine specific protein phosphatases.
5. Is present in activated glycogen synthase.

21. All statements pertaining to the following sentence are correct except:

Polypeptide hormones and growth factors bind to cell-surface receptors prior to their activation:

1. For receptor tyrosine kinases, receptor activation is a consequence of hormone (growth factor) mediated dimerization.
2. Receptor activation is a consequence of serine/threonine kinase modification of the ligand bound tyrosine kinase.
3. Receptor activation of the insulin receptor is a consequence of its tyrosine auto-phosphorylation within the catalytic domain.
4. Insulin receptor activation leads to the tyrosine phosphorylation of IRS-1.
5. Insulin receptor activation activates PI 3 kinase.

22. All statements pertaining to the insulin receptor are correct except:

1. Is mutated in patients suffering from type II diabetes.
2. Is down-regulated in obese type II diabetics.
3. Is desensitized in signal transduction in non-insulin dependent diabetes (type II).
4. Is normal in patients suffering from juvenile or type I diabetes.
5. Is expressed in insulin target cells.

23. All statements pertaining to insulin sensitive glucose transporters are correct except:

1. Are present in liver parenchyma (hepatocytes)
2. Are present in adipocytes (fat cells).
3. Are largely intracellular in the absence of insulin.
4. Depend on PI 3 kinase activation for their translocation.
5. Require insulin receptor activation for increased glucose transport across the cell membrane.

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SECTION I - CONTINUED

Each of the questions or statements below is followed by five suggested answers or completions. Select the one which is best in each case, and then on the answer card blacken the appropriate brackets with the corresponding number.

23. All statements pertaining to IRS-1 are correct except:

1. Is a downstream substrate of the activated insulin receptor tyrosine kinase.
2. Binds via its SH2 domain to the tyrosine phosphorylated activated insulin receptor.
3. Requires its own PH domain for the fidelity of signal transduction.
4. Docks and activates PI 3 kinase by an SH2 mediated recruiting mechanism.
5. Is present in insulin target cells.

23. Phosphatidyl inositol-4,5-bisphosphate (PIP2) turnover regulates carbohydrate and lipid metabolism.

1 Inositol 1,4,5-trisphosphate is liberated as a consequence of "G" protein activation of phospholipase C.
2. PIP2 turnover is implicated in mood swings of manic depressives due to its action on Li+ stores in the endoplasmic reticulum.
3. 1-steroyl-2-arachidonoyl-glycerol mediates PIP2 turnover as a consequence of its biosynthesis from the phorbol ester 12-0-tetradecanoyl phorbol-13 acetate.
4. The action of epinephrine on $-adrenergic receptors leads to the activation of protein kinase C.
5. None of the above.

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SECTION II

For each of the statements/questions below, ONE or MORE of the completions are correct. Decide which completions is/are correct and black the appropriate number.

1. If only A,B and C are correct
2. If only A and C are correct
3. If only B and D are correct
4. If only D is correct
5. If all are correct

26. Which of the following reactions in the citric acid cycle is (are) inhibited by a high NADH/NAD ratio?

A. Succinate dehydrogenase
B. Pyruvate dehydrogenase
C. Aconitase
D. alpha-ketoglutarate dehydrogenase

27. Which of the following inhibits citrate synthase?

A. ATP
B. NADH
C. Succinyl-CoA
D. Acetyl CoA

28. Current experimental evidence suggests that the (subunit of the mitochondrial ATP-ase:

A. Becomes phosphorylated
B. Drives the rotation of the $ subunits of F1
C. Is covalently attached to the Fo
D. Rotates between the three $ subunits of F1

29. Energy from the proton gradient is translated into ATP formation by:

A. Increasing the binding affinity for ADPand Pi.
B. Stimulating the ATP hydrolyzing mechanism.
C. Decreasing the binding affinity for ATP.
D. Changing its oxidation state

30. Incorporation of double bonds into a saturated fatty acid in mammals:

A. occurs on the endoplasmic reticulum
B. involves cytochrome P450
C. can utilize desaturase Œ9
D. produces the equivalent of 3 ATP

31. During a prolonged fast (eg >7 days)

A. lipoprotein lipase is increased
B. liver cells have an elevated NADH/NAD ratio
C. adipose tissue synthesizes large amounts of 3-oxybutyrates
D. the amount of the enzyme glucokinase is decreased

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SECTION II - CONTINUED

For each of the statements/questions below, ONE or MORE of the completions are correct. Decide which completions is/are correct and blacken the appropriate number.

(1) If only A,B and C are correct
(2) If only A and C are correct
(3) If only B and D are correct
(4) If only D is correct
(5) If all are correct

32. Propionyl CoA

A. is a product of the degradation of fatty acids containing an odd number of carbons
B. can be converted to glucose in mammals
C. the metabolic pathway for its utilization involves biotin
D. the metabolic pathway for its utilization involves Vitamin B12

33. Replenishment of the intermediates of the TCA cycle from pyruvate:

A. requires thiamine PP
B. involves a decarboxylation
C. is inhibited by acetyl CoA
D. consumes one high energy phosphate

34. Which of the following carbons can give rise to glucose? (gluconeogenesis)

A. carbon #15 of 15:0 fatty acid
B. carbon #1 of 17:0 fatty acid
C. carbon #2 of alanine
D. carbon #2 of leucine

35. The enzyme fatty acid synthase:

A. Is the main regulated step in the synthesis of fatty acids.
B. Is composed of two different types of polypeptide in yeast.
C. Produces primarily 18:0 fatty acids in mammals.
D. Must be a dimer to synthesize fatty acids in mammals.

36. Which of the following statements concerning phospholipid metabolism is/are true?

A. **Net** synthesis of choline in animals occurs only via modification of phosphatidylethanolamine.
B. Diacylglycerol (DAG) is an obligatory intermediate in the synthesis of TAG
C. Decarboxylation of phosphatidyl serine to phosphatidyl ethanolamine is a function of mitochondria
D. The synthesis of phosphatidyl inositol involves CDP-inositol.

37. During ketogenesis in an individual:

A. The TCA cycle is not the major source of energy for liver cells.
B. There is a massive release of fatty acids from adipose tissue.
C. The ratio of blood [lactate]/[pyruvate] increases.
D. Muscle glycogen is being used to maintain blood glucose levels.

38. A molecule of glucose is converted into carbons of a fatty acid that is stored in adipose tissue. It is then ultimately used for energy by the central nervous system. Which of the following is/are **not required** in this overall process?

A. Hormone sensitive lipase.
B. Glucose-6-P phosphatase.
C. Succinyl CoA - oxybutyrate transferase.
D. Lecithin cholesterol acyl transferase (LCAT).

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SECTION III

Each of the lists below contain possible responses for the group of questions immediately following it. Select the best answer for each question. A given response may be useful more than once or not at all.

For questions 39-43

1. **Phospholipase A2**
2. **Hormone sensitive lipase**
3. **Lipoprotein lipase**
4. **Phospholipase C**
5. **None of these**

39. Important in the re-tailoring of phosphatidyl inositol.
40. Glucagon increases the activity of this enzyme.
41. Involved in the process of storing dietary fatty acids in adipose tissue.
42. Used to generate arachidonic acid used in prostaglandin synthesis.
43. Involved in a Ca++ mediated regulatory pathway.

For questions 44-49

1. **HMG CoA reductase**
2. **HMG CoA lyase**
3. **Carnitine acyltransferase I**
4. **Fattyacyl CoA synthase**
5. **None of these**

44. Found in the matrix of the mitochondria of **muscle** cells.
45. Regulated by AMP-dependent protein kinase.
46. Located on the outer mitochondrial membrane of liver cells.
47. Phosphorylated by cAMP-dependent protein kinase.
48. A target of serum cholesterol-lowering drugs.
49. Found outside cells.

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SECTION IV

Answer in the space provided.

1. The enzyme glyceraldehyde-3-phosphate dehydrogenase catalyzes the reaction:

(6 pts).

(a) In the space provided draw the reaction mechanism of the enzyme:

(b) Name the types of covalent enzyme intermediates formed, if any, during the reaction:

.

SECTION IV - CONTINUED

Answer in the space provided.

2. What is the direct effect of ATP hydrolysis during nitrogen fixation?

(2 pts.)

3. (a) Beginning with the external aldimine derivative shown below illustrate the mechanism through which glutamate decarboxylase commits an unforced error and show the product(s) thus formed.

(4 pts.)

(b) Briefly explain how the enzyme is affected by this unforced error.

(2 pts.)

SECTION IV - CONTINUED

Answer in the space provided.

4. The reaction specificity of pyridoxal phosphate-containing enzymes is determined through a process known as stereochemical control. Use a diagram to illustrate what is meant by the term "stereochemical control".

(4 pts.)

5.(a) Describe the regulation of carbamoyl phosphate synthetase 1. (CPS-1).

(2 pts.)

(b) Explain in one or two sentences why CPS-1 is located in liver mitochondria..

(2 pts.)

6. Explain briefly why some patients with inherited defects in homocysteine catabolism can be treated successfully with elevated doses of pyridoxine.

(2 pts.)

7. How does the enzyme porphobilinogen deaminase acquire its cofactor (dipyrromethane)?

(2 pts.)

SECTION IV - CONTINUED

Answer in the space provided.

8. Starting with two molecules of acetylCoA and indicating all other cofactors and enzymes required, outline IN A DIAGRAM the first cycle of fatty acid synthesis by a mammalian system.

(7 pts.)

9. IN A DIAGRAM, outline the roles of chylomicrons, VLDL, LDL and HDL in fatty acid and cholesterol transport.

(7 pts.)