Name: _____

Student ID: _____

University of Guelph

BIOC*3560

Final Examination – Practice answers

Winter 2013 (April 10, 2013)

Time: 2 hours

16 pages. Check to make sure you have 16 different single-sided pages.
On the computer scoring sheet provided, use a **black lead pencil** to enter your seven-digit student ID number.

Illegible and otherwise unreadable, incomprehensible, or unclear answers will be considered incorrect.

Answer Part A, questions 1-50, on the computer-scoring sheet. Only one option is correct for each of these questions. Use a **black lead pencil**. Erase cleanly if you make a mistake. **Do not use ink or white-out** on the computer-scoring sheet.

Answer Part B and Part C directly on the question paper. **Answer only in ink (NOT RED) and only in the space provided**.

Part A 50 marks	
Part B 10 marks	
Part C 40 marks	
Total 100 marks	

Part A. Multiple Choice.
Please answer the following 50 questions on the provided computer scoring sheet. Answers for part A written on this sheet will <u>not</u> be graded.
1 Mark per question, 50 marks total. Only one answer in each question is correct.

1. The role of perilipin in the body is to:
   1) Transmit the signal to mobilize triacylglycerols
   2) Cleave glycerol from triacylglycerols
   3) Prevent inappropriate access of lipases to triacylglycerol ***
   4) Solubilize fatty acids as they move through the blood stream
   5) Help Fatty acids enter their target cell

2. Suppose we have a 16 carbon palmitoyl-CoA entering its first round of β-oxidation. Which enzyme will act on this substrate first?
   a) β-hydroxyacyl-CoA dehydrogenase
   b) Acyl-CoA dehydrogenase ***
   c) Enoyl-CoA hydrolase
   d) Thiolase
   e) 2,4-dienoyl-CoA reductase

3. In order to fully oxidize linoleate (C18:2 $\Delta^{9,12}$) you need all of the regular β-oxidation enzymes plus:
   a) 2-4-dienoyl-CoA reductase
   b) Δ^2,Δ^3 enoyl-CoA isomerase
   c) β-hydroxy-β-methylglutaryl-CoA lyase
   d) Both 2-4-dienoyl-CoA reductase and Δ^2,Δ^3 enoyl-CoA isomerase ***
   e) Both Δ^2,Δ^3 enoyl-CoA isomerase and β-hydroxy-β-methylglutaryl-CoA lyase

4. If the conventional β-oxidation enzymes break down (C17:0), how far can they break down this fatty acid before they need help from additional enzymes?
   a) C17:0 (β-oxidation enzymes cannot initiate breakdown of this product)
   b) No additional enzymes are needed, the conventional β-oxidation enzymes can completely degrade this substrate
   c) Malonyl-CoA
   d) Propionyl-CoA ***
   e) Methanyl-CoA

5. Which of the following molecules is an intermediate in ketone body biosynthesis?
   a) methylmalonyl-CoA
   b) carnitinyl-CoA
   c) β-methyl-β-hydroxy-glutaryl-CoA ***
   d) D–β-hydroxybutyryl-CoA
   e) propionyl-CoA

6. Which of the following is not true of acetyl-CoA carboxylase?
   a) It uses biotin as a cofactor
   b) It has separate carboxylase and transcarboxylase catalytic sites
   c) It catalyzes the first committed step of fatty acid synthesis
   d) ATP is required to complete the transcarboxylase catalytic step ***
   e) Malonyl-CoA is the product

7. Which of the following is a subunit of mammalian fatty acid synthases
   a) β-hydroxyacyl-CoA dehydrogenase
   b) acyl-CoA dehydrogenase
   c) 2,4-dienoyl-CoA reductase
   d) thioesterase ****
   e) thiolase

8. How many malonyl-CoA molecules do mammalian fatty acid synthases require to completely synthesize their product?
   a) Zero
   b) One
   c) Seven ***
   d) Eight
   e) Between six and ten; it depends on the fatty acid being produced

9. Suppose you wanted to radiolabel palmitic acid (C16:0) at C15 using fatty acid synthase extract from pig livers. Which of the following molecules would you need to ensure that the appropriate atom was labeled?
   a) malonyl-CoA labeled on the carboxylate carbon
   b) malonyl-CoA labeled on the methylene carbon
   c) malonyl-CoA labeled on the keto carbon
   d) acetyl-CoA labeled on the methyl carbon
   e) acetyl-CoA labeled on the keto carbon ***

10. Which of the following is not true of mammalian fatty acyl-CoA desaturases?
   a) The reaction occurs in the smooth ER
   b) Given stearate (18:0) as a substrate, oleate (18:1Δ^{9}) is the only possible product.
   c) Oleate can be desaturated to linoleate (18:2$\Delta^{9,12}$) ****
   d) Fatty acyl-CoA desaturases require oxygen
   e) Cytochrome b_5, is required for the reaction, and must be re-reduced using NADPH

11. Acetyl-CoA carboxylase is <u>not</u> regulated by:
   a) ATP ***
   b) Palmitoyl-CoA
   c) Citrate
   d) Epinephrine
   e) Insulin

12. Regulation of metabolism at the level of changes in levels of gene expression occurs on the time scale of
    a) Milliseconds to seconds
    b) Seconds to minutes
    c) Minutes to hours
    d) Hours to days ***
    e) Days to weeks

13. Glucose can not be made from:
    a) Glycogen
    b) Glycerol
    c) Fatty acids ***
    d) Most amino acids
    e) Oxaloacetate

14. How is the organization of acetyl-CoA carboxylase changed by phosphorylation?
    a) It is dissociated from tetramers into monomers
    b) It assembles into tetramers from monomers
    c) It assembles into a filament from individual subunits
    d) It disassembles into individual subunits from a filament ***
    e) While there is some internal motion, the overall organization does not change

15. Which of the following is not true of the liver?
    a) It is the first stop for newly absorbed nutrients
    b) It acts to detoxify harmful substances ingested
    c) It acts to keep blood glucose at roughly constant levels
    d) It prefers glucose as its primary energy source ***
    e) It can store excess glucose as glycogen

16. Which of the following is not true of the well-fed state?
    a) It is signaled by the release of insulin from the pancreas
    b) Glycolysis is down-regulated in the liver ***
    c) Fatty acid biosynthesis is up-regulated
    d) Glycogen synthesis is up-regulated
    e) None of a) – d) are false; they are all true

17. Which of the following is not true in an early fasting state:
    a) Ketone bodies are generated by the liver
    b) Glycolysis is down-regulated in the liver
    c) The brain switches to fatty acids as a primary fuel source ***
    d) Adipose tissue is stimulated to release fatty acids
    e) Glycogen in the liver is cleaved to release glucose-1-phosphate

18. During prolonged fasting, the citric acid cycle in the liver:
    a) Is shut down by the excessive accumulation of NADH/NAD^+
    b) Is shut down because the intermediates are used up in gluconeogenesis ***
    c) Is sustained by the break down products of amino acids from muscle tissue
    d) Is sustained by increased rates of fatty acid β-oxidation
    e) Is activated to increase liver activity, as required to deal with starvation

19. Which of the following is <u>not</u> true of cortisol
    a) It signals stress, such as low blood sugar
    b) It is a steroid hormone
    c) It acts on the liver and adipose tissue
    d) It acts more slowly than glucagon and epinephrine
    e) It modifies and thereby further increases the activity of target proteins ***

20. Which of the following is <u>not</u> true of glycogen synthase kinase 3?
    a) It is only active after casein kinase II phosphorylates its substrate
    b) It can be inhibited by phosphorylation of a serine residue near its N-terminus
    c) It phosphorylates serine residues 4 residues C-terminal to a phosphoserine ***
    d) It can be phosphorylated by protein kinase B (PKB)
    e) It is regulated by insulin signaling

21. If we number the three glycerol hydroxyl groups in a glycerolipid as 1, 2 and 3:
    a) Position 1 is occupied by a saturated fatty acid, position 2 by an unsaturated fatty acid ***
    b) Position 2 is occupied by a saturated fatty acid, position 1 by an unsaturated fatty acid
    c) All 3 positions are occupied by saturated fatty acids
    d) Both 1 and 2 are generally occupied by saturated fatty acids
    e) There is often one unsaturated fatty acid attached, but its position is random

22. A sphingomyelin is organized as
    a) A sphingolipid with an unmodified hydroxyl group
    b) A sphingolipoid modified with a complex carbohydrate group
    c) A sphingolipid modified with a phosphate group only
    d) A sphingolipid modified with a phosphocholine head group ***
    e) Two sphingolipid molecules linked by a phosphor-glycerol bridge

23. Sphingolipids do <u>not</u> have:
    a) A built in unsaturated acyl tail
    b) An fatty acid chain linked through an ester linkage ***
    c) An alcohol group that is never modified
    d) An alcohol group that may optionally be linked to a head group
    e) An attachment site for carbohydrates

24. Which of the following is not true of cholesterol:
    a) Its structure includes five linked carbon rings ***
    b) It has an alkyl side chain
    c) It is hydrophobic, except for a single alcohol group
    d) It is about as long as a palmitate
    e) It occurs in mammals as only a single chemical structure

25. Which of the following is <u>not</u> true of proteins that associate with the membrane through a lipid anchor?
    a) The myristoyl group can be attached to an internal cysteine residue ***
    b) Palmitoylated proteins interact with the inner leaflet of the membrane
    c) A protein could in principle have multiple palmitoyl groups, but not multiple farnesyl tails
    d) Myristoylated proteins preferentially associate with lipid rafts
    e) Proteins with a GPI anchor are found in the outer leaflet of the membrane

26. In order to traverse the central hydrophobic region of the membrane, and α-helix needs to be at least _____ residues long.
    a) Ten
    b) Fifteen
    c) Twenty ***
    d) Twenty-five
    e) Thirty

27. Glycophorin A can best be described as
    a) An extracellular peripheral membrane protein
    b) A lipid anchored protein
    c) A single spanning transmembrane protein with a small intracellular domain, and a larger glycosylated extracellular domain ***
    d) A seven-spanning α-helical protein with minimal extracellular domains
    e) A β-barrel transmembrane channel

28. In N-linked carbohydrates, the first sugar group attached to the protein is typically:
    a) Glucose
    b) N-acetylglucosamine ***
    c) Galactose
    d) N-acetylgalactosamine
    e) Ribose

29. Flippases:
    a) Move amine containing lipids from the outer to the cytosolic leaflet ***
    b) Move phospholipids from the outer to the cytosolic leaflet
    c) Move amine containing lipids from the cytosolic to the outer leaflet
    d) Move phospholipids from the outer to the cytosolic leaflet
    e) Move lipids randomly from one leaflet to the other

30. It is thought that individual lipid molecules are corralled by the presence of:
    a) Glycophorin
    b) Spectrin ***
    c) Ankyrin
    d) G-protein coupled receptors
    e) Peripheral membrane proteins

31. Which of the following processes does <u>not</u> require membrane transport?
    a) up-regulation of glucose transporters
    b) transport of membrane components between ER and Golgi
    c) neurotransmitter release
    d) Ca^{2+} release ***
    e) They all require membrane transport

32. Which of the following is not true of SNARE mediated membrane fusion:
    a) v-SNAREs and t-SNAREs are found as ~60 amino acid long single α-helices in the absence of their binding partners
    b) v-SNARE and t-SNARE need to interact with SNAP25 to allow membrane fusion
    c) The interaction between the SNARE complex proteins begins with the transmembrane domains ***
    d) Formation of a coiled-coil structure drive the membranes together
    e) An intermediate step with the inner leaflets of both membranes in contact occurs

33. Which of the following sets of molecules can all cross the membrane without help from membrane embedded proteins?
    a) Cortisol, CO_2, sucrose, insulin
    b) Glycerol, N_2, ethanol, thyroxine ***
    c) Water, O_2, Ca^{2+}, cortisol
    d) Glucose, asparagine, ethanol
    e) All of these lists have at least one molecule that cannot cross unassisted

34. Glucose in the GLUT1 transporter:
    a) Passes through a continuous pore in the membrane
    b) Binds a weakly specific binding site at the extra-membrane side, then is moved to a second site at the cytosolic side
    c) Has four distinct binding sites, only two of which bind glucose at a given time
    d) Binds to a single site in the middle of the membrane, which the protein pivots around ***
    e) Has both a sodium and a glucose binding site, which are utilized alternatively

35. Suppose you have a transporter that has the following properties:
    i. If lactose is bound at the central binding pocket, the transporter can flip from being open to the cytosol to being open to the extracellular space, or vice versa.
    ii. If a potassium ion is bound at the central binding pocket, the protein can flip from being open to the cytosol to being open to the extracellular space, or vice versa.
    iii. If neither ligand is bound in the central binding pocket, the protein cannot change conformations.

    We can infer that this protein is functionally a:
    a) Lactose uniporter
    b) Potassium uniporter
    c) Lactose – potassium antiporter ***
    d) Lactose - potassium symporter
    e) Both a lactose uniporter, and a potassium uniporter

36. Which of the following cellular ion concentrations is wrong?
    a) Na^+ concentrations are ~10 mM inside the cell, ~150 mM outside
    b) Cl^- concentrations are ~5 mM inside the cell ~110 mM outside
    c) K^+ concentrations are ~140 mM inside the cell ~5 mM outside
    d) Ca^{2+} concentrations are ~1 mM inside the cell ~5 mM outside
    e) All of the above concentrations are actually accurate ***

37. Starting with an empty unphosphorylated protein, what order do the following events occur in the Na^+ K^+ ATPase?
    I. K^+ binding
    II. Na^+ binding
    III. Phosphorylation
    IV. A conformational change from facing inside the cell to outside the cell

    a) I, II, III, IV
    b) I, III, IV, II
    c) II, I, III, IV
    d) II, III, IV, I ***
    e) III, II, IV, I

38. Na^+ K^+ ATPase uses the energy from one ATP molecule to move:
    a) 3 K^+ ions into the cell, 2 Na^+ ions out of the cell
    b) 2 K^+ ions into the cell, 3 Na^+ ions out of the cell ***
    c) 3 K^+ ions out of the cell, 2 Na^+ ions into the cell
    d) 2 K^+ ions out of the cell, 3 Na^+ ions into the cell
    e) 2 Na^+ ions out of the cell only – the name is a historical misnomer

39. Which of the following is not true of the selectivity of the potassium channel?
    a) K^+ ions must be stripped of water molecules to pass through the channel
    b) The helix dipole of the pore helix helps stabilize positive charges in the channel
    c) The size of the ions which will pass is dictated by the spacing between protein oxygen atoms
    d) The selectivity filter is built from the carbonyl oxygen atoms of five successive residues ***
    e) There are four K^+ binding sites, but only two are occupied at a time

40. Which of the following is not true of the organization of the voltage gated Na^+ channel?
    a) There are a total of 24 membrane-spanning helices
    b) Helix 4 is the voltage sensor
    c) Helix 6 is known as the activation gate
    d) Helix 5 lines the channel ***
    e) The inactivation gate is formed from the cytosolic loop joining domains III and IV

41. Which of the following is not a general property of signal-transducing systems?
    a) High specificity
    b) Signal amplification
    c) Desensitization and adaptation to a persistent signal
    d) Mechanisms to integrate conflicting signals
    e) Modification of the levels of transcription factors in the nucleus ***

42. Receptor affinity for their ligands is generally in what range?
    a) Millimolar
    b) Micromolar
    c) Nanomolar
    d) Picomolar ***
    e) Femtomolar

43. During the transmission of an action potential, the pattern of membrane potentials observed is:
    a) -60 mV, +30 mV, -75 mV, -60 mV ***
    b) -75 mV, -60 mV, + 30 mV, -75 mV
    c) -75 mV, + 30 mV, -60 mV, -75 mV
    d) +30 mV, -75 mV, -60 mV, +30 mV
    e) -60 mV, -75 mV, +30 mV, -60 mV

44. Which of the following is not true of the functioning of the nicotinic acetylcholine receptor?
    a) Two acetylcholine molecules need to bind to trigger the receptor
    b) The M2 helix lines the channel
    c) Binding of acetylcholine triggers rotation of the domains
    d) In the open state, the channel is lined by a leucine residue ***
    e) The open channel allows K^+ and Ca^{2+} to enter the cell

45. An inactive Gα-protein:
    a) Is complexed with GDP
    b) Forms a complex with the Gβ subunit
    c) Forms a complex with the Gγ subunit
    d) Anchored to the membrane by a fatty acid tail
    e) All of the above ***

46. Once activated by epinephrine binding the β-adrenergic receptor, the Gα subunit directly activates:
    a) Adenylyl cyclase ***
    b) IRS-1
    c) PKA
    d) PKB
    e) β-adrenergic receptor kinase

47. Which of the following is not true of the insulin receptor
    a) The receptor has two α and two β subunits
    b) Insulin binds to the subunit that possesses transmembrane helices ***
    c) The catalytic domains and insulin binding site are located on opposite sides of the plasma membrane
    d) The catalytic domain has tyrosine kinase activity
    e) The catalytic domains need to be activated before they are active on external substrates

48. The Protein Kinase A regulatory subdomain does not:
    a) Bind the catalytic subunit
    b) Have two cAMP binding sites
    c) Bind A Kinase Activating Protein
    d) Bind an activated G-protein ***
    e) Interact with a second copy of the regulatory subdomain

49. In insulin signaling, Raf-1 phosphorylates:
    a) ERK
    b) IRS-1
    c) MEK ***
    d) A variety of transcription factors
    e) Ras

50. Nuclear hormone receptors bind DNA through a domain known as a:
    a) DNA clamp
    b) Leucine zipper
    c) Helix-turn-helix motif
    d) Zinc finger ***
    e) Hormone response element

- End of Part A -

Part B.
Please write the appropriate term in the space provided.
Full names are required – no abbreviations.
1 Mark per question, 10 marks total.

1. During fatty acid synthesis, the growing acyl chain is mainly attached to a protein domain known as ___**Acyl carrier protein**__.

2. In addition to acetoacetate and acetone, ketone bodies are also comprised of the molecule ___**D-β-hydroxybutyrate**__.

3. The most important regulatory mechanism of fatty acid β-oxidation is malonyl-CoA inhibition of __**carnitine acyltransferase I**__.

4. Nutrients freshly absorbed in the small intestine enter the portal vein and are delivered to the ___**liver**___.

5. A lipid bilayer wrapped into a hollow sphere with aqueous solution on the inside is known as a _____**liposome**_____.

6. The layer of well-ordered lipids which adhere to the outside of proteins are known as ____**annular**____ lipids.

7. In the process known as __**facilitated diffusion**_____, a transmembrane protein allows a polar compound to cross the membrane down its electrochemical gradient.

8. The protein that allows water to cross membranes is called _____**aquaporin**_____.

9. The efflux of K^+ through a voltage gated potassium channel results in the __**hyper**_____ -polarization of the membrane.

10. As an alternative to tyrosine kinase activity, some receptor enzymes possess __**guanylyl cyclase**____ activity.

- End of Part B -

Part C.

Please answer the following questions in full in the space provided.
Marks are as indicated after each question. 40 marks total

1. Acetyl-CoA cannot escape from the mitochondria; however, this molecule is required in the cytosol to make fatty acids. Describe the process whereby acetyl-CoA from the mitochondria becomes available in the cytoplasm, naming all proteins and molecules involved and stating their locations. Note – you can ignore the complexities of returning four carbon metabolites back to the mitochondria. (*5 marks*)

   Citrate synthase in the mitochondrion interior reacts oxaloacetate and acetyl-CoA to make citrate; releasing CoA
   Citrate crosses the mitochondrial inner membrane through the citrate transmporter
   Citrate in the cytosol is reacted with cytosolic CoA and ATP to make acetyl-CoA and oxaloacetate

2. Suppose you have a β-ketoacyl-ACP molecule attached to the fatty acid synthase. What is the next enzyme subunit to act on this substrate (in the physiological sense), what is the (generic) name(s) of the product(s) produced, and what, if any, cofactor or substrate is required for this reaction. (*3 marks*)

   Enzyme: β-ketoacyl-ACP reductase
   Product: β-hydroxyacyl-ACP
   Cofactor: NADPH

3. Name four possible fates of glucose-6-phosphate in the liver in the well-fed state. (*4 marks)*

   be used to make glycogen for later use
   be phosphatased to glucose, to replenish blood glucose
   enter the pentose-PO_4 pathway – making NADPH and possibly nucleotides (ribose)
   enter glycolysis, with acetyl-CoA:
   - **entering the citric acid cycle to make ATP for the liver's energy needs**
   - **being used to make fatty acids**
   - **being used to make amino acids**

   any four of these 6 is acceptable

4. Explain how the metabolic disregulation observed in diabetics can result in ketosis. *(4 marks)*

   Acetyl-CoA carboxylase is inactive in the absence of insulin/presence of glucagon
   Acyl-carnitine transport is highly active because malonyl-CoA concentration is low
   Fatty acid β-oxidation is highly active but incomplete because high levels of $NADH/NAD^+$ inhibits citric acid cycle
   Excess acetyl CoA is turned into excess ketone bodies, causing ketosis

5. Putting cells of a given type in a blender and measuring total lipids is somewhat misleading, as the membranes in cells have non-uniform compositions in three distinct senses. Describe how lipid membranes are non-uniform, with an example in each case of a way in which a lipid that is non-randomly distributed. (6 marks)

   Lipids have different composition in different subcellular membranes. E.g. the cellular membrane is high in cholesterol
   Lipids are differentially distributed between leaflets – e.g. amine lipids (phosphotidyl ethanolamine and phosphotidyl serine) are depeleted in the outer membrane; phospholipids are depleted in the inner membrane
   Lipid rafts are local regions enriched in specific lipids – sphingolipids and cholesterol

6. The amino acids that sit on the surface of integral membrane proteins show marked differences from what is seen on typical soluble proteins. Describe how the amino acid composition varies by location on the surface of an integral membrane protein. (3)

   Hydrophobic residues are enriched in the portion of the protein that faces the lipid acyl groups
   Tyrosine and typtophan are enriched at the interface where the polar head groups meet the acyl chains.
   Charged residues are found almost exclusively in the aqueous phase

7. Hydrophilic solutes have a difficult time crossing the membrane. Describe in energetic terms why this is so, and what transporters and channels do that allows these solutes to get across membranes. *(3 marks)*

   To cross the lipid bilayer, solutes must be removed from their hydration shell
   The energy required to break these interactions presents a large energy barrier to crossing the membrane
   Transporters and channels function by lowering this energy barrier by providing strong interactions with the solute that compensate for the lost solvation energy

8. Describe the properties that allow membrane channels to be distinguished from membrane transporters (*4 marks)*.

   Saturability – transporter kinetics is saturable, channel kinetics is not
   Speed – channels are much faster than transporters, operating at near diffusion rates
   Channels have a continuous pore that crosses the membrane
   Transporters have a well defined binding site that allows one or a very few molecules to cross at once

9. Describe the steps that result in the internalization of the activated β-adrenergic receptor. (*4 marks*)

   The released GbGg complex recruits β-adrenergic receptor kinase (βARK)
   βARK phosphorylates Ser residues on the β-adrenergic receptor
   β-arrestin complex binds the phosphorylated β-adrenergic receptor, resulting in endocytosis of the complex

10. Describe the pathway that allows activation of the insulin receptor kinase to inactivate glycogen synthase kinase 3, allowing glycogen to form. *(4 marks)*

Phosphorylated IRS-1 binds the SH2 domain of phosphoinositide 3-kinase (PI-3K)
IRS-1 bound PI-3K phosphorylates PIP_2, producing the secondary messenger PIP_3
PIP_3 recruits protein kinase B (PKB)
PIP_3 bound PKB is phosphorylated by PDK1; phosphorylated PKB phosphorylates GSK3

- End of Part C -