

Biology 2120  
Spring 2011  
Midterm Exam #3

Multiple choice answers

Name (printed):

This exam contains 12 pages, *plus the multiple choice bubble sheet*. Please verify that you have all pages.

1. Write your name on both this exam *and* on the bubble sheet (fill in the bubbles for your name)
2. Write the *color* of your exam paper on the top edge of the bubble sheet
3. Answer all questions, using only the space available for the drawings/short answer section (part II).
4. You have until 11:30 AM to finish the exam- to receive credit for taking the exam, your exam *must* be handed in at the front of class when the proctor announces that the examination period has ended.
5. As indicated in the course syllabus, cheating in this course is strictly forbidden. Anyone who cheats on this exam will receive an F in the course and be referred for disciplinary action. By signing your name below, you indicate that you understand, and agree to comply with, this policy.

Name (signed)

Part I. Multiple Choice. Choose the single best ~~answer~~ to each question.

- ✓ 1. Which of the following is the main reason that a typical eukaryotic gene is able to respond to a far greater variety of regulatory signals than a typical prokaryotic gene or operon?

- A. Eukaryotes have three types of RNA polymerase.
- B. Eukaryotic RNA polymerases require general transcription factors.
- C. Transcription of a eukaryotic gene can be influenced by proteins that bind to DNA sequences far from the promoter.
- D. The protein-coding regions of eukaryotic genes are longer than those of prokaryotic genes.
- E. Eukaryotic genes are packaged into nucleosomes

- ✗ 2. The most abundant *intracellular cation* in the list below is:

- A.  $\text{Na}^+$
- B.  $\text{Ca}^{2+}$
- C.  $\text{Cl}^-$
- D.  $\text{K}^+$
- E. Positively charged macromolecules

- ✓ 3. How are most eukaryotic gene regulatory proteins able to affect transcription when their binding sites are far from the promoter?

- A. By binding to their binding site and sliding along DNA to the site of RNA polymerase binding.
- B. By folding DNA, thereby looping out the intervening DNA between their binding site and the promoter.
- C. By unwinding DNA between their binding site and the promoter.
- D. By phosphorylating RNA polymerase before it can bind to the promoter.
- E. By breaking hydrogen bonds between RNA polymerase and the promoter.

$\text{Cl}^-$  out  $\text{Na}^+$  out  
↓ ↓ ↓ ↓ ↓

X 4. An intravenous injection of a large amount of KCl is lethal because:

- A. KCl clogs the flow of blood through the heart.
- B. Raising the extracellular  $\text{K}^+$  concentration reduces the resting potential of heart muscle cells, so your heart stops beating.
- C. Raising the extracellular  $\text{K}^+$  concentration inhibits glucose uptake by heart muscle cells, so your heart stops beating.
- D. Raising the extracellular  $\text{Cl}^-$  concentration inhibits glucose uptake by heart muscle cells, so your heart stops beating.
- E. Raising the extracellular  $\text{Cl}^-$  concentration inhibits the  $\text{Na}^+/\text{K}^+$  pump in heart muscle cells, so your heart stops beating.

✓ 5. Estrogen stimulates the synthesis of many genes in the same cell because:

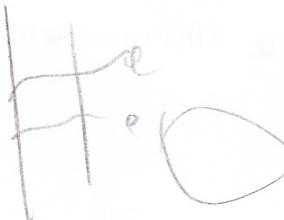
- A. It binds to multiple gene regulatory regions.
- B. It binds to multiple transcription factors.
- C. It binds to one transcription factor that then binds to multiple RNA polymerases.
- D. It binds to one transcription factor that then binds to an enhancer region present in the promoter region of many genes.
- E. There is more than one kind of transcription factor.

X 6. Which of the following does **not** happen in intracellular signaling pathways?

- A. Signals are physically transferred from one location of the cell to another.
- B. Signals are restricted from passing through any cellular membrane.
- C. Signals can change their physical form.
- D. Proteins bind to other molecules and change shape.
- E. Signals can become amplified as they are transduced.

X 7. Inositol phospholipids are found exclusively in the cytoplasmic face of the plasma membrane because:

- A. They are often secreted by neurons.
- B. They are phosphorylated.
- C. There are no inositol flippases in the ER.
- D. They are synthesized in the golgi apparatus.
- E. They bind clathrin.



✓ 8. Removal of a TATA box from a eukaryotic gene would likely result in which of the following outcomes?

- A. No transcription of that gene.
- B. Constitutive (constant) gene transcription.
- C. No splicing of gene transcripts
- D. Transcription of an incomplete gene sequence.
- E. Transcription of a mutant gene.

X 9. Which protein is responsible for establishing and maintaining a  $\text{Na}^+$  gradient across the plasma membrane?

- A. The ligand-gated  $\text{Na}^+$  channel
- B. The  $\text{Na}^+/\text{glucose}$  symporter
- C. The voltage-gated  $\text{Na}^+$  channel
- D. The  $\text{Na}^+/\text{K}^+$  ATPase
- E. The voltage-gated  $\text{Na}^+$  carrier

VESC  
LGSC

10. What is resting potential?

- A. A measure of ionic imbalance caused by DNA inside a nucleus and proteins in the cytosol; measured in millimoles
- B. A measure of ionic imbalance across the nuclear membrane, caused by unequal concentrations of ions in the cytosol vs. in the nucleus; measured in millivolts
- C. A measure of how many proteins are in the cytosol compared to in the lumen of the ER; measured in milligrams
- D. A measure of ionic imbalance across the plasma membrane, caused by unequal concentrations of ions in the cytosol vs. in the extracellular space; measured in millivolts
- E. A measure of the relative concentrations of  $\text{Na}^+$  and  $\text{K}^+$  after they have been transported across a membrane.

11. Which of the following is **not** an example of a "second messenger" in cellular signaling?

- A. Diacylglycerol.
- B. Calcium ions.
- C. Cyclic nucleotides.
- D. Inositol trisphosphate.
- E. Acetylcholine

12. G proteins can:

- A. Activate protein kinases.
- B. Cleave GTP to GDP.
- C. Bind cell surface receptors.
- D. Activate phospholipases.
- E. All of the above.

13. Which of the following mechanisms could **not** be used to inactivate at least one intracellular signaling pathway?

- A. Activation of phosphodiesterases.
- B. Degradation of a signaling protein.
- C. Depletion of the cellular ATP pool.
- D. Inhibition of a  $\text{Ca}^{+2}$  pump on the ER..
- E. Addition of GTP to cells.

14. Adrenaline acts at a G-protein linked receptor on heart muscle cells to make the heart beat more quickly by activating a cAMP-dependent signaling pathway. Which one of the following compounds would likely enhance the effect of adrenaline if it were added to the heart cells?

- A. A non-hydrolyzable analog of GTP (i.e., it cannot be cleaved to GDP + Pi).
- B. A non-hydrolyzable analog of ATP (i.e., it cannot be cleaved to ADP + Pi).
- C. Inhibitors of adenylate cyclase.
- D. Activators of p53.
- E. Activators of phosphodiesterase.

Checks DNA quality control wtf?

Digests cAMP



cAMP  
ATP  
Protein CAMP pathway

ATP

GDP

✓ 15. Which of the following signaling molecules stimulates a rise in cytosolic cAMP?

- A. Ras
- B. inositol trisphosphate *IP<sub>3</sub>*
- C. MAP kinase
- D.  $G\alpha_s$
- E.  $Na^+$

✓ 16. What is the source for this cAMP?

- A. Smooth endoplasmic reticulum
- B.  $Ca^{+2}$
- C.  $IP_3$
- D. ATP in the cytosol
- E. ATP in the nucleus

✓ 17. Which one is the most accurate description of the mechanism of the extrinsic pathway of apoptosis?

- A. A cell surface receptor initiates a cascade of protease activation events in the cytosol; the activated proteases digest the cell from the inside-out, so that none of the cellular proteins leaks into the extracellular space.
- B. A cell receives external signals that stimulate neighboring cells to engulf it, the cellular contents are eventually digested in the lysosomes of the neighboring cells.
- C. A cell receives external signals that cause the cell to secrete proteases that digest the surrounding extracellular matrix; the loss of contact with the ECM causes the plasma membrane to rupture, and the cell "bleeds to death."
- D. Apoptosis is also known as "Programmed Cell Death" and thus it is driven by a signal that diffuses from the extracellular space into the nucleus. The signal is then converted into mRNA, transported to the cytosol, and translated into protease proteins that digest the cell from the inside out.
- E. Cytochrome c leaks out of the mitochondrion and activates phospholipase C, and this initiates a cascade of protease activation; the activated proteases digest the cell from the inside-out, so that none of the cellular proteins leaks into the extracellular space

✓ 18. Identify the mismatched protein: functional location pair (Note: some proteins function in more than one location- the listed location may not be the only one for the corresponding protein in the answer; proteins can also exist in locations where they do *not* function- be sure you understand the difference).

- A. Estrogen receptor: nucleus
- B. MAP kinase: nucleus
- C. Troponin: nucleus
- D. Voltage-gated  $Ca^{+2}$  channel: Smooth ER membrane
- E. Myosin: cytosol

✓ 19. Complete this sentence: \_\_\_\_\_ directly inhibits a monomeric G protein, while \_\_\_\_\_ inhibits a heterotrimeric G protein signaling pathway.

- A. Acetylcholine; Mediator
- B. Integrin receptor; Sos
- C. RasGAP; phosphodiesterase
- D. Phospholipase C; cholera toxin
- E. GPCR; RTK

Ras  
What inhibits  
Ras?  
AM

20. Which statement best describes the function of CREB Binding Protein? CBP

- A. It unwinds the DNA double helix, making gene transcription easier
- B. It binds to the cAMP response element (CRE), thereby activating protein kinase A
- C. It binds to cAMP, thereby activating transcription
- D. It adds acetyl groups to lysines on histone proteins in nucleosomes
- E. It phosphorylates lysines on histone proteins in nucleosomes

21. What happens when a "G protein" cleaves GTP to GDP? X

- A. It changes shape, which causes a new phosphate to be added to the GDP in the protein
- B. It converts the GDP to GTP with a protein kinase
- C. It changes shape, and becomes "activated" so that it phosphorylates additional GDP molecules
- D. It changes shape, releases GDP, and binds a fresh GTP when it becomes available
- E. It releases Pi but remains otherwise unchanged

22. Cortisol receptors contain nuclear localization sequences, yet they are commonly found in the cytosol of cells. What is the most likely explanation for this observation? V

- A. Binding to cortisol induces a change in the receptor's shape; this in turn stimulates a cytosolic protease, which cleaves the receptor: this changes the shape of the receptor again, and unmasks a nuclear localization sequence that allows it to enter the nucleus.
- B. Binding to cortisol induces a change in the receptor's shape and unmasks a nuclear localization sequence that allows it to enter the nucleus.
- C. Cortisol binds to nuclear import receptors, and this causes the nuclear pore to open, thereby allowing all proteins, including the cortisol receptor, to enter the nucleus.
- D. Cortisol contains a nuclear localization sequence: Binding to the receptor induces a change in the cortisol's shape and unmasks a nuclear localization sequence that allows it and the receptor to enter the nucleus.
- E. Cortisol triggers the release of RanGTP from importin, thereby permitting new cargo (including the cortisol receptor) to undergo nuclear import.

23. How do DNA binding motifs, such as the helix-turn-helix, impact gene transcription? V

- A. They bind specifically to promoter sequences, including the CAAT box
- B. They act as helicases to unwind the major and minor grooves in helical DNA
- C. They bend double stranded DNA back to form a loop that can bring distant regulatory sequences close to the core promoter
- D. They bind RNA polymerase to the core promoter until TFIIH arrives
- E. They permit transcription factors to quickly find their DNA binding sequences by sliding in the major groove of helical DNA

24. A compound called PMA is a drug that mimics the structure of diacyl glycerol. If PMA is applied to the skin of lab animals, they can develop skin tumors. Which of the following best explains why this happens?

- A. Prolonged exposure to PMA results in a significant increase in cAMP, and this induces histone acetylation, causing increased mutation in dividing cells.
- B. Prolonged exposure to PMA results in activation of PKC; loss of PKC is accompanied by a loss of p21, so the cell cycle progresses more quickly.
- C. PMA disrupts the fluidity of the plasma membrane, so that receptor tyrosine kinases are locked in an activated state, resulting in prolonged activation of MAP kinase.
- D. PMA opens  $\text{Na}^+$  channels, so prolonged exposure to PMA results in a large flood of  $\text{Na}^+$  and subsequent activation of caspases.
- E. PMA causes an increase in  $\text{Ca}^{+2}$ , which then activates calmodulin and inhibits Akt, so cells grow continuously.

25. Why does signaling through a peptide growth factor (such as Platelet Derived Growth Factor) allow for more rapid responses in a cell than signaling through a steroid hormone such as estrogen?

- A. Steroid hormones do not enter cells as fast as peptide growth factors.
- B. Peptide growth factors are enzymes, steroid hormones are not
- C. Steroid hormones must be carried to the nucleus to exert their effects, while peptide growth factors can change the activity of cytosolic proteins
- D. Steroid hormones enter virtually every cell in the body, while peptide growth factors do not
- E. Peptide growth factors bind to dimerized receptors, while steroid hormones do not

26. Which statement best describes the mechanism of activation of heterotrimeric G proteins?

- A.  $\alpha$ ,  $\beta$  and  $\gamma$  subunits remain in a single complex, until stimulated by binding an GPCR; upon binding the activated receptor, the  $\alpha$  subunit releases GDP and binds GTP and separates from the  $\beta$  and  $\gamma$  subunits
- B. The  $\alpha$  subunit binds to a  $\beta/\gamma$  subunit and forms a homodimer. This dimer is split when GPCRs bind to GTP, thereby releasing activated  $\alpha$  subunits
- C. GTP binds to the  $\alpha$  subunit, which causes it to bind to a GPCR, thereby displacing a  $\beta/\gamma$  subunit
- D. GTP is swapped in for GDP by the  $\alpha$  subunit prior to binding of ligand to a  $\beta/\gamma$  subunit; the resulting complex binds to GPCR upon ligand binding
- E. The  $\alpha$  subunit cleaves GTP to GDP, then releases the  $\beta/\gamma$  subunit and binds a GPCR

27. Which of the following signaling molecules stimulates a rise in cytosolic  $\text{Ca}^{+2}$ ?

- A. Ras
- B. Inositol trisphosphate
- C. MAP kinase
- D. cAMP
- E.  $\text{Na}^+$

(P3)

28. What is the source for this  $\text{Ca}^{+2}$  (i.e., where is it stored)?

- A. The Trans Golgi Network
- B. The endoplasmic reticulum
- C. The lysosomes
- D. The nucleus
- E. The mitochondria

(ER)

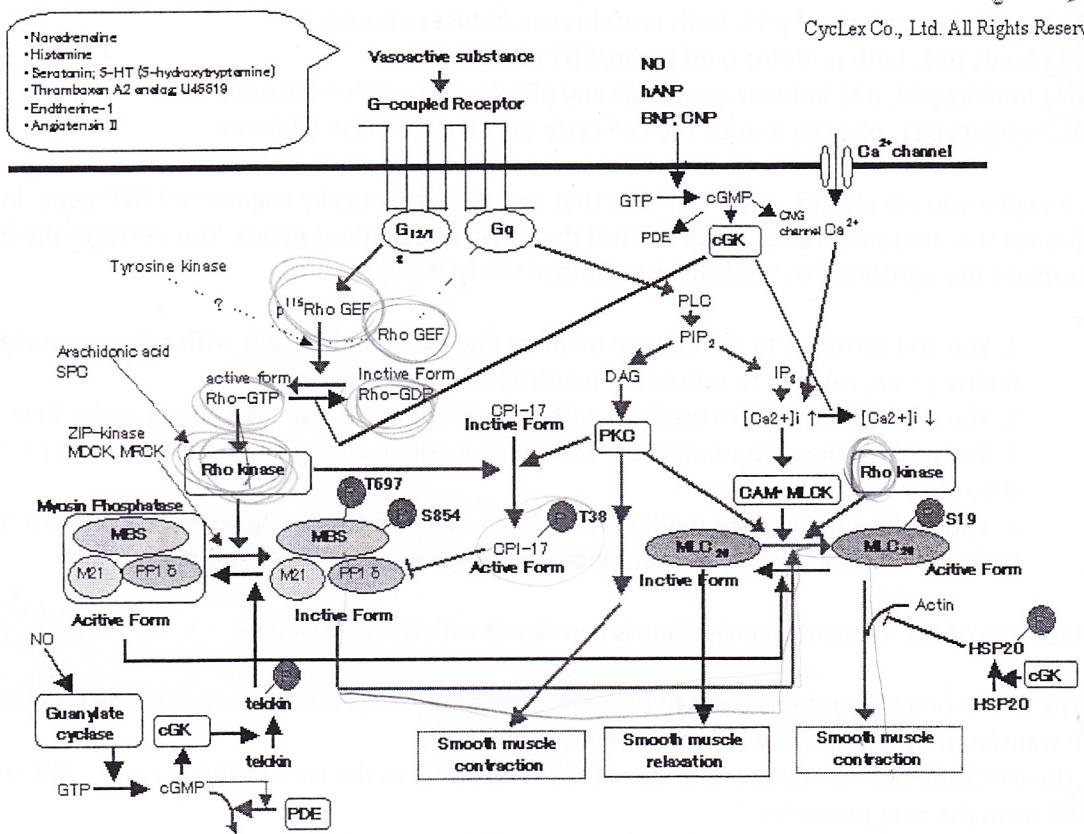
29. What can the "sarcoplasmic reticulum" in skeletal muscle cells do that the "smooth endoplasmic reticulum" in other cells cannot?

- A. Initiate an action potential
- B. Store calcium ions
- C. Depolarize in response to an action potential
- D. Bind to ribosomes
- E. Bind IP<sub>3</sub>

30. According to the diagram shown at right, which statement best describes the function of the G protein Rho in controlling smooth muscle cell contraction? Note that myosin light chain must be phosphorylated for smooth muscle cells to contract. (This requires some thought; be careful.)

### Signal transduction of smooth muscle contraction (1)

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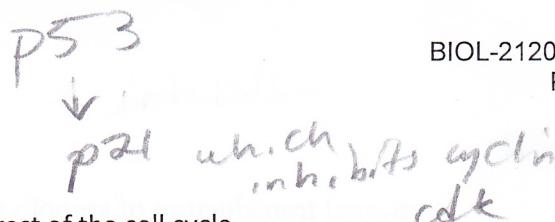


- A. Rho activates contraction, by activating an inhibitor (Rho kinase) of an inhibitor (Myosin phosphatase) of myosin light chain phosphorylation.
- B. Rho activates relaxation, by activating an inhibitor (Rho kinase) of an activator (Myosin Light Chain Kinase, MLCK) of myosin light chain phosphorylation.
- C. Rho inhibits contraction, by inhibiting an activator (Rho kinase) of an activator (Protein Kinase C, PKC) of myosin light chain phosphorylation.
- D. Rho inhibits relaxation, by activating an inhibitor (Rho kinase) of an inhibitor (CPI-17) of an inhibitor (myosin phosphatase) of myosin light chain phosphorylation.
- E. Rho activates contraction, by converting the signal from an activator receptor (GPCR) into activator second messengers (DAG and IP<sub>3</sub>) that both activate an activator (MLCK) of myosin light chain phosphorylation.

31. Would you expect p53 to be expressed in yeast (single-celled eukaryotes)?

- A. No, because yeast do not express integrin receptors
- B. Yes, because yeast cells must undergo apoptosis
- C. No, because apoptosis would not benefit a single celled organism like yeast
- D. Yes, because yeast infections can damage tissues
- E. No, because yeast cells do not contain cytochrome c, an important protein in apoptosis signaling

✓ 32. What is the relationship between p53 and p21?



- A. p53 induces expression of p21; both proteins can induce arrest of the cell cycle
- B. p21 induces expression of p53; both proteins can induce apoptosis
- C. p53 binds p21; both proteins bind cyclin/CDK complexes
- D. p21 inhibits p53; p21 induces apoptosis and p53 protects cells from apoptosis
- E. p53 inhibits p21; p53 can induce the cell cycle only if p21 is also inhibited

✗ 33. Imagine you are given a culture of cells that contain a genetically engineered GFP gene, including a promoter sequence that these cells also use to control their own endogenous genes. You perform the following experiments to determine the signaling mechanisms that control the GFP gene:

1. You add estrogen to the culture medium and examine the cells with a fluorescence microscope; they glow faintly green, relative to untreated (control) cells.
2. You replace the culture medium with fresh medium containing cholera toxin; they do not glow at all.
3. You replace the culture medium with fresh medium containing estrogen and a phosphodiesterase inhibitor; they glow bright green.
4. You replace the culture medium with fresh medium containing estrogen, cholera toxin, and a drug that inhibits Protein Kinase A; the cells glow faintly green, as in experiment 1.

Which one of the following conclusions is consistent with these findings?

Drug inhibits cholera

- A. The GFP promoter contains a cAMP Response Element (CRE) and a steroid response element (SRE) that both activate GFP transcription, completely independent of each other.
- B. The GFP promoter contains a CRE close (<20 base pairs) to the core promoter and a SRE that is far away (>100 base pairs) from the core promoter.
- C. TFIID is phosphorylated by estrogen receptor and PKA.
- D. The GFP promoter contains a cholera toxin response element (CTRE), a CRE, and a SRE, all in the proximal regulatory promoter.
- E. Access to the SRE is enhanced by CREB Binding Protein (CBP) in the GFP promoter.

✗ 34. Which statement best explains the difference between SH2 and SH3 domains?

Xyrosine  
Ala

- A. SH2 binds DNA, SH3 binds proteins
- B. SH2 binds G proteins, SH3 binds protein kinases
- C. SH2 binds phosphotyrosines, SH3 does not
- D. SH2 binds GPCRs, SH3 binds RTKs
- E. SH2 binds p53, SH3 binds p21

✗ 35. Which one of the following statements about regulation of gene expression is true?

- A. Activator sequences bind to enhancer proteins in the core promoter.
- B. Inhibitor sequences bind to inhibitor proteins in the proximal regulatory promoter.
- C. Suppressor proteins bind to inhibitor proteins that bind to activator proteins in the core promoter.
- D. Activator proteins bind to inhibitor proteins that bind to activator proteins in the proximal regulatory promoter.
- E. Activator proteins bind to enhancer sequences, and inhibitor proteins bind to suppressor sequences, and both types of sequences are in the proximal regulatory promoter.

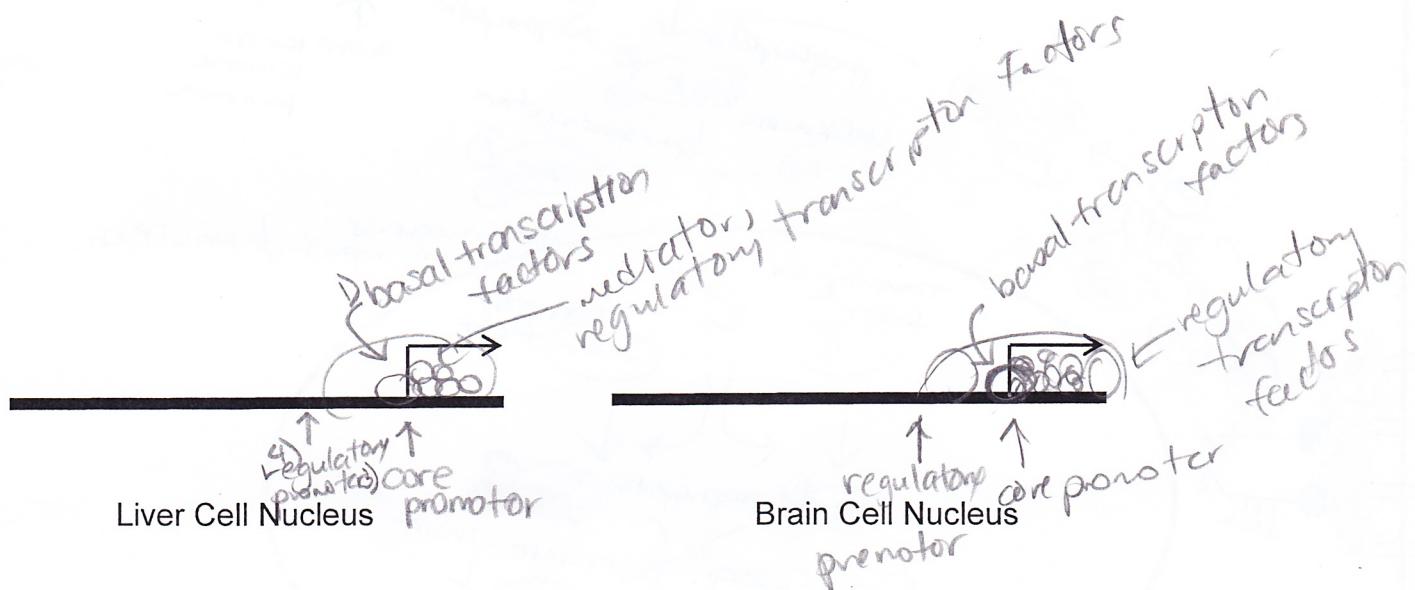
Part II

1. Draw a picture illustrating how the Combinatorial Model for Controlling Gene Expression works, using the diagram below to get you started. Include the following elements in your diagram:

- ✓ 1. Basal transcription factors +1
- ✓ 2. Regulatory transcription factors +2
- ✓ 3. Core promoter
- ✓ 4. Proximal regulatory elements (regulatory promoter) +1  
*before core*

6/7

Label the structures you draw.



In the box below, briefly explain your diagram.

The regulatory promoter is upstream of the core promoter, and basal transcription factors bind to the core promoter. The regulatory transcription factors, like the Mediator, then bind to the regulatory promoter and initiate gene transcription.

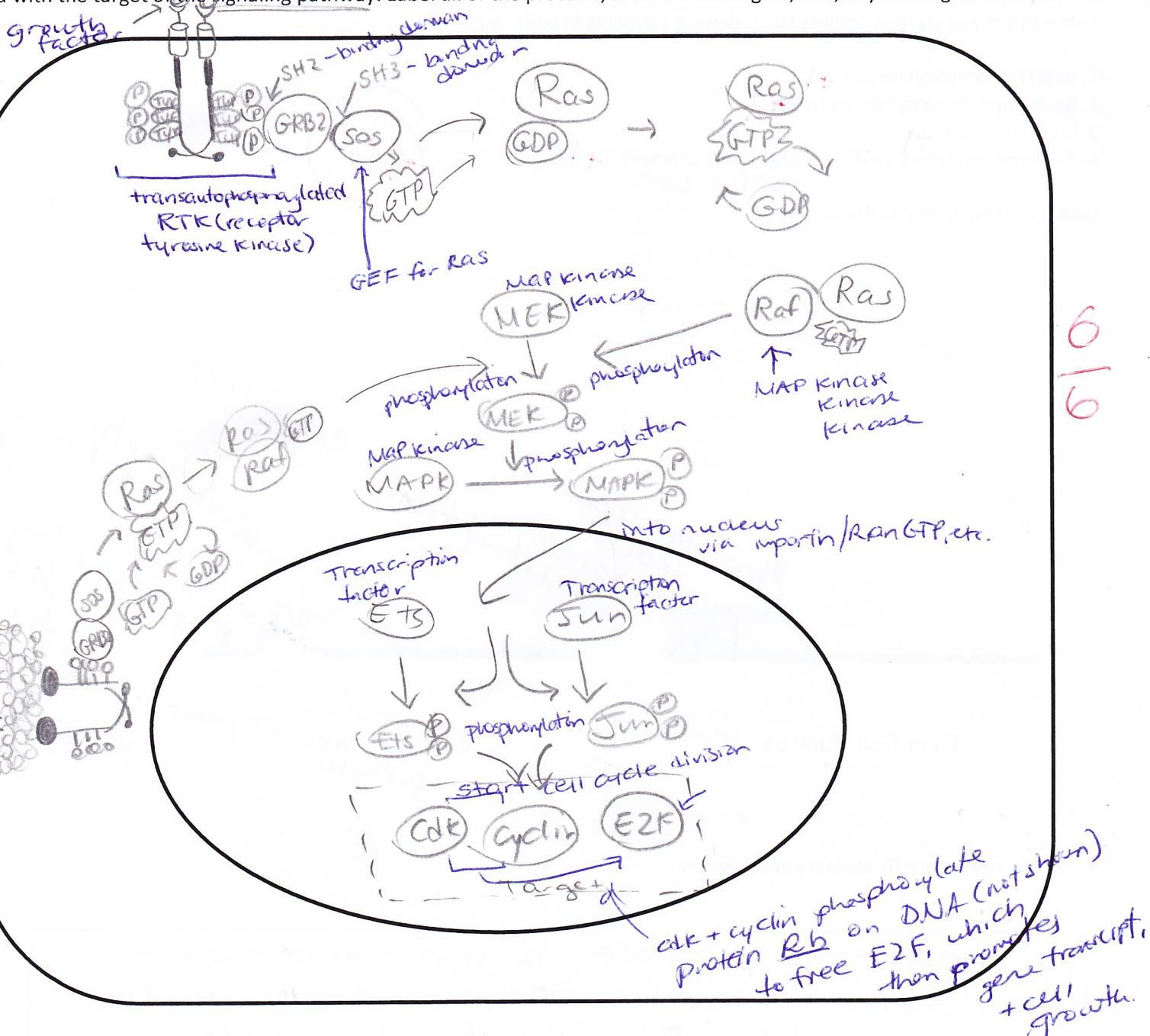
Not shown: regulatory transcription factors are different shapes in each diagram, but +1 process happens the same way.

6

# RTK

FAK

- 2A. Draw a picture illustrating how a receptor tyrosine kinase signaling pathway and an integrin receptor signaling pathway can converge into a single pathway that triggers cell growth. Begin with the extracellular signaling molecule and end with the target of the signaling pathway. Label all of the proteins, second messengers, etc., in your diagram.



6  
/ 6

- B. In the box below, briefly explain how the target of this pathway stimulates cells to grow. No diagram is necessary.

A growth factor binds to the extra cellular receptors on the RTK and integrin, causing a transautophosphorylation of the tyrosine tails on RTK. This causes the SH2 binding domain of GRB2 to bind to the phosphorylated tails, activating the SH3 binding domain on GRB2 so that proline-rich SOS binds to GRB2. SOS is the GEF for Ras. Therefore attracts GTP to replace GDP, activating a pathway that activates Raf, which phosphorylates MEK, then MAPK, then ultimately producing cyclin + cdk which promote M phase and cell growth, and E2F which, once activated by cdk + cyclin, can begin gene transcription.

2  
—  
2

3. Arrange the following events that occur during voluntary muscle contraction in the correct temporal sequence, from first to last, using the single letters (e.g, 1D; 2B; 3A, etc.):

- |  |
|--|
| A. Refractory period   |
| B. Simultaneous closing of voltage gated sodium channels and opening of voltage gated potassium channels |
| C. Electrical stimulus received  |
| D. Opening of voltage gated sodium channels  |
| E. Depolarization of neuronal membrane   |
| F. Closing of voltage gated potassium channels   |
| G. Repolarization of neuronal membrane   |

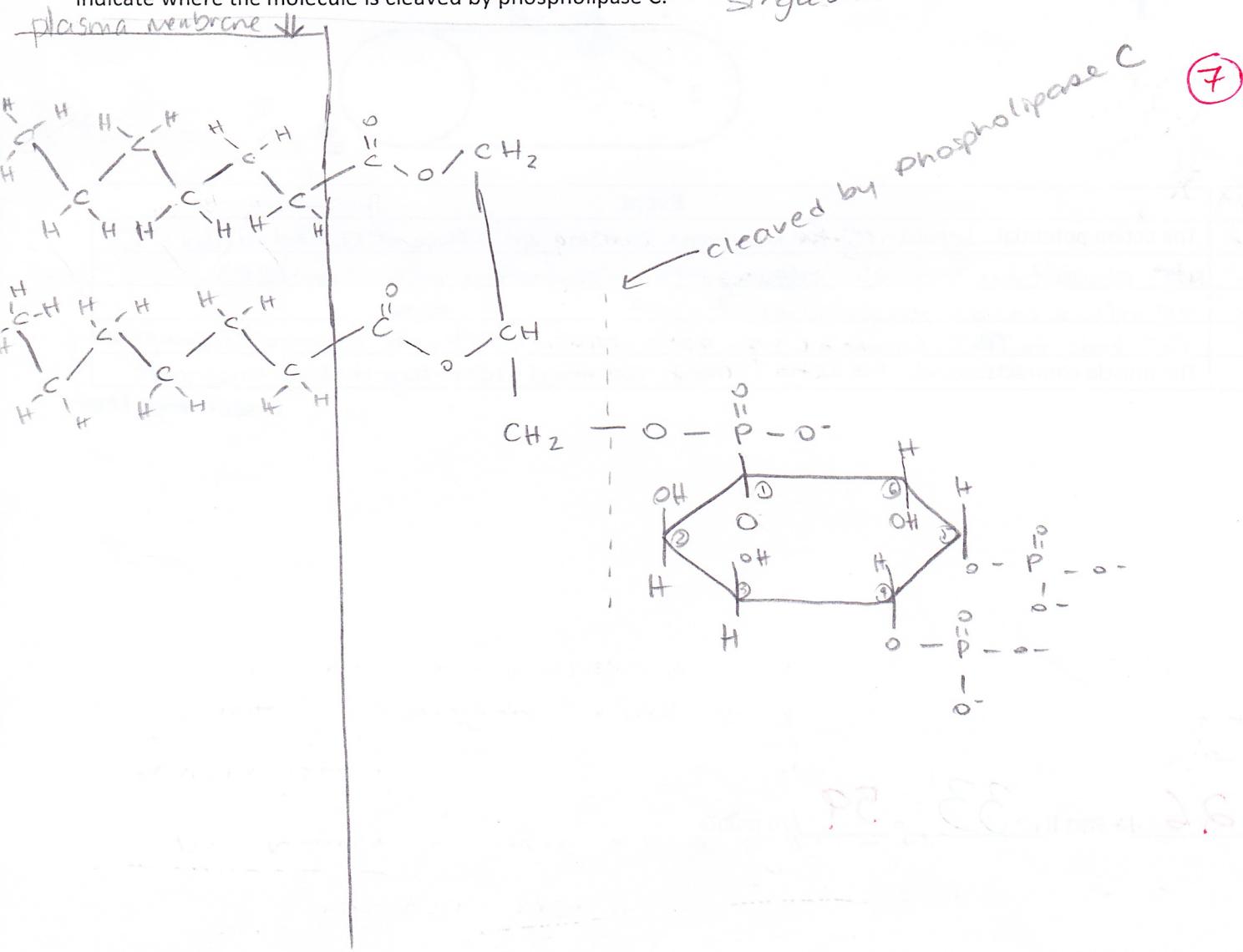
Sequence:

1. C; 2 D; 3 E; 4 B; 5 G; 6 F; 7 A

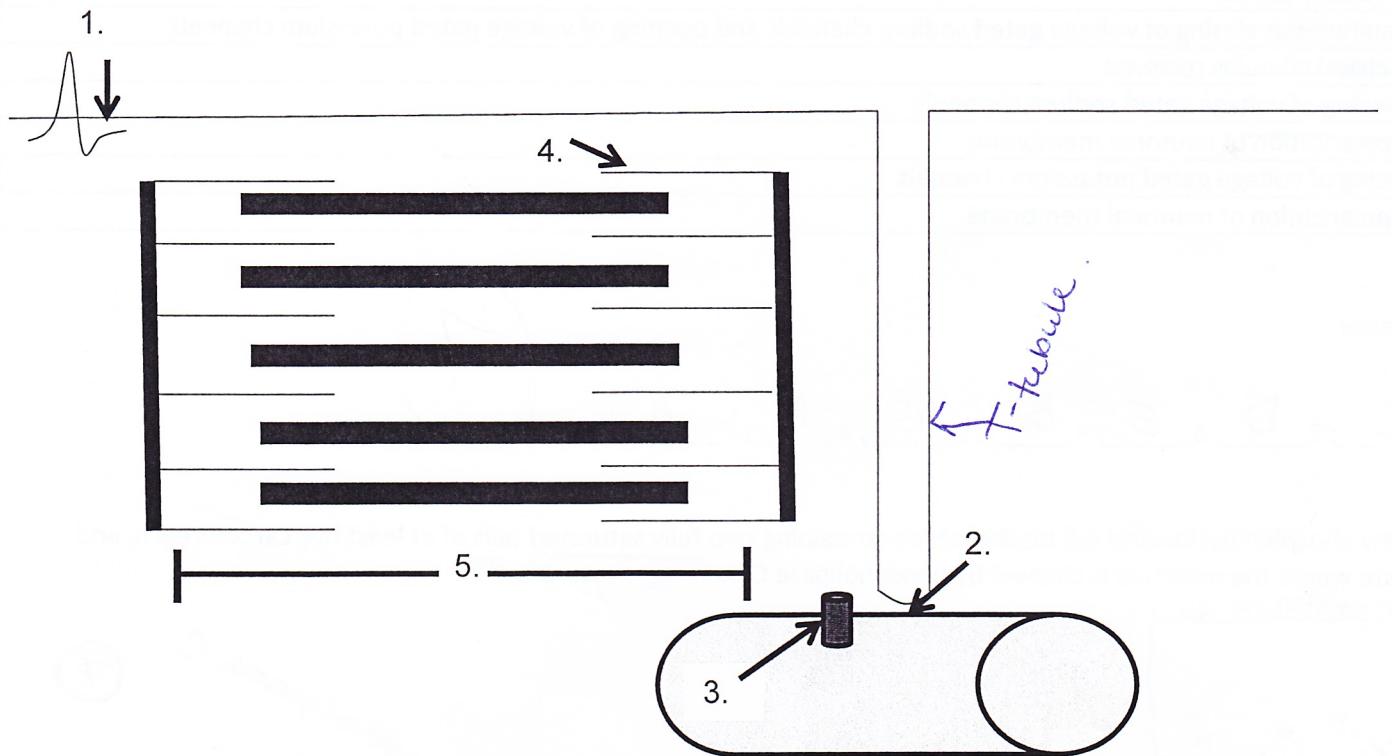
1

4. Draw phosphatidyl inositol 4,5 bisphosphate containing two fully saturated tails of at least five carbons each, and indicate where the molecule is cleaved by phospholipase C.

single bonds



5. Illustrate how the T tubule allows skeletal muscle cells to convert signals from nerve cells into muscle contraction, by briefly explaining what happens at the numbered steps. Start by explaining what happens to the action potential on the muscle cell as shown (#1), and end with muscle contraction (#5). The answers to #1 and #5 are started for you; simply complete the sentence.



Step	Event
1 ✓	The action potential... depolarizes the membrane causing an influx of $\text{Na}^+$ and outflux of $\text{K}^+$
2 ✓	$\text{Na}^+$ from T-tubule diffuses into sarcoplasmic reticulum (SR)
3 ✓	$\text{Na}^+$ influx causes an outflux of $\text{Ca}^{2+}$ <del>(<math>\text{Ca}^{2+}</math>)</del>
4	$\text{Ca}^{2+}$ binds to TP-C (troponin C) on actin, causing actin to contract/cross closer
5	The muscle contracts...and the actin filaments are moved closer together, Z lines move closer together