Trask

Zool 3200: Cell Biology
Exam 5
4/27/15

Answer each of the following short answer questions in the space provided, giving explanations when asked to do so. Circle the correct answer or answers for each multiple choice question. Recall that you are to work independently in completing this take-home exam. You are free to use all class notes and your text book, but not the internet when completing this exam. (80 points)

A growth factor known as RGF (rat growth factor) stimulates proliferation of cultured rat cells. The receptor that binds RGF is a receptor tyrosine kinase called RGF-R. Which of the following types of alteration to RGF would be most likely to prevent receptor dimerization? (1 point)

a.) a mutation that increases the affinity of RGF-R for RGF
b.) a mutation that prevents RGF-R from binding to RGF

c.) changing the tyrosines that are normally phosphorylated on RGF-R dimerization to alanines
d.) changing the tyrosines that are normally phosphorylated on RGF-R dimerization to glutamic acids

Antibodies are Y-shaped molecules that have two identical antigen binding sites. (See the diagram left) Suppose that you have obtained an antibody that is directed toward the extracellular domain of a Receptor Tyrosine Kinase (RTK), meaning that the antibody’s variable region binds go the receptor’s extracellular region. If cells containing the RTK were exposed to the antibody, what effect(s) on signaling from the receptor might you expect? Consider all possibilities, and explain your reasoning. (4 points)
Male cockroaches with mutations in a receptor tyrosine kinase gene, *gene A*, are oblivious to the charms of their female comrades. This particular receptor tyrosine kinase binds to a small molecule secreted by sexually-mature females. Most males carrying mutations in the gene for *Ras* protein are also unable to respond to females. You have just read a paper in which the authors describe how they have screened cockroaches with the defective *A* gene for additional mutations that partially restore the ability of males to respond to females. These latter mutants have a second defect in a gene that the authors call ‘*gene C*’. Which of the following proteins would be most likely to be encoded by *gene C*? Explain your answer by describing what you would expect if each of the potential compensatory mutations described below were introduced into male cockroaches with mutations in *gene A*. Be sure to include specifically what type(s) of mutation(s) would have to be present in order to observe your expected results. (10 points)

a.) A GEF (A.K.A., a GNRP) protein.

b.) A GAP protein.

c.) A protein kinase activated by the *Ras* protein.

d.) An adaptor protein that mediates the binding of the receptor *A* to the *Ras* protein.

e.) A transcription factor required for the expression of the *Ras* gene.

Despite their differences, there are several similarities between signaling through G protein coupled receptors and receptor tyrosine kinases. Name three similarities. (3 points)
While ligand binding to a 7-pass transmembrane receptor elicits a response, it is necessary to turn off this response so that continual cAMP production and PKA activation is halted. How is signaling through this pathway turned off? Be sure to name all of the things that must happen to silence signaling through this pathway. (4 points)

When epinephrine binds to 7-pass transmembrane adrenergic receptors on the surface of a muscle cell, it results in activation of a G-protein, initiating a signaling pathway where the activated α subunit activates adenyl cyclase. All of the downstream effects of adenyl cyclase then ensue, ultimately resulting in activation of enzymes that breakdown muscle glycogen (thus lowering cytoplasmic glycogen levels in muscle cells). You obtain muscle cells that are defective in various components of this signaling pathway. How would glycogen levels in each of the cells described below be affected in the presence of epinephrine? Explain your rationale in each case. (8 points)

a.) Cells that lack adenyl cyclase?

b.) Cells that lack cAMP phosphodiesterase?

c.) Cells that lack a functional protein kinase C?

d.) Cells carrying a mutation in Gα such that it could not be post-translationally modified with the addition of a lipid tail?
For each of the situations below, name a specific mutation (i.e., which protein(s) would be mutated and how it would be mutated) that would produce what is described. In addition, describe what would happen to cells in these situations with respect to their progression through the cell division cycle. (6 points)

a.) Cells are unable to degrade M-cyclin.

b.) Cells always express high levels of p21.

c.) Cells are unable to pass through “Start” of the cell division cycle.

You’re given two flasks of cultured cells, each containing a population of cells that has been ‘synchronized’ with respect to its division cycle. In other words, ALL of the cells in each of your two flasks are in the same phase of cell division. It has been revealed that one of the populations is just entering G1 phase and the other is at the G1-S checkpoint. Design two different experiments that would enable you to distinguish the two cultures? (i.e., what would you look for to tell me which population is in early versus late G1 phase?). (3 points)
Mitosis promoting factor, or MPF, is an activity that oscillates with the cell cycle, being highly active during M phase but rapidly declines near the end of mitosis. See diagram below. What are the two protein components of MPF? Name two of MPF’s substrates. What must occur (or not) in order for MPF to be active? (8 points)

With you knowledge of why MPF activity levels rise so rapidly at the beginning of M phase, and why they fall so precipitously at the end of M phase, predict what effect a mutation in the gene for Wee 1 phosphatase (such that the Wee 1 protein could not be phosphorylated) would have on MPF activity during the cell division cycle. How would this affect the shape of the curves in the graph above? Redraw the graph as you predict in the space provided below. (2 points for the prediction and 2 points for the graph; 4 points total)
Of the following mutations, indicate which are likely to cause cell-cycle arrest by marking them with an asterisk (*). If you predict a cell-cycle arrest, indicate whether the cell will arrest in early G₁, late G₁, or G₂. (5 points)

A. a mutation in a gene encoding a cell-surface mitogen receptor that makes the receptor active even in the absence of the mitogen

B. a mutation that destroyed the kinase activity of S-Cdk

C. a mutation that allowed G₁-Cdk to be active independently of its phosphorylation status

D. a mutation that removed the phosphorylation sites on the Rb protein

E. a mutation that inhibited the activity of Rb

Apoptotic cells are generally removed from a multicellular organism by the immune system. Describe how the immune system is able to recognize apoptotic cells from those that are normally functional. (1 point)

List the steps necessary to induce apoptosis through the intrinsic pathway. Name one condition that might induce this process. (7 points)

Name one condition that might induce the process of EXTRINSICALLY-INDUCED apoptosis. (1 point)
For each of the statements below, circle the adjective that appropriately describes the protein; 3 points)

*BCL-XL* is a protein that inhibits the function of *Bax*. *BCL-XL* is: Pro-apoptotic / anti-apoptotic

*Bim* inhibits *Bcl-2*. *Bim* is: Pro-apoptotic / anti-apoptotic.

*Bad* is: Pro-apoptotic / anti-apoptotic

Describe how connexins differ from occludins in the way they function and in their distribution (i.e, where they are in the body; 3 points).

Compare and contrast desmosomes with hemidesmosomes. (4 points)

Match the molecules (list 1) with the cell structures in which they are involved (list 2). Not all molecules in List 1 will be used, and some molecules in list 1 may be involved in more than one structure from list 2. (5 points)

<table>
<thead>
<tr>
<th>List 1</th>
<th>List 2</th>
<th>Related Molecules (letter[s])</th>
</tr>
</thead>
<tbody>
<tr>
<td>A. Cadherin</td>
<td>Tight junction</td>
<td></td>
</tr>
<tr>
<td>B. Cellulose</td>
<td>Gap junction</td>
<td></td>
</tr>
<tr>
<td>C. Adapter proteins</td>
<td>Adherens junction</td>
<td></td>
</tr>
<tr>
<td>D. Actin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E. Connexin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>F. Occludin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>G. Keratin</td>
<td></td>
<td></td>
</tr>
<tr>
<td>H. Integrin</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Everyone in my group contributed a reasonable intellectual effort toward the completion of this final group exam.

Signed: ________________________________