Name_____

Biology 169 -- Exam 1

February 2003

Answer each question, noting carefully the instructions for each.
Repeat- Read the instructions for each question before answering!!!
Be as specific as possible in each answer, within the set length limits; e.g., "tyrosine phosphorylation" is more specific than "phosphorylation", and " tyrosine phosphorylation by the EGF receptor" is even more specific.
Please print name on top of **each** page! (In case pages get separated)

I certify that I have performed my work on this examination in full conformity with the provisions of the Honor Code.

Signature_____

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1. The following three true-or-false questions are worth 4 points in total. Mark each as T or F and for any that is/are false, indicate briefly why in the space below.

a. T F Cancer cells can evade normal programmed cell death.

b. T F A single mutation is not enough to cause cancer.

c. T F Retroviral activation of Wnt-1 can contribute to mouse breast cancer.

_____

_____

_____

2. (7 points) Skin cells normally proliferate at a slow rate in the body, replacing those lost due to normal attrition, and remain firmly attached to the basal lamina. When the skin is wounded, what happens to the cell migration rate of skin cells?

(Choose ONE) It increases / It remains the same / It decreases.

In response to a wound, skin cells loosen their hold on the basal lamina and migrate into the wound site. This is stimulated by a signaling molecule called PDGF made by a particular type of blood cell. This ligand binds to PDGF receptors on skin cells—the cytoplasmic domain of the PDGF receptor has which
enzymatic activity? _____

Through a cascade of signal transduction events, a downstream protein called Src is activated. Src is normally inactive except when the cell sees the PDGF. Imagine two different types of mutation in Src. Mutation 1 (Src-ACTIVATED) renders it constitutively active. Mutation 2 (Src-INACTIVE) kills the normal function of the protein. Normal Src is designated " +". Two experiments were done, one in the absence and one in the presence of PDGF. Would skin cells of the following genotypes alter their adhesion to the ECM and migrate? In each blank, fill in either **STAYS PUT** or **MIGRATES**:

	Absence of PDGF	Presence of PDGF
+ / +	_____	_____
Src-INACTIVE / Src-INACTIVE	_____	_____
Src-INACTIVE / +	_____	_____
Src-ACTIVATED / +	_____	_____
Src-ACTIVATED / Src-ACTIVATED	_____	_____

3. (2 points: Circle one) The cell biological function of the normal Retinoblastoma protein is to:

A. Repair damaged DNA.
B. Turn on genes required for cell proliferation.
C. Phosphorylate integrins, promoting cell motility.
D. Turn off genes required for cell proliferation.

Name_____

4. (2 points- fill in the blanks) The NF1 gene is a tumor suppressor, analogous to Rb. The normal function of NF1 protein is to suppress cell proliferation, and its genetics are similar to those of Rb, with NF1 playing a role in neurofibroma development (tumors of the nervous system) similar to that Rb plays in retinoblastoma. Fill in the blanks with the letter corresponding to the most likely genotype from among those listed:

A. + / + B. $NF1^{mutant}$ / + C. $NF1^{mutant}$ / $NF1^{mutant}$

A skin cell from a normal individual? _____

A cell in a sporadic nervous system tumor that arose in a normal individual? _____

A skin cell from an individual with a familial predisposition to neurofibromas? _____

A nervous system tumor cell from an individual with a familial predisposition to neurofibroma? _____

5. (3 points) Advanced tumors become most difficult to treat when they have acquired the ability to metastasize, in other words to leave the original tumor and travel to distant parts of the body and form secondary tumors.
To do so, tumors turn **OFF** expression of which family of transmembrane proteins? _____

By what route do they travel to distant sites, and what normal type of cell also travels by this same route? _____

6. (1 point each) Choose among these choices the most likely phenotypes of the following animals:

Extra R7 Extra R8 No R7 No R8 Wild-type lethal

Hint for the following: In their genetic screen for enhancers, Simon et al. used the temperature 22.7° C.

sevenless ^{null}/ *sevenless* ^{null} at 18°C.

sevenless ^{null}/ *sevenless* ^{null} at 22.7°C.

sevenless ^{null}/ *sevenless* ^{null} at 25°C.

sevenless ^{null}/ + at 25°C

boss ^{null}/ *boss* ^{null} at 25°C

ras ^{null}/ *ras* ^{null} at 25°C

ras ^{null}/ + at 25°C

sevenless ^{ts}/ *sevenless* ^{ts} at 18°C.

sevenless ^{ts}/ *sevenless* ^{ts} at 22.7°C.

sevenless ^{ts}/ *sevenless* ^{ts} at 25°C.

sevenless ^{ts}/ *sevenless* ^{ts} ; *ras* ^{null}/ + at 22.7°C

sevenless ^{ts}/ *sevenless* ^{ts} ; *ras* ^{null}/ *ras* ^{null} at 22.7°C

(3 points) Explain the reason the phenotype of a phenotype of *ras* ^{null}/ *ras* ^{null} differs from that of *sevenless* ^{null}/ *sevenless* ^{null} ?

_____

_____

_____

Name_____

7. (15 points) Draw a diagram illustrating the signal transduction pathway for the EGF signal (aka the RTK-ras pathway). Indicate the name of each protein, its cellular location (extracellular, plasma membrane, cytoplasmic, nuclear), and the protein-protein or regulatory interactions that mediate signal transduction. I DO NOT WANT a lot of text—the diagram and labels should suffice.

Plasma membrane

Nucleus

Name_____

8. (3 points) What type (class) of virus is the most common cause of animal cancer?

_____

One mechanism by which this type of virus can contribute to tumor development is by picking up into its genome a mutant form of a normal cellular gene. What is the other mechanism by which this type of virus can help trigger cancer? Your explanation should include a description of an interesting thing that happens to the viral genome and the consequences of this.

_____

_____

_____

9. (4 points) Src normally exists in the OFF state, in which the kinase is inactive. What keeps the kinase off?

_____

_____

Why does the mutant form of Src carried by RSV have a constitutively active kinase?

_____

_____

10. (6 points) Ras is an enzyme—what enzymatic reaction does it catalyze?

_____

This ability to catalyze a chemical reaction allows Ras to cycle between and active and an inactive state. Diagram the Ras cycle, showing the active and inactive state, what molecule Ras is bound to in each, and the change that occurs in moving from active to inactive and from inactive to active.

11. (4 points) One class of proteins promotes ras assuming the **active** state—what are these proteins called and how do they promote this?

_____

_____

Another class of proteins promotes ras assuming the **inactive** state—what are these proteins called and how do they promote this?

_____

_____

Name_____

12. (4 points) Binding of EGF to the EGF receptor triggers TWO sequential changes in the receptor that ultimately lead to signal transduction. What are these two changes?

_____

_____

The second of these changes leads to the recruitment of another protein to the receptor. What protein-protein interaction results in this recruitment -i.e., what domain is involved, to what does it bind?

_____

_____

13. (7 points) In their genetic screen for genes that are in the same pathway as *sevenless* , Simon et al. used a temperature sensitive allele of *sevenless*. They screened for both suppressors (which made the *sevenless* phenotype less severe) and enhancers (which made the *sevenless* phenotype more severe). Classify the following genes as to whether loss of function mutations in them are likely to SUPPRESS or ENHANCE or HAVE NO EFFECT on the phenotype of *sevenless* ?

ras

E-cadherin

ras GAP

sos (a ras GEF)

Rb

raf

drk= Grb2

14. (2 points-all or none) The lin-34 mutation causes a Muv phenotype, in which all cells choose 1° or 2° cell fates. lin-3 and lin-45 mutations cause a Vul phenotype. To order these genes in a genetic pathway, scientists made double mutant combinations. The lin-34; lin-45 phenotype is Vul. The lin-34; lin-3 phenotype is Muv. Order the three genes in a linear pathway.

15. (6 points) lin-34 is a dominant gain-of-function allele of ras, and causes a Muv phenotype.

Mutations in which of the following would suppress the Muv phenotype and make either a wild-type animal or a Vul animal (circle the correct answer(s))?.

Worm homolog of EGF Receptor

Worm homolog of Raf

Worm homolog of FAK (focal adhesion kinase)

Worm homolog of MAP Kinase

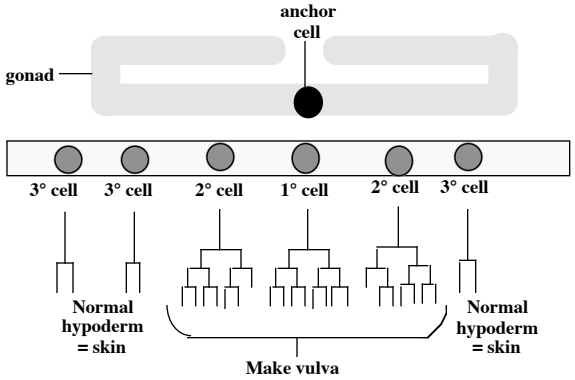
Worm homolog of Grb-2

Worm homolog of Src

Name_____

16. (10 points) The diagram shows the cell fates chosen by different cells of the vulval equivalence group in a wild-type worm. How many hypodermal cells (3° cell fates) and how many vulval cells (1° plus 2° cell fates) will be made in the cases listed below (the total will always be six)?
Hint: in the wild-type animal the answer would be:

Vulval cell fates ____3_____ Hypodermal cell fates _____3_____



In an animal in which the anchor cell was ablated using a laser (total =six)

Vulval cell fates _____ Hypodermal cell fates _____

In an animal in which the gonad was ablated using a laser (total =six)

Vulval cell fates _____ Hypodermal cell fates _____

In an animal in which all vulval precursor cells are heterozygous for a mutant form of Let-23 with a mutation analogous to that that Cori Bargmann found in the mammalian neu receptor

Vulval cell fates _____ Hypodermal cell fates _____

In a mosaic animal in which all of the vulval precursor cells are homozygous mutant for a null mutation in let-60 (ras), while the rest of the animal is heterozygous mutant (total =6)

Vulval cell fates _____ Hypodermal cell fates _____

In an animal which is heterozygous mutant for a dominant negative mutation in let-60 (ras);
i.e. which is let-60(dn) / +

Vulval cell fates _____ Hypodermal cell fates _____

17. (6 points) Herceptin is a promising new drug for treating certain cancers.

What oncogene does Herceptin target? _____

In MOST breast cancers, by what mechanism is this oncogene activated?

_____

What type of molecule is Herceptin? _____

This type of molecule could not be be used to target all types of proteins—for example, why couldn't you generate such a drug against ras?_____

_____

We also discussed another type of drug being developed against the same target as Herceptin—by what mechanism does this drug work?_____

_____