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2006 7.012 Problem Set 7

** Due before 5 PM on **FRIDAY**, December 8, 2006. **

Turn answers in to the box outside of 68-120.

PLEASE WRITE YOUR ANSWERS ON THIS PRINTOUT.

- 1.** Because producing effective HIV vaccines is problematic, the most common treatments for HIV infections are currently are anti-viral drugs.
- (a) Why do you think that there are no serious side effects to humans being treated for HIV by drugs that target the enzyme reverse transcriptase?
- (b) The drugs used to treat AIDS that are protease inhibitors need to be specific for HIV proteases, and cannot inhibit proteases in general. Why do you think this is?
- (c) You are attempting to come up with new ideas for HIV drugs. As a start you'd like to try to develop a drug you call anti-CD4, which would inhibit the function of CD4 proteins on the surface of helper T cells. Why would anti-CD4 be useful for preventing HIV infection?
- (d) What is the most major disadvantage of anti-CD4 treatment?
- (e) HIV viral particles cannot dock onto hamster cells, although it can dock onto human cells. You want to study HIV entry into host cells in lab using hamster cells. How do you think you might genetically manipulate hamster cells such that HIV viral particles can dock onto them?

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2. You are working in a lab that is trying to perform stem cell therapy on mice with Parkinson's Disease by inducing stem cells to become nerve cells *in vitro*, and then delivering these nerve cells to the diseased mouse's brain. The mouse strain you are trying to treat has a form of Parkinson's Disease that is autosomal recessive and is caused by loss-of-function in the PARK2 gene.

(a) You initially decide that you want to do the stem cell treatment with stem cells harvested from a wild-type mouse. What is a potential problem with treating the diseased mouse with stem cells taken from another mouse that is not related at all to the diseased mouse?

(b) You decide to try the kind of therapy discussed in part **(a)** anyway, regardless of the problem listed above. You decide that you will do the therapy using adult stem cells harvested from a wild-type mouse. What is one major problem with trying to use **adult** stem cells specifically for this therapy?

(c) You change your mind, and decide that you want to work with ES cells that are genetically identical to those of the diseased mouse, due to the problems listed in part **(a)** and **(b)**. Why can't you directly isolate ES cells from the diseased mouse?

(d) You decide to use Somatic Cell Nuclear Transfer in order to derive ES cells that are genetically identical to the diseased mouse. List the steps of the procedure you would need to do to accomplish this.

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(e) Before you induce the ES cells you derived in part **(d)** to become nerve cells, what must you do to the ES cells to make the stem cell treatment actually beneficial to the diseased mouse? (Hint: re-read the introduction to this question.)

(f) You do your treatment described in parts **(c)** – **(e)** on a female mouse, and the treatment is successful. Your mouse patient has now received the stem cells and has been relieved of its symptoms. For each cell in the treated mouse described below, state how many total alleles of the PARK2 gene are in that cell, and how many are wild-type versus mutant:

-- a nerve cell originally present in the mouse:

-- a nerve cell given to the mouse during the treatment:

-- an egg cell from the mouse:

3. Organismal cloning proves that an adult cell's nucleus contains all of the genetic material necessary to generate every cell type in an organism.

(a) All nucleated cells in the body of an adult human female contain the same DNA except for which three cell types?

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(b) Could you generate a mouse that was born if you created that mouse by doing organismal cloning, and if the adult cell you began with was a mature B cell? If yes, then predict what the phenotype would be of the organism as it develops from a newborn to an adult mouse. If no, explain why not.

(c) Could you generate a mouse that was born if you created that mouse by doing organismal cloning, and if the adult cell you began with was a red blood cell? If yes, then predict what the phenotype would be of the organism as it develops from a newborn to an adult mouse. If no, explain why not.

(d) Red blood cells (RBCs) are generated from precursor RBCs whenever needed. The body is capable of sensing when more RBCs must be generated, and produces a hormone that stimulates RBC production. What is the body sensing that allows it to know when more RBCs are necessary?

(e) What is the hormone that stimulates RBC formation, and what type of macromolecule is this hormone?

(f) In what cell type is this hormone produced?

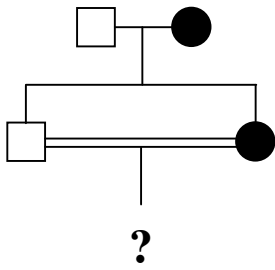
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- (g) In what cell type is the receptor protein for this hormone produced?
- (h) What is the enzymatic activity of this receptor protein and what is its substrate?
- (i) Patients with kidney disease/failure are typically anemic. Why do you think that is?
- (j) What is the most common way of treating the anemia of these patients?

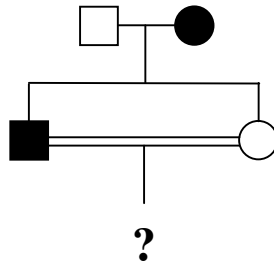
4. Throughout the course of the semester, we have learned about many different patterns of inheritance. In the unit on Mendelian inheritance, we learned about **autosomal** inheritance and **X-linked** inheritance. In the unit on Development, we learned about **maternal effect** inheritance. In the lecture on Molecular Evolution, we will discuss **Y-linked** inheritance and **mitochondrial** inheritance. Below are 5 pedigrees of mouse matings. For each pedigree below, assume that the mode of inheritance listed is the mode of inheritance for the trait. Assume for all pedigrees that the trait indicated by shaded circles and squares is recessive. Your task is to state how many mice in the next generation would be shaded versus not shaded, given each stated mode of inheritance. Assume that the next generation of mice contains 100 mice, 50 female and 50 male.

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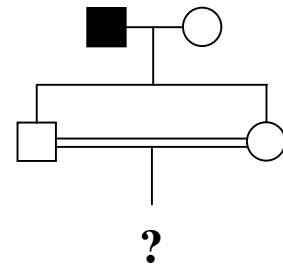
autosomal:



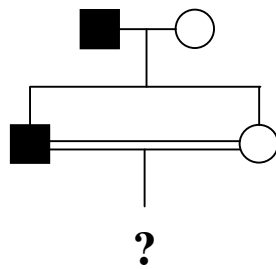
X-linked:



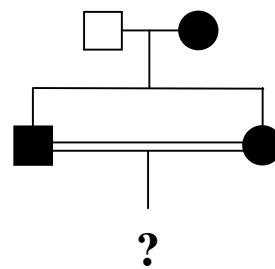
maternal effect:
(the gene is on an autosome)



Y-linked:



mitochondrial:



	Number of shaded females in next generation	Number of unshaded females in next generation	Number of shaded males in next generation	Number of unshaded males in next generation
autosomal				
X-linked				
maternal effect				
Y-linked				
mitochondrial				

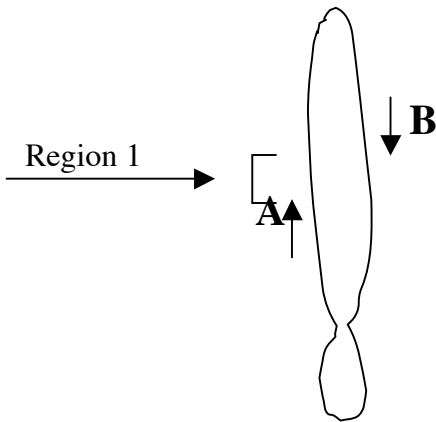
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5. During the last week of class, we will be discussing molecular medicine and the future of biology. To introduce you to just one of the many interesting topics relating to molecular medicine and the future of biology, we ask that you read a report from the US Government Accountability Office. The report is published at the website <http://www.gao.gov/new.items/d06977t.pdf>
Go to this website and print out pages 1-9 of the PDF (which includes 2 coversheets and pages 1-7 of the GAO article). Read this article and respond to it below in 8 sentences or less. By respond to the article, we DO NOT mean summarize the article, but rather we want to hear your reaction to this report. For instance, you could tell us something you found interesting or surprising about this article, or something this article made you think about. Write your response (handwritten) in the space below.

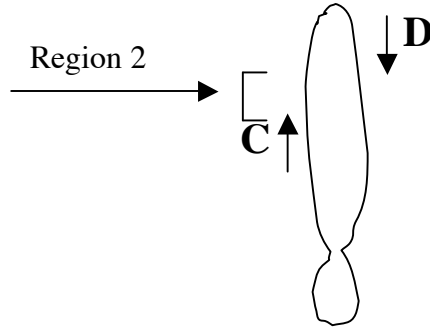
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6. You are a human geneticist studying cancer. You have four cell types that have been derived from four different tumors (Cell Types Q, R, S, and T, which are each from a different patient with a different type of cancer). You have designed a PCR-based assay to detect large chromosomal abnormalities such as deletions, duplications, inversions, and translocations. It turns out that each of the cancerous cell types has a different one of these abnormalities affecting either one or both of the following chromosomal regions (Regions 1 & 2). In each cell type, this chromosomal abnormality contributes to the development of the cancer in these cells. In the diagram below, the small arrows indicate PCR primers you will be using in your assay. Note that Regions 1 and 2 are not the same size (i.e. they are not drawn to scale in the drawing).

Schematic of Chromosome 3



Schematic of Chromosome 7



You do PCR using four different pairs of primers (in four separate reactions) on each of the four cell lines, and wild-type cells. The primers used are listed at the top of each lane in the gel.

A&B A&D B&C C&D A&B A&D B&C C&D A&B A&D B&C C&D A&B A&D B&C C&D



Wild-type Cells
or Cell Type T
(both look the same)
Cell Type Q
Cell Type R
Cell Type S

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(a) State which type of chromosomal abnormality is present in each cell type, and whether you think it is present in a heterozygous or homozygous state. If you cannot conclude, write “*inconclusive*.”

	Type of rearrangement	Heterozygous or homozygous
Cell Type Q		
Cell Type R		
Cell Type S		
Cell Type T		

(b) Do you think that each of the following chromosomal abnormalities is more likely to cause cancer by affecting an oncogene or a tumor suppressor gene?

-- Duplication

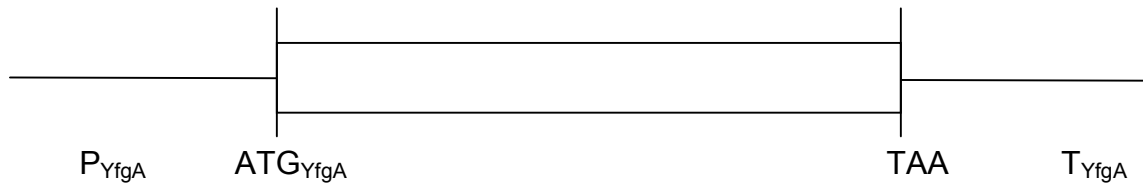
-- Deletion

We have discussed two different types of translocations that can affect oncogenes and cause cancer. One type (such as the translocation that places the myc open reading frame under control of the antibody gene promoter) is called a “transcriptional fusion.” The other type (such as the translocation that fuses the two open reading frames of Bcr and Abl in chronic myelogenous leukemia) is called a “translational fusion.”

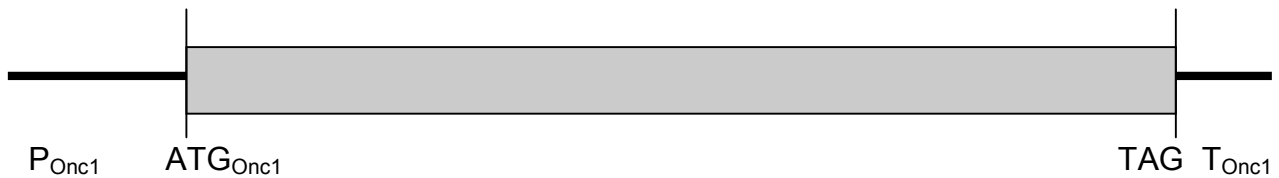
Assume you are studying an oncogene called Onc1. This oncogene can be activated by translocation in two ways. One translocation produces a transcriptional fusion of the gene YfgA to the gene Onc1; YfgA has a very strong promoter. This translocation causes the regulatory region (“P_{YfgA}”) that lies upstream of the YfgA open reading frame to be fused to the Onc1 coding sequence and terminator. The other translocation produces a translational fusion of the gene YfgA to the gene Onc1. This translocation causes almost the entire YfgA gene (beginning with its promoter and ending right before its stop codon) to be fused directly to a portion of the Onc1 gene (from the start codon through the terminator).

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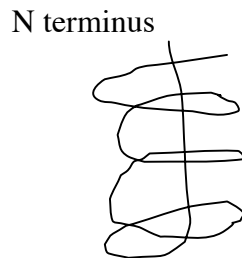
The gene for YfgA looks like this: (T = transcriptional terminator)



The gene for Onc1 looks like this:



The gene for YfgA produces a protein that looks like this:



The gene for Onc1 produces a protein that looks like this:



(c) Based on the diagrams above, draw a schematic of the transcriptional fusion gene that is produced by one type of translocation. Label all parts that are labeled in the original diagrams.

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(d) Based on the diagrams above, draw a schematic of the translational fusion gene that is produced by one type of translocation. Label all parts that are labeled in the original diagrams.

(e) Based on the diagrams above, draw a schematic of the transcriptional fusion protein that is produced by one type of translocation. Label the N and C termini.

(f) Based on the diagrams above, draw a schematic of the translational fusion protein that is produced by one type of translocation. Label the N and C termini.