Welcome to the Fourth Genetics Exam!

BIOL 213 GENETICS: Exam December 14-16, 2000

RULES OF THE GAME: Same rules as always.

One more: Have fun! We're all on a long trip. You might as well look out the window now and then.

The Questions

1. (1 pt) If you have neither received nor given aid regarding this exam, nor have you gained or given knowledge concerning a previous or future administration of this exam, then sign your name. Otherwise sign someone else's name.

2. (2 pts) This question has within it an example o fwhic ho fth efollowin g?

A. A frame shift mutation
B. A point mutation
C. A pointless mutation
D. I dunno. . . Looks OK to me

3. (10 pts + thanks) Did you submit an online questionnaire? Did you put your two filled out evaluations in an envelope at the front of the room?

4. (8 pts) Predisposition for freckles is a dominant trait. I've heard tell that it is the result of a mild defect in DNA repair. Freckles are not determined solely by genetic predisposition; there is also a strong environmental influence. Consider two opposing hypotheses as to how freckles form in people who have the susceptibility trait:

- **Hypothesis A:** Mutations occur at any time, at an abnormally high frequency and randomly in skin cells of susceptible individuals. Occasionally a mutation occurs that enables the gene encoding melanin to turn on. However, the brown color of melanin is only apparent upon prolonged exposure to UV.
- **Hypothesis B:** Mutations occur in skin cells of susceptible individuals upon prolonged exposure to UV, at an abnormally high frequency. When one occurs that turns on the synthesis of melanin, the cell becomes brown.

Both hypotheses presume that skin cells divide. What kind of observations would you make to distinguish between these two hypotheses?

5. (8 pts) The mutagen bisulfite reacts with cytosine to form a derivative (C*) that base pairs like thymine. Starting with the double stranded DNA fragment below, draw all the steps starting with the chemical reaction with bisulfite and ending with a stable mutation.

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ATTAGAT
TAATCTA
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6. (12) You are a world famous forensic geneticist, called on by the Environmental Protection Agency to testify against Squid Pharmaceuticals. The EPA claims that the company has spewed a chemical into the Hudson River that has increased the incidence of colorectal cancer in the local population. Squid claims that their effluent is nothing more than sparkling water (and the floating fish in the river merely represents a natural population dip that occurs every few hundred years or so). How can you pin the goods on them?

You are well aware that colorectal cancer is closely associated with mutations in a certain gene called *APC*. Your strategy is to analyze that gene from many afflicted residents for molecular clues. You are about to do this when Squid lawyers challenge your expert credentials and demand to put you to the test. You are called upon to consider a list of candidate mutagens (Table 1 below) and to identify which may have produced each mutant set of *APC* sequences shown below (Table 2). Each set (**a**, **b**, and **c**) of *APC* sequences was acted on by a single mutagen (or by none at all). For each set, identify the mutagen, if any, and state in about a half dozen words the mechanism you believe to be operating.

Table 1. List of candidate mutagens*

Candidate mutagen	Description of mutagen
A. hydroxyl amine	Industrial chemical that reacts with cytosine to form a derivative that base pairs with adenine
B. benzo(a)pyrene	Component of cigarette smoke that reacts with guanine to make the base unreadable by DNA polymerase
C. 2-amino-1-methyl-6-phenylimidazo-[4,5,b]-pyridine (PHIP)	Made when red meat is pan fried. Reacts with guanine to form a derivative that pairs with cytosine (as usual) but much less strongly than does guanine itself. As a result, the double stranded DNA often unpairs at that point.
D. ultraviolet light	Has the usual effect you know about
E. no mutagen	No particular pattern of mutation

* Exerpt from the legendary missing table

Table 2: Molecular line up of partial *APC* sequences[a]

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wt  AGTGGAGGTGGGATATTACGGAGTGTGTCCAAAATCCGGGAACTTCTTCGTGGAATGGTAAGTGGGATTA

a.#1  AGTGGAGGTGGATATTACGGAGTGTGTCCAAAATCCGGGAACTTCTTCGTGGAATGGTAAGTGGGATTAT
  #2  AGTGGAGGTGGGATATTACGGAGTGTGTCCAAAATCCGGAACTTCTTCGTGGAATGGTAAGTGGGATTAT
  #3  AGTGGAGGTGGGATATTACGGAGTGTGTCCAAAATCCGGGAACTTCTTCGTGGAATGGTAAGTGGATTAT

b.#1  AGTGGAGGTGGGATATTACTGAGTGTGTCCAAAATCCGGGAACTTCTTCGTGGAATGGTAAGTGGGATTA
  #2  AGTGGAGGTGGGATATTACGGAGTGTGTCCAAAATCAGGGAACTTCTTCGTGGAATGGTAAGTGGGATTA
  #3  AGTGGAGGTGGGATATTACGGAGTGTGTCCAAAATCCGGGAACTTCTTAGTGGAATGGTAAGTGGGATTA

c.#1  AGTGAAGGTGGGATATTACGGAGTGTGTCCAAAATCCGGGAACTTCTTCGTGGAATGGTAAGTGGGATTA
  #2  AGTGGAGGTGGGATATTACGGAGTGTCCAAAATCCGGGAACTTCTTCGTGGAATGGTAAGTGGGATTATA
  #3  AGTGGAGGTGGGATATTACGGAGTGTGTCCATAATCCGGGAACTTCTTCGTGGAATGGTAAGTGGGATTA
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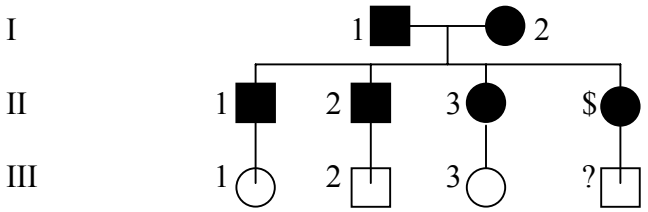
[a] Only one strand is shown. The approximate region of the mutation is underlined.

7. (6 pts) Think about the ways we can look at genetic variation at the DNA level.

a. If we are looking at any RFLP locus, what is the most likely change (e.g., bp substitution, deletion, etc.) and the minimal required unit of change (e.g., 1 bp, 10 bp, etc.) to account for one allele mutating to another allele?

b. Same question, except for a microsatellite locus encompassing a tandem array of a 120-bp repeat.

8. (10 pts) A multimillionaire (II-$) died, leaving no heir. Shortly after her death, a man (III-?) claiming to be her illegitimate son files suit demanding his inheritance. To test his claim, DNA was taken from the putative son and from one living relative of the deceased (see the pedigree below; those related by marriage not shown; living individuals as open symbols & deceased individuals as filled symbols).



The two DNA samples were digested with a particular restriction enzyme, ran on a gel, blotted, and the blot was hybridized to an autosomal RFLP probe. The hybridization patterns did not match in any way, so the judge throws out the claim. I, as the claimant's lawyer, cry foul and appeal the case. At the appeal, I call you as an expert witness. Please answer each of my following questions in 10 words or less. Don't go over that or I will ask the judge to consider you as a hostile witness!

a. Is it possible that my client could be the son of II-$ and yet have a completely different hybridization pattern than a first cousin for an autosomal RFLP probe? A simple yes or no answer will do.

b. Given that mutations are rare, let's ignore them for the moment. Does this change your answer to question a.? Explain yourself.

c. For this analysis with an autosomal RFLP probe, does it matter which first cousin was used for the comparison? If it does, who should or should not have been used?

d. Would a RFLP probe from the Y chromosome be of more use? Explain.

e. Would a RFLP probe from the X chromosome be of more use? Explain.

9. (12 pts) *Arabidopsis thaliana* is a small weedy flowering plant found along roadsides throughout the temperate regions. It can reproduce sexually by either cross-pollination or by self-pollination. You are studying two populations of *Arabidopsis*, one on the UR campus and one adjacent to a coal strip-mining pit in the Appalachian Mountains. Below (Table 3) are the genotype frequencies you find for the B1960 locus and for the G40 locus.

Table 3.: Genotype frequencies at two loci

	B1960 locus			G40 locus		
Population	**BB**	**Bb**	**bb**	**GG**	**Gg**	**gg**
UR Campus	0.6	0.2	0.2	0.12	0.16	0.72
Strip-Mining Pit	0.49	0.42	0.09	0	0	1

a. What is the frequency of the B allele for the UR campus population?

b. What is the frequency of the B allele for the strip-mining pit population?

c. What is the frequency of the g allele for the UR campus population?

d. What is the frequency of the g allele for the strip-mining pit population?

e. Is the UR campus population in H-W equilibrium for the B1960 locus?

f. Is the strip-mining pit population in H-W equilibrium for the B1960 locus?

g. Is the UR campus population in H-W equilibrium for the G40 locus?

h. Is the UR campus population in H-W equilibrium for the G40 locus?

i. In 10 words or less, give a plausible explanation for the genetic makeup of the UR campus population?

j. In 10 words or less, give a plausible explanation for the genetic makeup of the strip-mining pit population?

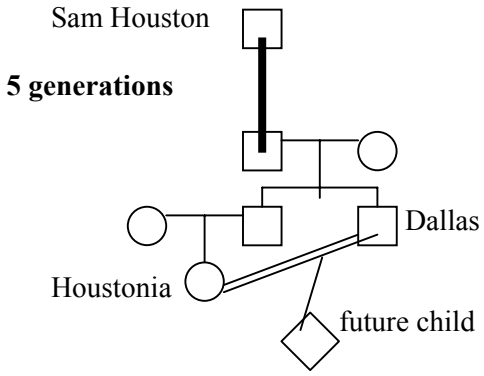
10. (10 pts) Many grasses accumulate silica in their cell walls, where its only role is to offer some protection against herbivory. Assume that silica uptake is a dominant trait controlled by a single gene called SUP. You take a very large sample of seeds from a randomly mating population of big bluestem grass, germinate some of them, and test the seedlings for silica uptake. 91% score positive.

a. What is the frequency of the sup+ allele in the generation represented by the seedlings?

b. You take some of the remaining seeds from the original sample and plant them in an open garden plot. The seeds germinate and the resulting plants are exposed to the normal insects, rabbits, and other potential herbivores. If plants that can take up silica have a fitness advantage (W = 1) compared to those that cannot take up silica (W = 0.5), determine the frequencies of the sup+ allele and of the silica uptake positive phenotype in

the seedlings that germinate from seeds produced by this generation. Assume that selection is the only violation of H-W occurring in this population.

11. (4 pts) Texans are fond of telling the rest of America that Texas is the only state of the U.S. that was once its own country (1836-1845) and that they reserve the right to do it again. The rest of the country finally calls their bluff and kicks Texas out of the union. "That's OK with us" reply the Texans, "since we have our own oil reserves, are major producers of beef, lamb, leather, wool, and mohair, and we can substitute high school football for the NFL!". But what to do about governance? The Texans decide to go for a monarchy and they turn to the family of Sam Houston, hero of the war of independence against Mexico. Now a monarchy calls for a royal bloodline, but the only two remaining direct descendants of Sam Houston are his great-great-great-great-great granddaughter Houstonia and her uncle Dallas (see pedigree below; you may assume that there is no inbreeding in this lineage prior to the mating in question). If Houstonia and Dallas become Queen Houstonia and King Dallas, what will be the risk of their future child having the disease *tennis shoeus*, where the feet will never fit into cowboy boots (a disease with devastating social consequences)? In the general Texas population, the frequency of the recessive allele is 1 in 100.



12. (8 pts) In the future, someone finds the records of an advanced human civilization under the sewer system of New York City that coexisted without the current city inhabitants ever finding them. There are only fragments of paper left, but you find one that appears to be concerned with the distribution of the **ABO** blood type locus for this previously unknown civilization. The only words you can make out are @#?#... 20.25% of our population has blood type **O** ... @%@$#&* ... and the frequency of the $I^B I^B$ genotype is 0.0625 . Based on this fragmentary information and assuming that the population was in H-W equilibrium, determine what you can about the **ABO** blood type distribution in this long-gone civilization.

Allele Frequency	f(I^A)	f(I^B)	f(i)			
Genotype Frequency	f($I^A I^A$)	f($I^A i$)	f($I^B I^B$) 0.0625	f($I^B i$)	f($I^A I^B$)	f($i i$)
Blood Type Frequency	f(**A**)	f(**B**)	f(**O**) 0.2025	f(**AB**)		

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