7.03 Exam 1

Name: _____

Section: _____ **TA:** _____

Exam starts at 11:05 and ends at 11:55

There are five pages including this cover page
Please write your name on each page.

Please...

• Look over the entire exam so you don't spend too much time on hard questions leaving easy questions unanswered.

• Check your answers to make sure that they make sense.

• To help us give partial credit, show your work and state any assumptions that you make.

Question 1	**30 points**
Question 2	**25 points**
Question 3	**20 points**
Question 4	**25 points**

Name: _____

1. You are studying the genetics of a new insect species and have identified three different recessive traits. For simplicity we will designate the phenotypes of the three distinct recessive traits **a**, **b**, and **c** and the corresponding wild-type phenotypes with a "**+**". Two different true-breeding lines are crossed and the F_1 progeny all appear as wild-type. These F_1 progeny are then crossed to individuals from a true breeding line that has all three recessive traits (**a b c**) and 100 progeny from this cross are analyzed. The phenotypes and numbers are as follows:

Phenotype	Number
+ + +	3
a b c	7
a + c	34
+ b +	36
+ b c	8
a + +	12

(a 5 pts.**)** What are the genotypes of the two parental true-breeding lines?

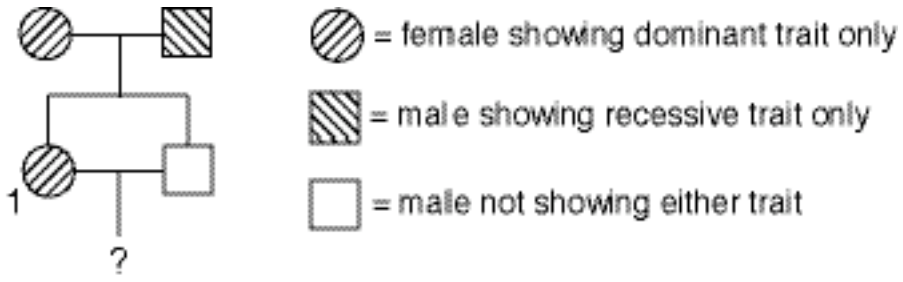
(b 5 pts.**)** Why are there only six phenotypic classes, rather than eight?

(c 10 pts.**)** Give as much information as you can about the chromosomal positions of the three markers **a**, **b**, and **c**. Include in your answer any relevant map distances in cM.

(d 10 pts.**)** Given the map distances in part (c), if F_1 insects are crossed to one another, what frequency of the resulting F_2 progeny would have all three recessive traits (i.e. phenotype: **a b c**)?

Name: _____

2. The following mouse pedigree shows the segregation of both a dominant and a recessive trait. (Assume all phenotypes are completely penetrant and that no new mutations arise).



(**a** 5 pts.**)**What is the genotype of mouse 1? For your answer use D to designate the allele for the dominant trait (with d representing the corresponding wild type allele) and r to designate the allele for the recessive trait (with R representing the corresponding wild type allele)

(**b** 5 pts.**)** If the genes for both traits are 30 cM apart on the X chromosome, what is the probability that a **female** progeny mouse indicated by **?** will show both traits?

(**c** 7 pts.**)** If the genes for both traits are 30 cM apart on the X chromosome, what is the probability that a **male** progeny mouse indicated by **?** will show both traits?

(**d** 8 pts.**)** If the genes for both traits are 30 cM apart on the same autosome, what is the probability that a progeny mouse indicated by **?** will show both traits?

Name: _____

3. You have isolated two different mutants of phage λ that make fuzzy plaques, which you name **fz-1⁻** and **fz-2⁻**. You cross **fz-1⁻** phage with **fz-2⁻** phage by coinfecting *E. coli* with phage of both types. Of 1000 plaques that result from the cross, all but 15 are fuzzy.

(a 8 pts.**)** What is the distance between the **fz-1⁻** and the **fz-2⁻** mutations in map units?

Mutations in the **cI** gene give clear plaques whereas wild-type phage have turbid plaques.

(b 12 pts.**)** You cross of a **cI⁻ fz-1⁻** double mutant to a **fz-2⁻** mutant and examine a total of 1000 plaques. Among the 15 plaques that are not fuzzy produced in this cross, 12 are clear and 3 are turbid. Draw a genetic map showing the order of the **cI⁻**, **fz-1⁻**, and **fz-2⁻** mutations as well as any relevant map distances in map units.

Name: _____

4. **(a** 5 pts.**)** You have isolated a new His^- yeast mutant. When you mate this mutant to a wild type yeast strain (His^+) you find that the resulting diploids are His^+. What does this tell you about the mutant that you isolated?

(b 10 pts.**)** When you sporulate the His^+ diploid from part (**a**) you find that tetrads of three types are produced. From a total of 100 tetrads, the following tetrad types are seen:

Type:	2 His^- : 2 His^+	3 His^- : 1 His^+	4 His^-
Number:	65	30	5

What does this result tell you about the original His^- strain? Give any relevant genetic distances (in cM) that you can calculate.

(c 10 pts.**)** There are a total of 240 His^- spore clones in the tetrads from part (**b**). If you picked two of these His^- clones (of opposite mating type) at random and mated them, what is the probability that the resulting diploid would be His^+? (You may find it helpful to consider the genotypes of the His^- spores in each tetrad type).

7.03 Exam 1

KEY

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Question 1	**30 points**
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Name: _____

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Phenotype	Number
+ + +	3
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a + c	34
+ b +	36
+ b c	8
a + +	12

(a 5 pts.) What are the genotypes of the two parental true-breeding lines?

$$\frac{a\ +\ c}{a\ +\ c} \quad + \quad \frac{+\ b\ +}{+\ b\ +}$$

(b 5 pts.) Why are there only six phenotypic classes, rather than eight?

Because there were no double crossovers

(c 10 pts.) Give as much information as you can about the chromosomal positions of the three markers **a**, **b**, and **c**. Include in your answer any relevant map distances in cM.

b ——10cM—— a ——20cM—— c

(d 10 pts.) Given the map distances in part (c), if F_1 insects are crossed to one another, what frequency of the resulting F_2 progeny would have all three recessive traits (i.e. phenotype: **a b c**)?

$$\frac{+\ a\ c}{b\ +\ +} \times \frac{+\ a\ c}{b\ +\ +}$$

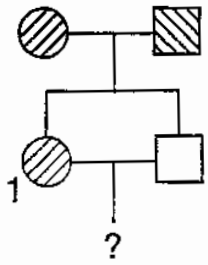
$\left(\frac{10}{100}\text{ x-overs between b+a}\right) - {}^{2}/_{10}(\text{double x-overs}) = {}^{8}/_{100}$ a+b+c or +++ alleles together

${}^{8}/_{100}({}^{1}/_{2}) = {}^{4}/_{100}$ abc gamete from either parent

$({}^{4}/_{100})({}^{4}/_{100}) = {}^{16}/_{10,000} = .16\%$ of F_2 progeny $\frac{abc}{abc}$

Name: _____

2. The following mouse pedigree shows the segregation of both a dominant and a recessive trait. (Assume all phenotypes are completely penetrant and that no new mutations arise).



= female showing dominant trait only

= male showing recessive trait only

= male not showing either trait

(**a** 5 pts.)What is the genotype of mouse 1? For your answer use D to designate the allele for the dominant trait (with d representing the corresponding wild type allele) and r to designate the allele for the recessive trait (with R representing the corresponding wild type allele)

Mouse 1 is $\frac{DR}{dr}$ (or $X^{DR}X^{dr}$). This mouse's father is $\frac{dr}{dr}$ or $X^{dr}y$ so one of mouse 1's chromosomes must be "dr." The other must be DR because of her phenotype -- she shows the dominant trait only.

(**b** 5 pts.) If the genes for both traits are 30 cM apart on the X chromosome, what is the probability that a **female** progeny mouse indicated by **?** will show both traits?

$P(X^{Dr}X^{-r}) = 0$ because this mouse's father must be $X^{dR}y$ and thus will always pass on a "R" allele to his daughters

(**c** 7 pts.) If the genes for both traits are 30 cM apart on the X chromosome, what is the probability that a **male** progeny mouse indicated by **?** will show both traits?

$P(X^{Dr}y)$ male is 15%; he will inherit his X chromosome from his mother, who is $X^{DR}X^{dr}$. Therefore she will pass on an X^{Dr} one half of the time she produces a gamete with a recombinant X chromosome, or $\frac{1}{2} \cdot 30\%$

(**d** 8 pts.) If the genes for both traits are 30 cM apart on the same autosome, what is the probability that a progeny mouse indicated by **?** will show both traits?

$P\left(\frac{Dr}{dr}\right) = 15\% \times 50\% = 7.5\%$; this mouse's father is $\frac{dR}{dr}$ and thus will donate "dr" 50% of the time. This mouse's mother is $\frac{DR}{dr}$ and thus will donate a "Dr" chromosome one half of the time she produces a gamete with a recombinant version of this chromosome, or $\frac{1}{2} \cdot 30\%$.

Name: _____

3. You have isolated two different mutants of phage λ that make fuzzy plaques, which you name **fz-1⁻** and **fz-2⁻**. You cross **fz-1⁻** phage with **fz-2⁻** phage by coinfecting *E. coli* with phage of both types. Of 1000 plaques that result from the cross, all but 15 are fuzzy.

(a 8 pts.) What is the distance between the **fz-1⁻** and the **fz-2⁻** mutations in map units?

$$\frac{15 \times 2}{1000} = 3 \text{ m.u.}$$

Mutations in the **cI** gene give clear plaques whereas wild-type phage have turbid plaques.

(b 12 pts.) You cross of a **cI⁻ fz-1⁻** double mutant to a **fz-2⁻** mutant and examine a total of 1000 plaques. Among the 15 plaques that are not fuzzy produced in this cross, 12 are clear and 3 are turbid. Draw a genetic map showing the order of the **cI⁻**, **fz-1⁻**, and **fz-2⁻** mutations as well as any relevant map distances in map units.

Rarest class (double crossover) → 3 turbid, no fuzzy (+ + +)

Therefore order is cI — fz-2 — fz-1

Distance between cI & fz-2:

$$p(\text{DC cI \& fz-1}) = p(\text{SC cI \& fz-2}) \times p(\text{SC fz-2 \& fz-1})$$

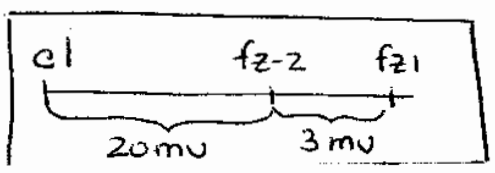
$$\frac{6}{1000} = \frac{x}{1000} \times \frac{30}{1000}$$

$$x = 0.2 \times 100 = \boxed{20 \text{ mU}}$$

or also

$$\frac{3}{15} \times 100 = 20 \text{ mU}$$

Therefore



Name: _____

4. (a 5 pts.) You have isolated a new His^- yeast mutant. When you mate this mutant to a wild type yeast strain (His^+) you find that the resulting diploids are His^+. What does this tell you about the mutant that you isolated?

The mutant is recessive to wildtype

(**b** 10 pts.) When you sporulate the His^+ diploid from part (**a**) you find that tetrads of three types are produced. From a total of 100 tetrads, the following tetrad types are seen:

	P	T	N
Type:	2 His^- : 2 His^+	3 His^- : 1 His^+	4 His^-
Number:	65	30	5

What does this result tell you about the original His^- strain? Give any relevant genetic distances (in cM) that you can calculate.

The original His^- strain was a double mutant (two mutations)

The distance between these two mutations is:

$$100 \times \frac{T + 6NPD}{2\Sigma} = \frac{30 + 6(5)}{2(100)} = \boxed{30\,cM}$$

(**c** 10 pts.) There are a total of 240 His^- spore clones in the tetrads from part (**b**). If you picked two of these His^- clones (of opposite mating type) at random and mated them, what is the probability that the resulting diploid would be His^+? (You may find it helpful to consider the genotypes of the His^- spores in each tetrad type).

To get a His^+ diploid the two (His^-) strains which must mate are a $His1^-His2^+$ and $His1^+His2^-$

$$P(\text{getting a } His1^+His2^- \text{ spore}) = \frac{30(1) + 2(5)}{240} = 1/6$$

$$P(\text{getting a } His1^-His2^+ \text{ spore}) = \frac{30(1) + 2(5)}{240} = 1/6$$

$$P(\text{getting a } His^+ \text{ diploid}) = \left[P(His1^-His2^+)_P(His2^-His1^+)\right] \times 2$$

$$P(His^+ \text{ diploid}) = (1/6)(1/6)(2) = \boxed{1/18}$$

P- 2 $His1^-His2^-$
2 $His1^+His2^+$

T- 1 $His1^+His2^+$
1 $His1^-His2^+$
1 $His1^+His2^-$
1 $His1^-His2^-$

N- 2 $His1^-His2^+$
2 $His1^+His2^-$

7.03 Exam 2

Name: _____

Section: _____ **TA:** _____

Exam starts at 11:05 and ends at 11:55

Please write your name on each page.

Only writing on the front sides of each page will be graded

Question 1	**40 points**
Question 2	**26 points**
Question 3	**34 points**

Name: _____

1. (a 6 pts.**)** The Mot genes of *E. coli* are required for motility. You have isolated a nonmotile mutant that you designate **Mot1⁻**. You grow P1 phage on an otherwise wild type strain that carries a **Tn5** insertion that is linked to one of the Mot genes and then use the resulting phage lysate to infect a **Mot1⁻** strain. From 50 transductants isolated by selecting for Kan^r you find that 35 are motile and 15 are nonmotile. What is the distance between the **Tn5** insertion and the **Mot1⁻** mutation (expressed as a cotransduction frequency)?

(b 6 pts.**)** You grow P1 phage on one of the nonmotile, Kan^r transductants (**Tn5 Mot1⁻**) isolated above and use the resulting phage lysate to infect a second nonmotile strain that carries a mutation designated **Mot2⁻**. A total of 200 Kan^r transductants are isolated and none are motile. Does this result tell you whether the **Mot1⁻** and **Mot2⁻** mutations are linked? Explain why or why not.

(c 8 pts.**)** Next, you grow P1 phage on a strain that carries both the **Tn5** insertion and the **Mot2⁻** mutation. When the resulting phage lysate is used to infect a strain that carries the **Mot1⁻** mutation, you find that 5 out of 200 Kan^r transductants are motile. Based on this result as well as the results from parts (**a**) and (**b**), draw a map showing the relative order of the **Tn5** insertion and the **Mot1⁻** and **Mot2⁻** mutations.

Name: _____

(d 6 pts.**)** You can detect the protein products of the Mot genes. You observe that one of these proteins is 58 kDa in a wild type strain but is 40 kDa in a **Mot1⁻** mutant and 30 kDa in a **Mot2⁻** mutant. Given this information, draw a diagram showing the direction of transcription of the Mot gene relative to the position of the **Tn5** insertion.

(e 6 pts.**)** You introduce an amber suppressing allele of a $tRNA^{ser}$ gene into a **Mot1⁻** mutant strain. The Mot protein in this **Mot1⁻ Su⁺** transductant is now 58 kDa. What kind of mutation is **Mot1⁻**?

(f 8 pts.**)** The sequence of the amber stop codon is $^{5'}UAG^{3'}$. Write out the DNA sequence of the anti-codon portion of an amber suppressing allele of $tRNA^{ser}$ (label the 5' and 3' ends of both strands and indicate which is the template strand during transcription of the tRNA).

Name: _____

2. Raffinose is a sugar that requires the lactose permease (LacY gene product) to enter an *E. coli* cell. However, raffinose does not act as an inducer for the Lac operon. Wild type (Lac^+) *E. coli* can not grow on raffinose as the only carbon source because without an inducer of the Lac operon there is not enough Lac permease synthesized to take up raffinose.

The ProA gene is linked to the Lac operon (cotransduction frequency is about 60%). Beginning with an *E. coli* strain that is $ProA^-$ Lac^+ you isolate a collection of ten different mutants that can grow on raffinose. You show that each of the mutants is linked to the Lac region by cotransduction with ProA.

(a 9 pts.**)** What three possible types of Lac mutations could you have isolated.

(b 5 pts.**)** You mate a strain carrying F' $ProA^+$ Lac^+ to each of your mutant strains by selecting for Pro^+ merodiploids. You find that all of the resulting merodiploids are no longer able to grow on raffinose. What type(s) of mutation from part (**a**) did you isolate?

(c 7 pts.**)** Using an *E. coli* strain with $ProA^-$ Lac^+ on the chromosome carrying F' Pro^+ Lac^+, you isolate a collection of mutants that can grow on raffinose. Which type(s) of mutations from part (**a**) could you isolate using this strategy? Explain why.

Name: _____

(d 5 pts.**)** You mate one of the mutant strains from part (**c**) an F^- $ProA^-$ Lac^+ strain. The resulting merodiploids that you isolate are *not* able to grow on raffinose. Where was the original mutation that allowed growth on raffinose located?

3. You are studying the regulation of ubiquinone synthesis in bacteria. The Ubi1 gene encodes a key enzyme in the pathway for ubiquinone synthesis. In order to study the regulation of the Ubi1 gene transcription you construct a promoter fusion by inserting Tn5::LacZ into the coding sequence for the Ubi1 gene (this hybrid gene is designated P_{ubi1}–LacZ). You find that ß-galactosidase is expressed at a high level when ubiquinone is *absent* from the growth medium, but ß-galactosidase is not expressed when ubiquinone is *present*. You find a mutation designated A^-, which gives constitutive ß-galactosidase expression from the LacZ fusion to the Ubi gene. Moreover, you find that A^- is closely linked to the Ubi1 gene. You have an F' that carries the Ubi1 gene along with neighboring genes and regulatory sites, you carry out the following genetic tests:

	ß-galactosidase activity	
	–ubiquinone	+ubiquinone
$A^+ P_{ubi1}$–LacZ	+	–
$A^- P_{ubi1}$–LacZ	+	+
$A^- P_{ubi1}$–LacZ / F' A^+ $Ubi1^+$	+	–
$A^+ P_{ubi1}$–LacZ / F' A^- $Ubi1^+$	+	–

(a 8 pts.**)** Characterize the A^- mutation (dominant vs. recessive, cis-acting vs. trans-acting) and propose a molecular function for the regulatory component that is affected by the A^- mutation.

Name: _____

Next, you isolate a second regulatory mutation designated B^- which causes constitutive expression of ß-galactosidase from the P_{ubi1}–LacZ promoter fusion. You find that the B^- mutation is *not* linked to the Ubi1 gene. An F' is isolated that carries the region of the chromosome where the B^- mutation lies. Genetic tests reveal the following properties:

	ß-galactosidase activity	
	–ubiquinone	+ubiquinone
$B^+ P_{ubi1}$–LacZ	+	–
$B^- P_{ubi1}$–LacZ	+	+
$B^- P_{ubi1}$–LacZ / F' B^+	+	–

(b 10 pts.**)** Draw *two* different linear regulatory pathways showing the possible relationships between the two different regulatory factors encoded by A and B. For your answer be sure to include the Ubi1 gene and to indicate where and how the inhibitor ubiquinone is acting.

(c 6 pts.**)** Why can't you use the A^- and B^- mutations you have isolated to distinguish the two models?

Name:_____

Next, you isolate an allele of the B gene that you call B^S that gives uninducible expression of P_{ubi1}–LacZ. The genotype and phenotype of strains carrying the B^C mutation are as follows:

Genotype	Phenotype
B^S P_{ubi1}–LacZ / F' B^+	uninducible
B^S A^- P_{ubi1}–LacZ	constitutive

(d 5 pts.**)** Draw out the model from part (**b**) that is consistent with these new results?

(e 5 pts.**)** How might the B^S mutation alter the function of the B protein to give uninducible expression of the Ubi1 gene?

Grading section

Question 1 40 points:_____

Question 2 26 points:_____

Question 3 34 points:_____

Total :_____

OFFICIAL KEY

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1. (**a** 6 pts.) The Mot genes of *E. coli* are required for motility. You have isolated a nonmotile mutant that you designate **Mot1**$^-$. You grow P1 phage on an otherwise wild type strain that carries a **Tn5** insertion that is linked to one of the Mot genes and then use the resulting phage lysate to infect a **Mot1**$^-$ strain. From 50 transductants isolated by selecting for Kan^r you find that 35 are motile and 15 are nonmotile. What is the distance between the Tn5 insertion and the **Mot1**$^-$ mutation (expressed as a cotransduction frequency)?

$$\frac{35}{50} \cdot 100\% = 70\%$$

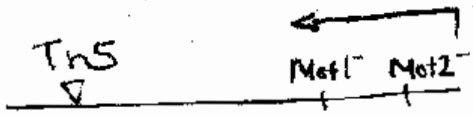
(**b** 6 pts.) You grow P1 phage on one of the nonmotile, Kan^r transductants (**Tn5 Mot1**$^-$) isolated above and use the resulting phage lysate to infect a second nonmotile strain that carries a mutation designated **Mot2**$^-$. A total of 200 Kan^r transductants are isolated and none are motile. Does this result tell you whether the **Mot1**$^-$ and **Mot2**$^-$ mutations are linked? Explain why or why not.

You cannot tell whether Mot1 and Mot2 are linked by this experiment. One possibility is that they are unlinked. In this case, all transductants will be Mot2$^-$ and non motile. Another possibility is that Mot1 and Mot2 are very tightly linked. In this case, recombination between Mot1 and Mot2 is rare enough that you never see the motile phenotype.

(**c** 8 pts.) Next, you grow P1 phage on a strain that carries both the **Tn5** insertion and the **Mot2**$^-$ mutation. When the resulting phage lysate is used to infect a strain that carries the **Mot1**$^-$ mutation, you find that 5 out of 200 Kan^r transductants are motile. Based on this result as well as the results from parts (**a**) and (**b**), draw a map showing the relative order of the **Tn5** insertion and the **Mot1**$^-$ and **Mot2**$^-$ mutations.

Name: _____

(d 6 pts.) You can detect the protein products of the Mot genes. You observe that one of these proteins is 58 kDa in a wild type strain but is 40 kDa in a **Mot1**$^-$ mutant and 30 kDa in a **Mot2**$^-$ mutant. Given this information, draw a diagram showing the direction of transcription of the Mot gene relative to the position of the **Tn5** insertion.



(e 6 pts.) You introduce an amber suppressing allele of a tRNA^{ser} gene into a **Mot1**$^-$ mutant strain. The Mot protein in this **Mot1**$^-$ **Su**$^+$ transductant is now 58 kDa. What kind of mutation is **Mot1**$^-$?

amber nonsense mutation

(f 8 pts.) The sequence of the amber stop codon is ^{5}'UAG^3'. Write out the DNA sequence of the anti-codon portion of an amber suppressing allele of tRNA^{ser} (label the 5' and 3' ends of both strands and indicate which is the template strand during transcription of the tRNA).

5'- CTA - 3'
3'- GAT - 5' ← template

Name: _____

2. Raffinose is a sugar that requires the lactose permease (LacY gene product) to enter an *E. coli* cell. However, raffinose does not act as an inducer for the Lac operon. Wild type (Lac$^+$) *E. coli* can not grow on raffinose as the only carbon source because without an inducer of the Lac operon there is not enough Lac permease synthesized to take up raffinose.

The ProA gene is linked to the Lac operon (cotransduction frequency is about 60%). Beginning with an *E. coli* strain that is ProA$^-$ Lac$^+$ you isolate a collection of ten different mutants that can grow on raffinose. You show that each of the mutants is linked to the Lac region by cotransduction with ProA.

(a 9 pts.) What three possible types of Lac mutations could you have isolated.

O^c

I^-

I^{-d}

(b 5 pts.) You mate a strain carrying F' ProA$^+$ Lac$^+$ to each of your mutant strains by selecting for Pro$^+$ merodiploids. You find that all of the resulting merodiploids are no longer able to grow on raffinose. What type(s) of mutation from part (a) did you isolate?

I^-

(c 7 pts.) Using an *E. coli* strain with ProA$^-$ Lac$^+$ on the chromosome carrying F' Pro$^+$ Lac$^+$, you isolate a collection of mutants that can grow on raffinose. Which type(s) of mutations from part (a) could you isolate using this strategy? Explain why.

$O^c + I^{-d}$

Because these are dominant mutations and dominant mutations can be isolated when you have two copies of the gene. Recessive mutations could not be isolated in this case because the recessive mutation would be masked by the wild-type allele.

Name:

(d 5 pts.) You mate one of the mutant strains from part **(c)** an F^- $ProA^-$ Lac^+ strain. The resulting merodiploids that you isolate are *not* able to grow on raffinose. Where was the original mutation that allowed growth on raffinose located?

on the e.coli chromosome

3. You are studying the regulation of ubiquinone synthesis in bacteria. The Ubi1 gene encodes a key enzyme in the pathway for ubiquinone synthesis. In order to study the regulation of the Ubi1 gene transcription you construct a promoter fusion by inserting Tn5::LacZ into the coding sequence for the Ubi1 gene (this hybrid gene is designated P_{ubi1}–LacZ). You find that ß-galactosidase is expressed at a high level when ubiquinone is *absent* from the growth medium, but ß-galactosidase is not expressed when ubiquinone is *present*. You find a mutation designated A^-, which gives constitutive ß-galactosidase expression from the LacZ fusion to the Ubi gene. Moreover, you find that A^- is closely linked to the Ubi1 gene. You have an F' that carries the Ubi1 gene along with neighboring genes and regulatory sites. you carry out the following genetic tests:

	ß-galactosidase activity	
	–ubiquinone	+ubiquinone
$A^+ P_{ubi1}$–LacZ	+	–
$A^- P_{ubi1}$–LacZ	+	+
$A^- P_{ubi1}$–LacZ / F' A^+ $Ubi1^+$	+	–
$A^+ P_{ubi1}$–LacZ / F' A^- $Ubi1^+$	+	–

(a 8 pts.) Characterize the A^- mutation (dominant vs. recessive, cis-acting vs. trans-acting) and propose a molecular function for the regulatory component that is affected by the A^- mutation.

The A^- mutation is [RECESSIVE] and [TRANS-ACTING]

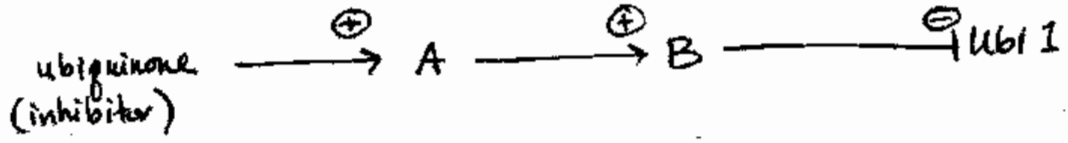
The regulatory component A can be a [REPRESSOR]

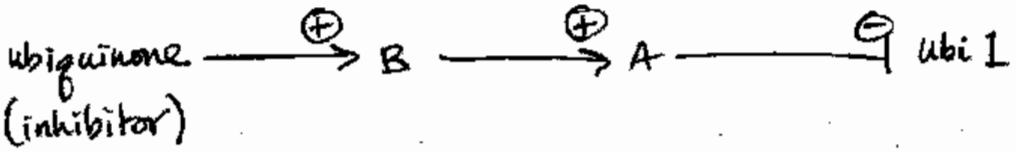
Name: _____

Next, you isolate a second regulatory mutation designated B^- which causes constitutive expression of ß-galactosidase from the P_{ubi1}–LacZ promoter fusion. You find that the B^- mutation is *not* linked to the Ubi1 gene. An F' is isolated that carries the region of the chromosome where the B^- mutation lies. Genetic tests reveal the following properties:

	ß-galactosidase activity	
	–ubiquinone	+ubiquinone
$B^+ P_{ubi1}$–LacZ	+	–
$B^- P_{ubi1}$–LacZ	+	+
$B^- P_{ubi1}$–LacZ / F' B^+	+	–

(b 10 pts.) Draw *two* different linear regulatory pathways showing the possible relationships between the two different regulatory factors encoded by A and B. For your answer be sure to include the Ubi1 gene and to indicate where and how the inhibitor ubiquinone is acting.





(c 6 pts.) Why can't you use the A^- and B^- mutations you have isolated to distinguish the two models?

Because both A^- and B^- are constitutive (i.e. these mutations result in constitutive expression of Ubi 1).

– OR –

Because both A^- and B^- mutants exhibit the same phenotype

Name: _____

Next, you isolate an allele of the B gene that you call B^S that gives uninducible expression of P_{ubi1}–LacZ. The genotype and phenotype of strains carrying the B^C mutation are as follows:

Genotype	Phenotype
B^S P_{ubi1}–LacZ/ F' B^+	uninducible
B^S A^- P_{ubi1}–LacZ	constitutive

(d 5 pts.) Draw out the model from part **(b)** that is consistent with these new results?

ubiquinone $\xrightarrow{\oplus}$ B $\xrightarrow{\oplus}$ A $\xrightarrow{\ominus}$ Ubi 1

A is epistatic to B

(e 5 pts.) How might the B^S mutation alter the function of the B protein to give uninducible expression of the Ubi1 gene?

B^S mutation causes:

① the B protein to always bind to the initiator sequence of the A gene

—OR—

② the B protein to become insensitive to the ubiquinone (that normally activates B).

Grading section

Question 1 40 points:_____

Question 2 26 points:_____

Question 3 34 points:_____

Total :_____

7.03 Exam 3

Name: _____

Section: _____ **TA:** _____

Exam starts at 11:05 and ends at 11:55

There are 6 pages including this cover page.

Please write your name on each page.

Only writing on the front side of each page will be graded.

Question 1	**26 points**
Question 2	**29 points**
Question 3	**21 points**
Question 4	**24 points**

Name: _____

1. To study the regulation of yeast genes for sucrose utilization you construct a fusion of **Suc1**, a gene encoding a sucrose-hydrolyzing enzyme, to the *E. coli* gene for ß-galactosidase. The resulting gene fusion **Suc1-LacZ**, located on an extrachromosomal plasmid, is expressed only when sucrose is provided to the yeast cells. A screen for mutations that affect the regulation of **Suc1-LacZ** has yielded two different mutations that you call **Suc2⁻** and **Suc3⁻**. The table below shows the behavior of the original mutants as well as heterozygous diploids produced by mating the mutants to wild type.

	ß-galactosidase activity	
	– sucrose	+sucrose
Wild type (**Suc1-LacZ**)	–	+
Suc2⁻ (**Suc1-LacZ**)	–	–
Suc2⁻ / Suc2⁺ (**Suc1-LacZ**)	–	+
Suc3⁻ (**Suc1-LacZ**)	+	+
Suc3⁻ / Suc3⁺ (**Suc1-LacZ**)	–	+

(a 4 pts.**)** When you mate a **Suc2⁻** mutant to a **Suc3⁻** mutant, the resulting **Suc2⁻ / Suc3⁻** diploid shows normal expression and regulation of **Suc1-LacZ**. What does this result tell you about the relationship between the **Suc2⁻** and **Suc3⁻** mutations?

(b 6 pts.**)** Next, you sporulate the **Suc2⁻ / Suc3⁻** diploid and dissect 50 tetrads. Among the tetrads, 10 are Type 1, 5 are Type 2, and 35 are Type 3.

Type 1	Type 2	Type 3
constitutive	uninducible	constitutive
uninducible	uninducible	constitutive
uninducible	regulated	uninducible
regulated	regulated	uninducible

Are the **Suc2⁻** and **Suc3⁻** mutations linked? Briefly explain your answer.

Name: _____

(c 6 pts.**)** Is a **Suc2⁻ Suc3⁻** double mutant regulated, constitutive, or uninducible? Briefly explain your answer.

(d 10 pts.**)** On the basis of your answer for part **c** and from the rest of the information given in this problem, diagram a molecular model to explain the regulation of the **Suc1** gene. For your model, include the **Suc2** and **Suc3** genes. Also show how sucrose itself might act.

2. Consider an autosomal recessive trait that is present in 1 per 250,000 newborn individuals in a random-mating population. We will call the recessive allele **b** and the dominant allele **B**.

(a 4 pts.**)** What is the frequency of allele **b**?

(b 8 pts.**)** What proportion of all **b** alleles are present in **bb** homozygotes?

Name: _____

(c 5 pts.**)** Suppose that homozygotes have 90% as many offspring as average individuals in the population. What mutation rate (**B→ b**) would account for the frequency of allele **b** in the population? (Assume h = 0.)

(d 12 pts.**)** Consider the effect of a change in mating patterns such that every person mates with a cousin of one of their parents. Calculate the frequency of the recessive **trait** in the first generation following this change. Show your calculations. (Assume S = 0, h = 0, _ = 0.)

3. You discover a frame-shift mutation in an X-linked gene called SPG in a man who is infertile because of poor sperm production. You postulate that the SPG mutation is the cause of the man's poor sperm production.

(a 6 pts.**)** You obtain genomic DNA samples from other men with poor sperm production and sequence their SPG gene. You find that six such men, apparently unrelated, are mutant in SPG. Are these six men likely to carry the same frame shift mutation found in the first man because of the mutation having been passed through many generations, or are they more likely to carry independent mutations that arose in recent generations? Explain your answer.

Name: _____

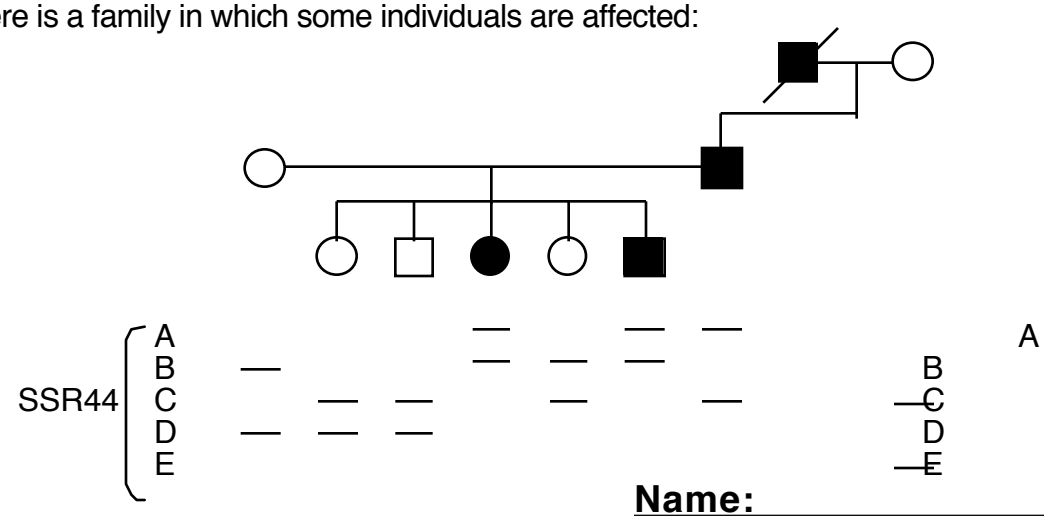
Your classmate discovers an X-linked male-sterile mutant that arose spontaneously in her mouse colony. Having heard about your studies of the human SPG gene, she points out that most genes on the human X chromosome have counterparts on the mouse X chromosome, and that her male-sterile mice might be mutant in the mouse SPG gene. You are unsure whether the human and mouse SPG genes are functionally interchangeable.

(b 9 pts.**)** Propose an experiment involving a mouse transgene (but no knockouts and no sequencing) that would test whether your classmate's mouse mutation is in the mouse SPG gene. Diagram your transgene, describe where it would integrate into the mouse genome, and describe any crosses required.

(c 6 pts.**)** Let's assume that your classmate's mouse mutation is in the mouse SPG gene. Propose an experiment involving a human transgene (but no knockouts) to test the hypothesis that the mouse and human SPG genes are functionally interchangeable.

4. You are genetically mapping a rare skin disease that shows autosomal dominant inheritance.
Alleles: + (normal) SD (associated with skin disease)

Here is a family in which some individuals are affected:



Name: _____

(a 2 pts.**)** Which parent(s) is/are informative with respect to linkage between the skin disease gene and SSR44?

(b 3 pts.**)** What allele at SSR44 did the affected father inherit from his father (deceased)?

(c 5 pts.**)** Diagram the phase relationship between the SD alleles and the SSR44 alleles in the affected father.

(d 10 pts.**)** Calculate the LOD score for linkage at $\theta = 0.1$ between the skin disease gene and SSR44 in this family.

(e 4 pts.**)** How many families of this exact type would be needed to achieve a publishable LOD score at $\theta = 0.1$?

Grading section

Question 1 26 points: _____

Question 2 29 points: _____

Question 3 21 points: _____

Question 4 24 points: _____

Total: _____

7.03 Exam 3

OFFICIAL ANSWER KEY

Name: _____

Section: _____ TA: _____

Exam starts at 11:05 and ends at 11:55

There are 6 pages including this cover page.

Please write your name on each page.

Only writing on the front side of each page will be graded.

Question 1	**26 points**
Question 2	**29 points**
Question 3	**21 points**
Question 4	**24 points**

Name: KEY

1. To study the regulation of yeast genes for sucrose utilization you construct a fusion of **Suc1**, a gene encoding a sucrose-hydrolyzing enzyme, to the *E. coli* gene for ß-galactosidase. The resulting gene fusion **Suc1-LacZ**, located on an extrachromosomal plasmid, is expressed only when sucrose is provided to the yeast cells. A screen for mutations that affect the regulation of **Suc1-LacZ** has yielded two different mutations that you call **Suc2⁻** and **Suc3⁻**. The table below shows the behavior of the original mutants as well as heterozygous diploids produced by mating the mutants to wild type.

	ß-galactosidase activity	
	– sucrose	+sucrose
Wild type (**Suc1-LacZ**)	–	+
Suc2⁻ (**Suc1-LacZ**)	–	–
Suc2⁻ / Suc2⁺ (**Suc1-LacZ**)	–	+
Suc3⁻ (**Suc1-LacZ**)	+	+
Suc3⁻ / Suc3⁺ (**Suc1-LacZ**)	–	+

(**a** 4 pts.) When you mate a **Suc2⁻** mutant to a **Suc3⁻** mutant, the resulting **Suc2⁻ / Suc3⁻** diploid shows normal expression and regulation of **Suc1-LacZ**. What does this result tell you about the relationship between the **Suc2⁻** and **Suc3⁻** mutations?

The Suc2⁻ & Suc3⁻ mutations complement each other, which means that Suc2⁻ & Suc3⁻ are in two different genes.

(**b** 6 pts.) Next, you sporulate the **Suc2⁻ / Suc3⁻** diploid and dissect 50 tetrads. Among the tetrads, 10 are Type 1, 5 are Type 2, and 35 are Type 3.

TT	NPD	PD
Type 1	Type 2	Type 3
constitutive	uninducible	constitutive
uninducible	uninducible	constitutive
uninducible	regulated	uninducible
regulated	regulated	uninducible
10	5	35

Are the **Suc2⁻** and **Suc3⁻** mutations linked? Briefly explain your answer.

For two mutations to be linked PD>> NPD or the 1 PD : 4 TT : 1 NPD ratio must not be true.

PD>> NPD ∴ Suc2⁻ and Suc3⁻ mutations are linked.

type 3 = 35 type 2 = 5

Name: KEY

(c 6 pts.) Is a **Suc2⁻ Suc3⁻** double mutant regulated, constitutive, or uninducible? Briefly explain your answer.

Suc2⁻ Suc3⁻ double mutant is **uninducible**. We can tell that this is the case by either looking at the NPD or TT expected genotypes and comparing them with the observed phenotypes

TT

2⁻ 3⁺ - uninducible
2⁺ 3⁺ - regulated
(2⁻ 3⁻) → must be uninducible
2⁺ 3⁻ - constitutive

NPD

2⁺3⁺ regulated
2⁺3⁺ regulated
(2⁻ 3⁻)
(2⁺ 3⁻)] must be uninducible!

(d 10 pts.) On the basis of your answer for part c and from the rest of the information given in this problem, diagram a molecular model to explain the regulation of the **Suc1** gene. For your model, include the **Suc2** and **Suc3** genes. Also show how sucrose itself might act.

From part c) we can deduce that Suc2⁻ epistatic to Suc3⁻

Suc2 is a net activator of suc1
Suc3 is a net repressor of suc1

Therefore:

Sucrose ⊖| Suc3 ⊖| Suc2 ⊕→ Suc1

2. Consider an autosomal recessive trait that is present in 1 per 250,000 newborn individuals in a random-mating population. We will call the recessive allele **b** and the dominant allele **B**.

(a 4 pts.) What is the frequency of allele b?

$$f(b) = q = \sqrt{\frac{1}{250{,}000}} = \frac{1}{500} = 0.002$$

(b 8 pts.) What proportion of all **b** alleles are present in **bb** homozygotes?

f(b in homozygotes) = q^2
f(b in heterozygotes) = pq

$$\frac{q^2}{q^2+pq} = \frac{q}{p+q} = q = 0.002$$

Alternate solution:

$$\frac{2Nq^2}{2Nq+2Nq^2} = \frac{q}{1+q} \approx 0.002$$

*Here p is approximated to 1.

Name: KEY

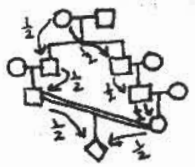
(c 5 pts.) Suppose that homozygotes have 90% as many offspring as average individuals in the population. What mutation rate (**B→ b**) would account for the frequency of **allele b** in the population? (Assume h = 0.)

$S = 1 - 0.9 = 0.1$

$\mu = Sq^2$

$= (0.1)(1/250{,}000) = 4 \times 10^{-7}$

(d 12 pts.) Consider the effect of a change in mating patterns such that every person mates with a cousin of one of their parents. Calculate the <u>frequency of the recessive trait in the first generation following this change</u>. Show your calculations. (Assume S = 0, h = 0, μ = 0.)



$F = 4 \cdot \left(\frac{1}{2}\right)^7 = \frac{1}{32} = 0.03125$

$f(bb) = Fq = \frac{1}{32} \cdot \frac{1}{500} = \frac{1}{16000} = 6.25 \times 10^{-5}$

3. You discover a frame-shift mutation in an X-linked gene called SPG in a man who is infertile because of poor sperm production. You postulate that the SPG mutation is the cause of the man's poor sperm production.

(a 6 pts.) You obtain genomic DNA samples from other men with poor sperm production and sequence their SPG gene. You find that six such men, apparently unrelated, are mutant in SPG. Are these six men likely to carry the same frame shift mutation found in the first man because of the mutation having been passed through many generations, or are they more likely to carry independent mutations that arose in recent generations? Explain your answer.

Given that all seven men carry the same frameshift mutation in the SPG gene, two possibilities exist. All seven of the men could have acquired this mutation spontaneously and independently, <u>OR</u> this SPG frameshift mutation could have been passed on through the generations from a distant common ancestor via carrier females. Of these two possibilities, the latter is more likely.

Name: KEY

Your classmate discovers an X-linked male-sterile mutant that arose spontaneously in her mouse colony. Having heard about your studies of the human SPG gene, she points out that most genes on the human X chromosome have counterparts on the mouse X chromosome, and that her male-sterile mice might be mutant in the mouse SPG gene. You are unsure whether the human and mouse SPG genes are functionally interchangeable.

(b 9 pts.) Propose an experiment involving a mouse transgene (but no knockouts and no sequencing) that would test whether your classmate's mouse mutation is in the mouse SPG gene. Diagram your transgene, describe where it would integrate into the mouse genome, and describe any crosses required. Start with fertilized eggs from an X^+X^{spg} carrier mother. Isolate those eggs and inject them with a wildtype mouse Spg^+ gene. Investigate the fertility of any transgenic sons created in this manner. If all transgenic sons are fertile, then your classmate's mutation is in the Spg gene.

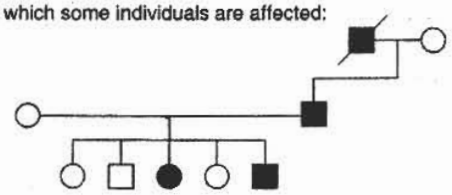
transgene: ~~wt Mm SPG~~, which would integrate randomly into the genome

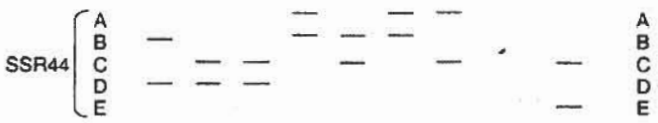
(c 6 pts.) Let's assume that your classmate's mouse mutation is in the mouse SPG gene. Propose an experiment involving a human transgene (but no knockouts) to test the hypothesis that the mouse and human SPG genes are functionally interchangeable. Start with fertilized eggs from an X^+X^{spg} carrier mother. Isolate those eggs and inject them with a wildtype human Spg^+ gene. Investigate the fertility of any transgenic sons created in this manner. If all transgenic sons are fertile, then the human and mouse Spg genes are interchangeable.

4. You are genetically mapping a rare skin disease that shows autosomal dominant inheritance.

Alleles: + (normal) SD (associated with skin disease)

Here is a family in which some individuals are affected:





Name: KEY

(a 2 pts.) Which parent(s) is/are informative with respect to linkage between the skin disease gene and SSR44?

father

(b 3 pts.) What allele at SSR44 did the affected father inherit from his father (deceased)?

A

(c 5 pts.) Diagram the phase relationship between the SD alleles and the SSR44 alleles in the affected father.

—A— SD —
—C— (+) —

(d 10 pts.) Calculate the LOD score for linkage at $\theta = 0.1$ between the skin disease gene and SSR44 in this family.

$$LOD_{\theta=.1} = \log \frac{(.45)^5}{(.25)^5} = 1.28$$

(e 4 pts.) How many families of this exact type would be needed to achieve a publishable LOD score at $\theta = 0.1$?

publishable LOD ≥ 3 so 3 families

Grading section

Question 1 26 points: _____

Question 2 29 points: _____

Question 3 21 points: _____

Question 4 24 points: _____

Total: _____

7.03 Final Exam 2002

Name: _____

Section: _____ **TA:** _____

There are 15 pages including this cover page.

Verify that you have all 15 pages.

Please write your name on each page.

Question 1	**25 points**
Question 2	**25 points**
Question 3	**25 points**
Question 4	**30 points**
Question 5	**15 points**
Question 6	**20 points**
Question 7	**30 points**
Question 8	**30 points**

Name: _____

1. You have isolated a Tn5 insertion in an otherwise wild-type *E. coli* strain that is linked to the gene encoding the MalT activator protein. Tn5 carries a marker for kanamycin resistance (Kan^R). You grow P1 phage on the strain with the Tn5 insertion and use the resulting phage to infect a $MalT^-$ strain. Among 100 resulting Kan^R transductants, 20 express no maltase activity and 80 express maltase normally. Note that the MalT gene is unlinked to the gene encoding the maltase enzyme MalQ.
(a 4 pts.**)** What is the distance between the Tn5 insertion and MalT, as expressed as a cotransduction frequency?

(b 10 pts.**)** You grow P1 phage on a $MalT^-$ Kan^R transductant isolated in part (a), and use the resulting phage to infect a $MalT^C$ mutant in an otherwise wild-type strain. The $MalT^C$ protein binds DNA regardless of whether the inducer maltose is present. The following results are obtained:

Phenotype	number of Kan^R transductants
uninducible	80
constitutive	19
regulated	1

Next you perform the reciprocal cross by growing P1 phage on a $MalT^C$ Kan^R strain carrying the same Tn5 insertion as above. You use the resulting phage to infect a $MalT^-$ mutant in an otherwise wild-type strain. The following results are obtained:

Phenotype	number of Kan^R transductants
uninducible	20
constitutive	80

Draw a diagram of the recombination event(s) that gave rise to the single regulated transductant from the first cross. Your diagram should clearly show the relative order of Tn5, $MalT^-$, and $MalT^C$ (but cotransduction distances are not necessary).

Name: _____

(c 4 pts.**)** You have isolated a Tn10 insertion that is linked (50% cotransduction) to an ochre tRNA suppressor allele (Su^+) in an otherwise wild-type *E. coli* strain. The Tn10 insertion carries a marker for tetracycline resistance (Tet^R) and is not linked to MalT. You grow P1 phage on this Tet^R Su^+ strain and use the resulting phage to infect a $MalT^-$ strain. Out of the 100 Tet^R transductants, 50 express maltase normally and 50 express no maltase activity. What type of mutation is $MalT^-$? (Be as specific as possible.)

(d 7 pts.**)** You grow P1 phage on the Tet^R Su^+ strain from part (c) and use the resulting phage to infect a $MalT^-$ $MalT^C$ double mutant. Out of the 100 Tet^R transductants, 50 express maltase constitutively and 50 express no maltase activity. Is the phenotype of a $MalT^-$ $MalT^C$ double mutant regulated, constitutive, or uninducible?

Name: _____

2. You are studying the regulation of Gln1, a yeast gene involved in glutamine synthesis. Gln1 is not expressed when glutamine is present in the growth medium and is expressed when glutamine is absent. To begin your analysis of regulation, you fuse the promoter region of the Gln1 gene to the LacZ coding sequence and then place this hybrid gene on a yeast plasmid. You find that yeast cells carrying this plasmid (P_{Gln1}–LacZ) only express ß-galactosidase activity when glutamine is absent. You next identify two different mutants that show abnormal regulation of your reporter. You call these mutants $Gln7^-$ and $Gln8^-$. The table below shows the phenotypes of a variety of haploid and diploid yeast strains containing the P_{Gln1}–LacZ reporter. A filled circle indicates a yeast colony that expresses ß-galactosidase activity.

	ß-galactosidase activity	
	– glutamine	+ glutamine
wild type (P_{Gln1}–LacZ)	●	○
$Gln7^-$ (P_{Gln1}–LacZ)	●	●
$Gln7^-$ / $Gln7^+$ (P_{Gln1}–LacZ)	●	○
$Gln8^-$ (P_{Gln1}–LacZ)	○	○
$Gln8^-$ / $Gln8^+$ (P_{Gln1}–LacZ)	●	○

(a 5 pts.**)** When you mate a $Gln7^-$ (P_{Gln1}–LacZ) mutant to a $Gln8^-$ mutant, the resulting $Gln7^-$ / $Gln8^-$ (P_{Gln1}–LacZ) diploid shows normal ß-galactosidase expression and regulation. After sporulatation, this diploid produces three different tetrad types. Out of a total of 50 tetrads, 5 are Type 1, 38 are Type 2, and 7 are Type 3.

Type 1		Type 2		Type 3	
ß-galactosidase activity		ß-galactosidase activity		ß-galactosidase activity	
– glutamine	+ glutamine	– glutamine	+ glutamine	– glutamine	+ glutamine
●	○	●	●	●	○
●	●	●	●	●	●
●	●	○	○	○	○
●	○	○	○	●	●

Is a $Gln7^-$ / $Gln8^-$ double mutant regulated, constitutive, or uninducible?

Name: _____

(b 6 pts.**)** Are the Gln7$^-$ and Gln8$^-$ mutations linked? If so, how far apart are they in cM?

(c 4 pts.**)** In the 50 tetrads you analyze, there are a total of 200 spores. Out of those 200 spores, 17 are Gln7$^-$ Gln8$^-$ double mutant spores. What fraction of those 17 came from NPDs?

(d 10 pts.**)** On the basis of your answer for part (a) and from the rest of the information given in this problem, diagram a model to explain the regulation of the Gln1 gene. Your model should include the Gln7 and Gln8 gene products, as well as glutamine.

Name: _____

3. You have isolated two different mutations in the **mi** gene of phage □ that make tiny plaques. These mutations are called **mi-1**$^{-}$ and **mi-2**$^{-}$. From DNA sequencing, you know that the **mi-1**$^{-}$ mutation is a +1 frameshift, but you do not know the nature of the **mi-2**$^{-}$ mutation. You cross an **mi-1**$^{-}$ phage with an **mi-2**$^{-}$ phage by coinfecting *E. coli* with phage of both types so that each cell receives at least one phage of each type. Of the 1000 plaques that result from the cross, only 8 form large plaques while the rest are tiny.

(a 7 pts.**)** Your lab partner sequences the phage genomes from the phage that formed the 8 large plaques. She observes that 4 of those genomes are wild-type for the **mi** gene, and four contain both the **mi-1**$^{-}$ and **mi-2**$^{-}$ mutations. Give a specific description of the molecular nature of the **mi-2**$^{-}$ mutation that would explain these results.

(b 6 pts.**)** What is the distance between the **mi-1**$^{-}$ and **mi-2**$^{-}$ mutations in map units?

(c 6 pts.**)** The genome of phage □ is 5 X 10^{4} bp in physical length and 200 map units in genetic length. What is the distance between the **mi-1**$^{-}$ and **mi-2**$^{-}$ mutations in base pairs?

Name: _____

(d 6 pts.**)** Next you isolated an **mi-3**$^{-}$ mutation that is a UGA stop mutation in an otherwise wild-type phage background. You find that the wild-type **Mi** protein is 30 kDa, but in the **mi-3**$^{-}$ strain this protein is only 20 kDa in length. When you combine the **mi-1**$^{-}$ and the **mi-3**$^{-}$ mutations, the **Mi** protein produced is 22 kDa. Diagram the **mi** mRNA, labelling the 5' and 3' ends and the relative locations of the **mi-1**$^{-}$ and **mi-3**$^{-}$ mutations.

4. Consider an autosomal recessive disease in humans that is caused by a single loss-of-function allele at a single gene locus. Assume complete penetrance and no selection or new mutations.

(a 6 pts.**)** In population I, the disease has an incidence of 4×10^{-8}. Assuming that mating in the population is random, what is the frequency of the disease allele (**q**)?
What fraction of all matings in population I are between heterozygotes? Show your calculations.

(b 6 pts.**)** A second population (population II) is also characterized by random mating, but here the disease has an incidence of 10^{-6}. Now suppose that human migration produces a new, mixed population, with 90% of the members of the new population deriving (randomly) from population I and the remaining 10% deriving (randomly) from population II. One generation later, what would the incidence of the disease be in the new, mixed population if mating were random? Show your calculations.

Name: _____

(c 6 pts.**)** What would the incidence of the disease be in the new, mixed population (from part **b**) if mating were strictly assortative (that is, if individuals originating from population II mated only with other individuals originating from population I and vice versa for population I)? Show your calculations.

(d 3 pts.**)** Assume that the new, mixed population from part **(b)** has undergone at least one generation of random mating. What is the probability that a child whose parents are first cousins will have the disease?

(e 3 pts.**)** Now assume that the disease allele in population I differs from (but is in the same gene as) that in population II. Would you modify your response to question **(b**)? To question **(c)**? (No calculations needed.)

(f 6 pts.**)** Now assume that the disease allele in population I is in a different gene from that in population II. Would you modify your response to question **(b)**? To question **(c)**? (No calculations needed.)

5. The genetics of the eye disease known as retinitis pigmentosa (RP) are complex in humans, with many dozens of genes implicated. You decide to model this hereditary disease in mice using transgene and/or gene knockout methods.

For both **(a)** & **(b)** indicate:

1. The method you would use (transgene or knockout)
2. The DNA to be introduced into mouse cells
3. The cell type you would use (fertilized egg or ES cells)
4. The site of integration
5. Any additional breeding required

Name:

(a 5 pts**)** You identify a human family in which RP displays autosomal dominant inheritance and is caused by a specific missense mutation in the RP5 gene, on human chromosome 5. Describe how you would create a mouse model of this family's disease. (You have access to a BAC that contains the mutant RP5 gene from an affected member of the family.)

(b 5 pts**)** In another human family, you find that RP displays autosomal recessive inheritance and is caused by a loss-of-function mutation in the RP11 gene, on human chromosome 11. Describe how you would create a mouse model of this family's disease. (You have access to a BAC that contains the wild type RP11 gene from a wild-type mouse.)

(c 5 pts**)** You also obtain a true-breeding strain of mice, called Rpx, which has retinitis pigmentosa. You do not observe retinitis pigmentosa among offspring of Rpx mice mated with wild-type mice. The Rpx mutant has not yet been characterized molecularly, but you suspect that the Rpx strain is mutant in the RP11 gene. Describe how you could use the mouse model created in part **(b)** to test this hypothesis without any sequencing.

6. For each of the following diseases, estimate the concordance rates that you might expect in MZ and DZ twins.

(a 5 pts**)** Chicken pox, a very common and contagious viral disorder.

(b 5 pts**)** Tay-Sachs disease, a rare autosomal recessive disorder in which environmental contributions are negligible.

Name: _____

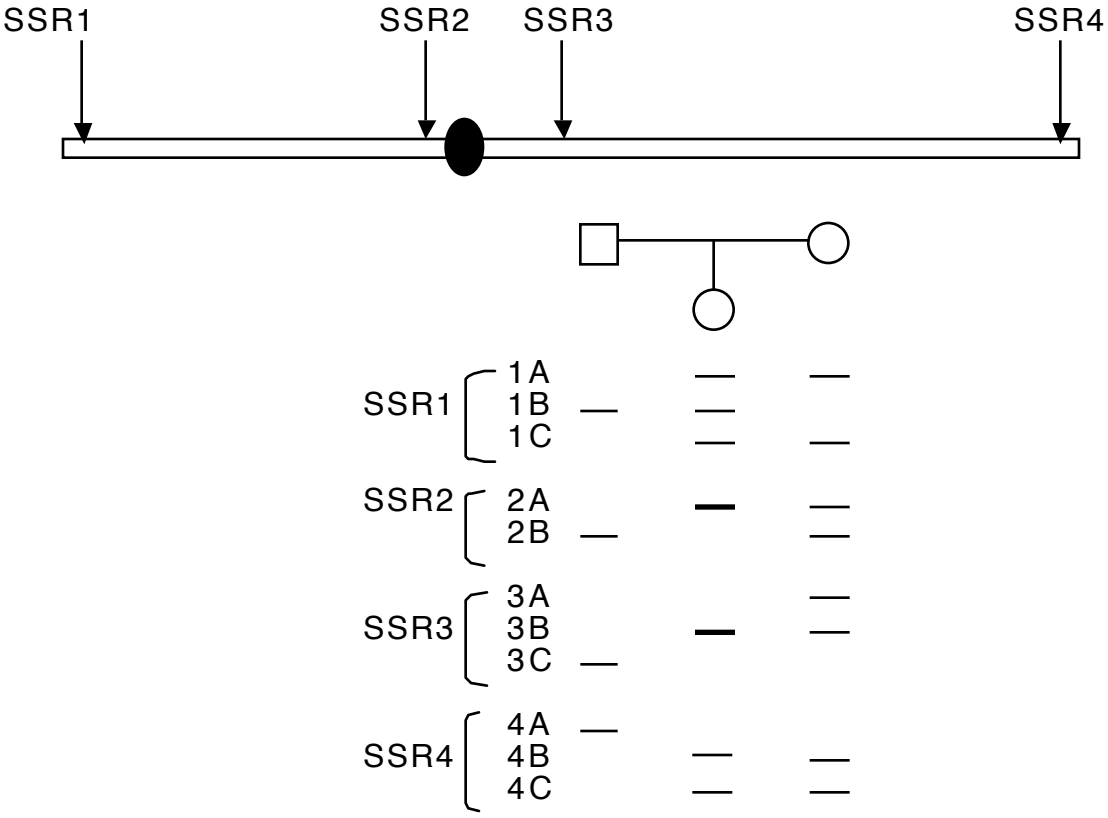
(c 5 pts**)** A rare disease in which both environment and a single gene contribute **equally** to risk. Assume that the allele that predisposes to disease is dominant.

(d 5 pts**)** A rare disease in which both environment and a single gene contribute **equally** to risk. Assume that the allele that predisposes to disease is recessive.

Name: _____

7. While home on winter break, your neighbor, who is a medical geneticist, seeks your help in interpreting a patient: a 47,XXY girl.

You prepare genomic DNA samples from the girl and from her parents. You confirm that the stated father is in fact the biological father by testing the family for a large number of autosomal SSRs. You also test the family for a series of SSRs distributed along the X chromosome:



(a 3 pts**)** In which parent did nondisjunction occur?

(b 4 pts**)** In which division of meiosis did nondisjunction occur? Briefly explain your answer.

Name: _____

(c 9 pts**)** Sketch the meiosis in which nondisjunction occurred (include both divisions in your sketch). Your drawing should include the SSRs present along the X chromosome. Assume that SSR alleles 1A and 2A are on a single chromosome in the mother's somatic cells. Assume that SSR alleles 3A and 4C are on a single chromosome in the mother's somatic cells.

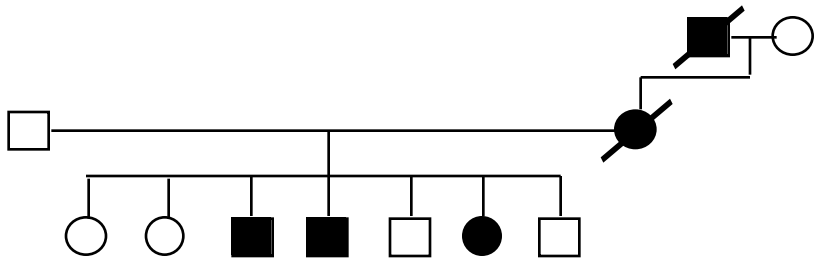
(d 4 pts**)** How many chromatids were present in the first polar body? In the second polar body?

(e 5 pts.**)** What might account for this girl having developed as a female despite the presence of a Y chromosome?

(f 5 pts.**)** Explain how you would test your hypothesis from part **(e)** without the use of sequencing.

Name: _____

8. Your neighbor also seeks your advice regarding a family in which several individuals (filled circles or squares below) developed colon cancer in their 30's or 40's. All living, unaffected individuals are in their 50's or older.



You speculate that colon cancer in this family might be caused by either:

1) germline transmission of a mutation in the APC gene (the autosomal dominant disease known as FAP, familial adenomatous polyposis)

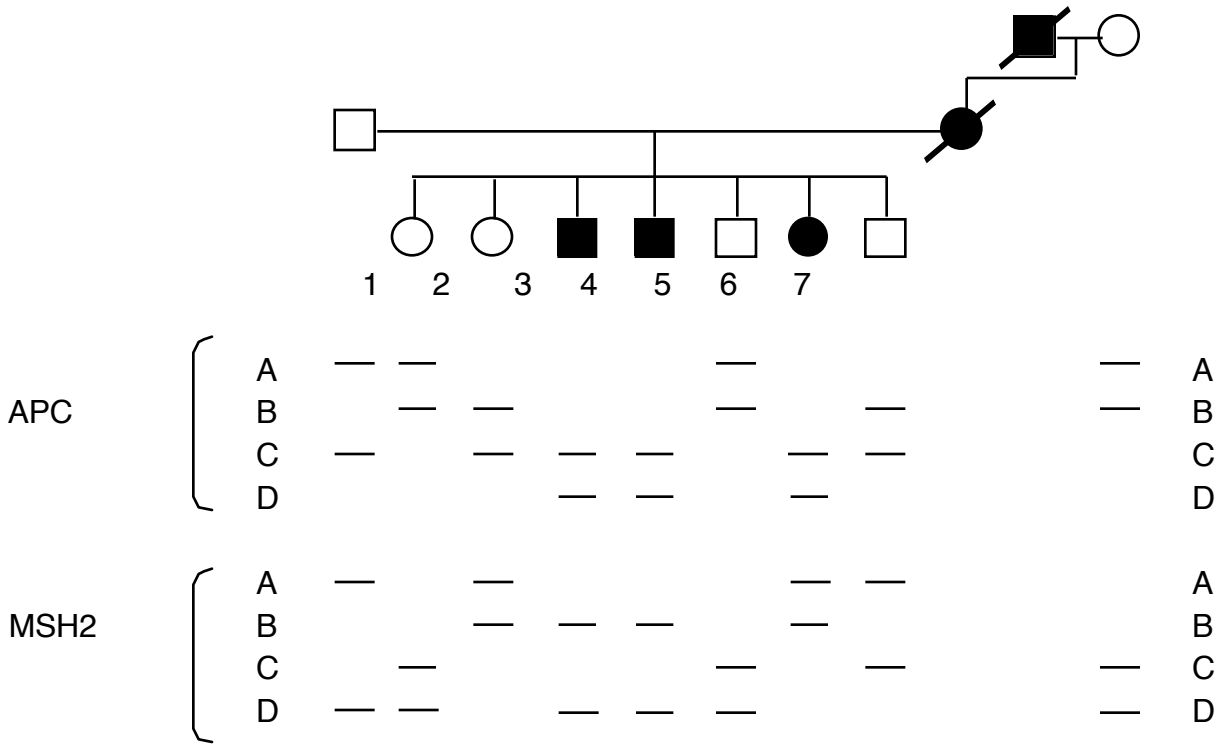
or

2) germline transmission of a mutation in a gene involved in DNA mismatch repair (the autosomal dominant disease known as HNPCC, hereditary nonpolyposis colon cancer)

(a 4 pts.**)** You obtain blood DNA samples from all living family members, as well as colon tumor DNA samples from the three living, affected individuals. Your neighbor is surprised when you test both the blood and colon tumor DNAs for several SSRs known to show no genetic linkage to either HNPCC or FAP. How would you use these test results in considering the likelihood of FAP versus HNPCC?

Name: _____

You identify an SSR that is located within an intron of the APC gene, and a second SSR that is located within an intron of the MSH2 gene (which is involved in mismatch repair). You type blood DNA samples for these SSRs and obtain the following results:



You find out that individuals 3 and 4 are twins, but it has not been determined whether they are monozygotic (MZ) or dizygotic (DZ).

(b 6 pts.**)** Calculate a LOD score for linkage at $\theta = 0$ between colon cancer and APC in this family, assuming that individuals 3 and 4 are DZ twins. Show your calculations.

(c 8 pts.**)** Does your calculation in part **(b)** change if you assume that individuals 3 and 4 are MZ twins? If so, show how it changes.

Name: _____

(d 4 pts.**)** Are these data consistent with the hypothesis that colon cancer in this family is caused by germline transmission of a mutation in APC? Briefly justify your answer.

(e 4 pts.**)** Are these data consistent with the specific hypothesis that colon cancer in this family is caused by germline transmission of a mutation in MSH2? Briefly justify your answer.

(f 4 pts.**)** Would your answer to part **(e)** change if you learned that individual 2 had been diagnosed with cancer of the ovary at the age of 35? Briefly explain your answer.

Grading section

Question 1	25 points:	_____
Question 2	25 points:	_____
Question 3	25 points:	_____
Question 4	30 points:	_____
Question 5	15 points:	_____
Question 6	20 points:	_____
Question 7	30 points:	_____
Question 8	30 points:	_____
	Total:	_____

Name: _____

2. You are studying the regulation of Gln1, a yeast gene involved in glutamine synthesis. Gln1 is not expressed when glutamine is present in the growth medium and is expressed when glutamine is absent. To begin your analysis of regulation, you fuse the promoter region of the Gln1 gene to the LacZ coding sequence and then place this hybrid gene on a yeast plasmid. You find that yeast cells carrying this plasmid (P_{Gln1}–LacZ) only express ß-galactosidase activity when glutamine is absent. You next identify two different mutants that show abnormal regulation of your reporter. You call these mutants Gln7$^-$ and Gln8$^-$. The table below shows the phenotypes of a variety of haploid and diploid yeast strains containing the P_{Gln1}–LacZ reporter. A filled circle indicates a yeast colony that expresses ß-galactosidase activity.

	ß-galactosidase activity	
	– glutamine	+ glutamine
wild type (P_{Gln1}–LacZ)	●	○
Gln7$^-$ (P_{Gln1}–LacZ)	●	● → constitutive, recessive repressor
Gln7$^-$ / Gln7$^+$ (P_{Gln1}–LacZ)	●	○
Gln8$^-$ (P_{Gln1}–LacZ)	○	○ → uninducible, recessive activator
Gln8$^-$ / Gln8$^+$ (P_{Gln1}–LacZ)	●	○

(**a** 5 pts.) When you mate a Gln7$^-$ (P_{Gln1}–LacZ) mutant to a Gln8$^-$ mutant, the resulting Gln7$^-$ / Gln8$^-$ (P_{Gln1}–LacZ) diploid shows normal ß-galactosidase expression and regulation. After sporulatation, this diploid produces three different tetrad types. Out of a total of 50 tetrads, 5 are Type 1, 38 are Type 2, and 7 are Type 3.

NPD = 5

Type 1

ß-galactosidase activity		
– glutamine	+ glutamine	
●	○	reg
●	●	const
●	●	const
●	○	reg

double mutant

PD = 38

Type 2

ß-galactosidase activity		
– glutamine	+ glutamine	
●	●	const
●	●	const
○	○	unind
○	○	unind

TT = 7

Type 3

ß-galactosidase activity		
– glutamine	+ glutamine	
●	○	reg
●	●	const
○	○	unind
●	●	const

double mutant

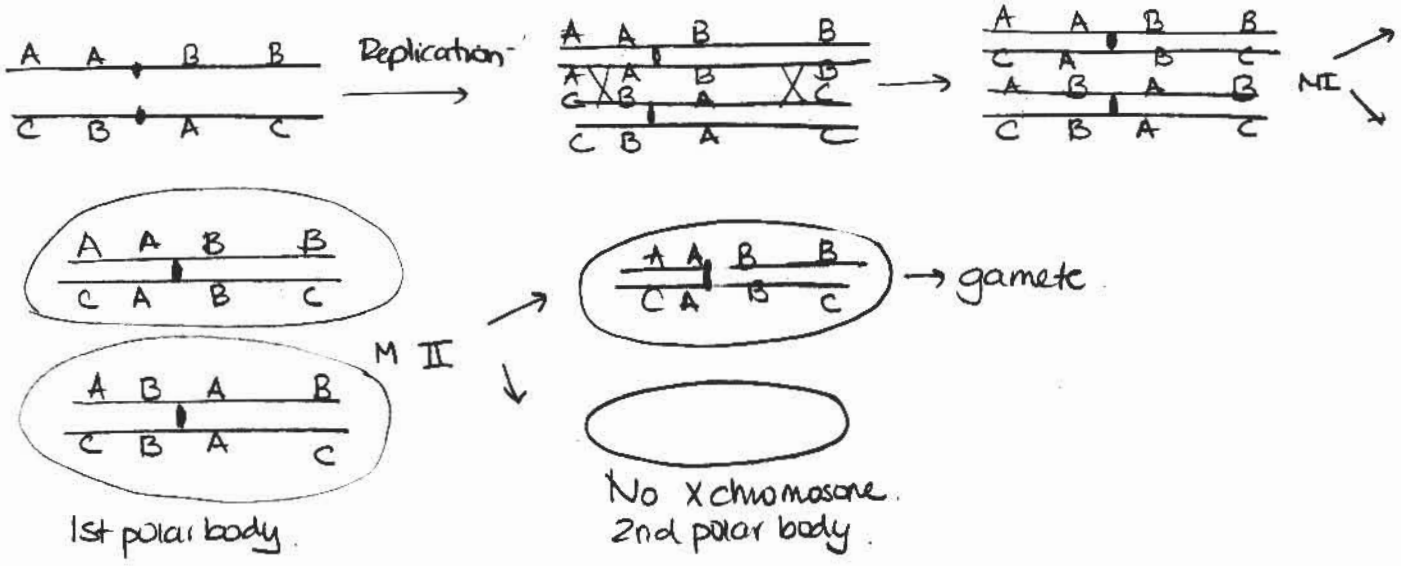
Is a Gln7$^-$ / Gln8$^-$ double mutant regulated, constitutive, or uninducible?

Double mutant is constitutive

Gln7 is epistatic to Gln8

Name: _____

(c 9 pts) Sketch the meiosis in which nondisjunction occurred (include both divisions in your sketch). Your drawing should include the SSRs present along the X chromosome. Assume that SSR alleles 1A and 2A are on a single chromosome in the mother's somatic cells. Assume that SSR alleles 3A and 4C are on a single chromosome in the mother's somatic cells.



(d 4 pts) How many chromatids were present in the first polar body? In the second polar body?

46 22
1st 2nd

(e 5 pts.) What might account for this girl having developed as a female despite the presence of a Y chromosome?

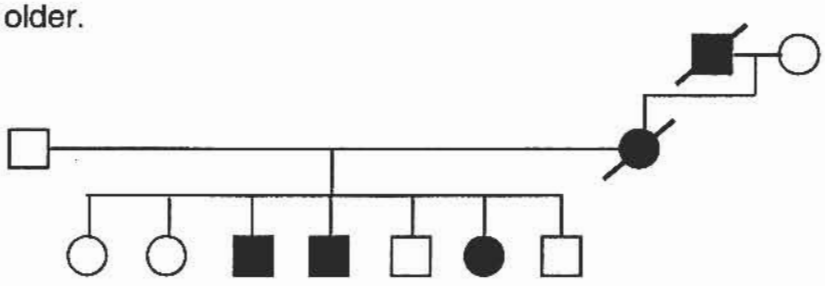
Recombination event bet/ x & y chromosomes in the dad where the SRY allele was recombined out of the Y.

(f 5 pts.) Explain how you would test your hypothesis from part **(e)** without the use of sequencing.

1. STS testing → see if there are certain STS along the Y missing in this XXY girl.
2. Use primers for the SRY gene and PCR the SRY gene from DNA sample from this XXY girl. IF there is no PCR product → SRY is absent. and the recombination event in part e could explain why XXY is a girl

Name: _____

8. Your neighbor also seeks your advice regarding a family in which several individuals (filled circles or squares below) developed colon cancer in their 30's or 40's. All living, unaffected individuals are in their 50's or older.



You speculate that colon cancer in this family might be caused by either:

1) germline transmission of a mutation in the APC gene (the autosomal dominant disease known as FAP, familial adenomatous polyposis)

or

2) germline transmission of a mutation in a gene involved in DNA mismatch repair (the autosomal dominant disease known as HNPCC, hereditary nonpolyposis colon cancer)

(a 4 pts.) You obtain blood DNA samples from all living family members, as well as colon tumor DNA samples from the three living, affected individuals. Your neighbor is surprised when you test both the blood and colon tumor DNAs for several SSRs known to show no genetic linkage to either HNPCC or FAP. How would you use these test results in considering the likelihood of FAP versus HNPCC?

Look for SSR instability in tumor DNAs ↗ YES → HNPCC ↘ NO → ~~FAP~~.

Name: _____

(c 5 pts) A rare disease in which both environment and a single gene contribute **equally** to risk. Assume that the allele that predisposes to disease is dominant.

MZ DZ
50% 25%

MZ/DZ
~2 → 1 gene, dominant
~4 → 1 gene, recessive
≥4 → more than one gene

(d 5 pts) A rare disease in which both environment and a single gene contribute **equally** to risk. Assume that the allele that predisposes to disease is recessive.

MZ DZ
50% 12.5%.

Name:

(c 6 pts.) What would the incidence of the disease be in the new, mixed population (from part **b**) if mating were strictly assortative (that is, if individuals originating from population II mated only with other individuals originating from population I)? Show your calculations.

$$q^2_{NEW} = \underset{(\text{from pop I})}{q^2} + \underset{(\text{from pop II})}{q^2}$$

$$(4\times10^{-8})(0.9) + (1\times10^{-6}) \times (0.1) = 3.6\times10^{-8} + 1\times10^{-7} = \boxed{1.36\times10^{-7}}$$

(d 3 pts.) Assume that the new, mixed population from part **(b)** has undergone at least one generation of random mating. What is the probability that a child whose parents are first cousins will have the disease?

$$F = 1/16$$

$$f(a|a) = Fq = 1/16 \times 2.8\times10^{-4} = \boxed{1.75\times10^{-5}}$$

(e 3 pts.) Now assume that the disease allele in population I differs from (but is in the same gene as) that in population II. Would you modify your response to question **(b)**? To question **(c)**? (No calculations needed.)

No No.

(f 6 pts.) Now assume that the disease allele in population I is in a different gene from that in population II. Would you modify your response to question **(b)**? To question **(c)**? (No calculations needed.)

Yes No

5. The genetics of the eye disease known as retinitis pigmentosa (RP) are complex in humans, with many dozens of genes implicated. You decide to model this hereditary disease in mice using transgene and/or gene knockout methods.

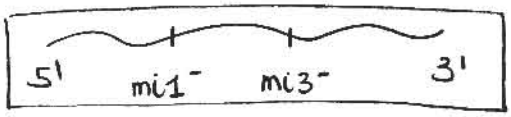
For both **(a)** & **(b)** indicate:

1. The method you would use (transgene or knockout)
2. The DNA to be introduced into mouse cells
3. The cell type you would use (fertilized egg or ES cells)
4. The site of integration
5. Any additional breeding required

Name:

(d 6 pts.) Next you isolated an **mi-3**$^-$ mutation that is a UGA stop mutation in an otherwise wild-type phage background. You find that the wild-type **Mi** protein is 30 kDa, but in the **mi-3**$^-$ strain this protein is only 20 kDa in length. When you combine the **mi-1**$^-$ and the **mi-3**$^-$ mutations, the **Mi** protein produced is 22 kDa. Diagram the **mi** mRNA, labelling the 5' and 3' ends and the relative locations of the **mi-1**$^-$ and **mi-3**$^-$ mutations.

$mi^+ \rightarrow$ 30 kDa
$mi3^- \rightarrow$ 20 kDa
$mi1, mi3^- \rightarrow$ 22 kDa ∴ mi1 must come earlier than mi3 so that it can shift the mi3 stop codon out of frame.



4. Consider an autosomal recessive disease in humans that is caused by a single loss-of-function allele at a single gene locus. Assume complete penetrance and no selection or new mutations.

(a 6 pts.) In population I, the disease has an incidence of 4×10^{-8}. Assuming that mating in the population is random, what is the frequency of the disease allele (**q**)?
What fraction of all matings in population I are between heterozygotes? Show your calculations.

$q = \sqrt{4 \times 10^{-8}} =$ **0.0002**

$f(Aa) = 2pq = 2(1)(0.0002) =$ **0.00039**

$f(Aa) \times f(Aa) = (0.00039)^2 =$ **1.6×10^{-7}**

(b 6 pts.) A second population (population II) is also characterized by random mating, but here the disease has an incidence of 10^{-6}. Now suppose that human migration produces a new, mixed population, with 90% of the members of the new population deriving (randomly) from population I and the remaining 10% deriving (randomly) from population II. One generation later, what would the incidence of the disease be in the new, mixed population if mating were random? Show your calculations.

$q_{\text{polII}} = \sqrt{10^{-6}} = 0.001$

$q_{NEW} = (0.0002)(0.9) + (0.001)(0.1) = 2.8 \times 10^{-4}$

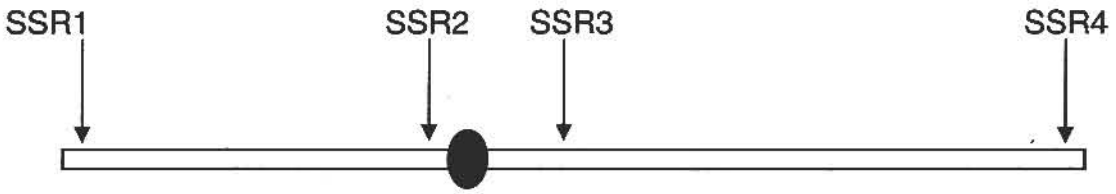
($q_{\text{pol I}}$ = 0.0002, $q_{\text{pol II}}$ = 0.001)

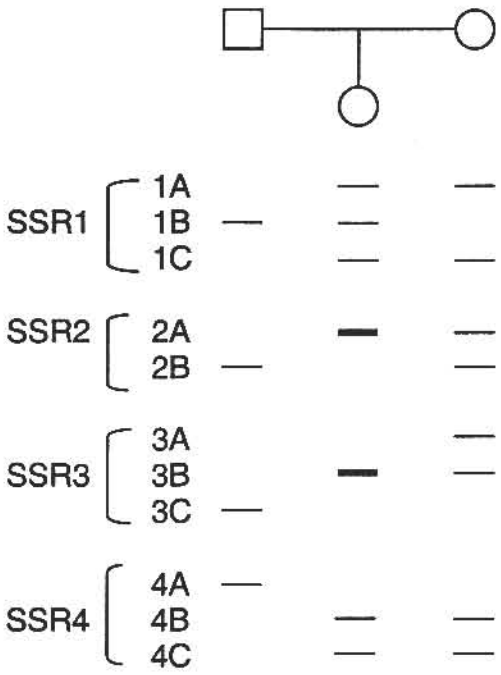
$q^2 = 7.8 \times 10^{-8}$

Name: _____

7. While home on winter break, your neighbor, who is a medical geneticist, seeks your help in interpreting a patient: a 47,XXY girl.

You prepare genomic DNA samples from the girl and from her parents. You confirm that the stated father is in fact the biological father by testing the family for a large number of autosomal SSRs. You also test the family for a series of SSRs distributed along the X chromosome:





(a 3 pts) In which parent did nondisjunction occur?

Mother

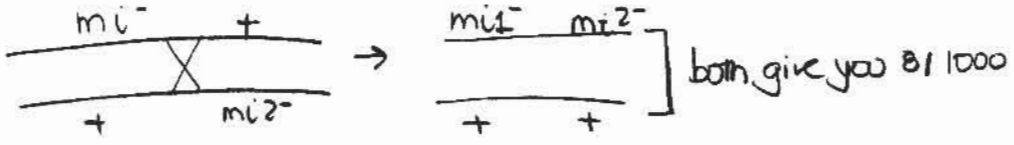
(b 4 pts) In which division of meiosis did nondisjunction occur? Briefly explain your answer.

Meiosis II → Alleles near centromere are duplicated.

Name:

3. You have isolated two different mutations in the **mi** gene of phage λ that make tiny plaques. These mutations are called **mi-1**$^-$ and **mi-2**$^-$. From DNA sequencing, you know that the **mi-1**$^-$ mutation is a +1 frameshift, but you do not know the nature of the **mi-2**$^-$ mutation. You cross an **mi-1**$^-$ phage with an **mi-2**$^-$ phage by coinfecting *E. coli* with phage of both types so that each cell receives at least one phage of each type. Of the 1000 plaques that result from the cross, only 8 form large plaques while the rest are tiny.

(a 7 pts.) Your lab partner sequences the phage genomes from the phage that formed the 8 large plaques. She observes that 4 of those genomes are wild-type for the **mi** gene, and four contain both the **mi-1**$^-$ and **mi-2**$^-$ mutations. Give a specific description of the molecular nature of the **mi-2**$^-$ mutation that would explain these results.



Mi-2⁻ is a -1 frameshift because when both combine it gives you a wild type phage

(b 6 pts.) What is the distance between the **mi-1**$^-$ and **mi-2**$^-$ mutations in map units?

Distance = 8/1000 x 100 = 0.8 m.u

(c 6 pts.) The genome of phage λ is 5 X 10^4 bp in physical length and 200 map units in genetic length. What is the distance between the **mi-1**$^-$ and **mi-2**$^-$ mutations in base pairs?

$$0.8 \text{ m.u} \times \frac{5 \times 10^4 \text{ bp}}{200 \text{ m.u}} = 200 \text{ bp}$$

Name:

(a 5 pts) You identify a human family in which RP displays autosomal dominant inheritance and is caused by a specific missense mutation in the RP5 gene, on human chromosome 5. Describe how you would create a mouse model of this family's disease. (You have access to a BAC that contains the mutant RP5 gene from an affected member of the family.)

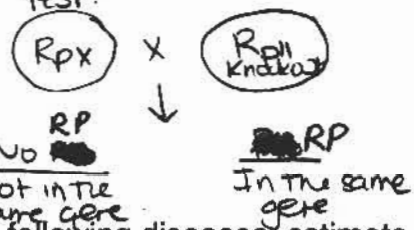
1. Transgene
2. BAC containing RP5 (or RP5 mutant allele by itself).
3. Fertilized egg
4. Randomly
5. No additional breeding req.

(b 5 pts) In another human family, you find that RP displays autosomal recessive inheritance and is caused by a loss-of-function mutation in the RP11 gene, on human chromosome 11. Describe how you would create a mouse model of this family's disease. (You have access to a BAC that contains the wild type RP11 gene from a wild-type mouse.)

1. Knakoot
2. use BAC to create homologous regions and then get a reo marker fused to those regions.
3. ES cells.
4. Specifically (homologous recombination)
5. Additional breeding to obtain a homozygous knockout (recessive needs it)
   chimera x wt → het x het → homo (1/4)

(c 5 pts) You also obtain a true-breeding strain of mice, called Rpx, which has retinitis pigmentosa. You do not observe retinitis pigmentosa among offspring of Rpx mice mated with wild-type mice. The Rpx mutant has not yet been characterized molecularly, but you suspect that the Rpx strain is mutant in the RP11 gene. Describe how you could use the mouse model created in part **(b)** to test this hypothesis without any sequencing.

Complementation Test:



6. For each of the following diseases, estimate the concordance rates that you might expect in MZ and DZ twins.

(a 5 pts) Chicken pox, a very common and contagious viral disorder.

MZ = DZ (should be relatively high)
↑
because it's all environmental

(b 5 pts) Tay-Sachs disease, a rare autosomal recessive disorder in which environmental contributions are negligible.

MZ	DZ
100%	25%

DZ twins are 1/2 related and bc/ this is an autosomal recessive trait → it will need two copies

Name: _____

(d 4 pts.) Are these data consistent with the hypothesis that colon cancer in this family is caused by germline transmission of a mutation in APC? Briefly justify your answer.

No because the SSR chose came from within an intron of APC and we see no recombinants → just not enough to publish

(e 4 pts.) Are these data consistent with the specific hypothesis that colon cancer in this family is caused by germline transmission of a mutation in MSH2? Briefly justify your answer.

No, there is one recombinant (girl 2)

(f 4 pts.) Would your answer to part **(e)** change if you learned that individual 2 had been diagnosed with cancer of the ovary at the age of 35? Briefly explain your answer.

Yes because this would mean that girl 2 exhibits a mutator phenotype and that she may eventually also be affected w/ colon cancer (No longer recombinant)

Grading section

Question 1	25 points:	_____
Question 2	25 points:	_____
Question 3	25 points:	_____
Question 4	30 points:	_____
Question 5	15 points:	_____
Question 6	20 points:	_____
Question 7	30 points:	_____
Question 8	30 points:	_____
	Total:	_____

Name: _____

(b 6 pts.) Are the Gln7$^-$ and Gln8$^-$ mutations linked? If so, how far apart are they in cM?

Yes because PD>> NPD or 1:4:1 not true
PD TT NPD

Distance is $\frac{6NPD+TT}{2\,total} = \frac{6\times 5+7}{2\times 50} = 37/100 =$ 37 cM

(c 4 pts.) In the 50 tetrads you analyze, there are a total of 200 spores. Out of those 200 spores, 17 are Gln7$^-$ Gln8$^-$ double mutant spores. What fraction of those 17 came from NPDs?

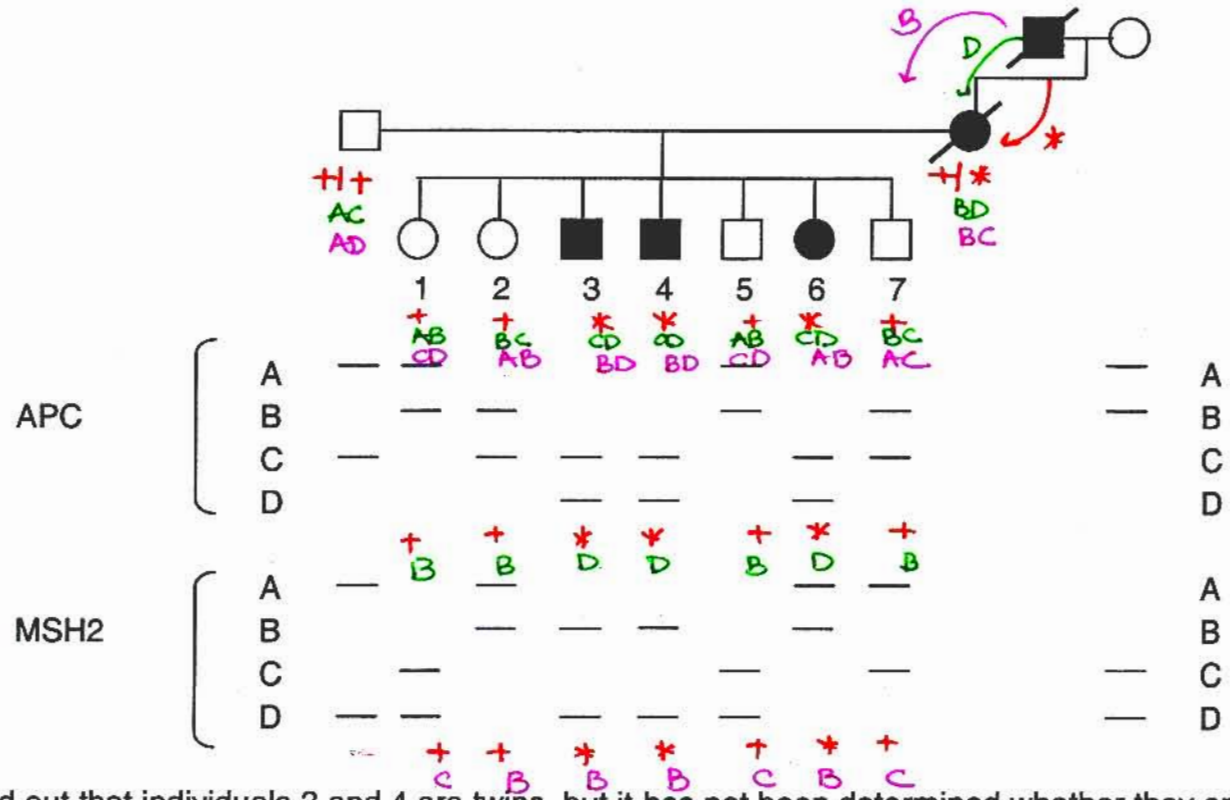
10/17 (2 dabe mutant spors per each NPD → there are 5).

(d 10 pts.) On the basis of your answer for part (a) and from the rest of the information given in this problem, diagram a model to explain the regulation of the Gln1 gene. Your model should include the Gln7 and Gln8 gene products, as well as glutamine.

glutamine ⊣ Gln8 ⊣ Gln7 ⊣ Gln 1

Name: _____

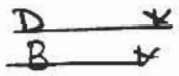
You identify an SSR that is located within an intron of the APC gene, and a second SSR that is located within an intron of the MSH2 gene (which is involved in mismatch repair). You type blood DNA samples for these SSRs and obtain the following results:



You find out that individuals 3 and 4 are twins, but it has not been determined whether they are monozygotic (MZ) or dizygotic (DZ).

(b 6 pts.) Calculate a LOD score for linkage at $\theta = 0$ between colon cancer and APC in this family, assuming that individuals 3 and 4 are DZ twins. Show your calculations.

Mom- informative, Phase known



$$LOD_{\theta=\emptyset} = \log\left[\frac{(0.5)^7}{(0.25)^3}\right] = \boxed{2.1}$$

(c 8 pts.) Does your calculation in part **(b)** change if you assume that individuals 3 and 4 are MZ twins? If so, show how it changes.

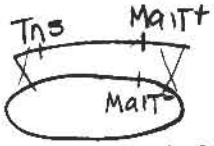
Yes → (only one meiotic event)

$$LOD_{\theta=\emptyset} = \log\left[\frac{(0.5)^6}{(0.25)^6}\right] = \boxed{1.8}$$

Name: _____

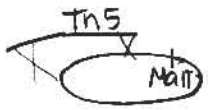
1. You have isolated a Tn5 insertion in an otherwise wild-type *E. coli* strain that is linked to the gene encoding the MalT activator protein. Tn5 carries a marker for kanamycin resistance (Kan^R). You grow P1 phage on the strain with the Tn5 insertion and use the resulting phage to infect a $MalT^-$ strain. Among 100 resulting Kan^R transductants, 20 express no maltase activity and 80 express maltase normally. Note that the MalT gene is unlinked to the gene encoding the maltase enzyme MalQ.

(a 4 pts.) What is the distance between the Tn5 insertion and MalT, as expressed as a cotransduction frequency?



Tn5 MalT+ 80%

OR



Tn5 MalT- 20%

80%

+4 points correct
+1 for writing either formula or 20/100×100.

(b 10 pts.) You grow P1 phage on a $MalT^-$ Kan^R transductant isolated in part (a), and use the resulting phage to infect a $MalT^C$ mutant in an otherwise wild-type strain. The $MalT^C$ protein binds DNA regardless of whether the inducer maltose is present. The following results are obtained:

Phenotype	number of Kan^R transductants
uninducible	80
constitutive	19
regulated	1

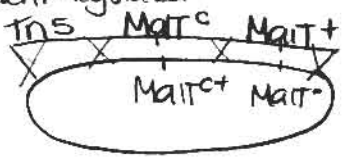
Next you perform the reciprocal cross by growing P1 phage on a $MalT^C$ Kan^R strain carrying the same Tn5 insertion as above. You use the resulting phage to infect a $MalT^-$ mutant in an otherwise wild-type strain. The following results are obtained:

Phenotype	number of Kan^R transductants
uninducible	20
constitutive	80

Draw a diagram of the recombination event(s) that gave rise to the single regulated transductant from the first cross. Your diagram should clearly show the relative order of Tn5, $MalT^-$, and $MalT^C$ (but cotransduction distances are not necessary).

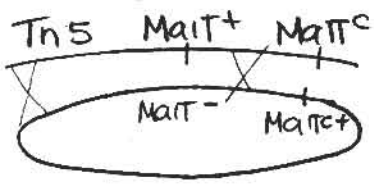
+4 correct crossover event
+

Cross 2 - Rare event - regulated



Tn5 MalTC+ MalT+

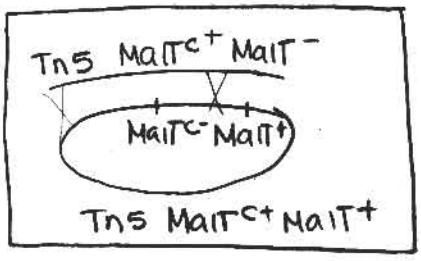
OR



Tn5 MalTC+ MalT+

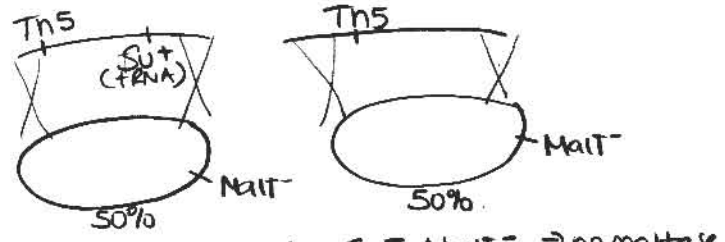
Therefor order is Tn5 MalTC MalT

Event that gave rise to regulated in cross 1



Name: _____

(c 4 pts.) You have isolated a Tn10 insertion that is linked (50% cotransduction) to an ochre tRNA suppressor allele (Su^+) in an otherwise wild-type *E. coli* strain. The Tn10 insertion carries a marker for tetracycline resistance (Tet^R) and is not linked to MalT. You grow P1 phage on this Tet^R Su^+ strain and use the resulting phage to infect a $MalT^-$ strain. Out of the 100 Tet^R transductants, 50 express maltase normally and 50 express no maltase activity. What type of mutation is $MalT^-$? (Be as specific as possible.)



Su+ MalT- → regulated Su- MalT- → no maltase

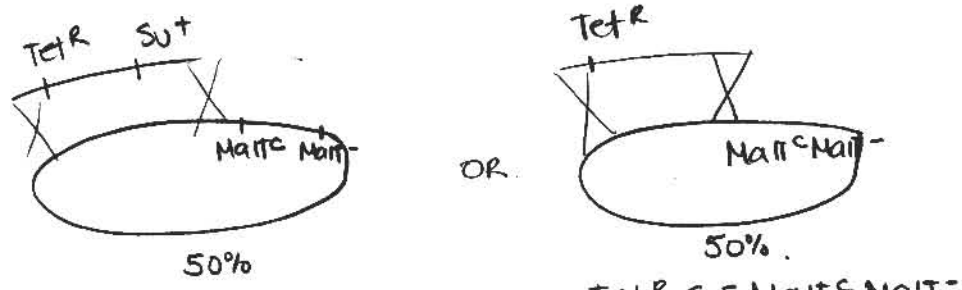
Su is a tRNA ochre suppressor.

MalT- → ochre mutation

↓

Nonsense mutation

(d 7 pts.) You grow P1 phage on the Tet^R Su^+ strain from part (c) and use the resulting phage to infect a $MalT^-$ $MalT^C$ double mutant. Out of the 100 Tet^R transductants, 50 express maltase constitutively and 50 express no maltase activity. Is the phenotype of a $MalT^-$ $MalT^C$ double mutant regulated, constitutive, or uninducible?



TetR Su+ MalTc MalT-

↓

constitutive

TetR Su- MalTc MalT-

↓

uninducible

7.03 Final Exam 2002

Name: _____

Section: _____ **TA:** _____

There are 15 pages including this cover page.

Verify that you have all 15 pages.

Please write your name on each page.

Question 1	25 points
Question 2	25 points
Question 3	25 points
Question 4	30 points
Question 5	15 points
Question 6	20 points
Question 7	30 points
Question 8	30 points