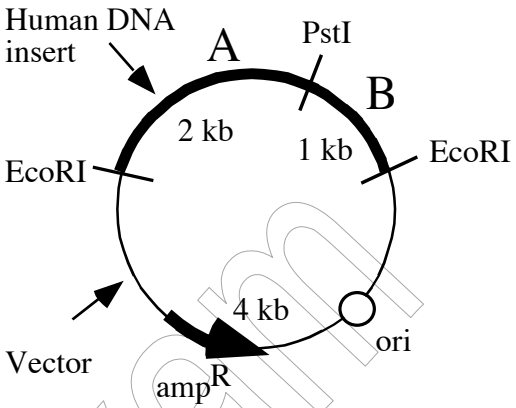
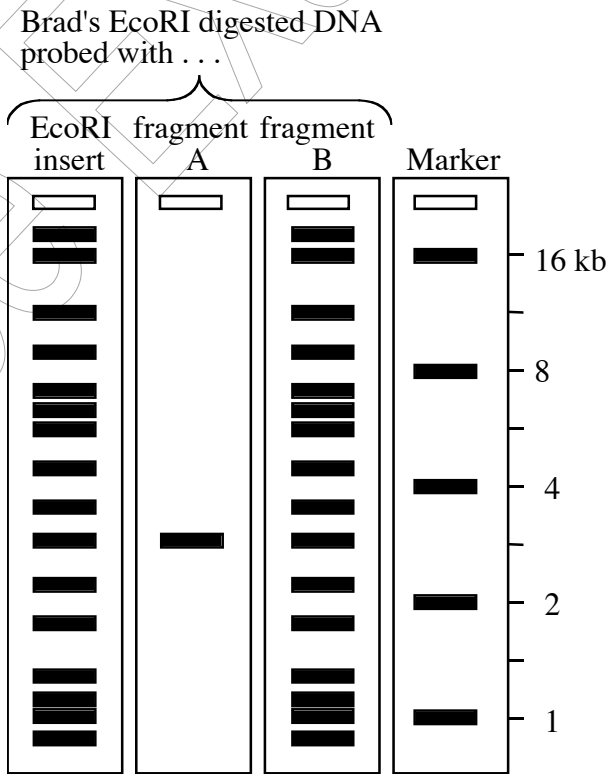
GENOME 371; A 03 Name:_____

Berg/Brewer Practice Exam 3; Nov 19, 2003

1. (20 pts) A student (Brad) in Mary-Claire King's lab in Genome Sciences was given a DNA clone with a 3 kb human insert in a bacterial vector. She wanted him to do some basic characterizations on the insert in this DNA plasmid (see map to the right). Brad does the following set of experiments and then leaves for Christmas vacation. Mary-Claire is looking through his lab notebook trying to interpret Brad's results.



A. Brad did three Southern blots using his own DNA that was cut with EcoRI. Each blot was hybridized with a different radioactive probe (see below right). What do the results mean?

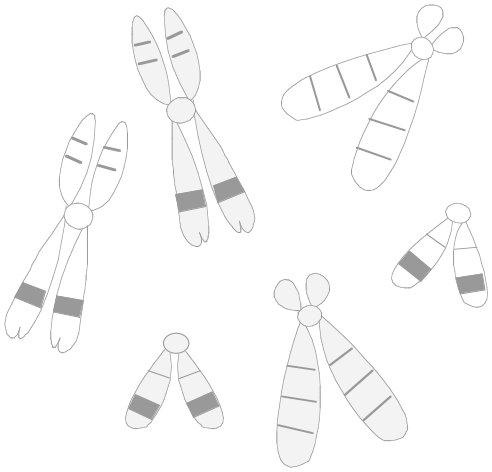


EcoRI insert?

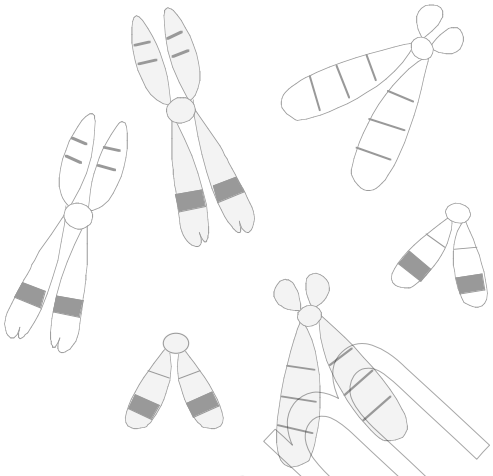
Fragment A?

Fragment B?

B. Brad did two separate Fluoresence In Situ Hybridization (FISH) experiments to his own karyotype. On one karyotype he used labeled A fragment; on the other he used labeled B fragment. What result was he expecting? Draw clearly the expected results on these three pairs of homologues.

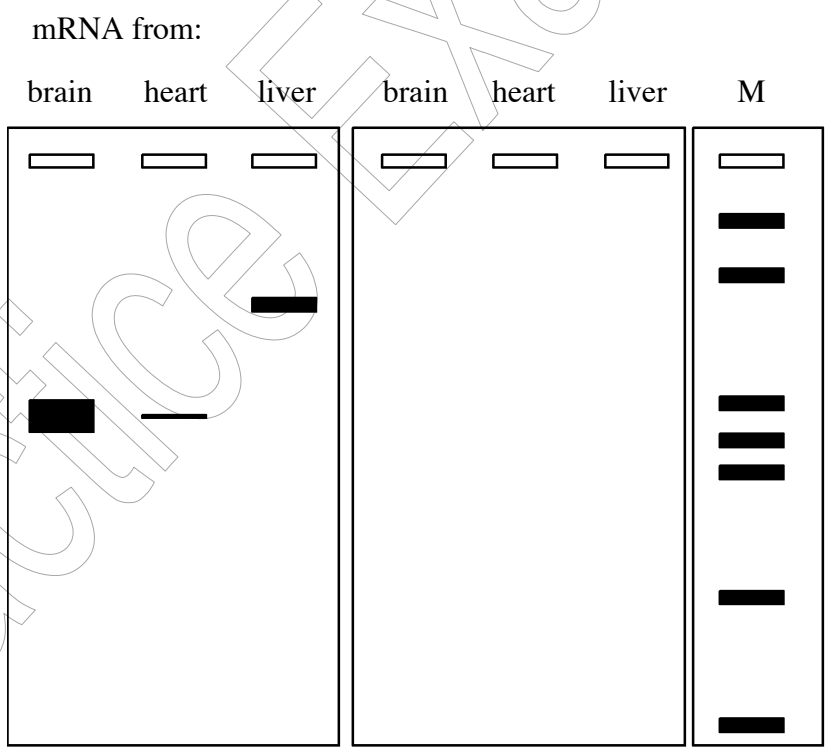


Probe



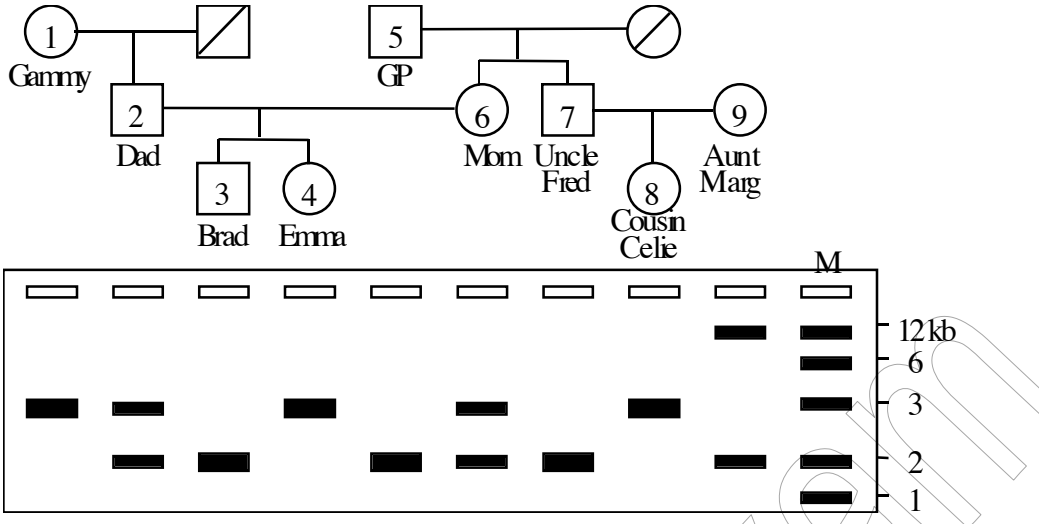
Probe B

C. Brad obtained autopsy samples of liver, heart and brain from a young girl who died in a car accident. He isolated mRNA from these samples and did two northern blots. One he hybridized with labeled fragment A and the other he hybridized with labeled fragment B. What do these results tell M-C? Be quantitative and specific.



A probe B probe

2. (15 pts) When Brad (from question 1) went home for Thanksgiving, he collected hair samples from all of his family members. Back in lab, he isolated DNA from each person's hair follicles. He then cut the DNA samples with EcoRI and PstI and probed the Southern blot with the A fragment. Use these data to answer questions about the location of this 3 kb of DNA, the PstI site and his family.



A. Does this DNA fragment lie on an autosome or the X chromosome? _____

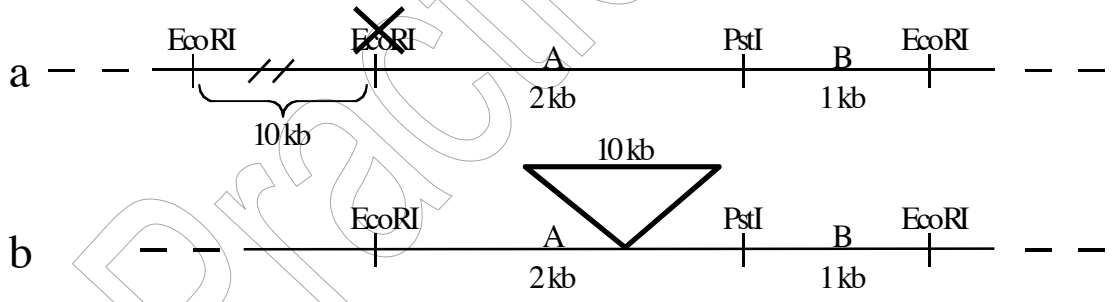
B. What do you conclude about the Pst I site? _____

C. What is the genotype of Brad's deceased maternal grandmother? _____

D. Is Emma illegitimate? _____

E. What is the simplest explanation for Cousin Celie's genotype? _____

F. Brad imagines two possible explanations for Aunt Marg's 12 kb band (see the maps **a** and **b** below).



What could Brad do to distinguish between the two hypotheses for the 12 kb band?

3. (14 pts) You have just been handed a tube of DNA containing an amplified PCR fragment from the dog genome. Below on the left are a series of questions regarding this DNA sample. On the right is a list of tools that could be used to answer the question about the PCR sample. Pick up to two of the most important tools (numbers 1-14) for each question. What would you do . . .

Answer	Experimental questions:
_____	to determine if this sequence is transcribed?
_____	to map this DNA molecule to a chromosome?
_____	to determine if the PCR fragment is repeated elsewhere in the dog genome
_____	to see if it is homologous to DNA sequences in other organisms?
_____	to see if it is polymorphic in dog populations?
_____	to find a BAC clone containing this fragment?
_____	to determine if the PCR fragment contains a minisatellite

Tools:

1) FISH (Fluorescent *In Situ* Hybridization)

2) Colony hybridization of a dog genomic library

3) Sequence the PCR fragment and do a BLAST search of yeast and Drosophila databases

4) Southern blot of restriction-enzyme digested dog genomic DNA

5) Insert the PCR fragment into a vector

6) Hybridize the PCR fragment to allele-specific oligonucleotides specific to this sequence

7) DNA sequencing of this particular PCR fragment

8) Sequence the PCR fragment and do a BLAST search of dog EST libraries

9) Northern blot

10) PCR amplification of this fragment from different dogs

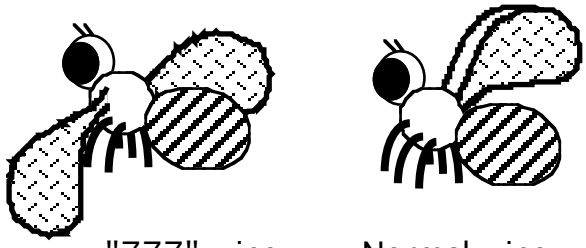
11) Zoo blots

12) Colony hybridization of a dog cDNA library

13) Measure CpG frequency

14) Sequence the PCR fragment and look by computer for syntenic regions in the human genome

4. (7 points) You are working in Dr. Berg's lab as chief fly stock keeper and you notice that your **wild-type** stock of flies contains a single male fly with unusual wings. This male's wings are held out from the body, much like wings of an airplane. You think this mutation might represent a new gene and, being from Seattle, you name the gene "Boeing 777".



"777" wing Normal wing

To start mapping the 777 gene to a particular chromosome, you mate this male to a pure-breeding strain that carries three dominant mutations: Garnet eye (X-linked), Thin bristle (second chromosome) and Fat body (third chromosome).

$\frac{G}{G}$; $\frac{T}{T}$; $\frac{F}{F}$ females (normal wings) X "Boeing 777" male (all other traits are wild type)

You obtain the following data:

Phenotype of progeny				# of female progeny	# of male progeny
garnet eye	thin bristle	fat body	777 wing	25	25
garnet eye	thin bristle	fat body	normal wing	25	25

Is "777" dominant? YES / NO / Can't determine from these data

Is "777" sex-linked? YES / NO / Can't determine from these data

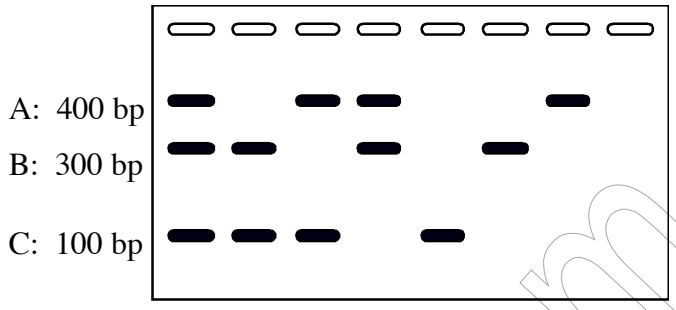
Is "777" on the second chromosome? YES / NO / Can't determine from these data

Is "777" on the third chromosome? YES / NO / Can't determine from these data

Using nomenclature consistent with the above results, give ONE POSSIBLE genotype for the boxed males.

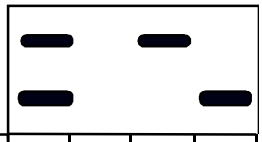
5. (20 pts) In the process of PCR, the primers must be a perfect complementary match to the template to get amplification of a DNA fragment. This fact is used to assay DNA samples for SNPs (Single Nucleotide Polymorphisms)--alleles that differ by one base pair.

A single male mouse, heterozygous at three SNP loci, has sperm collected and subjected to single cell PCR using primers for three SNP loci. Primer set A generates a 400 bp fragment if no mismatches occur between primer and template. Similarly, PCR primer set B generates a 300 bp fragment and PCR primer set C generates a 100 bp fragment. Below are the results compiled from 25 individual sperm amplifications, grouped by gel pattern.



Number of sperm that gave specific gel pattern: 1 3 1 8 8 0 2 2

A) Fill in this worksheet based on data from the gel.



number of AB genotypes				
number of BC genotypes				
number of AC genotypes				

B) Yes or No:
Are A and B linked? _____

Are B and C linked? _____

Are A and C linked? _____

C) Show the arrangement of SNP alleles on the chromosomes of the male who produced these sperm. Use A, B and C to indicate the presence of the amplifiable allele and a, b, and ¢ to indicate the absence of the amplifiable allele.

Indicate the distances between the linked loci.

6. (12 pts) You have been hired to work in a forensic laboratory that is gathering and studying evidence from a recent murder scene in the area. The police suspect a man who lives several states away. He, of course, claims that he is innocent. However, the police collected an oak leaf sample from the man's car that looks like it came from the same type of oak tree that was at the murder scene.

The district attorney wants you to demonstrate that the oak leaf from the suspect's car came from the oak tree at the murder scene. You collect the following PCR allele information from the literature about the population of oak trees from across the country.

locus	allele number	allele frequency
"A"	1	25%
	2	75%
"B"	10	20%
	11	30%
	12	50%
"C"	23	30%
	27	70%

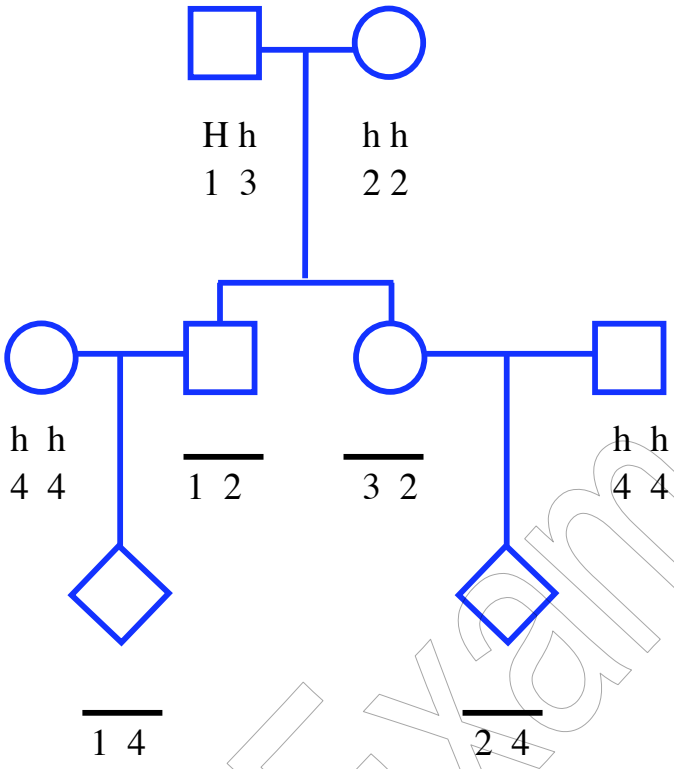
A) You test for the above PCR markers using DNA you isolated from the leaf found in the suspect's car and a leaf taken from the tree at the murder scene. For these three PCR markers, the two leaves have the identical genotypes (shown below):

"A" locus – 1, 1
"B" locus – 10, 11
"C" locus – 23, 27

What can you tell the district attorney about the possibility that the leaf from the suspect's car is NOT from the tree at the crime scene?

B) What would you do to improve the odds for a conviction?

7. (12 points) Individual I-1 suffers from a dominant autosomal disease. The mutant allele (H) is linked to allele #1 of a DNA marker locus, which has four alleles total and maps 5 cM from the disease gene.



A. Given the inheritance pattern of the marker locus, what is the most likely genotype of individual II-2? Fill in the blank provided.

B. What is the probability that individual II-2 will exhibit the disease syndrome?

C. Given the inheritance pattern of the marker locus, what is the most likely genotype of individual II-3? Fill in the blank provided.

D. What is the probability that individual II-3 will exhibit the disease syndrome?

E. What is the probability that individual III-1 will exhibit the disease syndrome?

F. What is the probability that individual III-2 will exhibit the disease syndrome?