Genome 371, Fall 2003 Name _____KEY_____
Berg/Brewer; Exam 1A

1. (30 pts) A tropical fish breeder for the local pet store is interested in creating a new type of fancy tropical fish. She observes consistent patterns of inheritance for the following traits:

P_1: solid color X dotted (color with white dots)

F_1: dotted

F_2: 3 dotted : 1 solid

P_1: blue X yellow

F_1: yellow

F_2: 3 yellow : 1 blue

A. What are your hypotheses for the inheritance of these two traits?

There is a gene in fish that determines pattern. It has two alleles, solid and dotted. Dotted is dominant to solid.
There is a gene in fish that determines color. It has two alleles, blue and yellow. Yellow is dominant to blue.

B. A pure breeding yellow fish with white dots is crossed with solid blue fish. The F_1 are yellow with white dots. These fish are then crossed to the solid blue fish. The following offspring are produced:

Phenotype	Observed	Expected	$(O-E)^2$	$(O-E)^2/E$
dotted yellow	10	**8**	**4**	**0.5**
solid yellow	8	**8**	**0**	**0**
dotted blue	0	**8**	**64**	**8**
solid blue	14	**8**	**36**	**4.5**

What would Mendel have predicted for this cross? Put his values in the table above under the "expected" column.

C. Do these data conform to Mendel's predictions? Use a Chi-square test to answer this question.

Calculate a Chi-square value for these data. **13**

How many degrees of freedom are there for this cross? **3**

What is the P value? **< 0.005**

Do you reject or accept the Mendel's hypothesis? **Reject**

D. What are you rejecting or accepting in this cross: That is, what (specifically) is the "null" hypothesis in this example?

Pattern (solid/dotted) and color (blue/yellow) are independently assorting traits and the data are not different from a 1:1:1:1 ratio.

E. There are two possible explanations for the absence of dotted blue fish.

Hypothesis #1. The combination of alleles for dots and blue color are lethal.
Hypothesis #2. The allele for blue is epistatic to dots.

How do these hypotheses differ in terms of predicted outcomes in the cross of the dotted yellow F_1 with the solid blue fish? (A Punnett square may help you with your predictions.)

Hypothesis #1 suggests that one class of expected offspring, the dotted blue fish, are dead. We would predict that dotted yellow F1 x solid blue fish would produce 1/4 fewer adult progeny than expected from the number of fertilized eggs (if we had a way to count all the fertilized eggs and then count the number of surviving fish – not practical with fish!). More importantly, the surviving offspring would appear in a 1:1:1 ratio (yellow dotted: yellow solid: blue solid).

Hypothesis #2 suggests that the "dotted blue" fish survive, but the presence of dots is masked by the blue color. Thus, we would predict that all the eggs survive to adults and, more importantly, the adults appear in a 1:1:2 ratio (yellow dotted: yellow solid: blue solid).

F. Chi-square analysis was performed on these two hypotheses. The values are presented below

Hypothesis #1: Chi-square value = 0.75
Hypothesis #2: Chi-square value = 1.75

Pick one of these two hypotheses and evaluate the Chi-square results:

Hypothesis# **1**

Degress of freedom? **2**

P-value? **0.5 – 0.9**

Reject or accept? **Accept**

Hypothesis# **2**

Degress of freedom? **2**

P-value? **0.1 – 0.5**

Reject or accept? **Accept**

G. What cross would you do to test your hypothesis? (How would Mendel have figured this out?) Be specific as to the cross, the expected offspring and how this outcome proves the hypothesis.

We do not know if the solid blue fish are all dd yy or if some are actually Dd yy and blue is masking the dotted allele. To distinguish these possibilities, cross many, solid blue individuals to solid yellow fish, whose yellow color would let us see the presence or absence of dots.

? solid blue fish? X solid yellow fish

(dd yy and Dd yy?) X (dd YY)

Hypothesis #1: If the Dd yy (dotted blue) fish are all dead, then the solid blue fish are of a single genotype (dd yy) and I would never see any dotted offspring from the proposed cross.

Hypothesis #2: If the blue color masks (is epistatic to) dots, and the Dd yy fish look the same as the dd yy fish, then the offspring from 1/2 the crosses will be solid yellow (those whose parents are dd yy) but the other half will result in a 1:1 ratio of dotted yellow: solid yellow (those with parents of genotype Dd yy).

2. (20 pts) Your neighbor is a cat breeder and owns a rare, solid brown male. Your tabby female (see picture) gets loose when she is in heat and ends up pregnant with kittens fathered by your neighbor's brown cat. Your tabby has five offspring:

2 tabbies just like mom
2 solid black kittens
1 silver tabby

At first, you are puzzled by the solid black kittens, by the lack of brown kittens and by the sudden appearance of the silver tabby. Use your knowledge of cat coat color to resolve these issues.

A. Given the phenotypes of the parents and offspring, deduce as much as possible about all of the cats' genotypes. Give genotypes for only the genes that matter in this cross. For example, there is no white on these cats so you can ignore W, C and S. Other genes that you don't need to consider are D, T, O and Y. If there isn't enough information to determine genotypes completely, indicate the unknown allele with a question mark (?).

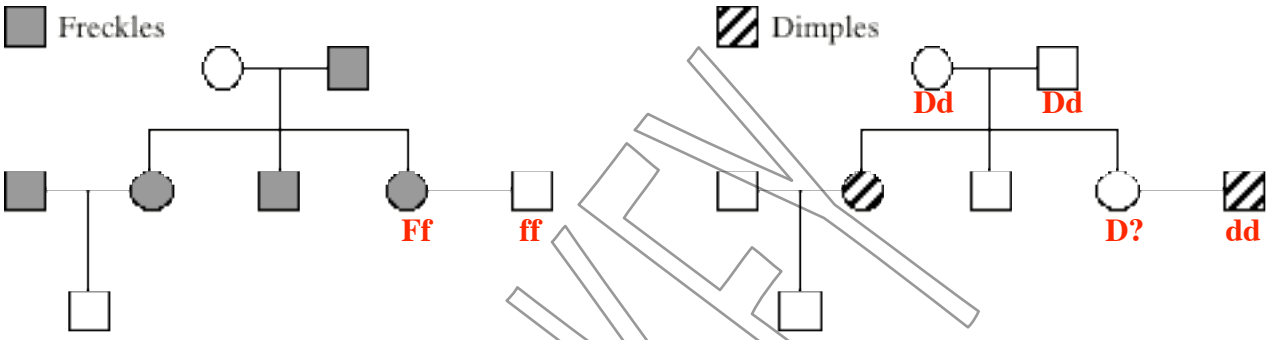
brown male	X	tabby female
aa bb Ii		**Aa B? ii**

2 tabbies	**Aa Bb ii**
2 black	**aa Bb I?**
1 silver tabby	**Aa Bb Ii**

B. Based on the pathway of pigment formation in cats, how do you explain the birth of a silver tabby to parents who are not silver? Discuss the important parts of the cat pigment pathway that support your hypothesis.

Non-agouti (*aa*) is epistatic to silver (*II*, *Ii*, or *ii*). To see either yellow or silver, the cat must shut off eumelanin synthesis for some period of time. Functional Agouti protein (encoded by the *A* allele) is needed to block black pigment production and thereby reveal the presence (yellow) or absence (silver) of phaeomelanin in the hair. The solid brown cat is genotype *aa* and thus masks the presence of the *I* allele.

3. (15 pts) The pedigree below shows the inheritance of two independently assorting, single-gene traits in a particular family: freckles and dimples. Individuals with freckles are shaded gray; individuals with dimples are striped. Answer the following questions based on the pedigree.



A. In this family freckles are inherited as a(n)
   a. autosomal dominant
   b. autosomal recessive
   c. sex-linked dominant
   d. sex-linked recessive
   e. cannot be determined from these data.

B. In this family dimples are inherited as a(n)
   a. autosomal dominant
   b. autosomal recessive
   c. sex-linked dominant
   d. sex-linked recessive
   e. cannot be determined from these data.

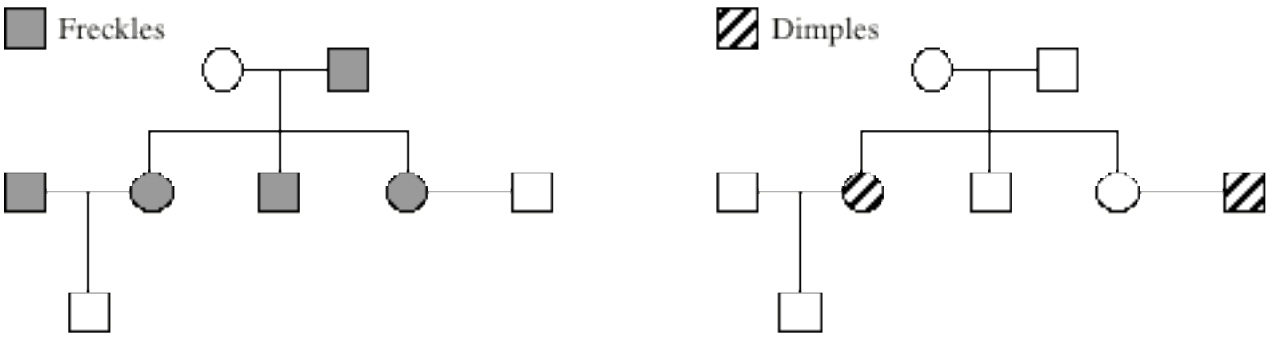
C. If individuals II-4 and II-5 have a child . . .

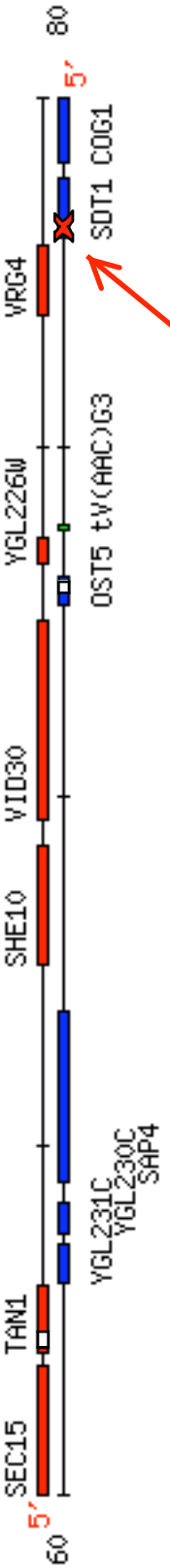
what is the probability that the child will have freckles? **1/2**

what is the probability that the child will have dimples? **1 x 2/3 x 1/2 = 1/3**

what is the probability that the child will have both freckles and dimples? **1/2 x 1/3 = 1/6**

(more copies of the pedigree if you need them)





4. (10 pts) On the left is a 20 kb region from the yeast genome as illustrated in SacchDB. Examine the features in this region and answer the questions below.

A. From what chromosome is this 20 KB region? **VII (seven)**

B. Where is the centromere, to the left or the right? **To the right**

C. Approximately how far away (in kb) is the centromere from YGL226W?

226 x 2 kb (average size of yeast gene) = ~ 450 kb

(or, if you calculated directly from the data here**:**
20 kb / 12 ORFs x 226 = 376.7 kb)

D. Place an X on the map to illustrate where the stop codon for gene SDT1 would be. Be sure to indicate the correct end of the gene and the correct strand.

E. Is there a tRNA gene in this region of the genome? **Yes** If yes, what is its name? **tV(AAC)G3**

F. What are the fundamental differences between a tRNA gene and an ORF (such as VID30)?

tRNA genes encode RNAs that act as RNA and are not translated into protein. ORFs encode messenger RNAs that are translated into protein. tRNAs are adapters that allow the decoding of the message to construct a proper protein.

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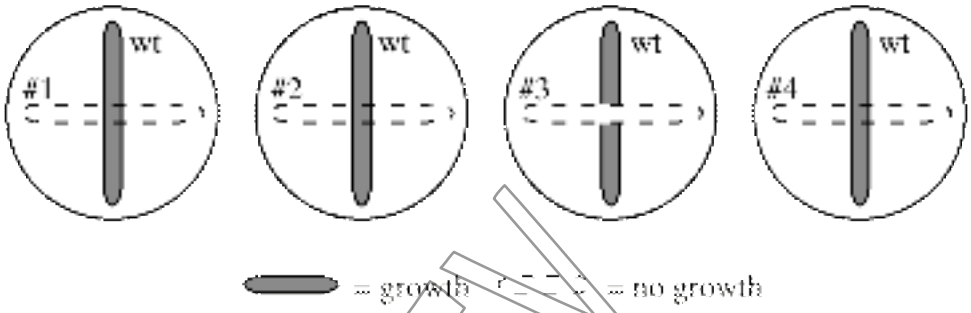
5. (25 pts) Mike is a student in Lee Hartwell's lab using genetics to study mitosis in his favorite haploid organism, yeast. He was given four temperature sensitive mutants (#s1-4) that grow fine at 23°C but stop growing when replica-plated and placed at 37°C. He crossed each mutant individually to wild type yeast on complete plates at 23°C, replica plated the crosses and grew the replica plates at 37°C.

Growth at 37°C



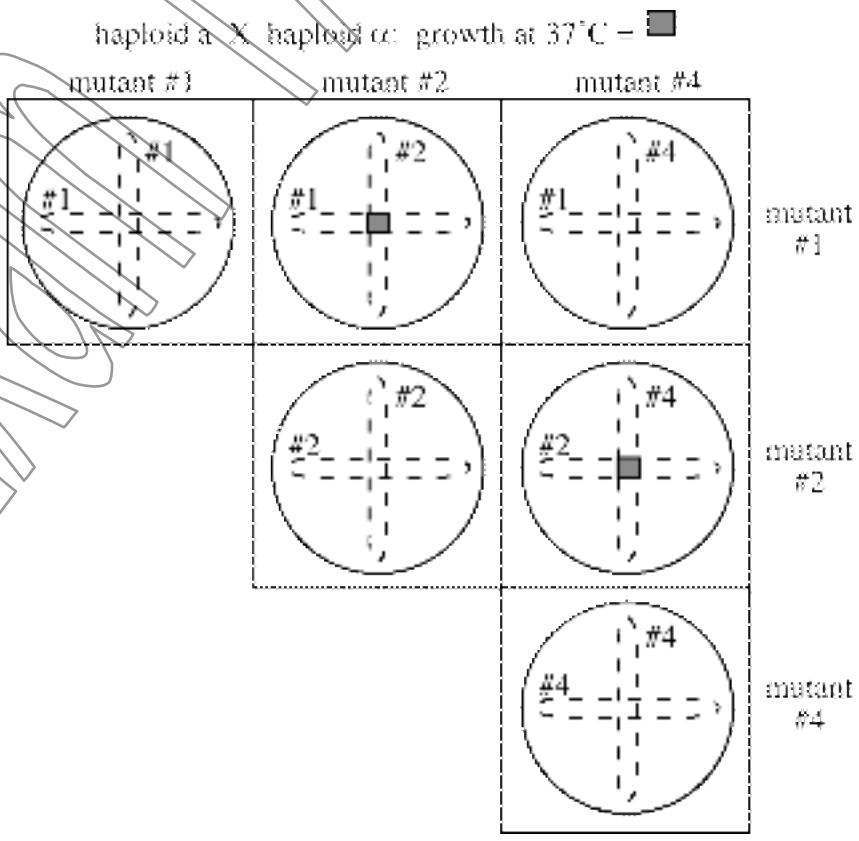
A. What cells are present at the junction between the two strains?

a/α diploid cells

B. What did these results tell Mike about each of his mutants?

Mutants #1, #2, and #4 are recessive to wild type.
Mutant #3 is dominant to wild type.

C. Mike generated haploid α strains for each of his mutants and crossed them in pair-wise combinations to some of the starting haploid a strains. After growing the crosses at 23°C, he replica-plated and placed the replica plates at 37°C. His results are shown below.

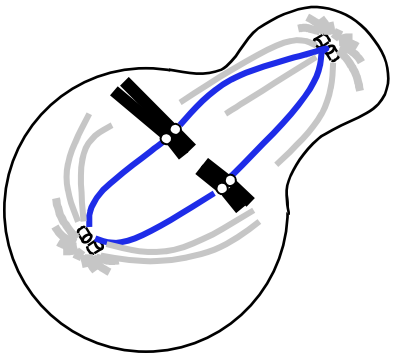


What did these results tell Mike?

#1 and #4 fail to complement and therefore likely affect the same gene.

 # 2 complements both #1 and #4 and therefore affects a different gene.

D. To see what was going wrong with the cell cycle, Mike examined his haploid mutant strains in the microscope. After incubating them at 37˚C for a period of time long enough for cells to complete ANAPHASE, he found that ALL four of the mutants had the phenotype shown below: the cells were arrested at metaphase with the chromosomes stuck on the metaphase plate. (Only two of the sixteen yeast chromosomes are shown.)



Mike suspects that one or more of the following proteins may be defective in his mutant strains: APC, Cohesin, Securin, or Separase.

Choose any one of the four mutant strains (1, 2, 3, or 4) and choose one of the proteins listed above that could be altered in the mutant you chose. Answer the following questions:

--What mutant number? **See chart below**

--What protein? **APC, Cohesin, Securin, or Separase**
And how is it specifically altered in the mutant?

Mike's mutants are all temperature sensitive. At 23°C, the mutant protein is made and functions normally, but when the yeast are shifted to 37°C, the protein no longer works correctly. The most likely explanation for this behavior is that the mutant allele contains a missense mutation that introduces an aberrant amino acid into the protein. This change causes a destabilization of the protein at higher temperatures, so that the protein denatures and cannot fold or function properly. In this respect, Mike's temperature-sensitive mutations resemble the c^s or c^h alleles of Siamese cats. For full credit, the answer must state explicitly what aspect of protein function goes wrong. See chart below.

--Is it a dominant or recessive mutation? **1, 2 and 4 = recessive; 3 = dominant. Mutant number must match description of phenotype (e.g., Mutant #1 = APC, recessive loss of function; see example below)** (Keep in mind the data from page 7.)

--Is the mutation a loss of function mutation or a gain of function mutation? **See chart below**

--How does your proposed alteration in that protein result in the observed phenotype at 37˚C?

Protein	Recessive loss of function	Dominant loss of function	Recessive gain of function EXTREMELY rare	Dominant gain of function
APC	Unable to bind or cleave Separase	Poison subunits	Not possible *	Not possible *
Securin	Not possible *	Can't be bound or cleaved by APC	Not likely	Always binds Separase
Separase	Unable to bind or cleave Cohesin	Poison subunits	Not likely	(Always binds Securin)
Cohesin	Not possible *	Can't be bound or cleaved by Separase	Not likely	Always binds the sister chromatids

*** will not give "stuck at metaphase" phenotype**

Example: Mutant #1, APC, recessive, loss of function. At high temperatures, APC denatures and can no longer bind Securin and destroy it. Thus, even though all the chromosomes experience tension by microtubules bound to their kinetochores, APC cannot promote anaphase by destroying Securin. Securin stays bound to Separase. In the absence of active Separase, Cohesin will not be cleaved to liberate the sister chromatids from Cohesin's constraints. As a result, the cells will remain in metaphase.