

Final review and Homework due **Dec. 11**

The final exam will be given on Thursday, **December 13 at 8:00 am**

This review sheet covers lectures 18-23. Half of the points on the final exam will come from these lectures. The other half of the points are comprehensive. Review material for the earlier sections was provided on earlier homeworks and review sheets.

Vocabulary Many of these words are in the glossary in Hartwell.

conditional lethal	multivulva	vulvaless
cell autonomous	yeast integrating plasmid	yeast centromeric plasmid
yeast episomal plasmid	<i>HO</i>	<i>MAT</i>
sporulation	tetrads	T-DNA
<i>Agrobacterium</i>	RNA-mediated interference	imaginal disc
homeotic mutation	P element	enhancer trap
ectopic expression	chimeric embryo	ES cells
inbred strains	recombinant inbred strains	congenic lines
epistasis	spliced leader RNA	balancer chromosome
hybrid dysgenesis	P strains and M strains	plasmid shuffle

Concepts. Be sure to understand the following concepts from section IV

yeast mating type	forward vs. reverse genetics
mosaic analysis	conservation of synteny
epistasis analysis	transgenic mice
ectopic expression vs. overexpression vs. antisense or dominant negative	

For each of the model organisms know

- Know the approximate size of the genome and the approximate number of genes.
- Be able to explain how one carries out reverse genetics in each of the model organisms.
- Be able to explain how one can determine the location of gene function in each of the multicellular model organisms. Be able to explain how GAL4 is used, and how FRTs are used, for this purpose.
- Be able to explain the advantages and disadvantages of each model organism.

From section I, you should be aware of basic concepts in probability, including intersection, union, and sample space. You should be able to know when to apply the binomial or Poisson distributions, the formula for the binomial and the formula for the zero term of the Poisson. You should know how to adjust the probability of an outcome to account for a change in the sample space.

Study questions (you may have questions like these on the exam).

1. Is the phenotype of a null mutation in the *AGAMOUS* gene in *Arabidopsis* autonomous or nonautonomous?
 2. Speculate on whether, among mutations **in the coding region of a gene**, a missense or a nonsense mutation is more likely to be dominant.
 3. Be able to explain the role of the TK gene in mammalian gene replacement. Is there a corresponding marker used in gene replacement in yeast? If so, which marker is normally used? If not, why not? What marker would you use if you did need to use such a marker?
 4. Review solved problems at the end of chapters 20 and 22 and References A thru E, especially the questions at the end of 20 .
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HOMEWORK QUESTIONS

1. (2 points) You have isolated a new recessive **lethal** mutation in *Drosophila*. You tentatively call the mutation (and the gene it's in) *Einstein*, or simply *ei* (because of the phenotype of the dead embryos, which have an overgrowth of the central nervous system). You have mapped *ei* to the second chromosome, and wish to refine its map position further. To do this, you use *cinnabar* (*cn*, which has a recessive cinnabar eye color phenotype) and *curved* (*c*, which has the recessive phenotype that the wings are curved). You cross *ei / SM5* females (*SM5* is a balancer chromosome for second chromosome) to *cn c* males, and then mate virgin heterozygous G1 *ei / cn c* females to *cn c* homozygotes. You then examine and test male G2 flies that carry a (potentially) recombinant chromosome over the *cn c* tester chromosome. (recomb. / *cn c*)

You first test 100 G2 flies that are homozygous for both *cn* and *c* and find that **none** of those 100 recombinant chromosomes carry the *ei* mutation. This convinces you that the *ei* mutation must lie in the region of these markers, so you test only recombinants, working until you collect 100 recombinant males of each of the two reciprocal classes, ignoring thousands of nonrecombinants.

<u>Class of male progeny</u>	<u>number carrying the <i>ei</i> allele</u>
cinnabar eyes, normal wings	72 <i>ei</i> chromosomes of 100 tested
wild-type eyes, curved wings	30 <i>ei</i> chromosomes of 100 tested

Examine the *Drosophila* genetic map (see pg. 141 of Hartwell, Fig. 5.13, or flybase: <http://flybase.bio.indiana.edu/>) and **estimate the position of *einstein* on the genetic map** (i.e. its location in map units). For example, *cn* is at 2-57.5).

2. (1 point) Use the information from question 1 to infer an approximate position of your gene (*einstein*) on the **cytological** map (for example, the cytological position of *cn* is 43E16. You will probably need to visit flybase to correlate the two maps.

3. (1 points) Name at least one candidate gene that maps in this region. Explain why *einstein* might be an allele of your candidate gene.

4. (2 points) *Drosophila* larvae that were heterozygous for a null mutation of the *brown* gene (*bw*) and its wild-type allele (*bw*⁺) were irradiated with X rays and then reared to adulthood. When the adults emerged from the pupal cases, a few had brown patches in their otherwise red eyes. These patches were otherwise normal in every other way. What caused these patches to develop? Given this observation, do you think it more likely that the product of the *brown* gene acts in pigment deposition or in the metabolic pathway for pigment synthesis? Explain. This result does not resolve the issue; just tell us if this result favors one of those two possibilities, and why. It is known that pigments are synthesized elsewhere and then transported to the eyes.

5. (2 points) You repeat this experiment using the same protocols, but this time with *Drosophila* larvae that are heterozygous for mutations in the linked genes *cinnabar* (*cn*) and *brown* (*bw*) and derived from a cross between wild-type and *cn bw* parents. Together, these mutations cause a white eye (you can read about these genes on flybase). Again, larvae were irradiated with X rays and then reared to adulthood. When the adults emerged from the pupal cases, a few had brown patches in their otherwise red eyes, but no white or cinnabar patches were observed. Explain your observations.

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6. (6 points) For each of the following types of animal, indicate

First, whether the individual animals are all genetically identical and

Second, whether or not the cells present in each animal are homozygous at all or nearly all loci:

- a) chimeric mice derived from wild-type 129/SvJ ES cells and B6 blastocysts.
- b) mice from a standard laboratory strain such as C57BL/6J
- c) F1 mice from a cross between two inbred lines such as C57BL/6J and 129/SvJ.
- d) *Arabidopsis thaliana* from a standard laboratory strain such as Col-0
- e) *Arabidopsis thaliana* from a single recombinant inbred line
- f) *C. elegans* worms from a standard wild-type laboratory strain such as N2.

7. (1 point) Is it possible to exclude paternity by examination of a single locus (examination of the same single polymorphic locus in a child and the presumed father?

Explain (If so, how? [give an example of how you could do this]. If not, why not?).

8. (1 point) Is it possible to exclude the possibility that two people are siblings by examination of a single locus (examination of the same single locus in the two individuals that may be siblings)? Explain (if so, how? if not, why not).

9 (2 points). In diagramming developmental signaling pathways, the symbol ---| is used to indicate repression; the activity of one gene negatively regulates the activity of the next. For the pathway **A ---| B ---> C** if A is on, then B will be off. If B is on, then C will also be on. You are studying mutations that affect the sensory rays in the male tail development of *C. elegans* and you have defined two genes, *ray-1* and *ray-2*. Loss-of-function mutations in *ray-1* result in males with extra rays, more than the normal number. Loss-of-function mutations in *ray-2* result in males with no sensory rays in the tail. Which of the following regulatory pathways would be consistent with these results?

- a) *ray-1* ---> *ray-2* ---> ray formation.
- b) *ray-1* ----| *ray-2* ---> ray formation.
- c) *ray-1* ---> *ray-2* ----| ray formation.
- d) *ray-1* ----| *ray-2* ----| ray formation.
- e) *ray-2* ---> *ray-1* ---> ray formation.
- f) *ray-2* ----| *ray-1* ---> ray formation.
- g) *ray-2* ---> *ray-1* ---| ray formation.
- h) *ray-2* ----| *ray-1* ---| ray formation.

10. (2 pts.) In further studies you find that a *ray-1; ray-2* double mutant looks identical to a *ray-2* single mutant (i.e. no rays are produced). Which of the pathways is most consistent with this result? (Refer to answers a through h in problem 9)