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
- HO
- MAT
- sporulation
- tetrads
- T-DNA
- Agrobacterium
- RNA-mediated interference
- imaginal disc
- homeotic mutation
- P element
- enhancer trap
- ectopic expression
- chimeric embryo
- ES cells
- cre
- lox
- flp
- 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 probabilty 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 Refs A thru E (esp. Ch. 20).
HOMEWORK QUESTIONS

1. You have isolated a new recessive lethal mutation in Drosophila. You tentatively call the mutation (and the gene it's in) mozart, or simply moz (because of the phenotype of the dead embryos, which have an overgrowth of the central nervous system). You have mapped moz to the second chromosome, and wish to refine it's 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 moz / SM5 females (SM5 is a balancer chromosome for second chromosome) to cn c males, and then mate virgin heterozygous G1 moz / 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 moz mutation. This convinces you that the moz 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.

<table>
<thead>
<tr>
<th>Class of male progeny</th>
<th>number carrying the ei allele</th>
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<tbody>
<tr>
<td>cinnabar eyes, normal wings</td>
<td>28 moz chromosomes of 100 tested</td>
</tr>
<tr>
<td>wild-type eyes, curved wings</td>
<td>70 moz chromosomes of 100 tested</td>
</tr>
</tbody>
</table>

(2 points) 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 mozart on the genetic map (i.e. it's location in map units). For example, cn is at 2-57.5).

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

3. (2 points) Name one candidate gene that maps in this region. Explain why mozart 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.
The final exam will be given on Monday, December 15 at 8:00 am

HOMEWORK QUESTIONS continued

6. (6 points) For each of the following types of organism, indicate
First, whether the individuals are all genetically identical and
Second, whether or not the cells present in each individual 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 (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.

8. (2 pts.) In further studies you find that a ray-1; ray-2 double mutant looks identical to a
ray-1 single mutant (i.e. extra rays are produced). Which of the pathways is most consistent
with this result? (Refer to answers a through h in problem 7)