

Your name: _____

Define each of the following terms, explaining what it is and how it is used for molecular genetics research in one or more of the genetic model organisms we discussed (5 points each):

recombinant inbred lines

Balancer chromosomes

ES cells

Your name: _____

The cre site-specific recombinase

T-DNA

GAL4 (in this case, explain how it is used in model organisms other than *S. cerevisiae*)

Your name: _____

1. (6 points) At a given locus, three alleles, 1, 2 and 3 are present in a population in Hardy-Weinberg equilibrium and no other alleles are present at appreciable frequencies. Homozygotes for allele 1 represent 25% of the population. Do you know what fraction of the population is heterozygous for allele 1? If so, what is that fraction?

2. (4 points) Building on question 1, heterozygotes between alleles 1 and 2 represent 20% of the population. What fraction of the population is homozygous for allele 2?

3. (4 points) Building on questions 1 and 2, what fraction of the population is homozygous for allele 3?

4. (4 points) You isolate DNA from a haploid strain of yeast and from a closely related and highly inbred diploid strain. In separate reactions of the same volume you allow 100 micrograms of DNA from each strain to denature and hybridize.

- a) DNA from the haploid strain would hybridize faster by a factor of 4
- b) DNA from the haploid strain would hybridize faster by a factor of 2
- c) DNA from the two strains would hybridize at the same rate
- d) DNA from the diploid strain would hybridize faster by a factor of 2
- e) DNA from the diploid strain would hybridize faster by a factor of 4

5. (4 points) You repeat this experiment using DNA from the same number of cells rather than the same mass of DNA. This time

- a) DNA from the haploid strain would hybridize faster by a factor of 4
- b) DNA from the haploid strain would hybridize faster by a factor of 2
- c) DNA from the two strains would hybridize at the same rate
- d) DNA from the diploid strain would hybridize faster by a factor of 2
- e) DNA from the diploid strain would hybridize faster by a factor of 4

Your name: _____

You are studying a new mutation in the yeast *Saccharomyces cerevisiae* that is uv sensitive (no growth when irradiated 30 Jm^{-2} of ultraviolet light). You have named your mutation *mrd2*, for **my radiation sensitive 2** (although you anticipate re-naming it if it turns out to be allelic to an existing *RAD* gene). It may be a new gene, and you want to investigate.

First, you cross your haploid *mrd2* strain to a haploid strain of the opposite mating type carrying *can1* and *cup5*, both recessive markers on chromosome V. The phenotype of *can1* is resistance to canavanine. The phenotype of *cup5* is sensitivity to copper.

CAN1 lies at position -50 cM (50 cM to the left of the centromere) and *CUP5* lies at -18 cM (32 map units to the right of *CAN1*, so the expected recombination frequency between *can1* and *cup5* is about 23.6%).

The resulting *mrd2/MRD2; can1 cup5 / CAN1 CUP5* diploids are wild-type (they grow after exposure to 30 Jm^{-2} of ultraviolet light) and sporulate normally.

You induce sporulation and examine the haploid spores.

6. Among the resulting haploid spores 50% are *cup5*. (5 points) What fraction of the *cup5* haploids are also resistant to canavanine?

You identify 20 colonies that are *can1 CUP5* using plates with canavanine and copper.

7. (5 points) If *MRD2* is unlinked (not on chromosome V), what fraction of these 20 colonies do you expect to continue growing after exposure to 30 Jm^{-2} of ultraviolet light?

8. (6 points) In this case (*MRD2* is unlinked) could you determine whether it is near the centromere of the chromosome that it is on? Is so, how would you do that?

9. (5 points) If *MRD2* is at -52 cM., 2 cM. to the left of *CAN1*, what fraction of these 20 colonies do you expect to continue growing after exposure to 30 Jm^{-2} of ultraviolet light?

10. (5 points) If *MFT2* lies at -34 cM. (precisely between *CAN1* and *CUP5*) what fraction of these 20 colonies do you expect to continue growing after exposure to 30 Jm^{-2} of uv light?

11. (5 points) If *MFT2* lies at -16, 2 cM. to the right of *CUP5*, what fraction of these 20 colonies do you expect to continue growing after exposure to 30 Jm^{-2} of ultraviolet light?

Your name: _____

(2 points per item; think of each question as multiple true/false statements). Circle, check or otherwise designate **each** correct statement (i.e. check all that apply). Again, ambiguous marks (checking both, placing a mark between the two statements, etc.) will be considered wrong.

18. The F plasmid

- a) contains genes for lysis of the host cell.
- b) is a conjugative plasmid.
- c) forms an **Hfr** bacterium upon integration into the *E. coli* chromosome.
- d) integrates into a single preferred location on the *E. coli* chromosome.
- e) contains genes for synthesizing connections between donor and recipient cells.
- f) is the basis for the vector used in construction of BAC clones.

19. The fidelity of replication in vivo is increased about 100-fold by

- a) recBCD.
- b) mismatch repair
- c) the 3'-to-5' exonuclease activity of DNA polymerase itself
- d) double-strand break repair

For each of the following statements, indicate for which of the five model organisms (*Saccharomyces cerevisiae*, *Drosophila melanogaster*, *Caenorhabditis elegans*, *Arabidopsis thaliana*, *Mus musculus*) it is true. These are 25 true-false questions, worth 1 point each.

Statement.	<i>S. c.</i>	<i>D. m.</i>	<i>C. e.</i>	<i>A. t.</i>	<i>M. m.</i>
Gene disruption using homologous recombination is routinely used for reverse genetics.					
XX individuals are females and XY individuals are males.					
Self-fertilization allows a heterozygous allele in a single individual to be homozygous in the next generation.					
The genome size is under 300 Mb..					
The majority of genes have no introns.					

Your name: _____

(4 points each). In each of the following there are two or more statements. One is true (generally, it is taken directly from your textbook) and the others have been modified so that to be untrue or misleading. Circle, check or otherwise designate the correct statement. Ambiguous marks (checking both, placing a mark between the two statements, etc.) will be considered wrong.

20. a) In reverse genetics, one starts with the gene sequence and determines the phenotype.
b) In forward genetics, one starts with the gene sequence and determines the phenotype
21. a) *FMR-1* alleles with an intermediate number of CGG triplet repeats (between 50 and 200) have no greater risk of mutation to alleles with a greater number of repeats (which are more likely to show symptoms), but do increase penetrance in the next generation (thereby increasing the chance that their progeny will show symptoms).
b) *FMR-1* alleles with an intermediate number of CGG triplet repeats (between 50 and 200) do not generate fragile X symptom in most carriers, but have an increased risk of mutation to alleles with a greater number of repeats that do show symptoms.
22. a) DNA methylation in mammals is specific for GATC tetranucleotides.
b) DNA methylation in mammals is specific for CG dinucleotides.
23. a) miRNAs are produced through processing from precursors that are encoded in non-protein-coding regions of plant and animal genomes.
b) miRNAs are produced through processing from double-stranded RNA molecules such as viral genomes or experimentally produced RNAi molecules.
24. a) Autozygosity is a term used to refer to homozygosity that results from mitotic recombination.
b) Autozygosity is a term used to mean homozygosity for markers identical by descent and inherited from a recent common ancestor.
25. a) Wild-type yeast (*S. cerevisiae*) can grow vegetatively as either haploid or diploid cells.
b) Wild-type yeast (*S. cerevisiae*) grow vegetatively as diploid cells; haploid cells mate soon after sporulation and die if they do not mate.
26. a) Small regulatory RNAs like *lin-4* RNA are a novel feature of gene regulation in nematodes.
b) Small regulatory RNAs like *lin-4* RNA may play a much larger role in development than originally suspected, and not only in nematodes.
27. a) Congenic mouse strains are identical except for a single locus and are generated by repeated backcrossing.
b) Congenic mouse strains are obtained by transformation of a standard (non-inbred) strain with recombinant DNA.

Your name: _____

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In diagramming developmental signaling pathways, the symbol ---| is used to indicate repression (the activity of one gene negatively regulates the activity of the next) and the symbol ---> indicates activation (the activity of one gene positively regulates the activity of the next). Thus, 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 vulval development in *C. elegans* and you have defined two genes, *vuv-1* and *vuv-2*. Null alleles of *vuv-1* result in hermaphrodites with a vulvaless phenotype while loss-of-function mutations in *vuv-2* result in the multivulva phenotype.

28. (5 points) Which of the following regulatory pathways would be consistent with these results? List all that apply.

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

29. (5 points) In further studies you find that a *vuv-1*; *vuv-2* double mutant looks identical to a *vuv-2* single mutant (i.e. multivulva). Which of the pathways is most consistent with this result? Please refer to the options listed above (a through h), picking one.

30. (6 points) You have a piece of DNA that includes the sequence:

5' - **CGTACCATGTACCTGTACCTGTACTATCTATCGGGTGACTGCTTATCCA** - 3'

To amplify this DNA by PCR you would use a pair of primers containing which **two** of the following eight primers (you must get both primers right to get any credit -- circle **two** letters):

- a) 5' - CAGGTACATGGTACG - 3'
- b) 5' - GTCCATGTACCATGC - 3'
- c) 5' - CGTACCATGTACCTG - 3'
- d) 5' - GCATGGTACATGGAC - 3'
- e) 5' - TGGATAAGCAGTCAC - 3'
- f) 5' - ACCTATTCGTCAGTG - 3'
- g) 5' - GTGACTGCTTATCCA - 3'
- h) 5' - CACTGACGAATAGGT - 3'