**Problem set 6 answers**

1. You find a mouse with no tail. In order to determine whether this mouse carries a new mutation, you cross it to a normal mouse. All the F1 progeny of this cross are wild type. What does this mean?

**The mutation is recessive**

You then mate all the F1 males to their sisters and observe that three out of 42 F2 animals have no tail and two have short tails. What could explain this pattern of inheritance?

**There should be 1/4 m/m progeny from this cross, so many of these animals are wild type. The mutation results in a partially penetrant phenotype with variable expressivity (no tails and short tails).**

You map the no tail mutation by recombination and realize that there is a stock available that is heterozygous for a deletion that removes the region where the no tail mutation maps. You cross animals without tails to animals that are heterozygous for the deletion. All the progeny for this cross are wild type. Assuming that the deletion really removes the gene mutated by your mutation, explain this result.

**The m/Df animals die.**

2. You are studying the regulation of the *lac* operon in *E. coli* and perform a merodiploid (partial diploids) analysis with various regulatory and structural gene variants that you isolated. Your first results are shown below (in units of ß-galactosidase activity).

| Experiment | Genotype | ß-galactosidase activity | |
|---|---|---|---|
| | | + Inducer | - Inducer |
| 1. | $lacI^+O^+Z^+$ | 100 | 0.1 |
| 2. | $lacI^-O^cZ^+$ | 100 | 100 |
| 3. | $lacI^-O^cZ^-$ | 1 | 0.1 |
| 4. | $lacI^-O^+Z^+/lacI^+O^+Z^+$ | 200 | 0.1 |

*lac*I encodes the lac repressor and is active in the absence of inducer (i.e., lac repressor binds to the lac operator and inhibits transcription from the lac promoter). Addition of inducer inhibits the repressor and stimulates transcription from the lac promoter. *lacO* is the operator, the region to which lac repressor binds, and $lacO^c$ mutations are constitutive operator mutations, causing *lacZ* expression in the presence of repressor and absence of inducer. *lacZ* encodes ß-galactosidase, an enzyme that functions as a tetramer.

a) Why is the induced activity in experiment 4 twice that of 1.

**There are two copies of *lacZ* in 4, and only one copy in 1.**

You generate additional merodiploids and get the surprising results shown below.

| Experiment | Genotype | Induced | Uninduced |
|---|---|---|---|
| 5. | $lacI^-O^cZ^-/lacI^+O^+Z^+$ | 10 | 0.1 |
| 6. | $lacI^+O^cZ^-/lacI^-O^+Z^+$ | 10 | 0.1 |
| 7. | $lacI^-O^+Z^-/lacI^+O^cZ^+$ | 10 | 100 |
| 8. | $lacI^+O^cZ^+/lacI^-O^+Z^-$ | 10 | 100 |

b) Describe a hypothesis to explain the results of experiments 5-8.

**The *lacZ-* mutant allele is an antimorphic or dominant negative mutant. When it is expressed it inhibits the function of the wild-type *lacZ* gene. Since beta-galatosidase functions as a tetramer, incorporation of the mutant protein into the complex poisons the complex even if they contain wild-type protein.**

3. *Drosophila* homozygous for an allele of the *thick veins* gene, $tkv^{Sz2}$, are normal-appearing adults except that the veins on the wings are much thicker than the wild-type wing veins. Flies hemizygous for that allele and a deficiency of the gene ($tkv^{Sz2}$/Df) die as embryos.

a. What is the nature of the $tkv^{Sz2}$ allele (amorph, hypomorph, haploinsufficient, hypermorph, antimorph, neomorph)?

**The *tkv*$^{Sz2}$ allele is probably a hypomorphic mutation of a gene that is essential for development. Only because the mutation is weak do the animals survive. Lowering the dose by putting the mutation over a deficiency drops its levels below a threshold essential for viability.**

b. Based on the mutant phenotypes, what are the functions of the wild
type *thick veins* gene?

It plays an essential role during development of flies and also functions in regulating the morphology of wing veins.

4. You compare the phenotype of animals that are homozygous for a mutation (m/m), that are heterozygous for the mutation (m/+), that are hemizygous for the mutation (m/Df), that contain an extra copy of the wild-type gene (m/m/+), and that are hemizygous for the locus (Df/+). Which of these animals will exhibit a wild-type phenotype, and of the animals that exhibit a mutant phenotype, which will exhibit the more severe phenotype (order the mutants based on strength of phenotype) when the mutation is:

a. Hypomorphic (Explain your reasoning for each example.)
**The m/+, Df/+ and m/m/+ animals will be wild type, since most loss-of-function mutations are recessive to their wild-type alleles.**

**Since the mutant allele retains some function, reducing the levels of the gene produce (m/Df) could make the phenotype more severe.**

**m/Df > m/m**

b. haploinsufficient

**Haploinsufficiency means that reducing the levels of a product by 50% results in a mutant phenotype, and m/+, Df/+ and m/m/+ animals will exhibit the phenotype. m/m and m/Df will be more severe than m/+ and m/Df.**

c. antimorphic

**Antimorphic mutations antagonize the wild-type product so increasing the ratio of the mutant to wild-type alleles enhances the phenotype.**

**m/Df = m/m > m/m/+ > m/+**

5. The *C. elegans lin-14* gene controls the timing of development in *C. elegans*. LIN-14 protein is high early in development and gradually decreases as development proceeds. *lin-14* is defined by both dominant and recessive mutant alleles. Animals that are homozygous for recessive alleles develop precociously (developmental events occur much earlier than normal) because LIN-14 protein levels are lowered or eliminated, similar to the levels seen later in development. Animals that contain dominant alleles are retarded in development (developmental events occur much earlier than normal) because LIN-14 levels are higher than they should be late in development. You are given three *lin-14* mutants.

a) Animals that are homozygous for mutation A develops precociously and development is even more precocious when the mutation is placed over a deficiency of the locus. What type of a mutation is this?

**Hypomorphic, because the phenotype of the mutation is enhanced in trans to a Df.**

b) Animals that are homozygous for mutation B develops precociously and development is similar when the mutation is placed over a deficiency of the locus. What type of a mutation is this?

**Amorphic or null, because the phenotype is not enhanced when the mutation is placed in trans to a Df.**

c) Animals that are heterozygous for mutation C are retarded. Development is less retarded when the C mutation is placed over a deficiency and more retarded when the animals contain one C mutant gene and two wild-type genes. What type of a mutation is this?

**Hypermorphic, because the phenotype is enhanced when more wild-type genes are added to the mutant gene.**