MIDTERM1 REVIEW QUESTIONS :

1. Several mutants of grasshoppers were found: the first type, a lazy jumper that jumped less frequently and not very far compared to wild-type grasshoppers and the second type a grasshopper that did not chirp. You want to determine something about the inheritance of these mutations.

a. Why do we cross each of these mutants to true-breeding wild-type first?

When the lazy jumper was crossed to a true-breeding wild-type grasshopper: 79 wild-type and 81 lazy jumpers were produced. When two lazy jumpers were crossed to each other 80 lazy jumpers and 40 wild-type and were produced. After 70 crosses between lazy jumpers a similar ratio of wild-type to lazy jumpers were always produced.

b. Create a hypothesis to account for this result.

When the non-chirping grasshopper was crossed to true-breeding wild-type the F1 were all wild-type but the F2 produced 119 wild-type chirping grasshoppers and 40 non-chirping grasshoppers

c. What do you conclude about non-chirping?

d. If you cross a number of non-chirping females to a number of lazy jumper males what do you expect to see in the F1? If you self the chirping, lazy jumpers to generate the F2 what so you expect to see in terms of genotypes, phenotypes and relative ratios?

2. Loppins (*Loppinicus loopy*) are fictitious, but very useful diploid invertebrates with a total of 6 chromosomes in their somatic cells. Of those 6 chromosomes, 4 are autosomes and 2 are sex chromosomes. Like humans, male loppins are XY while females are XX.
The gene that determines loppins' blood type is called *bt* and is on chromosome 1, the gene that determines the presence or absence of eyelashes is called *eye* and is on chromosome 2, and the gene that determines ability to digest cellulose is called *cel* and is on the X chromosome.
bt^A, bt^B; $eye^{W,}$ eye^D, *celWT* and *celM* are alleles of these three genes.

a) A female loppin is a triple heterozygous with the genotype bt^A/bt^B; eye^{WT}/eye^D; X^{celWT}/X^{celM}.
Her mother was homozygous for bt^A, for eye^D and for *celWT*.
Draw a somatic cell of our triple heterozygous female loppin in G1 stage of the cell cycle (that is, before DNA replication). Make sure that the chromosomes are properly drawn and clearly label all the relevant genes and alleles.

b) What alleles did the triple heterozygous female loppin inherit from her mother, and what alleles did she inherit from her father?

c) For research purposes you remove three meiocytes from the triple heterozygous female, you let them undergo the cell cycle and meiosis, and you analyze the genotype of the gametes that are produced. The first meiocyte produces two gametes of genotype bt^A; eye^{WT}; X^{celWT} and two gametes of genotype bt^B; eye^D; X^{celM}.

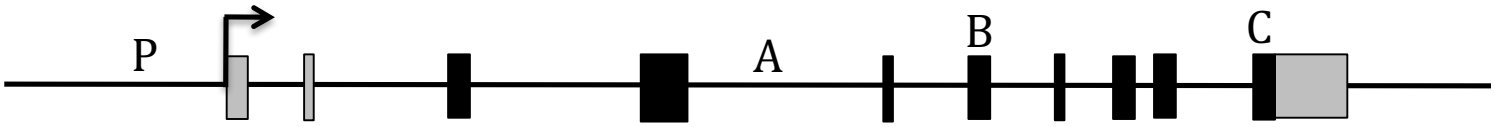
i) Draw this meiocyte at metaphase of meiosis I (this is when the homologous chromosomes are paired and lined up in the centre of the cell). Make sure to clearly label all the relevant genes and alleles.

ii) The second meiocyte produces two gametes of genotype bt^B; eye^{WT}; X^{celWT} and two gametes of genotype bt^A; eye^D; X^{celM}. Explain what must have happened differently in this meiocyte compared to the one in part i) to produce this result. You may refer to the diagram that you drew above to illustrate your rationale.

iii) If we looked at the gametes produced by 100 different meiocytes from this triple heterozygous female loppin, what are all the genotypes that we would expect to find, and in what proportions? *(Note: 100 different meiocytes will produce a total of 400 gametes)*

3. Below is shown the gene structure of the gene *isocitrate dehydrogenase* (*ic*) from yeast *Saccharomyces cerevisiae* . Based on sequence analysis there are no known enhancers in this gene. The protein coded for by this gene is an enzyme within the citric acid cycle operating in the mitochondria that converts isocitrate to alpha ketoglutarate. The ultimate purpose of this cycle is produce reduced NADH which is then converted to energy through other major metabolic reactions. Yeast cells that cannot produce NADH through this cycle then have to perform anerobic fermentation to obtain energy.

The locations of 3 different mutations are shown.



Mutation A is an insertion of 2 nucleotides in the middle of the 4th intron.
Mutation B is the deletion of 4 nucleotides in the 6th exon, which also happens to be part of the active site of the enzyme.
Mutation C is the substitution of 1 nucleotide which causes a missense mutation in the last exon and causes the enzyme to be found in the cytoplasm rather than the mitochondria where it is normally found.

a) In the table below explain what the phenotype of each of these mutations will likely be (when homozygous) at the different levels

genotype	mRNA (sequence, size amount)	Protein (sequence, size, amount, function)	Whole organism (single yeast cell)
ic^A/ic^A			
ic^B/ic^B			
ic^C/ic^C			

b) If the normal job of isocitrate dehydrogenase is to convert isocitrate into alpha ketoglutarate explain whether or not each mutation could be rescued by adding alpha ketoglutarate to the cell (and we are assuming the alpha ketoglutarate makes it into the mitochondria)

c) Rank and explain the relative severity of the three heterozygous allele combinations. State any assumptions you are making.

ic^A/ic^B;

ic^A/ic^C;

ic^B/ic^C

4. Sex linkage in dogs is similar to humans. An unusual female bulldog is found that walks on its tiptoes. When this bulldog is crossed to a 'wildtype' (not tiptoeing) bulldog, all their offspring tiptoe.

i) How could we evaluate whether there is an environmental vs. genetic cause of tiptoeing?

ii) What could be an environmental cause of the tiptoeing phenotype we observe in the female bulldog and all her pups? Speculate

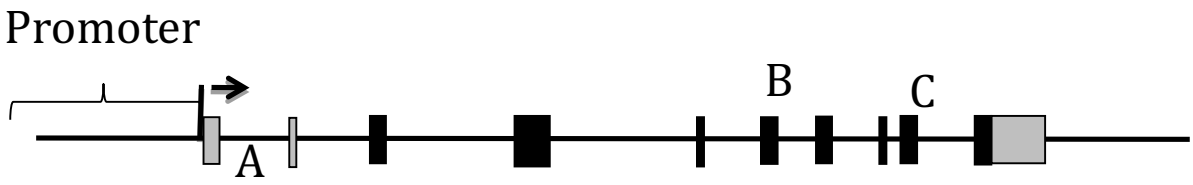
iii) If all environmental causes of the phenotype are ruled out then what can we conclude about the inheritance of the tiptoeing mutation from the information above

iv) What would allow you to tell if the mutation is autosomal or X-linked? (Suggest two things)

5. Researchers are investigating a rare condition in humans called congenital insensitivity to pain, or CIP. The condition results in the inability to sense pain (e.g. if cut, a person or mouse with CIP can be unaware they cut themselves and will not experience pain). If they discover more about this condition, it could provide useful information for the development of medicine to treat pain disorders. You also have a second population of people that have the condition: extreme pain disorder (EPD). People with EPD can experience feelings of pain even when there is no painful stimulus.

From your research you have determined that both CIP and EPD are the result of mutations in the *same* gene, called *SCN9A*. *SCN9A* codes for a sodium channel protein that allows action potentials to occur when stimulated. When stimulated, the channels open and sodium ions flood into the cell, causing an action potential and the ability to feel pain.

The locations of 3 different known mutations in SCN9A are shown below.



Mutation A is an insertion of 25 nucleotides in the middle of the 1st intron.
Mutation B is a base substitution in the 6th exon.
Mutation C is a base substitution in the 3' splice site of the 9th intron.

a. For each mutation, predict if you think it is involved in either of the disorders, and if so, which one (CIP or EPD). Explain your prediction and state any assumptions you are making and/or if more information is needed to make a more accurate prediction.

b. What do you predict the phenotype would be for a person with the following genotypes? Explain. Note that $SCN9A^{+}$ is the wild-type allele, and the superscript A, B, C refer to the alleles mentioned in part a.

i. $SCN9A^{+}/SCN9A^{A}$
ii. $SCN9A^{+}/SCN9A^{B}$
iii. $SCN9A^{+}/SCN9A^{C}$
iv. $SCN9A^{B}/SCN9A^{C}$
v. $SCN9A^{A}/SCN9A^{C}$

c. Draw the resulting bands on a gel for the DNA, RNA, and protein for the following individuals:

$SCN9A^{+}$ / $SCN9A^{+}$
$SCN9A^{+}$ /$SCN9A^{A}$
$SCN9A^{+}$ /$SCN9A^{B}$
$SCN9A^{+}$ /$SCN9A^{C}$