BB2920-C15 Name:_____

Genetics

Exam 3

Professor Farny

**Instructions:**

**Do not open this exam until instructed to do so.**

**You will have 60 minutes to complete the exam.**

**You may not leave the examination room during the exam.**

**Phones, tablets, computers, and any other electronic device are strictly prohibited.**

**They must be completely out of sight for the entirety of the exam.**

**You may use a calculator. Phones, tablets, laptops, etc. may not be used as**

**calculators. It must be a separate calculator.**

Question 1

a) Match the genome designations on the right with each of the following terms on the left, assuming that the normal state of the organism's somatic cells are diploid:

monoploid __D__

trisomic __E__

tetraploid __A__

monosomic __C__

A. 4n
B. 2n + 2
C. 2n - 1
D. n
E. 2n + 1
F. 3n

b) Which specific type of aneuploidy causes Down Syndrome?

_____2n+1 (trisomy Chr 21)_____

Problem 2: In the human genome, brown eyes (B) are dominant over all categories of "light" eyes (b, which includes blue, gray, hazel and green). In the Scandinavian countries of northern Europe, it is estimated that approximately 80% of the population have light colored eyes. In the southern European countries of Spain, Portugal and Greece, it is estimated that only about 20% of the population have light colored eyes.

a) In Scandinavia, what percentage of the population are brown-eyed **heterozygotes**?

bb = 0.8 = q^2 q = 0.894 p = 1-q = 0.106
2pq = 2 x 0.894 x 0.106 = 0.1895 or 18.95%

b) In southern Europe, what percentage of the population are brown-eyed **homozygotes**?

bb = 0.2 = q^2 q = 0.447 p=1-q=0.553
p^2 = 0.553^2 = 0.3058 or 30.58% of the population

c) Myotonia Congenita (MC) is a rare autosomal recessive genetic disorder that causes muscle weakness and rigidity. It affects 1/100,000 live births worldwide, but affects 1/10,000 live births in Scandinavia.
In Scandinavia, what percentage of the population are carriers for the MC allele?
MC = 1/10,000 = q^2 = 0.0001 q = 0.01 p=1-q=0.99
carriers = 2pq = 2 x 0.01 x 0.99 = 0.0198 or 1.98%

d) In Scandinavia, what percentage of the population are brown eyed heterozygotes AND carriers for MC?
Assuming that the eye color gene and the MC gene assort independently, you can apply the product rule.
probability of brown eyed het from part a = 0.1895
probability of carrier of MC from part b = 0.0198
0.1895 x 0.0198 = 0.00375 or 0.375%

e) Give two hypotheses as to why there is a higher incidence of blue eyes and Myotonia Congenita among the Scandinavian population (these are the factors we discussed that affect the Hardy-Weinberg equilibrium).
Many possible answers, including inbreeding that increases the allele frequencies of blue eyes and MC alleles, positive assortative mating (blue eyed people prefer blue eyed mates), geographic isolation (people born in Scandinavia tend to remain there for their lives), and others

Question 3 (21 points)

a) For the lac operon, the allosteric effector(s) of the system is/are: (circle all that apply)

glucose **lactose** galactose **cAMP** ATP

b) For the GAL-UAS regulatory system, the allosteric effector(s) of the system is/are: (circle all that apply)

glucose lactose **galactose** cAMP ATP

c) Which component(s) of the lac operon contain the allosteric binding site(s) for the effector(s) in the system? _____Lac I and CAP_____

d) Which component(s) of the Gal4-UAS system contain the allosteric binding site(s) for the effector(s) in the system? _____Gal3_____

e) Indicate the effect of the following mutations on the transcription of lacZ and LacY (Circle the appropriate response: will the transcription be inducible upon addition of lactose, always on, or always off?). The endogenous genome is indicated before the slash, and the F' plasmid after the slash. Consider only the negative regulation for this section. Assume anything not indicated is wild type. Assume no mutations in lacZ or lacY.

| mutation(s) | LacZ/LacY regulation: | | |
|---|---|---|---|
| I- / F' I+ | inducible | always on | always off |
| $O^C$ / F' O+ | inducible | always on | always off |
| $I^S$ / F' I- | inducible | always on | always off |
| P- $O^C$/ F' P+ O+ | inducible | always on | always off |
| $I^S$ P+ O+ / F' I+ P- $O^C$ | inducible | always on | always off |

f) Indicate the effect of the following mutations on the level of transcription of lacZ and lacY under the indicated glucose (Glu) and lactose (Lac) conditions. (circle one). Consider both positive and negative regulation for this section. Assume all mutations are within the genomic copy of the operon (no plasmid). Anything not listed is wild type. Assume no mutations in lacZ or lacY.

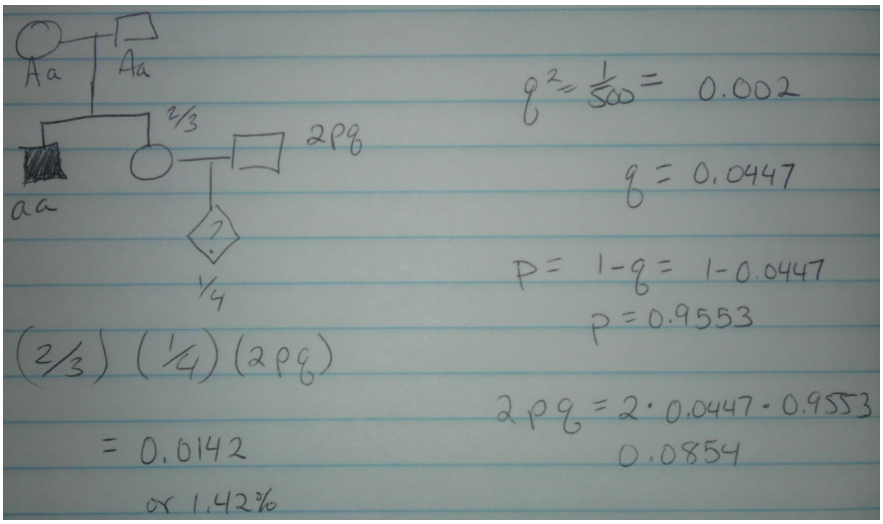
| mutation(s) | Glu+ Lac- | Glu + Lac + | Glu - Lac + |
|---|---|---|---|
| CAP- | **OFF** **LOW** **HIGH** | **OFF** **LOW** **HIGH** | **OFF** **LOW** **HIGH** |
| $I^S$ | **OFF** **LOW** **HIGH** | **OFF** **LOW** **HIGH** | **OFF** **LOW** **HIGH** |
| $O^C$ | **OFF** **LOW** **HIGH** | **OFF** **LOW** **HIGH** | **OFF** **LOW** **HIGH** |
| $P^{CAP}$ I- | **OFF** **LOW** **HIGH** | **OFF** **LOW** **HIGH** | **OFF** **LOW** **HIGH** |

g) Indicate the effect of the following mutations on the transcription of the *GAL* genes (*GAL1*, *GAL2*, *GAL7*, *GAL10*) in the Gal4-UAS system in the absence (gal-) or presence (gal+) of galactose. Circle the appropriate response. Assume anything not listed is wild type.

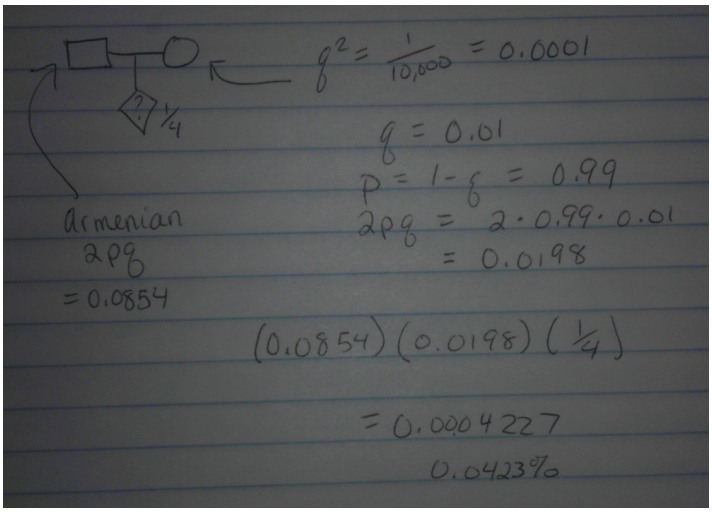
| Mutation: | *GAL* gene transcription<br>Gal - | Gal + |
|---|---|---|
| No mutations | **ON** **OFF** | **ON** **OFF** |
| Deletion of the Gal4 DNA-binding domain | **ON** **OFF** | **ON** **OFF** |
| Deletion of the Gal80 protein | **ON** **OFF** | **ON** **OFF** |
| Deletion of the allosteric site on Gal 3 | **ON** **OFF** | **ON** **OFF** |

Question 4: Familial Mediterranean Fever (FMF) is an autosomal recessive disease, characterized by recurrent attacks of fever, inflammation of the abdominal lining (peritonitis), inflammation of the lining surrounding the lungs (pleurisy), painful swollen joints and a characteristic ankle rash. Within the Armenian population, FMF is estimated to affect 1 in 500 individuals. Worldwide, the prevalence of FMF is about 1 in 10,000.

a) An Armenian woman with a brother affected by FMF marries an Armenian man with no immediate family history of FMF. What is the probability that this couple will have a child affected by FMF? Show your work!




b) The couple above separate, and the Armenian man (with no family history of FMF) marries a different woman that is not of Armenian descent and has no family history of FMF. What is the probability that this couple will have a child affected by FMF? Show your work!



Question 5

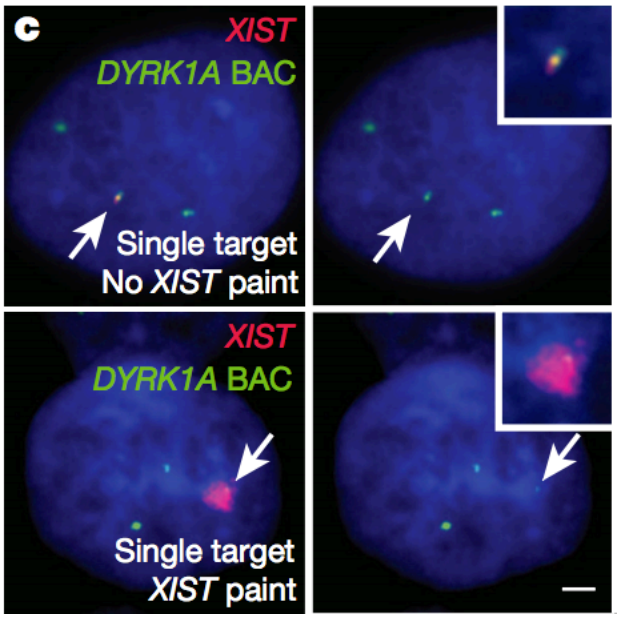
Explain ***why*** additional copies of autosomes are typically lethal in humans, whereas additional copies of the X chromosome cause very few negative phenotypes.

Additional copies of the X chromosome can be "turned off" by X chromosome inactivation, thereby normalizing the gene dosage. Additional copies of autosomes cannot be shut off, and so the gene dosage is too high and the organism cannot survive.

Question 6: Describe two ways in which the basic process of gene regulation differs between prokaryotes and eukaryotes.

Many possible responses, including:
ground state in prok. is on and in euk. its off
euk. have chromatin and prok. don't
euk. have extensive regulation by distal regulatory elements and prok. don't
prok. have several genes organized into a operon (multiple proteins made from a single mRNA) and euk. have only one-mRNA-to-one-protein.

Question 7 (10 points): In the article "Translating Dosage Compensation to Trisomy 21" by Jiang et al., the authors inserted the *XIST* gene into a copy of chromosome 21 in order to silence the chromosome. Below is a panel of Figure 1 that demonstrates that the authors were successful in targeting the *XIST* gene to the correct chromosome.




Legend, Figure 1C: DNA/RNA FISH in interphase Down's syndrome iPS cells shows thatXIST overlaps one of three DYRK1Agenes (left panels and insets) in a non-expressing cell (top, arrows), and a cell induced to express a large XIST RNA territory over theDYRK1A locus after 3 days in doxycycline (bottom, arrows). Right panels show green channel (DYRK1A) alone. Nuclear DNA is stained with 49,6-diamidino-2-phenylindole (DAPI blue). Scale bar, 2mm.

a) What technique is being used to detect *XIST* RNA and Chromosome 21 gene loci in this figure? Briefly explain how this technique works.

Fluorescence In situ hybridization

Probe hybridizes to Xist RNA and contains a red fluorescent marker, indicates the location of Xist RNA expression.

b) How can the authors be sure that the red signal they see coming from this cell is from *XIST* RNA on the targeted chromosome 21 and not a normal X chromosome?

One way is that the cells are male, so their shouldn't be an endogenous Barr body

Another way is the colocalization with the DYRK1A locus, which wouldn't occur on the X chromosome