Biol 321  Winter 2010  Final Exam  [80 points]

NAME________________________________________

•  REMEMBER: carefully inspect problems and pay attention to detail!
•  YOU ARE NOT ALLOWED TO USE CALCULATORS OR CELL PHONES DURING THIS EXAM or to send or receive signals of any kind
•  READ EACH QUESTION CAREFULLY BEFORE ANSWERING.
•  REMEMBER: carefully inspect problems and pay attention to detail!

This exam is divided into two sections:
Section 1: 50 pts total.  You must answer every question in this section
Section 2: 30 pts total.  You must answer two of the four options

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Section 1 (50 pts.) You must answer each question in this section

1. a. (2 pts.) What is the estimate for the total number of genes in the (haploid) human genome?

b. (3 pts.) Here is a quote from a Science paper published this week. “We analyzed the whole genome sequences of a family of four, consisting of two siblings and their parents. Family-based sequencing allowed us to …………….. directly estimate a human intergeneration mutation rate of ~1.1 \times 10^{-8} per position per haploid genome.”

How many total base pair differences were detected between a particular child and its parents? Show your work and circle your answer.

2. (3 pts.) In two sentences or less, define a neutral mutation. NOTE: I am looking for a general definition here NOT an example.

3. (6 pts.) A map of the Drosophila X chromosome is shown on the data sheet (pg **).

(i) A female of genotype ${lz^+ \text{cv}^+ / lz \text{cv}}$ is crossed with a phenotypically wild-type male. All female progeny are wild-type. The percentage of males who will be wildtype for both traits is: a. 7%  b. 14%  c. 43%  d. 50%  e. 86%  f. not enough info to determine.

(ii) Answer the same question for a female of genotype ${bb^+ \text{sc} / bb \text{sc}^+}$. a. 0%  b. 17%  c. 25%  d. 34%  e. 50%  f. 66%  g. not enough info to determine.

(iii). Survey the gene names. In one sentence using proper terminology, how were most (if not all) of these genes named?

4. (2 pts.) Recall the assigned reading on Mutation or Polymorphism? By each statement circle True/False/Not addressed in the article. Answer false if any part of the statement is false.

T  F  N  Any new sequence variant, even if it is neutral or beneficial, will start off as a rare mutation.

T  F  N  Although polymorphic sequence variants usually do not cause overt debilitating diseases, this generalization does not apply in all cases, as a sequence variant may be considered a rare disease mutation in one population and a beneficial polymorphism in another
In the life cycle of wasps and bees, unfertilized eggs develop as haploid males while fertilized eggs develop as diploid females.

Wild-type wasps have "dark purple" eyes. Mutants with scarlet eyes have been isolated. **Experiment 1:** Your lab partner isolates two recessive mutations resulting in a scarlet-eyed phenotype (called Scarlet 1 & 2). He crosses true-breeding females of one mutant strain with males of the other mutant strain and observes female progeny with wild-type (purple) eyes. **Experiment 2:** Your lab partner then allows the F1 females to lay eggs unmated. He examines 100 male progeny: 99 have scarlet eyes and 1 has wildtype (purple) eyes.

Choose all correct restatements of these data:

a. This is a linkage test showing that the Scarlet 1 and Scarlet 2 mutations are alleles of the same gene.
b. This is a complementation test showing that the Scarlet 1 and Scarlet 2 mutations are alleles of different genes.
c. The Scarlet 1 and Scarlet 2 mutations are linked on the same gene
d. The genes mutated in the Scarlet 1 and Scarlet 2 strains assort independently and are likely to be located on different (non-homologous) chromosomes.
e. The genes mutated in the Scarlet 1 and Scarlet 2 strains are closely linked.
f. None of the conclusions is a valid restatement of the data.

5. (2 pts.) Circle all correct answers. An individual line represents:

a. a double-stranded DNA molecule
b. one strand of a double-stranded DNA molecule
c. a chromatid
d. a duplicated homolog
e. none of these interpretations is correct
6. (8 pts.) The pedigree below (in duplicate) shows the inheritance pattern of a disease caused by a completely penetrant, autosomal dominant mutation that is 10 map units from a polymorphic marker locus (that has no phenotype on its own). The marker locus has three alleles, numbered 1, 2 and 3. The phenotypes of the individuals A and B (indicated with question marks) are unknown.

a. (2 pts.) Ignoring the genotypes of the polymorphic marker locus, what is the probability that both kids (A & B) are heterozygous for the disease allele? Show your work and circle your answer.

b. (2 pts.) Using proper notation for linked alleles, indicate the genotypes of the parents of A & B. Don’t forget to define your allele symbols.

b. (2 pts.) Taking into account the genotypes of the linked marker locus, what is the probability that individual A is heterozygous for the disease allele? Show your work and circle your answer.

c. (2 pts.) If individual B is the product of parental gametes only, what is the probability that she is homozygous for the normal allele. Show your work and circle your answer.
7. (5 pts) Recall the discussion in class of the Braf protooncogene which is mutated in many cancers including about 50% of all melanomas examined to date. The third article in the New York Times series described how the anti-Braf magic bullet that sent many melanoma patients into remission was not a long-term cure. The researchers speculate that the resurgence of the cancers might result from selection for cells that have other driver mutations in addition to the Braf mutations. Using proper terminology, briefly describe what types of mutations could act as drivers in a cancer cell. 2 sentences. Be very explicit. You don’t need to name specific genes, but you should name gene categories. List all possibilities and indicate loss vs gain-in-function.

8. (5pts.) In three sentences of less, decode this statement: SNPs can be easily detected as RFLPs after PCR and restriction digest. Feel free to add a labelled figure or diagram.
9. (pts.) R-spondin revisited. See pg 2 of data sheet for info taken from a paper entitled: R-spondin1 is essential in sex determination, skin differentiation and malignancy.

Here is the abstract of the paper:
R-spondins are a recently characterized small family of growth factors. Here we show that human R-spondin1 (RSPO1) is the gene disrupted in a syndrome characterized by XX sex reversal, palmoplantar hyperkeratosis and predisposition to squamous cell carcinoma of the skin. Our data show, for the first time, that disruption of a single gene can lead to complete female-to-male sex reversal in the absence of the testis-determining gene, SRY

True/False/Not enough Info to decide. Answer false if any part of the statement is false. If there are two statements the first statement is true and you are to decide if the second statement is true or false. 2pts if explanation required; otherwise 1pt per question.

T    F    N These researchers used a positional cloning strategy to identify the specific gene that was mutated in this disease state. This information suggests that the researchers suspected from the outset that the R-spondin gene coded for a growth factor.

One sentence defense of your answer.

T    F    N (Examine data on extra sheet.) Unaffected family members are heterozygous for many of the molecular polymorphisms examined (listed on the right) whereas affected family members tend to be homozygous for these same loci.

T    F    N (Examine data on extra sheet.) The box on the right side of the figure indicates the disease gene lies outside of this particular region of chromosome 1

T    F    N (Examine data on extra sheet.) Individual IV7 carries a paternal chromosome that is either the product of double cross over event between the same two chromatids or a new mutation due to strand slippage (during DNA replication in her father’s germline).

One sentence defense of your answer.

T    F    N (Examine data on extra sheet.) Since individual AN from family A is homozygous for a different haplotype from Family F, he is likely to be homozygous for a mutation in a different gene.

One sentence defense of your answer.

T    F    N (Examine data on extra sheet.) Individual IV 4 in Family F is likely to be heterozygous for the mutation.

One sentence defense of your answer.
Section 2 (30 pts): This section consists of four 15 pt problems. You must answer TWO of these problems. If you answer more than two, you must indicate which ones I should grade. Otherwise, I will grade the first two questions that have answers.

1. Essay: I am what I am
2. Data analysis: direct detection of mutation
3. Cross analysis: genotypes & gene interactions
4. Data analysis: PWS

Section 2 Option 1 ESSAY
“i yam what i yam!”

See cartoon on pg1 of data sheet. Fully explore Popeye’s statement in the context of what you have learned this quarter about the relationship between genotype and phenotype:

• Be sure to address both simple (single-gene) and complex traits.
• Illustrate each of your major points with specific examples. At least one example should be relevant to the cartoon – in a general sense at least. You can use hypothetical examples; be imaginative but don't let your creativity get in the way of the science.
• Figure/diagrams are fine but you must also include text that explains it/them.
• NOTE: this is a serious question. Your essay will be graded on content, coherence and the proper use of scientific/genetic terminology.

Hints for writing an effective essay:

• Your essay should be in paragraph form. A list of talking points is not sufficient.
• Use proper genetic terminology.
• Take time to organize the major points of your essay before you start writing.

PUT ESSAY ON the extra sheet of paper included with your test
Kidney stones affect 12% of males and 5% of females in the western world, and are familial (inherited) in 45% of patients. They are commonly associated with hypercalciuria (high urinary calcium levels). The family discussed in this problem exhibits a variety of phenotypes, including hypercalciuria, resulting from a mutation in the gene CLCN5, which codes for a kidney chloride channel.

The molecular data show direct detection of the mutation in the CLCN5 gene. Note that the TaqI is a restriction enzyme from Thermus aquaticus, different from Taq DNA polymerase. Its recognition sequence is 5’TCGA3’.

(a). Given this trait is dominant, is it X linked or autosomal? Briefly explain your answer, indicating relevant observations.

(b). Examine the table of mutations. Is this a gain or loss-of-function? Explain very briefly.

(c). II#3 is expecting another child. Her brother (II#1) recently died from this disease state, and she decides that a prenatal test is in order. She wants to know whether the test will tell her for sure whether her child will die of end stage renal failure.

What do you tell her? Be very explicit about what can and cannot be said with certainty.

(d). For this part of the question, assume individual I#1 has hypercalciuria, but none of the other phenotypes. Taking all of the information given into account (including his genotype), provide two different possible explanations for this observation.
Many genes function in fruitflies to specify the production and distribution of body hairs. You have a true-breeding line of wild-type fruitflies (normally hairy). One day, buzzing around your mangoes, you find a remarkable female fly that is bald. You do the series of crosses shown below. Define allele symbols and fill in the genotypes for the parental, F1 and F2 animals in each cross. For the F1 Cross C give predicted outcomes of cross: genotype and phenotype ratios.

### Allele symbols (indicate dominance):

### Type of gene interaction:

<table>
<thead>
<tr>
<th>Parental</th>
<th>wildtype (normally hairy) X bald</th>
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</thead>
<tbody>
<tr>
<td>F1</td>
<td>1/2 F1 extra hairy</td>
</tr>
<tr>
<td></td>
<td>1/2 F1 wild-type (normally hairy)</td>
</tr>
</tbody>
</table>

**F1 Cross A:**  extrahairy F1 males X extrahairy F1 females:

| F2       | 9/16 Extrahairy                  |
|          | 3/16 wild-type (normally hairy)  |
|          | 4/16 bald                        |

**F1 Cross B:**  wildtype (normally hairy) F1 males X wildtype F1 females:

| F2       | 3/4 normally hairy               |
|          | 1/4 bald                         |

**F1 Cross C:**  extrahairy F1 males and wildtype F1 females:

<table>
<thead>
<tr>
<th>F2</th>
<th>Give genotypic and phenotypic ratios for the progeny of this cross</th>
</tr>
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Section 2 Option 4  DATA ANALYSIS

See pg 4 of data sheet about Prader-Willi syndrome.

(i). Examine the gel. What does the difference in PCR product length represent? In other words, what is the molecular basis of the polymorphism. One sentence.

(ii). Examine the pedigree and gel data on the extra sheet. What is surprising about the genotype of the affected child (#2)? Be explicit.

(iii). Non-disjunction refers to a situation where either paired homologs or sister chromatids fail to separate during a cell division. The gamete that #2 received from his mother was produced by non-disjunction of chromosome 15 during meiosis in her germline. Assuming no crossing-over between the site of the microsatellite polymorphism and the centromere, in which meiotic division did the non-disjunction event occur?  
Circle the correct answer:

- a. Meiosis I
- b. Meiosis II
- c. either Meiosis I or II
- d. not enough info to determine

Defend your answer with a labelled diagram and one or two sentences of text. Don’t show all stages of meiosis - just the most relevant one(s). Be sure to label division and stage.

(iv) Now assume that a cross-over event did occur between the site of the microsatellite polymorphism and the centromere. In which meiotic division did the non-disjunction event occur?  
Circle the correct answer:

- a. Meiosis I
- b. Meiosis II
- c. either Meiosis I or II
- d. not enough info to determine

Defend your answer with a labelled diagram and one or two sentences of text. Don’t show all stages of meiosis - just the most relevant one(s). Be sure to label division and stage.

(v) Reread the introduction to the problem. Why does #2 have PWS?  
2 sentences max.