Biol 322 F12 Study Problems for Final Quiz

The final quiz is worth 47 points and will be held on Tues Dec 11 at 10:30 in CB385.

Fair game for the final quiz

- RNAi lab and lecture
- Model organisms & Forward and Reverse genetics
- Nasonia lab and complementation
- A do-over of the him-5 question from the last quiz
- One 5 (all-or-nothing) dilution problem
- Basic Mendel: segregation and independent assortment
- Chi square analysis
- Handouts, lecture material and problem sets covering the above topics
- The final quiz will include one question lifted directly from this study sheet

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1. *C. elegans* "rollers" are animals to move in a circle rather than a straight line. Your lab partner does a mutant hunt for new roller strains. He finds one which he names Roller #2. Using various dpy and unc genetic markers, he shows that his new roller mutation is tightly linked to the *rol-1* gene on chromosome III. From this work he concludes that his new mutation is an allele of the *rol-1* gene. *He decides to do some follow-up experiments which involve the following crosses with true-breeding strains:*

Parental *Roller #1 males X Roller #2 hermaphrodites*

↓

F1 Progeny *wild-type (non-roller)* hermaphrodites and males

↓ self

F2 1/2 wild-type (non-roller)
1/2 roller

a. Your lab partner does not know how to explain these data. He comes to you for help. ***Using proper terminology***, in 1-2 sentences, briefly explain what is going on in the F1 and the F2 generations.

b. Define allele symbols and indicate the genotypes **(using proper notation) for the parental, F1 (cross progeny only) and F2 generations. Respect allele symbols and use *proper allele notation*. Use an extra sheet of paper if desired.**

2. ***Deaf by Design*** *Multiple choice*
Recall that John and Karen are both deaf but that genetic testing has shown that it was extremely unlikely that they would have a deaf child. Assuming that both are deaf due to a single gene mutation, the best interpretation is:

a. Since mutations in a relatively large number of gene are known to cause inherited deafness, the offspring of John and Karen will have to show complementation.
b. Since mutations in a relatively small number of gene are known to cause inherited deafness, the offspring of John and Karen will have to fail to complement.
c. John and Karen are homozygous for mutant alleles in two different genes; these genes complement and are likely to be unlinked.
d. John and Karen are homozygous for mutant alleles in two different genes; their offspring will show complementation.
e. John and Karen are homozygous for mutant alleles in two genes that assort independently; a non-deaf offspring will be produced.
f. None of these statements accurately describes the situation as described in the article.

3. Exerpt from Wolf Wiki: FILL in the blanks:

_____ **genetics** refers to the process of identifying a phenotype and then characterizing the mutant gene that is responsible for that phenotype. This approach would involve mutagenizing a population and conducting a screen for a particular phenotype. Once the mutant phenotype is characterized, the mutation is mapped to determine which gene's or protein's activity is being affected.

_____ **genetics** involves starting with a known gene and then disrupting the function of that gene to produce a phenotype and gain insight into what that gene does. For well-characterized species such as *Arabidopsis*, genetics tools are abundant: T-DNA insertional mutants have been produced by a number of groups. If a researcher wishes to obtain information about the function of a candidate gene, he/she may request a T-DNA insertion line and begin a detailed phenotypic analysis.

4. " To study biological processes, geneticists employ a policy of destruction *while biochemists employ a policy of reconstruction"*

In 4-6 well-crafted sentences explain the geneticist half of the statement.

- Be sure to use & explain the terms ***forward genetics*** and ***reverse genetics*** in your answer.
- Take a couple of minutes to think through your answer before you start writing.
- Give a specific example

5. a. Recall our C. elegans RNAi experiment. Was this experiment an example of forward or reverse genetics? Defend your answer in one sentence.

b. Read the abstract below edited from a recent Science paper.

- Is this experiment an example of forward or reverse genetics? Defend your answer in one sentence.
- What is insertional mutagenesis? Give one specific example from a lab exercise or reading assignment this quarter.

Haploid Genetic Screens in Human Cells Identify Host Factors Used by Pathogens

Jan E. Carette,[1] Carla P. Guimaraes,[1] Malini Varadarajan,[1] Annie S. Park,[1] Irene Wuethrich,[1] Alzbeta Godarova,[1] Maciej Kotecki,[2] Brent H. Cochran,[2] Eric Spooner,[1] Hidde L. Ploegh,[1,3] Thijn R. Brummelkamp[1,*]

Loss-of-function genetic screens in model organisms have elucidated numerous biological processes, but the diploid genome of mammalian cells has precluded large-scale gene disruption. We used random insertional mutagenesis to generate null alleles in a human cell line haploid for all chromosomes except chromosome 8. Using this approach, we identified host factors essential for infection with influenza by screening mutant lines for resistance to HlN1 influenza virus. This approach has both conceptual and practical parallels with genetic approaches in haploid yeast and other model organisms.

6. See crosses on next page.

(i) Choose the statement that describes <u>experiment #2</u> most accurately.

a. This is a set of complementation tests that tells you which of the genes are linked.

b. This is a set of complementation tests that tells you how many different genes in Drosophila can be mutated to produce a short-wing phenotype.

c. This is a set of complementation tests that tells you how many different genes are mutated in this set of short-winged mutants and which strains have mutations in the same gene.

d. This is a set of complementation tests that tells you how many different genes are mutated in this set of mutants and whether the genes are linked or unlinked.

e. None of these statements accurately describes what you can determine from this set of crosses.

(ii) From the data in tables #1 and #2, you can conclude that this collection of short-winged strains represents mutations in at least five different genes.

a. True **b.** False c. Not enough information

Explain/defend your answer (no credit if no explanation):

(iii) The mutation in strain #5 could be allelic with the mutation in strain #3.

a. Yes, this is consistent with the data given

b. No, the data eliminate this possibility

Explain/defend your answer (no credit if no explanation):

Six mutant strains (#1 - 6) of Drosophila have been identified that have shorter wings than wild-type. Two sets of experiments are performed with the mutant strains. All strains used are truebreeding.

Experiment #1: Reciprocal crosses between mutant and wild-type:

Parent		Progeny		
Female	Male	female	male	
M#1	wt	wt	wt	wt = wild type (long wing)
wt	M#1	wt	wt	
				m = mutant (short wing)
M#2	wt	wt	wt	
wt	M#2	wt	wt	
M#3	wt	wt	m	
wt	M#3	wt	wt	
M#4	wt	wt	wt	
wt	M#4	wt	wt	
M#5	wt	m	m	
wt	M#5	m	m	
M#6	wt	wt	wt	
wt	M#6	wt	wt	

Experiment #2: The mutant strains are crossed to each other and the F1 examined:

		Female Parent 1	2	4	6	
Male parent	1	--	+	+	+	-- means all progeny mutant
	2	+	--	+	+	+ means all progeny wild-type
	4	+	+	--	+	
	6	+	+	+	--	

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7. Read each statement carefully and then indicate whether the statement is TRUE or FALSE. Answer false is any part of the statement is false.

a. Biologists believe that RNA predated DNA and proteins in the evolution of living systems because it is functionally a more versatile molecule than DNA.
Circle: True or False ***One sentence explanation:***

b. The researchers who initially discovered evidence for RNAi had a hunch that there were basic cellular processes still to be uncovered that had been overlooked by molecular biologists in 1960s, 70s & 80s. *Circle: True or False*

c. The dicer component of RNAi systems is responsible for making the endonucleolytic cut that destroys the target mRNA
Circle: True or False ***One sentence explanation:***

d. In principle, C. elegans RNAi knockdown "feeding" libraries could be used in both forward and reverse genetic screens.

e. The source of dsRNAs that trigger RNAi can either be exogenous or endogenous; an example of the latter would be normal transcription of specific type of non-protein coding sequences. *Circle: True or False*

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8. ESSAY Your mom is an avid reader of the New York Times. In the Jan 16. 2003 issue she sees the following article:

From Worm Genes, Human Obesity Clues by Nicholas Wade

"Biologists at MIT have laid a new basis for studying human obesity by identifying almost all the genes that regulate fat storage and metabolism in a small animal, the laboratory roundworm.

The finding should provide leads to the many unknown genes that regulate fat storage in people and to the defects in the genes that underlie many obesity cases……."

Your mom is an astute individual, but she is a bit mystified with respect to the relationship between worms and humans and wonders how the statement in the second paragraph can be justified. She phones you (or maybe sends an email) and asks you to explain all of this to her. ***Briefly discuss the rationale for studying an organism like C. elegans. In your essay be sure to include the following:***

- explicit definition of a model organism
- two specific advantages of studying a model organism
- an explicit discussion of why what we learn about one organism can often be applied to understanding a different organism
- Please take time to organize your thoughts before you start writing

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9. Read through the entire question before you answer it. Don't forget about haplodiploidy: segregation patterns in male reflect the meiotic output in the female.

You are interested in the genetic control of eye development in insects and you choose to use a forward genetics approach with the model *Nasonia vitripennis*. In the progeny of mutagenized females you discover a male with very small eyes. You name this male Squinty. You cross the mutant male with wild-type females from a true-breeding line – see outcome of crosses on next page.

Part 1

a) First, define allele symbols assuming that this is a standard single gene trait. Indicate genotypes of parents, F1 and F2 progeny. *What F2 progeny ratios do you predict under this scenario?*

b) You re-inspect the data and conclude that the Squinty phenotype results from a combination of mutations in two different genes (that assort independently). You also propose that a wasp carrying a mutation in only one of these genes has a wild-type phenotype. Indicate genotypes of parents, F1 and F2 progeny. *State clearly why this explanation fits the F2 data.*

c) Your somewhat contentious lab partner argues that your data doesn't eliminate the possibility that the Squinty phenotype is a single gene trait. In other words, she thinks that you have come up with a complicated explanation without sufficient experimental evidence. ***What is your response to your lab partner's criticism? Do the appropriate chi square calculation and state explicitly in words what, from the statisticians viewpoint, your calculations tell you.***

d) Your lab partner's response to your statistical arguments is that there are other explanations for your data. He thinks that you haven't considered the issue of penetrance or other factors that might affect the number of squinty males observed. Re-explore the data in this context. NOTE, you don't have to do additional chi square calculations, but rather explore explanations for the data set other than what you proposed in part b

Part 2: *Nasonia* has a sequenced genome (hooray!) and the usual sets of shared genes (recall Genes We Share lecture) with predicted molecular functions as well as some genes that are specific to the hymenoptera (bees wasps ants). Your lab partner is big into Reverse Genetics and thinks that you are using the wrong approach with your forward genetics.

- Briefly explain how you might handle a reverse genetics approach. Be sure to make it clear how a reverse genetics approach would differ from your original experiment.
- Mention how you might abrogate gene function. Just suggest one possibility.
- Be as explicit as possible.
- 5-6 sentences here or a detailed, labeled diagram or flow chart (with a one sentence caption.

Part 1 a Genotypes if single gene trait:

Parental Wild-type females X squinty male

↓

F1 wild-type females and males

↓

set F1 females unmated and collect male progeny

F2 15 wild-type males
5 squinty males

Part 1 b Genotypes if two gene trait:

Parental Wild-type females X squinty male

↓

F1 wild-type females and males

↓

set F1 females unmated and collect male progeny

F2 15 wild-type males
5 squinty males

$$\chi^2 = \sum \frac{|O - E|^2}{E}$$

df	0.995	0.99	0.975	0.95	0.90	0.10	0.05	0.025	0.01	0.005
1	---	---	0.001	0.004	0.016	2.706	3.841	5.024	6.635	7.879
2	0.010	0.020	0.051	0.103	0.211	4.605	5.991	7.378	9.210	10.597
3	0.072	0.115	0.216	0.352	0.584	6.251	7.815	9.348	11.345	12.838