

ANSWERS TO Problem set questions from Exam 3 – Eukaryotic Gene Regulation, Genome Modifications in Eukaryotes, Population Genetics

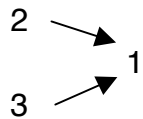
Characterizing novel pathways that control the expression of yeast genes

1. You are studying regulation of the yeast enzyme glutamine synthetase (GS), which is encoded by the GLN1 gene.

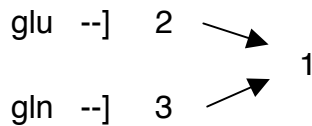
(a) they are both activators, because recessive trans uninducible

(b) $3 \rightarrow 2 \rightarrow 1$

$2 \rightarrow 3 \rightarrow 1$



(c)



(d) never express GS no matter what conditions

(e) 300 – 250 is the glu response element, is a UAS, may bind GLN2

200 -- 100 is the gln response element, is a UAS, may bind GLN3

50 -- 1 is the promoter

(f) with neither amino acid added = 50

with only glu added = 50

with only gln added = 0

(g) with neither amino acid added = 0

with only glu added = 0

with only gln added = 0

2. Consider a eukaryotic gene regulatory pathway where a small molecule X activates the expression of a reporter gene.

(a) $X \rightarrow A \rightarrow B \rightarrow$ reporter gene

OR

$X \rightarrow B \rightarrow A \rightarrow$ reporter gene

(b) A always activates B, regardless of whether X is present (upper model)

OR

A always activates the reporter gene, regardless of whether B is activated or not (lower model)

(c) if the upper model is correct, you would get a 1 PD: 1 NPD: 4 TT ratio

PD	NPD	TT
Constitutive	uninducible	regulated
Constitutive	uninducible	uninducible
Uninducible	regulated	constitutive
Uninducible	regulated	uninducible

if the lower model is correct, you would get a 1 PD: 1 NPD: 4 TT ratio

PD	NPD	TT
Constitutive	constitutive	regulated
Constitutive	constitutive	constitutive
Uninducible	regulated	constitutive
Uninducible	regulated	uninducible

(d) the F1s would all be constitutive, regardless of the model for the F2s:

if the upper model is correct, you would get a ratio of 9 constitutive: 3 uninducible: 3 regulated: 1 uninducible

if the lower model is correct, you would get a ratio of 9 constitutive: 3 constitutive: 3 regulated: 1 uninducible

3. You are studying the regulation of an enzyme in yeast.

(a) both trans

(b)

<u>Type 1</u>	<u>Type 2</u>	<u>Type3</u>
regulated (1+ 2+)	regulated (1+ 2+)	constitutive (1 ⁻ 2+)
regulated (1+ 2+)	constitutive (1 ⁻ 2+)	constitutive (1 ⁻ 2+)
uninducible (1 ⁻ 2 ⁻)	uninducible (1 ⁻ 2 ⁻)	uninducible (1+ 2 ⁻)
uninducible (1 ⁻ 2 ⁻)	uninducible (1+ 2 ⁻)	uninducible (1+ 2 ⁻)

(c) no

(d) uninducible

(e) inducer --] 1 --] 2 → reporter gene

4. You have discovered a gene in yeast that is involved in repairing damaged DNA.

(a) repressor, because constitutive, trans, recessive

(b) UV --] Reg1 --] Rad66

(c) UV --] Reg1 --] Reg2 → Rad66

OR

UV → Reg2 --] Reg1 --] Rad66

(d) constitutive

(e) UV → Reg2 --] Reg1 --] Rad66

(f) region 2 is the Reg1 binding site, and region 6 is the promoter

(g) The DNA sequence of regions 3 – 5 are not necessary for proper Rad66 regulation, and the spacing between elements 2 and 6 is not critical.

5. In the examples of gene expression that we have covered in class, the genes were regulated in some way or another.

(a) yes, at 27 cM

(b) zero

(c)



(d) Con 1 binds region 4, and Con2 binds region 2

Altering the genomes of mice -- Transgenics and Gene targeting

1. You hypothesize that a loss of function of the *Pindrop* gene is the cause of the recessive phenotype of deafness in a strain of mice called the *Ard* strain.

- (a)
- i) gene targeting
 - ii) the *Pindrop* gene, with a antibiotic resistance gene disrupting that gene
 - iii) ES cells
 - iv) wild-type ES cells
 - v) at the *Pindrop* gene locus
 - vi) yes it would make a chimera
 - vii) you would have to breed the chimeric heterozygote to wild-type to generate a non-chimeric heterozygote. You would then have to mate two non-chimeric heterozygotes together, and 1/4 of their offspring would be the animal you are looking for.
 - viii) if the mouse is deaf, then *Pindrop* is required. If the mouse can hear, then *Pindrop* is not required.

(b) breed the mice from above to the *Ard* strain. If the resulting animals are deaf, then *Pindrop* was mutated in the *Ard* strain. If the resulting animals can hear, then a different gene was mutated in the *Ard* strain.

- (c)
- i) transgenic
 - ii) the wild-type human *Pindrop* gene
 - iii) egg
 - iv) homozygous *Pindrop* mutant egg
 - v) randomly
 - vi) no
 - vii) none
 - viii) if the mouse is deaf, then human and mouse are not interchangeable. If the mouse can hear, then the human and mouse genes are interchangeable.

2. In mammals, including humans and mice, growth hormone (a protein) is speculated to play a prominent role in determining adult size.

(a) i) transgenic

ii) the wild-type mouse GH gene

iii) egg

iv) wild-type egg

v) randomly

vi) no

vii) none

viii) if the mouse is bigger, then more copies of GH do yield larger mice. If the mouse is not bigger, then more copies of GH is ineffective.

(b) i) gene targeting

ii) the GH gene, with a antibiotic resistance gene disrupting that gene

iii) ES cells

iv) wild-type ES cells

v) at the GH gene locus

vi) yes it would make a chimera

vii) you would have to breed the chimeric heterozygote to wild-type to generate a non-chimeric heterozygote. You would then have to mate two non-chimeric heterozygotes together, and 1/4 of their offspring would be the animal you are looking for.

viii) If the mouse is smaller, then one copy of GH is not sufficient to control size normally. If the mouse is normal size, then one copy of GH is enough for sufficient GH function.

(c) breed two mice from part **(b)** and 1/4 of their offspring will have zero copies of GH

(d) breed two mice from part **(a)** and 1/4 of their offspring will have four copies of GH

(e) i) transgenic

ii) the wild-type mouse GH gene

iii) egg

iv) an egg created by the breeding of two mice from part **(d)**

v) randomly

vi) no

vii) none

viii) if the mouse is bigger, then more copies of GH do yield larger mice. If the mouse is not bigger, then more copies of GH is ineffective.

(f) breed two mice from part **(e)** and 1/4 of their offspring will have six copies of GH

3. As we will study later in the semester, there are genes in the human and mouse genomes that control cell proliferation.

- (a) yes
- (b) yes
- (c) a transgenic mouse, because the process is quicker and requires less mating
- (d) add a mutant copy of the Ras gene
- (e) the mutant copy of the Ras gene would insert randomly
- (f) wild-type fertilized egg
- (g) no further steps
- (h) no
- (i) yes
- (j) you don't have a choice
- (k) disrupt both copies of the Rb gene
- (l) the Rb gene that is disrupted by a gene encoding antibiotic resistance, which would insert at the endogenous Rb locus
- (m) wild-type ES cells
- (n) you would have to breed the chimeric heterozygote to wild-type to generate a non-chimeric heterozygote. You would then have to mate two non-chimeric heterozygotes together, and 1/4 of their offspring would be the animal you are looking for.

4. Many mouse genes are expressed in a “tissue-specific” manner; that is, the genes themselves are present in all cells in the body, but the genes are expressed (transcribed and translated) in only one of the animal's many tissue types.

- (a) no
- (b) homozygotes should have the same expression pattern as heterozygotes
- (c) your transgene, when it randomly inserted, must have inserted into a locus that is important for heart function
- (d) Just make another transgenic mouse – there is essentially no way that the transgene will randomly insert into the same locus for heart function
 - i) transgenic
 - ii) the LacZ gene under the control of the amylase promoter
 - iii) egg
 - iv) a wild-type egg
 - v) randomly
 - vi) no
 - vii) mate two transgenic mice together, and 1/4 of their offspring will be homozygous for the transgene

viii) If the mouse has a heart defect, then the transgene itself causes the heart defect. If the mouse has a heart that is fine, then the insertion site of the transgene in the original mouse is what caused the heart defect.

(e) i) gene targeting

ii) the amylase gene, disrupted by LacZ (without its own promoter) followed by an antibiotic resistance gene

iii) ES cells

iv) wild-type ES cells

v) at the amylase gene locus

vi) yes it would make a chimera

vii) you would have to breed the chimeric heterozygote to wild-type to generate a non-chimeric heterozygote. You would then have to mate two non-chimeric heterozygotes together, and 1/4 of their offspring would be the animal you are looking for.

viii) If the mouse only expresses beta-galactosidase in the pancreas, then amylase is only expressed in the pancreas. If the mouse expresses beta-galactosidase elsewhere also, then amylase is expressed elsewhere also.

Population Genetics – populations at Hardy-Weinberg Equilibrium

1. Consider a rare autosomal recessive trait that is possessed by one in every 3,000 children in the U.S.

(a) $q = 0.018$

(b) $2pq = 2 (0.982) (0.018) = 0.036$

(c) $(1/4) (2pq)^2 = (1/4) [2 (0.982) (0.018)]^2 = 0.00033$

(d) $(1/2) (2pq) = (1/2) (2 * (0.982) (0.018)) = 0.018$

(e) $(2/3) (1/4) (2pq) = (1/6) (2 * (0.982) (0.018)) = 0.006$

(f) $(1/2) (2pq) = (1/2) (2 * (0.9905) (0.0095)) = 0.0095$

2. Consider the gene that determines which blood type a human is (A, B, AB, or O).

(a) $f(I^A I^A) = (0.26)^2 = 0.0676$

$f(I^B I^A) = 2 * (0.26) * (0.07) = 0.0364$

$f(I^B I^B) = (0.07)^2 = 0.0049$

$f(I^A i) = 2 * (0.26) * (0.67) = 0.3484$

$f(I^B i) = 2 * (0.07) * (0.67) = 0.0938$

$f(i i) = (0.67)^2 = 0.4489$

(b) $f(A) = f(I^A I^A) + f(I^A i) = [(0.26)^2] + [2 * (0.26) * (0.67)] = 0.416$

$f(B) = f(I^B I^B) + f(I^B i) = [(0.07)^2] + [2 * (0.07) * (0.67)] = 0.0987$

$f(AB) = f(I^B I^A) = 2 * (0.26) * (0.07) = 0.0364$

$f(O) = f(i i) = (0.67)^2 = 0.4489$

(c) $f(I^A) = 0.5$

$f(i) = 0$

3. In the 1950's, a screening of Europeans revealed that 30% were unable to taste the chemical compound phenylthiocarbamide (PTC).

(a) $q = 0.55$

(b) 0.55

(c) 0.87

(d) 0.64

(e) $q = 0.1$

(f) 0.1

4. Consider two large but completely isolated populations of rabbits: population X (consisting of 100,000 randomly mating rabbits) and population Y (consisting of 50,000 randomly mating rabbits).

(a) $q = 0.1$

(b) 18,000

(c) $\frac{(1/2)(2pq)}{1-q^2} = \frac{(0.68)(0.32)}{0.900} = 0.24$

(d) $p(\text{brown}) = 0.98$

(e) 0.172

(f) $2pq + p^2 = [2 * (0.172)(0.828)] + [(0.828)^2] = 0.97$

(g) one generation

5. In humans, albinism (unpigmented skin, hair, and eyes) is due to an enzymatic deficiency, and it is an autosomal recessive trait.

(a) $q = 0.005$

(b) $p = 0.995$

(c) number of $aa = q^2 * 1,000,000 = 25$

number of $Aa = 2pq * 1,000,000 = 9950$

(d) no

(e) no

(f) $(1/4)(9950/1,000,000)^2 = 2.48 * 10^{-5}$

(g) $2 * (1/4)(9000/999,500)(2 * 0.995 * 0.005) = 2.24 * 10^{-5}$

(h) $1/2 * 2pq = (1/2)(2)(0.005)(0.995) = 5 * 10^{-3}$

Population Genetics – populations not at equilibrium (because of selection and/or mutation)

1. In answering the various parts of this question, assume that mating is random.

(a) $\mu = (1/3000)$

(b) $h = \sqrt{(1/3000)} = 1.83\%$

(c) $2pq = 2 (0.05) (0.95) = 9.5\%$

(d) $q^2 = (0.05)^2 = 0.25\%$

2. Consider a heritable autosomal disease with an incidence in the population of 1 per thousand.

(a) $\mu = 0.0001$

(b) $\mu = 0.0002$

(c) $h = 0.0064$

3. Cystic fibrosis is an autosomal recessive disease that currently affects about 1 in 1600 children in Europe.

(a) $q = 0.025$

(b) lower

(c) lower

4. In practice, it can be very difficult to detect subtle selection for or against the heterozygote for an allele that causes an obvious recessive phenotype.

(a) $\mu = (0.0004)^2 = 1.6 * 10^{-7}$

(b) $q^2 + 0.01q - (0.0004)^2 = 0$

so $q = 0.000016$

(c) $-q^2 + 0.01q + (0.0004)^2 = 0$

so $q = 0.01$

- 5.** Suppose that body color in cockroaches is controlled by an autosomal gene “gene G.”
- (a) $f(g) = 0.01$
 - (b) $\mu = 0.00008$
 - (c) $q = 0.014$
 - (d) $q = 0.33$ (Note that you cannot estimate that $p = 1$ in this part of this problem.)

Population Genetics – populations not at equilibrium (because of non-random mating)

1. In answering the various parts of this question, show your calculations, and state any additional simplifying assumptions that you employ.

(a) $Fq = (1/4) (0.01) = 0.0025$

(b) $Fq = (1/8) (0.01) = 0.00125$

(c) $Fq = (1/64) (0.01) = 1.56 \times 10^{-4}$

(d) $F = (5/16)$

2. “Double first cousins” are the result of either two brothers marrying two sisters, or of a brother/sister pair marrying another brother/sister pair.

(a) $F = (1/8)$

(b) $f(aa) = (0.002)^2 = 4 \times 10^{-6}$

(c) $f(aa) = (80\%) (0.002)^2 + (15\%) (1/16) (0.002) + (5\%) (1/8) (0.002) = 0.000034$

(d) $f(a) = 0.01$

(e) $(1/10,000) = (80\%) q^2 + (15\%) (1/16)q + (5\%) (1/8)q$

so $q = 0.0051$

(f) $= \frac{(15\%) (1/16) (0.0051) + (5\%) (1/8) (0.0051)}{(1/10,000)} = 0.79$

(g) $= \frac{(15\%) (1/16) (0.002) + (5\%) (1/8) (0.002)}{0.000034} = 0.91$

3. Consider two large but completely isolated human populations (populations M and N).

(a) for M: $q = (1/50) = 0.02$

(b) for N: $(1/2500) = (90\%) q^2 + (10\%) (1/16)q$

so $q = 0.018$

(c) for M: $q = (1/5000)$

(d) for N: $q = (1/5000)$

(e) for M: $q = (1/2500)$

(f) for N: $q = (1/2500)$

4. Johnny Lunchbucket and Betty Juicebox were both raised by single mothers.

(a) $F = (1/8)$

(b) $q = 0.0016$

(c) frequency of half-sibling marriages = x

$$\frac{200}{1} = \frac{(1-x)(0.0016)^2}{(0.0002)x}$$

so $x = 0.000064$

(d) $(1/8) + 0.04 = 0.165$

5. In this question we will consider the interaction of selection and inbreeding in determining the incidence of autosomal recessive diseases.

(a) $q = 0.005$

(b) $0 = -S(90\% q^2 + 10\% Fq) + 0.00001$

$$0 = (-0.36)q^2 - 0.0025q + 0.00001$$

so $q = 0.002839$

$$\text{incidence} = (90\%)q^2 + (10\%)(1/16)q$$

so incidence = 0.000025

(c) $q^2 = 8 * 10^{-6}$

(d) rise

(e) $q = 0.005$