

Note: These brief answers are not complete. In many cases, writing exactly what is on this sheet would not be sufficient for full credit. If you are using this answer key to review the material, you should also consult the relevant sections in the book or your lecture notes.

1. (10 points). Compare and contrast the initiation of translation in prokaryotes and eukaryotes. Your answer should incorporate information about differences in gene organization and cellular structure.

This was covered in lecture 14 and chapter 8. The major point are summarized in Figure 8.24 and Table 8.1. Polycistronic mRNAs make operons possible.

For grading, the following point guide was used:

- Prokaryotes: Shine-Dalgarno 2 pts
- Polycistronic 2 pts
- Eukaryotes: Cap scanning 2 pts
- Monocistronic 2 pts

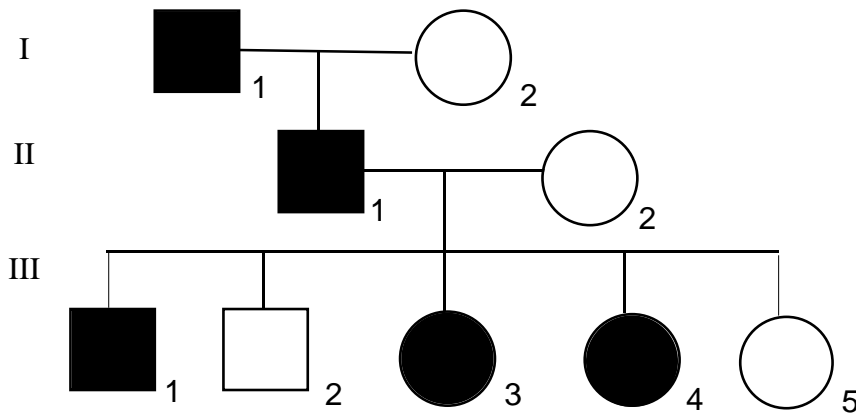
Coupled transcription and translation in prokaryotes 2 pts

2. (10 points) Discuss mechanisms for the elimination of aberrant mRNAs that contain misplaced in-frame translation stop codons. Once again, contrast eukaryotes and prokaryotes, mentioning the role of splicing and mRNA export in this process.

This was covered in lecture 14 (actually, lecture 15, given Nov. 2).

- You needed to describe nonsense-mediated decay (NMD) 4 pts
- including the role of the Exon Junction Complex (EJC) 4 pts
- Rho-dependent termination after premature termination of translation in prokaryotes 2 pts

This pedigree shows a family affected by an autosomal dominant genetic disease. Genotypes for three markers, A, B and C, are shown



The genotypes are:

Your name \_\_\_\_\_

I-1	A <sub>1,3</sub> B <sub>1,2</sub> C <sub>1,2</sub>	III-1	A <sub>1,4</sub> B <sub>1,4</sub> C <sub>1,4</sub>
I-2	A <sub>1,3</sub> B <sub>3,3</sub> C <sub>3,3</sub>	III-2	A <sub>3,4</sub> B <sub>3,4</sub> C <sub>3,4</sub>
II-1	A <sub>1,3</sub> B <sub>1,3</sub> C <sub>1,3</sub>	III-3	A <sub>1,4</sub> B <sub>1,4</sub> C <sub>3,4</sub>
II-2	A <sub>4,4</sub> B <sub>4,4</sub> C <sub>4,4</sub>	III-4	A <sub>1,4</sub> B <sub>1,4</sub> C <sub>1,4</sub>
		III-5	A <sub>3,4</sub> B <sub>3,4</sub> C <sub>3,4</sub>

3. (8 points). Indicate the haplotypes of individual II-1 by checking which of the following are possible (check all that apply):

a) A<sub>1</sub> B<sub>1</sub> C<sub>1</sub> / A<sub>3</sub> B<sub>3</sub> C<sub>3</sub>

d) A<sub>3</sub> B<sub>1</sub> C<sub>1</sub> / A<sub>1</sub> B<sub>3</sub> C<sub>3</sub>

4. (6 points; two points per pair of markers) For each individual in the third generation (III-1, III-2, III-3, III-4 and III-5) indicate whether they are **recombinant**, **nonrecombinant** or **indeterminate** for each pair of **markers** in this pedigree (Fill in each of the 15 squares with **yes**, **no** or **maybe**).

Because the phase of A is unknown, the status of recombination involving A is unknown (indeterminant).

individual	A B recombinant	B C recombinant	A C recombinant
III-1	maybe	no	maybe
III-2	maybe	no	maybe
III-3	maybe	yes	maybe
III-4	maybe	no	maybe
III-5	maybe	no	maybe

5. (4 pt.) Considering only the data for marker locus A (i.e. ignoring B and C), what is the approximate lod score for linkage **between A and the disease gene** with  $\theta = 0$ ?

Either 5 R or 5 NR, so  $Z = \log_{10}[(0.5 \cdot 1^5 \cdot 0^0 + 0.5 \cdot 0^5 \cdot 1^0) / (0.5)^5] = 1.2$

6. (4 pt.) Considering only the data for marker locus **B**, what is the approximate lod score for linkage **between B and the disease gene** with  $\theta = 0$ ?

5 NR, so  $Z = \log_{10}[1^5 \cdot 0^0 / (0.5)^5] = 1.5$

Note that for these questions, I also told you that the maximal lod score ( $\theta = 0$  and no recombinants) is 0.3 per child. (0.3 is  $\log_{10}(2)$ ) and (for problem 4) that not knowing the phase costs you the equivalent of one child.

7. (4 pt.) Considering only the data for marker locus **C**, what is the **approximate** lod score for linkage **between C and the disease gene** with  $\theta = 0$ ?

4 NR, 1 R, so  $Z = \log_{10}[1^4 \cdot 0^1 / (0.5)^5] = \text{negative infinity}$

In other words, linkage at  $\theta = 0$  is excluded.

8. (16 points) This question concerns amorphic (null), neomorphic, hypermorphic and antimorphic dominant alleles. I'm asking you to consider how the mutant phenotype caused by each type of dominant allele is affected by an extra dose of the normal allele (duplication) or by reduced activity (a hypomorphic allele) at the other allele. In the following table, label each of the eight empty squares as **unchanged**, **enhanced** (a more extreme mutant phenotype) or **suppressed** (a less severe mutant phenotype – more like wild-type).

	Dominant/+ The typical situation	Dominant+/+ <i>i.e.</i> an extra dose of the wild-type allele	Dominant/hypomorphic (in trans to a hypomorph)
amorphic	unchanged (compare to this)	suppressed	enhanced
neomorphic	unchanged (compare to this)	unchanged	unchanged
hypermorphic	unchanged (compare to this)	enhanced	suppressed
antimorphic	unchanged (compare to this)	suppressed	enhanced

These are just Muller's rules for each class of dominant. The first case (an amorphic allele that is dominant) is also known as haploinsufficiency. This was presented in lecture 17.

(4 points each).

9. a) It is only when Myc and Max come together in a heterodimer that a transcriptional activator is formed.
10. a) Autozygosity is a term used to refer to homozygosity by descent from a common ancestor.
11. a) In forward genetics, one starts with the mutant phenotype.
12. b) The relation between physical and genetic distances is not constant across the genome; the approximation 1 cM = 1 Mb. is a useful rule of thumb in the case of humans, but the actual value varies widely for different chromosomal regions.
13. a) Alleles at separate loci that are associated with each other at a frequency significantly higher than expected by chance are said to be in linkage disequilibrium.
14. a) Recombinant progeny can result from either the recombination of genes or markers on the same chromosome or by independent assortment of genes on nonhomologous chromosomes.
15. a) Epigenetic imprints generally persist throughout the life of a mammal, but are erased during the passage of a gene through the germ line into the next generation.

16. (10 points)

Define, compare and contrast siRNAs and miRNAs. Spell out the abbreviations, explain what they do, how they work and what species have them. Include a definition of the RISC complex.

This was all explained in lecture 15.

siRNA: small interfering RNA (from dsRNA)

2 pts

miRNA: microRNA (endogenous, from a precursor)

2 pts

eukaryotes have them

1 pt

RISC: RNA-induced silencing complex

2 pts

Mechanism (RISC, mRNA cleavage, translation arrest)

3 pts