
Your name:

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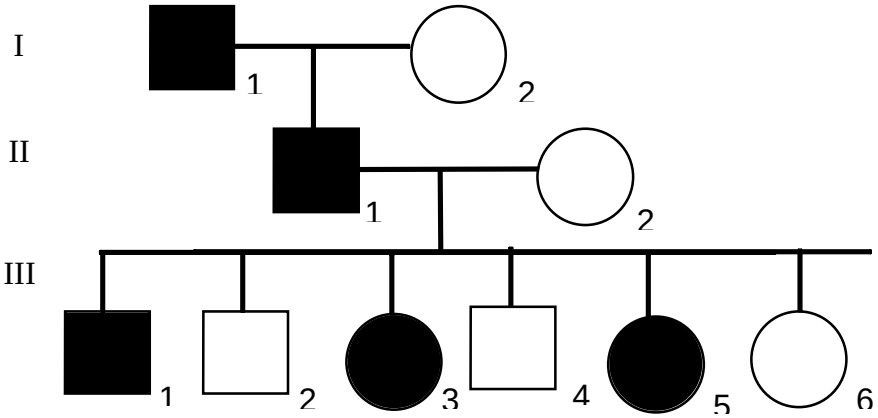
This pedigree shows a family affected by an autosomal dominant genetic disease.
Genotypes for five markers, A through E, are shown



The genotypes are:

I-1	$A_{1,2}$ $B_{1,2}$ $C_{1,2}$ $D_{1,2}$ $E_{1,2}$
I-2	$A_{3,3}$ $B_{3,3}$ $C_{3,3}$ $D_{3,3}$ $E_{3,3}$
II-1	$A_{1,3}$ $B_{1,3}$ $C_{1,3}$ $D_{1,3}$ $E_{1,3}$
II-2	$A_{4,4}$ $B_{4,4}$ $C_{4,4}$ $D_{4,4}$ $E_{4,4}$
III-1	$A_{1,4}$ $B_{1,4}$ $C_{1,4}$ $D_{3,4}$ $E_{1,4}$
III-2	$A_{3,4}$ $B_{3,4}$ $C_{3,4}$ $D_{3,4}$ $E_{3,4}$
III-3	$A_{1,4}$ $B_{3,4}$ $C_{3,4}$ $D_{1,4}$ $E_{1,4}$
III-4	$A_{3,4}$ $B_{3,4}$ $C_{3,4}$ $D_{3,4}$ $E_{3,4}$
III-5	$A_{1,4}$ $B_{1,4}$ $C_{3,4}$ $D_{1,4}$ $E_{1,4}$
III-6	$A_{3,4}$ $B_{3,4}$ $C_{3,4}$ $D_{1,4}$ $E_{1,4}$

1. (12 points; two points per pair of markers) For each individual in the third generation (III-1, III-2, III-3, III-4, III-5 and III-6) of this pedigree indicate whether they are **recombinant**, **nonrecombinant** or **indeterminate** for each pair of **markers listed** (Fill in each of the 36 squares with **yes**, **no** or **maybe**). (Yes, there are another four pairs -- BE, CD, CE and DE -- not listed on the table.)

individual	A B recombinant ?	A C rec.	A D rec.	A E rec.	B C rec.	B D rec.
III-1						
III-2						
III-3						
III-4						
III-5						
III-6						

2. (3 pt.) Considering only the data for marker locus **A** (i.e. ignoring the other markers), what is the approximate lod score for linkage **between A and the disease gene** with $\theta = 0$?

3. (3 pt.) Considering only the data for marker locus **B**, what is the approximate lod score for linkage **between B and the disease gene** with $\theta = 0$?

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4. (3 points) These five marker loci are linked. What is the most likely order on the genome? You know that A is to the left of B. Possibilities are ABCDE, CDEAB, ACDEB, AEDCB etc..

5. (3 points) What is the minimum number of recombination events observed, and which progeny are recombinant (from III-1, III-2, III-3, III-4, III-5 or III-6; **list all that apply**)?

6. (3 points) Which one of the following statements best describes the location of the disease gene?

a) At A	f) Between A and B	k) Between B and D
b) At B	g) Between A and C	l) Between B and E
c) At C	h) Between A and D	m) Between C and D
d) At D	i) Between A and E	n) Between C and E
e) At E	j) Between B and C	o) Between D and E

(4 points each). In each of the following there are two or more statements. One is true. Usually, it is taken directly from your textbook or from my lecture. In other cases, it might come from the scientific literature. Others have been modified so as to be untrue or misleading. Circle the letter next to the one correct statement. In some cases, you might not know enough to be sure that statement is correct but you should be able to identify the others as bogus in some way.

7. DNase I hypersensitivity sites are typically:
   a) cell type-specific and within the coding region.
   b) cell type-specific and intergenic.
   c) found in all cells and within the coding region.
   d) found in all cells and intergenic.

8. a) The autoregulatory Sxl protein **promotes** its own synthesis through RNA splicing, resulting in a productive mRNA, thereby acting **as a self-reinforcing on/off switch**.
   b) The autoregulatory Sxl protein **inhibits** its own synthesis through RNA splicing, resulting in less productive mRNA, thereby acting **to finely tune its level and activity**.

9. a) Nonsense mediated decay is a cellular mechanism of mRNA surveillance leading to degradation of **proteins** truncated by premature stop codons.
   b) Nonsense mediated decay is a cellular mechanism of mRNA surveillance leading to degradation of **mRNAs** bearing premature stop codons.

10. a) Epigenetic imprints **gradually decay** during the life of a mammal and are rarely transmitted through the germ line into the next generation.
   b) Epigenetic imprints generally **persist** throughout the life of a mammal, and are often **transmitted** through the germ line into the next generation.
   c) 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.

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11. a) Autozygosity is a term used to refer to homozygosity **by descent from a common ancestor**.
b) Autozygosity is a term used to refer to homozygosity **that results from mitotic recombination**.

12. a) There is **great** conservation of the primary sequence of histones among all eukaryotes and this correlates with conservation in the nature of regulatory histone modifications between species.
b) There is **little** conservation of the primary sequence of histones among all eukaryotes and this correlates with variation in the nature of regulatory histone modifications between species.

13. a) **Prokaryotic** mRNAs tend to be **polycistronic** while **eukaryotic** mRNAs tend to be monocistronic.
b) **Eukaryotic** mRNAs tend to be **polycistronic** while **prokaryotic** mRNAs tend to be monocistronic.

14. a) The variable θ in lod score analysis represents **expected recombination frequency**.
b) The variable θ in lod score analysis represents **genetic map distance**.

Which of the following is true (4 points):

15. a) **Both** autozygosity mapping and lod score analysis both depend on common ancestry and you cannot combine results from different populations with either method.
b) **Neither** autozygosity mapping nor lod score analysis both depend on common ancestry and you can combine results from different populations with either method.
c) **Lod score analysis but not autozygosity mapping** depends on common ancestry and you can combine results from different populations autozygosity mapping but not lod score analysis.
d) **Autozygosity mapping but not lod score analysis** depends on common ancestry and you can combine results from different populations in pedigree analysis but not autozygosity mapping.

16. Explain your answer to number 15 (5 points):

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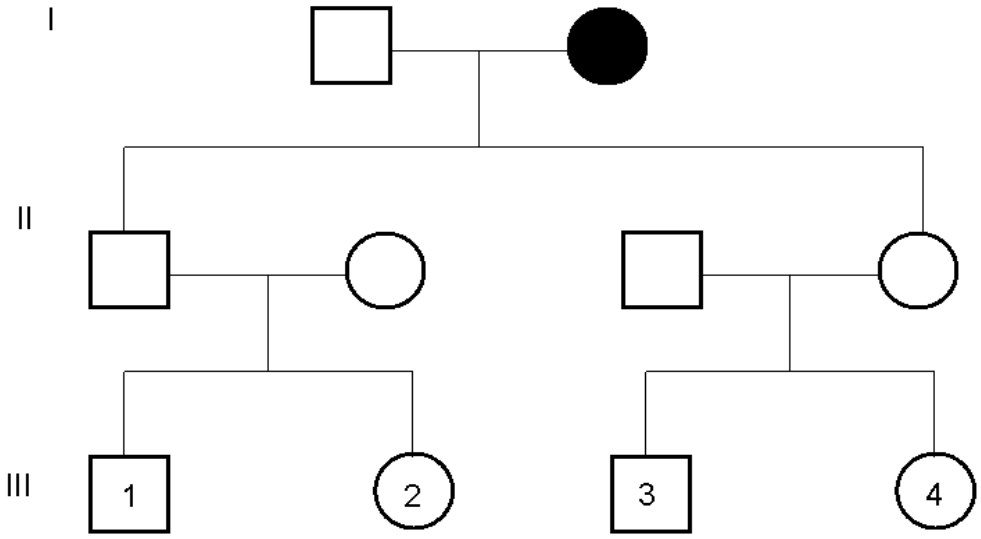

17. (3 points) In the case of an autosomal dominant trait with incomplete penetrance
    a) 1 and 2 are at risk but 3 and 4 are not.
    b) All of the grandchildren are at equal risk.
    c) 3 and 4 are at risk but 1 and 2 are not.

18. (3 points) In the case of a maternally imprinted trait with incomplete penetrance
    a) 1 and 2 are at risk but 3 and 4 are not.
    b) All of the grandchildren are at equal risk.
    c) 3 and 4 are at risk but 1 and 2 are not.

19. (3 points) In the case of a paternally imprinted trait with incomplete penetrance
    a) 1 and 2 are at risk but 3 and 4 are not.
    b) All of the grandchildren are at equal risk.
    c) 3 and 4 are at risk but 1 and 2 are not.

20. (3 points) In the case of a (rare) sex-linked trait
    a) Only 1 is at risk.
    b) Only 3 is at risk.
    c) 1 and 3 are at risk but 2 and 4 are not.
    d) 3 and 4 are at risk but 1 and 2 are not.
    e) All of the grandchildren are at equal risk.

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21. (12 points) Compare and contrast the mechanism of action of cellular microRNAs in animals with the action of siRNAs derived from double-stranded RNA precursors. Be sure to describe both similarities and to illustrate how the two differ.

22. (8 points) Explain the difference between genetic heterogeneity and polygenic determination, using examples (You have to define the terms. You can make up the examples).