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HST.161 Molecular Biology and Genetics in Modern Medicine
Fall 2007

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HST 161 – Fall 2004
Molecular Biology & Genetics in Modern Medicine
November 2, 2004

Quiz #2

This quiz should take you less than an hour to complete, but you may use the full hour if necessary. Please print your name on each page. Please write concise, to-the-point answers rather than long explanations. Good luck! ☺

1. (25 points) The ABO blood group is the major determinant of transfusion reactions. There are four major blood types, A, B, AB, and O. These are the consequence of a multiallelic polymorphism in a glycosyltransferase that modifies a red blood cell surface protein. The protein encoded by the *A* allele adds N-acetylgalactosamine, the protein encoded by the *B* allele adds galactose, while the protein encoded by the *O* allele is inactive and adds no sugar. People with genotypes *AO* and *AA* have blood group A, *BO* and *BB* have blood group B, *AB* have blood group AB, and *OO* have blood group O.

- a. Imagine a population where the allele frequency of *A* is 60%, *O* is 40%, and *B* is 0. Using the Hardy-Weinberg equilibrium, derive the frequency of the **four blood groups** A, B, AB, and O in this population (10 points).

Blood group A	$AO = 2(0.6)(0.4) = 0.48$ $AA = (0.6)^2 = 0.36$ $AO + AA = 0.84$	Blood group AB	$AB = 0$
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Blood group B	$BO = 0$ $BB = 0$ $BO + BB = 0$	Blood group O	$OO = (0.4)^2 = 0.16$
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- b. Imagine instead that the population has allele frequencies: *A* = 60%, *B* = 20%, and *O* = 20%. Derive the frequency of the **four blood groups** (15 points).

Blood group A	$AO = 2(0.6)(0.2) = 0.24$ $AA = (0.6)^2 = 0.36$ $AO + AA = 0.60$
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Blood group B	$BO = 2(0.2)(0.2) = 0.08$ $BB = (0.2)^2 = 0.04$ $BO + BB = 0.12$
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Blood group AB	$AB = 2(0.6)(0.2) = 0.24$
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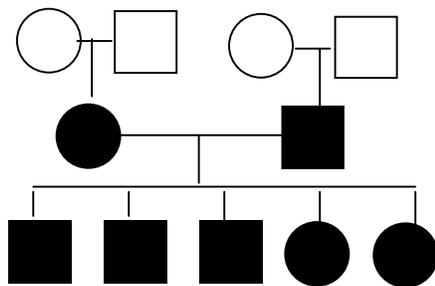
Blood group O	$OO = (0.2)^2 = 0.04$
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2. (25 points) Put a checkmark next to the boxes that are possible disease models for the given triads. For the genetic models, assume that the disease is FULLY PENETRANT and that there is no new mutation (1 point per box).

Autosomal recessive	X	X	X	X	X
Autosomal dominant	X	X	X	X	
X-linked recessive		X	X	X	
X-linked dominant	X	X	X		
Mitochondrial inheritance	X		X		

3. (30 points) Draw out the pedigree for this family as you solve this problem (3 points).

a. Anne Smith and Richard Jones were both born deaf, attended the same school for the deaf, married and had five children, three boys and two girls. All of their children were born deaf. Neither Anne's parents nor Richard's parents were deaf. Based on these facts alone what modes of Mendelian inheritance would be compatible with Anne and Richard's family? For each mode of inheritance comment on whether new mutation or incomplete penetrance could be relevant to explaining the pattern of inheritance in the family.



4 points each for at least 3 possible modes of inheritance:

Autosomal Recessive

Autosomal Dominant with Incomplete Penetrance

Autosomal Dominant with New Mutations

(Problem 3 continued)

b. Anne's sister Rachel, who was not deaf, met Richard's brother, Mark, who also was not deaf, while visiting at the school. Rachel and Mark married and had four children. Two of the children were born deaf. What is the most likely mode of inheritance for deafness in the family based on these new facts? (5 points)

Autosomal Recessive

c. Candidate genes on chromosomes 4, 7 and 19 have been identified for the deafness in this family. DNA samples are collected from Anne and Rachel's parents and Mark and Richard's parents as well as Anne, Rachel, Richard, Mark and all of their children. DNA markers within 50 kilobases of each candidate gene were identified.

The marker on chromosome 7 tested was a VNTR with eight possible alleles. The following genotypes were obtained:

- Anne's father 2,6
- Anne's mother 4,5
- Anne 2,5
- Rachel 5,6
- Richard's father 4,7
- Richard's mother 3,3
- Richard 3,7
- Mark 3,4
- Mark and Rachel's deaf son 3,5
- Mark and Rachel's deaf daughter 3,5
- Mark and Rachel's hearing daughter 3,6
- Mark and Rachel's hearing son 4,5

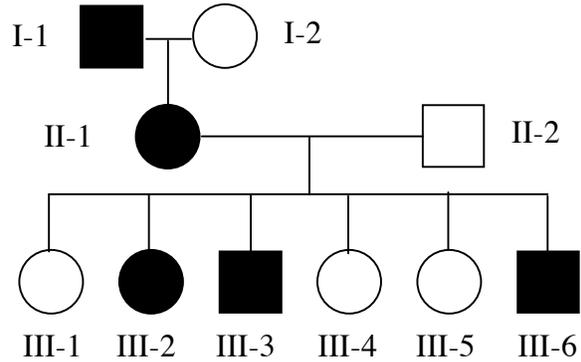
Do these data exclude the candidate gene on chromosome 7? Alternatively, do they suggest linkage to specific VNTR alleles? If so, which allele(s)?

Given this data, you cannot exclude a candidate gene on chromosome 7 (5 points).

Rather, the data above suggests linkage to alleles 3 and 5 with an autosomal recessive mode of inheritance (5 points). Alleles 2 and 7 also cannot be excluded with the little data given.

4 (20 points) You would like to determine the mutation responsible for segregation of familial hypertrophic cardiac myopathy in the pedigree below. You test three SNP markers from three different chromosomal regions: an SNP 50 kbp from the troponin T gene on 1q, an SNP in the promoter of the myosin heavy chain gene on 14q, and an SNP in intron 3 of the tropomyosin gene on 15q.

	1q	14q	15q
I-1	aa	Bb	Cc
I-2	AA	bb	cc
II-1	Aa	Bb	Cc
II-2	aa	BB	Cc
III-1	Aa	Bb	cc
III-2	aa	BB	Cc
III-3	aa	Bb	Cc
III-4	Aa	BB	Cc
III-5	Aa	BB	Cc
III-6	aa	Bb	CC



a. Which marker gives the highest LOD score for linkage at $\theta = 0$ to the disease locus? Explain your answer. Note: It is not necessary to solve the LOD score mathematically to answer part (a) and (b).

1q- there are no recombination events for the disease gene a. Therefore 1q has the highest LOD score (5 points).

b. Which marker gives the lowest LOD score for linkage at $\theta = 0$ to the disease locus? Explain your answer.

14q has the lowest LOD score, and is not linked (4 recombination events) (5 points). The meioses of 15q is uninformative.

c. What is the LOD score at $\theta = 0$ for linkage between the 1q marker and the disease locus?

$$\text{LOD} = \frac{(1-\theta)^{NR} \theta^R}{(1/2)^{NR+R}} = \log \frac{(1)^6 (0)^0}{(1/2)^6} = \log 64 = 1.8$$

(10 points)