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

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Pset 1 Solutions

1.

a)  $\theta = 0$        $\text{LOD} = \log [0^0 \cdot (1-0)^{10} / 0.5^{10}] = 3.01$   
 $\theta = 0.1$        $\text{LOD} = \log [0.1^0 \cdot (1-0.1)^{10} / 0.5^{10}] = 2.55$

b)  $\theta = 0$        $\text{LOD} = \log [0^3 \cdot (1-0)^7 / 0.5^{10}] = -\text{infinity}$   
 $\theta = 0.1$        $\text{LOD} = \log [0.1^3 \cdot (1-0.1)^7 / 0.5^{10}] = -0.31$

2. a) We should sequence MS2, the **cardiac troponin T** gene. Allele 6 of MS2 co-segregates with the disease in every case.

b) We should sequence MS3, the  **$\alpha$ -tropomyosin** gene. Allele 3 of MS3 co-segregates with the disease in every case except for Tyler, but he is too young to exhibit symptoms of FHC.

c) We should sequence MS1, the  **$\beta$ -cardiac myosin gene**. Allele 5 of MS1 co-segregates with the disease. Allele 5 of MS4 also co-segregates with the disease, but Arthur is homozygous for allele 5, so we don't know which allele 5 each child receives, i.e. we have an uninformative meiosis.

3. a) A lower LOD score is obtained for D7S3313 compared to D7S669 because there are a smaller number of informative meioses for D7S3313. Specifically, IV-1, IV-9 and IV-12 are informative for D7S669 but not for D7S3313. It is important to note that the lower LOD score at  $\theta = 0$  is a consequence of fewer informative meioses for D7S3313 compared to D7S669 but there are no meioses which identify an obligate crossover between D7S3313 and the disease locus so there is no reason to presume that it is more distant from the disease locus based on the lower LOD score.

b) The likelihood of the site of the mutation causing the disease being at any given position across the entire 27.2 Mb interval is equal. There are no obligate crossovers within the interval which exclude any part of the interval. The variation in the values of the LOD scores for the different markers within the interval reflects the number of informative meioses vs. the number of uninformative meioses for each marker but does not tell us that the mutation causing the disease is more likely to be close to a marker with a higher LOD score.

c) Yes, additional markers could be chosen to reduce the interval in which the disease gene might reside. Specifically, a recombination crossover occurred between D7S506 and D7S1485 at one end of the 27.2 Mb interval. Markers between D7S506 and D7S1485 could be chosen to potentially narrow down this ~6 Mb region.