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Lab 5

1. Families 1, 3, 6, 7, 8, 9, 11, 15, and 17 produce negative LOD scores while families 2, 4, 5, 10, 12,13, 14, and 16 produce positive LOD scores. Why?

In the families with the negative LOD score affected individual(s) exhibit different alleles in ApoB locus. Presence of such individuals is the evidence against linkage hypothesis, hence the negative LOD scores. Rest of the families has the same alleles in ApoB locus, so they provide evidence for the linkage and therefore positive LOD scores.

2. Families 2 and 4 share the same pedigree structure, but family 2 produces LOD scores that are considerably lower than for family 4. Why?

Family 2 has two instances of allele 3 in ApoB locus, while family 4 has two instances of allele 1. In the Caucasian sample, a frequency for allele 1 is 0.219, and for allele 3 it is 0.402. Therefore in case of family 2 the genotype is less rare than in case of family 4, hence it is more probable that the diseased individual is having this genotype by the coincidence that leads to lower LOD scores.

3. From the total lods scores for your 3 merlin runs, the two using the Caucasian allele frequencies should indicate some evidence for linkage near the ApoB marker (LOD scores about 2.0). Using the Japanese allele frequencies, there is no longer much support for linkage in the region. Why?

A significant proportion of affected individuals in the sample have two instances of allele 1 at ApoB locus. In Japanese population this allele is about 3 times more frequent than in the Caucasian one. Therefore observed frequency of 1,1 genotype in affected population is the anomaly if Caucasian frequencies are used, and such anomaly provides evidence for linkage. With Japanese frequencies it is no longer an anomaly, therefore individuals with two instances of allele 1 do not provide significant evidence for linkage.

4. Compare the lod score curves from the two analyses. You should see that the LOD scores are fairly similar. Does this mean that the Japanese and Caucasian allele frequencies are similar for the markers along this chromosome? Is it possible to have some of the allele frequencies wrong, but still end up with reasonably correct LOD scores? Comment.

Similar LOD scores do not mean that frequencies are the same, and they, in fact, differ significantly. It is possible to have different frequencies but get the same LOD score. As we have seen before LOD score from individuals homozygous at marker locus with some allele decreases with the increase in frequency of that allele, and increases with the decrease in frequency. Since change in frequencies makes some alleles more and some less frequent, it can, under some conditions, preserve the total lod score (simplest example: in case of two alleles with unequal frequencies but with the equal number of observed affected homozygotes for each allele, swapping the frequencies of alleles will preserve the lod score).