

# Genome 371 LOD practice -- key

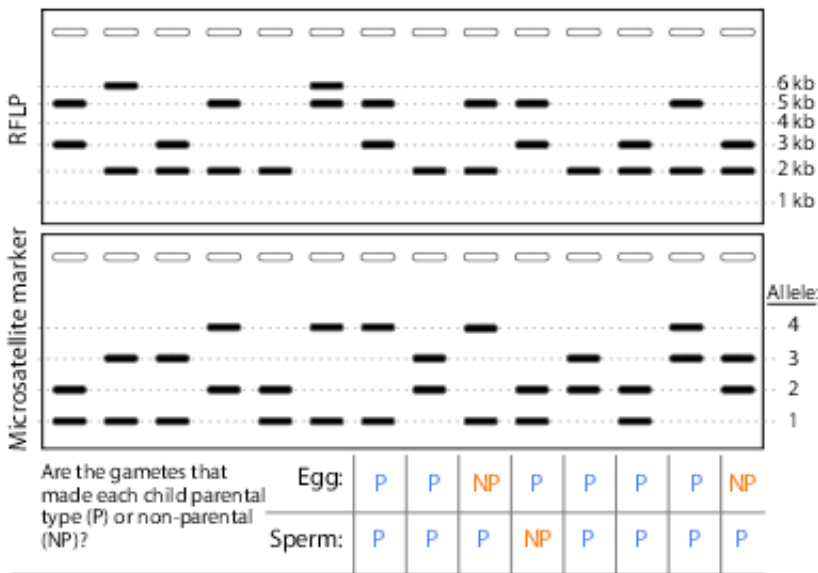
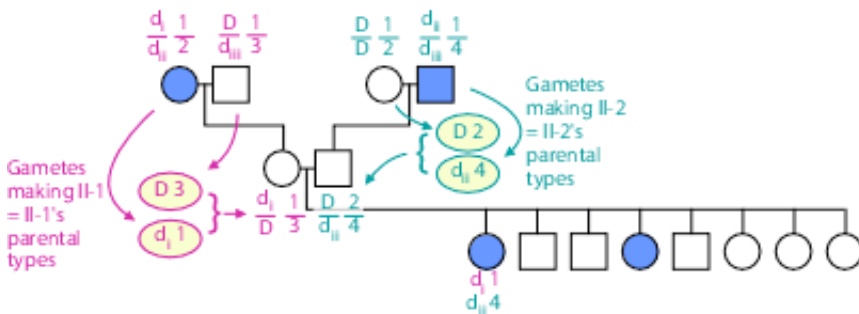
The disease gene alleles can be recognized based on the RFLP fragment sizes on the gel:

- D = 2 kb
- $d_i$  = 3 kb
- $d_{ii}$  = 5 kb
- $d_{iii}$  = 6 kb

Anyone inheriting D does not show the disease.

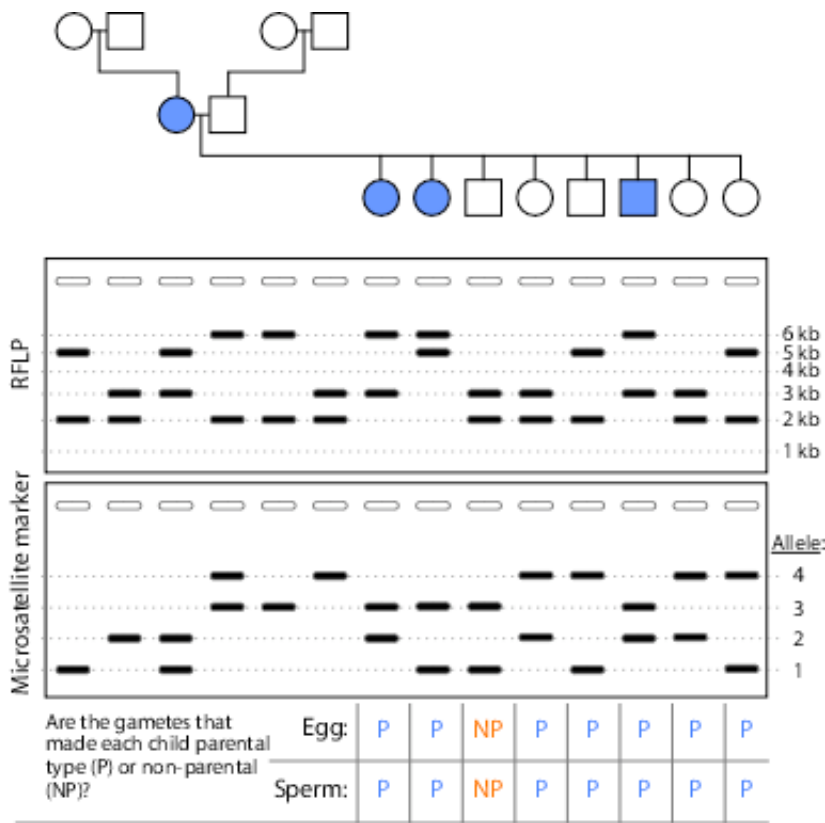
After reading off each person's genotype from the gels, we can determine whether the gametes making each child are parental or non-parental. The genotypes of II-1 and II-2 and of their first child are shown on one pedigree as an example.

## Pedigree #1:



3 non-parental out of 16 total gametes =  $(3/16) \times 100 = 18.75$  cM.

## Pedigree #2:



2 non-parental out of 16 total gametes =  $(2/16) \times 100 = 12.5$  cM.

If we were to average the two calculations, we'd say that the estimated map distance was  $\sim 15.6$  cM.

LOD score calculations

Parental vs. non-parental gamete frequencies if the loci are linked at a map distance ( $\theta$ ) = 5 cM (for example):

Non-parental gametes = 5% = frequency of 0.025 each.

Parental = 0.475 each.

If independently assorting... each gamete frequency = 0.25.

There are 13 parental and 3 non-parental gametes (between all the children), so the LOD score equation can be written as

LOD score for map distance of 5 cM =

$$\log \frac{(0.475)^{13} \times (0.025)^3}{(0.25)^{16}}$$

= **0.62**.

NOTE: You can also write the probabilities child-by-child, i.e., probability of child #1 for linkage at 5 cM =  $0.475 \times 0.475$ ; probability of 4th child for linkage at 5 cM =  $0.025 \times 0.475$ , etc.

Map distance (theta)	LOD score for...		Total
	Pedigree #1	Pedigree #2	
5	0.62	1.90	2.53
10	1.22	2.18	3.40
15	1.43	2.18	3.61
20	1.46	2.06	3.52
25	1.39	1.86	3.25
30	1.23	1.60	2.84
35	1.02	1.29	2.30
40	0.74	0.91	1.65
45	0.40	0.49	0.89
50	0.00	0.00	0.00

So, although each pedigree by itself does not give statistically significant evidence for or against linkage between the disease gene and the polymorphic locus, we can sum the values from the two pedigrees and get results that are statistically significant. The assumption is that we are looking at the segregation of alleles of the same gene in the two pedigrees. (I'll leave it up to you to plot the data on the graph.)

The combined data show evidence in favor of linkage between the disease gene and the polymorphic site at a minimum distance of  $\sim 7$  cM and a maximum distance of  $\sim 27$  cM, with the maximum probability of linkage at  $\sim 15$  cM.