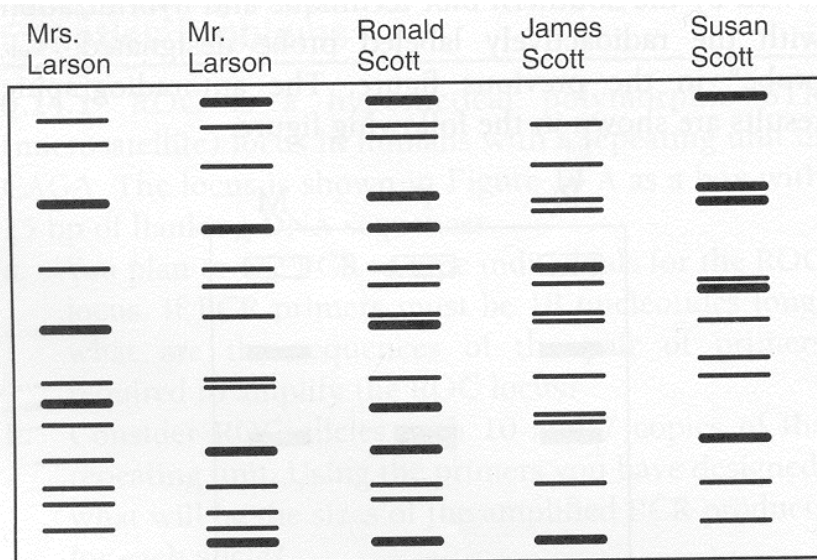


One application of DNA fingerprinting technology has been to identify stolen children and return them to their parents. Bobby Larson was taken from a supermarket parking lot in New Jersey in 1978, when he was 4 years old. In 1990, a 16-year-old boy called Ronald Scott was found in California, living with a couple named Susan and James Scott, who claimed to be his parents. Authorities suspected that Susan and James Scott might be the kidnappers and that Ronald Scott might be Bobby Larson. DNA samples were obtained from Mr. And Mrs. Larson and from Ronald, Susan, and James Scott. PCR of several VNTR loci was used to generate a DNA fingerprint of each individual with the results shown in the figure below. (10 points)

A. What is a mini-satellite sequence (VNTR)?

A repeat sequence of between 10 and 100 basepairs

B. From the information in the figure, what can you say about the parentage of Ronald Scott? Explain.



The Larsons are likely to be Ronald Scott's parents. Almost all of his bands on the gel are found in either Mr or Mrs Larson. There is not a significant match with the Scotts.

The ectodermal dysplasias (EDs) are a large and group of diseases that have in common anomalies of the hair, teeth, nails, and sweat glands, with or without anomalies in other organs and systems. The incidence is estimated to be ~7 in 10,000 births. So far, >200 different pathological clinical conditions have been recognized and defined as EDs, all with Mendelian modes of inheritance.

More than 30 different loci have been shown to produce ED phenotypes when individuals are homozygous for mutations in these genes. The following is taken from an analysis that demonstrated that mutations in the WNT10A gene were responsible for ED in three consanguineous Lebanese Shiite Muslim families. The geneticists mapped the location of the mutation to the WNT10A gene using both linkage analysis with LOD scores and homozygosity mapping.

1. The team of geneticists used these three families to perform linkage analysis using different microsatellite alleles located on several different chromosomes.
 - a. All the families were informative/phase-known for the marker alleles the researchers used. What does it mean for a family to be phase-known?

It means that you can identify which marker allele appears to be linked to the disease gene you are mapping.

- b. When determining the distance between a known marker locus and an unknown mutation, why is it important to know the phase of a particular allele of the marker and the disease phenotype?

It is important to know the phase so that you can identify the recombinant and non-recombinant progeny. This is the information that is required for the linkage analysis.

- c. The table below shows the results of their linkage analysis using 5 different marker loci on 4 different chromosomes. The table shows the marker, its chromosomal location, and the calculated LOD scores for several different recombination distances.

Marker	Chromosome	Recombination Distance (Θ)							
		.0	.01	.05	.1	.2	.3	.4	
<i>D2S2211</i>	1p15.1	-1.32	-1.27	-1.07	-.85	-.49	-.23	-.07	
<i>D2S2722</i>	2q35	3.4	3.7	2.5	2.0	1.0	.21	.06	
<i>D2S335</i>	2q38.1	1.04	2.0	3.0	4.2	3.2	1.95	.06	
<i>D3S1263</i>	9q5.32	-1.21	-1.18	-1.06	-.92	-.62	-.36	-.15	
<i>D4S1572</i>	12p3.43	-.98	-.95	-.85	-.72	-.47	-.24	-.07	

Which markers are unlinked? *Explain.*

***D2S2211*, *D3S1263*, and *D4S1572*. They all have negative LOD scores for all recombination distances.**

Which markers are likely to be linked to the mutation causing ED in these families? *Explain.*

***D2S2722* and *D2S335*. They have positive LOD scores for all recombination distances**

What is the most likely distance between each linked marker and the disease causing mutation? *Explain.*

***D2S2722* is likely to be 1% recombination or 1 map unit away from the disease mutation.**

***D2S335* is likely to be 10% recombination or 10 map units away from the disease mutation**

2. All three pedigrees show consanguineuity indicating that affected individuals are likely homozygous for the chromosomal region that carries the ED mutation. All three families are members of a close knit Lebanese Shiite Muslim religious community and the researchers hypothesize that affected individuals in these three families all carry the same exact disease mutation and may share marker alleles surrounding the disease mutation.
- a. What is the name given to the shared set of marker alleles found around the disease mutation?

Disease haplotype

- b. Given the nature of this population, why is it likely that they are carrying the same mutation and surrounding marker alleles?

They are from a close knit religious community that shares a common ancestry making it likely that they all have a mutation from a single founder individual. They will share the disease mutation and some of the surrounding alleles that are closely linked.

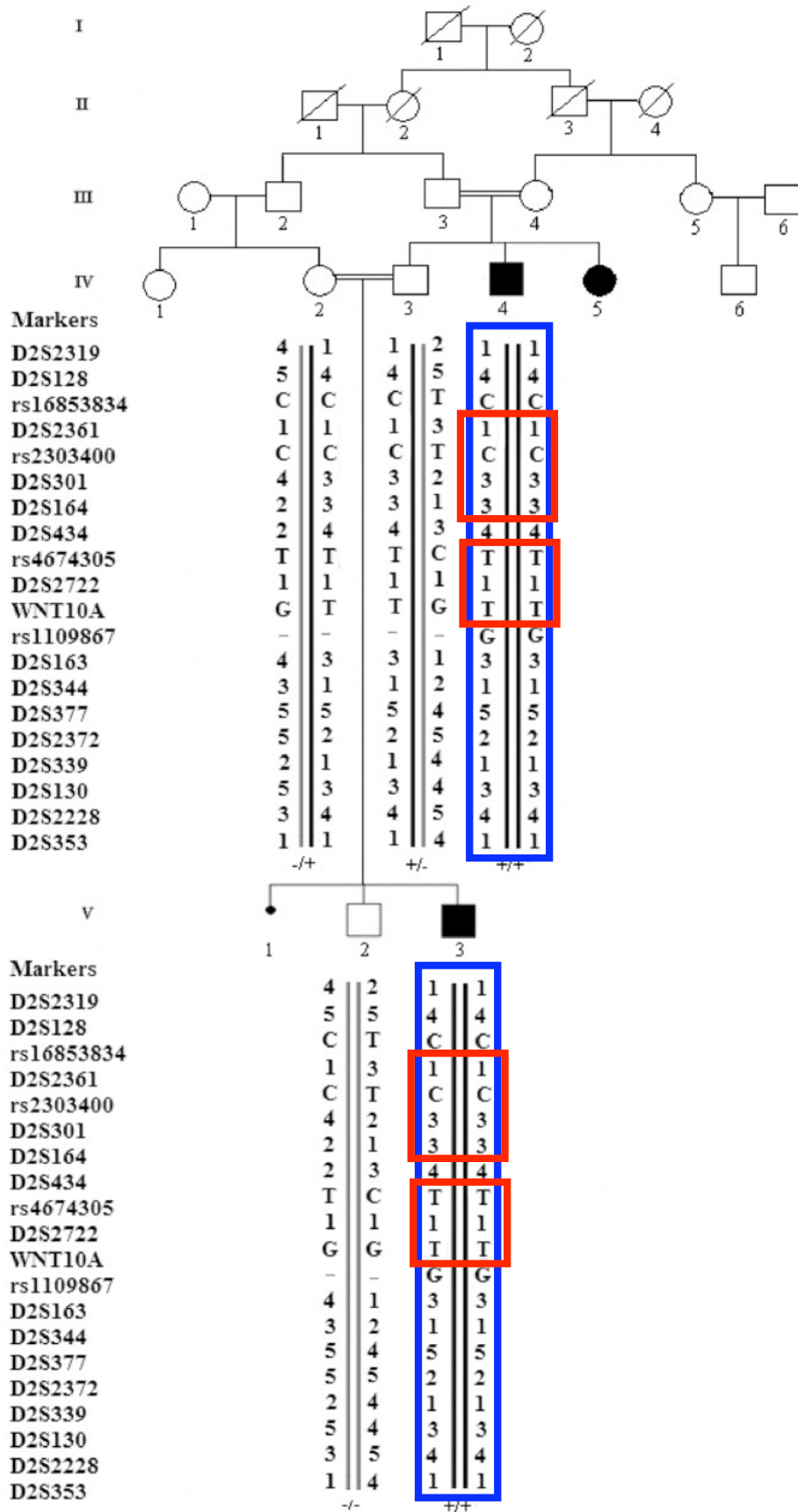
3. Below are the three pedigrees showing the inheritance pattern of the ED phenotype. Based on their linkage analysis results, the researchers determined the haplotypes of several individuals in each family in the 2q34-36 region. Beneath some of the individuals, the haplotypes for both chromosomes are given. The haplotypes for each individual contains their alleles for specific microsatellite markers (1,2,3, etc.) and their alleles of particular SNPs (A, G, C, or T) in the region.
- a. Use the information in the following three pedigrees to determine the region of homozygosity in all affected individuals in the pedigree. *Place a box around this region in each affected individual.*

Part A asks you to just look at affected individuals and label the region of homozygosity (Blue Box).

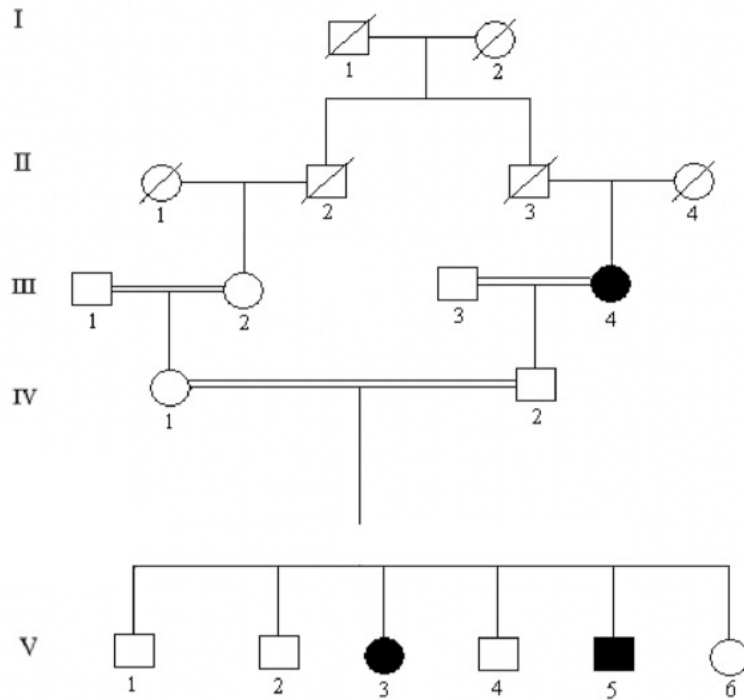
- b. Now, given the assumption that these three families although not directly related are likely carrying the same founder chromosomes, determine the minimal region of homozygosity that is required to produce the ED disease. Hint: you will need to compare your boxed regions in part from all three families.

Part B asks you to just look at the boxes you made in A and find a common haplotype that is found in all of them (Red Box).

B



C



Markers

D2S2319
 D2S128
 rs16853834
 D2S2361
 rs2303400
 D2S301
 D2S164
 D2S434
 rs4674305
 D2S2722
 WNT10A
 rs1109867
 D2S163
 D2S344
 D2S377
 D2S2372
 D2S339
 D2S130
 D2S2228
 D2S353

1	1
T	T
1	1
C	C
3	3
3	3
4	3
T	T
1	1
T	T
G	G
2	2
1	3
2	1
4	3
1	1
1	2
1	2
-	-

+/+

1	3
T	C
1	4
C	T
3	5
-	-
4	1
T	C
1	1
T	G
G	T
2	3
1	3
2	3
4	5
1	3
1	1
1	3
-	-

+/-

A

