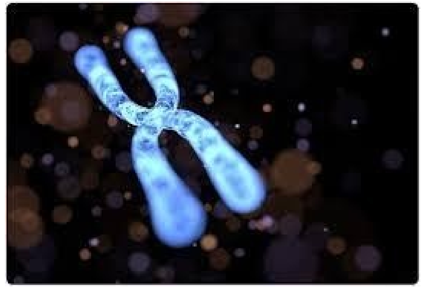
Chapter 5

Human



Pedigree analysis part 2:
gene localization

Part 2: determining the localization of a gene.

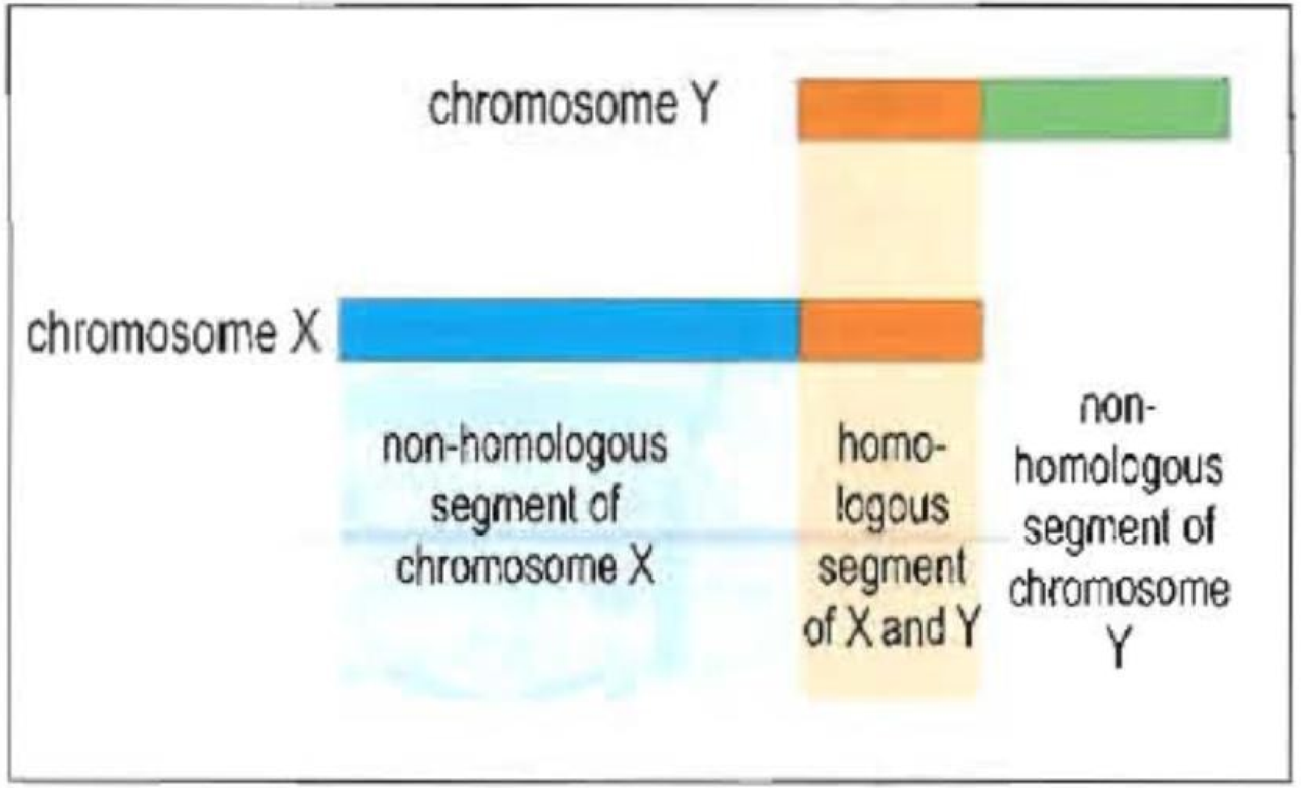
Is it on the sex chromosomes Y?

Is it on the sex chromosome X?

Is it both on X and Y?

Is it on an autosome?

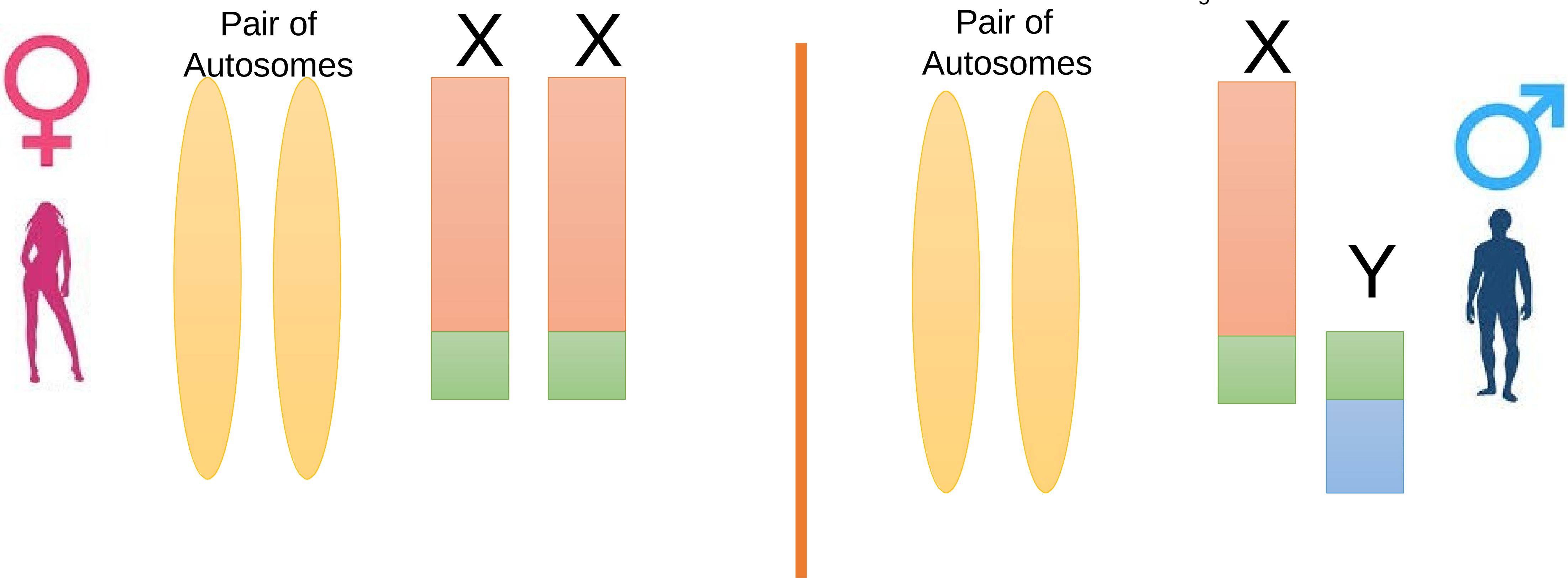
A closer look at the sex-chromosomes X and Y



Doc.a *Shematic representation of X and Y sex chromosomes.*

Fill in the following table:

	Gene location	Number of copies		Expression of alleles	
		In a female	In a male	In a female	In a male
	On autosomes	2	2	Dominant expressed	Dominant expressed
On gonosomes	Homologous region of X & Y	2	2	Dominant expressed	Dominant expressed
	Non-homologous region of X	2	1	Dominant expressed	Allele expressed regardless
	Non-homologous region of Y	0	1	Not expressed	Allele expressed regardless



Strateg

Steps:

1- Check of there is sexual discrimination in the expression of the disease:

- **If Yes:** then the disease is probably sex-linked (on non-homologous region of X or Y)
- **If No**; continue with analysis.

2- Try to eliminate the possibility that the gene is on the non-homologous region of Y, then try to eliminate the possibility that the gene is on the non-homologous region of X and finally try to eliminate the possibility that the gene is located on the homologous region of X & Y.

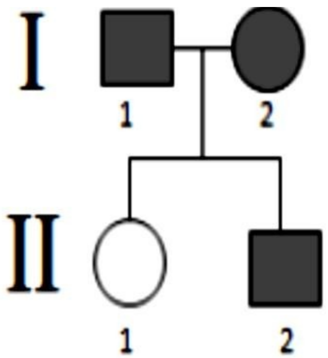
3- If all these 3 cases eliminated, then the gene is autosomal.

Examples for elimination of the gonosomal locations

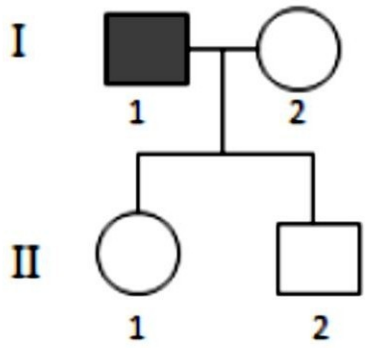
Note: these examples are small and limited for the case indicated in each sub-part.

A- How to eliminate the possibility that the gene is Y-linked (on the non-homologous region of Y)

Hint: look for a female with the trait or look at fathers and their sons

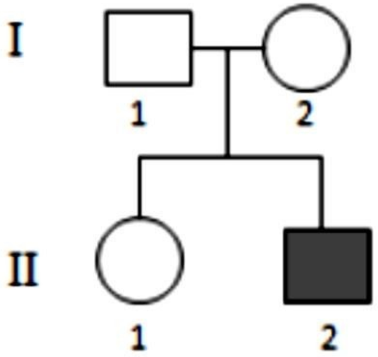


If the gene coding for the disease is Y-linked (on the non-homologous region of Y) no females should be affected by this disease, since they have no Y; but here the female I_2 is affected, then it can't be Y-linked.



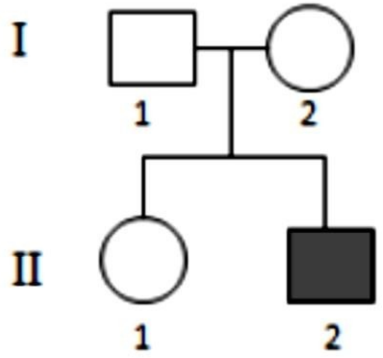
If the gene coding for the disease were Y-linked (on non-homologous region of Y)

Father I_1 is diseased then he should have a Y carrying the disease allele (XY^D) and all his sons should receive a Y^D from him in addition to an X from their mother to become also XY^D (diseased), but here the son II_2 is normal; hence it is not Y-linked.



If the gene coding for the disease were Y-linked (on non-homologous region of Y)

Father I_1 is normal then he should have a Y carrying the normal allele (XY^N) and all his sons should receive a Y^N from him in addition to an X from their mother to become also XY^N (normal), but here the son II_2 is diseased; hence it is not Y-linked.



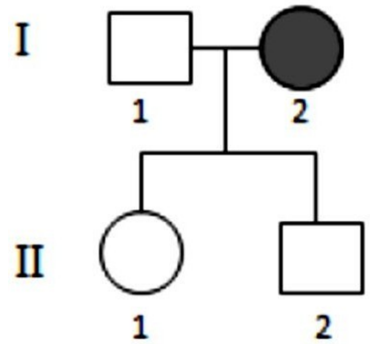
If the gene coding for the disease were Y-linked (on non-homologous region of Y)
Father I_1 is normal then he should have a Y carrying the normal allele (XY^N) and all his sons should receive a Y^N from him in addition to an X from their mother to become also XY^N (normal), but here the son II_2 is diseased; hence it is not Y-linked.

B- How to eliminate the possibility that the gene is X-linked (on the non-homologous region of X)

Hint: look at fathers and their daughters or mothers and their sons

Example 1

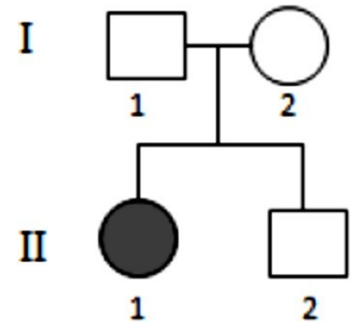
<u>Case 1:</u> (the allele of the disease is recessive) N>d



If the allele coding for the disease were X-linked (on the non-homologous region of X) then female I_2 would be X^dX^d (she should carry only allele d and no N which would otherwise be expressed), then all her sons should get an X^d from her in addition to a Y from the father to become X^dY (diseased) but here the son II_2 is normal then it can't be X-linked.

Example 2

Case 1: (the allele of the disease is recessive) N>d

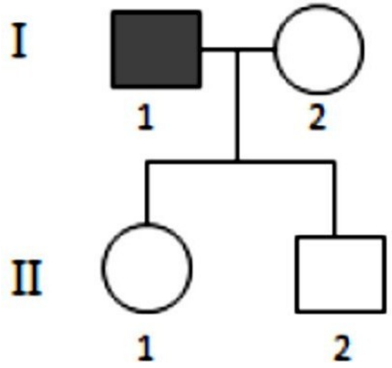


If the allele coding for the disease were X-linked (on the non-homologous region of X) then female II_1 would be X^dX^d (she should carry only allele d and no N which would otherwise be expressed), then she must have received an X^d from her father I_1 in addition to a Y to become X^dY (diseased) but here the father is normal then it can't be X-linked.

. But then the father would be affected (X^dY) and here he his normal, hence this gene

Case 2: (the allele of the disease is dominant) D>n

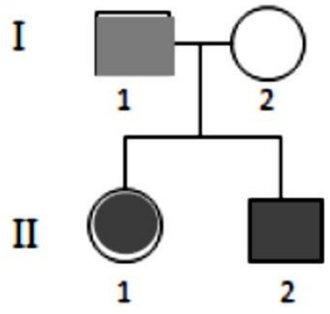
Example 1



If the allele coding for the disease were X-linked (on the non-homologous region of X) then father I_1 would be X^DY, then all his daughters should get an X^D from him and would be then diseased regardless of what their mother gives them as D is dominant, but here the daughter II_1 is normal then it can't be X-linked.

<u>Case 2:</u> (the allele of the disease is dominant) D>n

Example 2

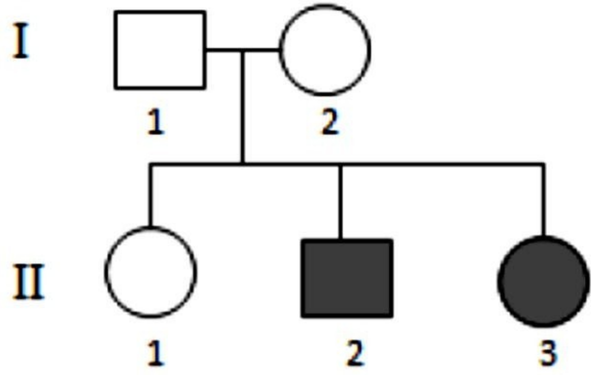


If the allele coding for the disease were X-linked (on the non-homologous region of X) then son II_2 would be X^DY, then he must have received an X^D from his mother I_2 who would be then diseased regardless of what her other X carries as D is dominant, but here the mother I_2 is normal then it can't be X-linked.

C- **<u>How to eliminate the possibility that the gene is XY-linked (on the homologous region of X & Y)</u>**

<u>Hint: look at a brother and a sister who are similar but opposite to their father)</u>

Case 1: (the allele of the disease is recessive) N>d

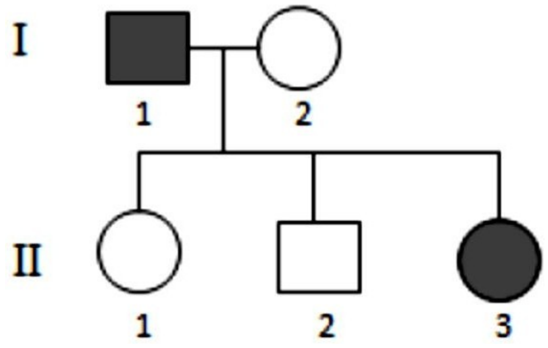


If the gene were on the homologous region of X & Y (XY-linked) then:

- II_3 would be X^dX^d, and she gets X^d from her father I_1
- II_2 would be X^dY^d, and he gets Y^d from his father I_1;

Then I_1 would be X^dY^d (diseased) but he is normal, then the disease allele is not XY-linked.

Case 2: (the allele of the disease is dominant) D>n

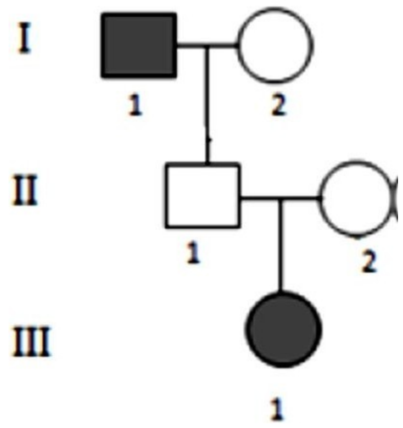


If the gene were on the homologous region of X & Y (XY-linked) then:

- II_1 would be X^nX^n, and she gets X^n from her father I_1
- II_2 would be X^nY^n, and he gets Y^n from his father I_1;

Then I_1 would be X^nY^n (normal) but he is diseased, then the disease allele is not XY-linked.

Special case:



In the adjacent pedigree, let's say that the allele of the disease is recessive (N>d)

If the gene concerned with the disease were on the homologous region of X and Y (XY-linked) then:

- I_1 would be X^dY^d and his son II_1 would get a Y^d from him.
- Also, III_1 would be X^dX^d and would get X^d from her father II_1
- Hence II_1 should be X^dY^d (diseased) but here he is normal, hence the disease is not XY-linked.