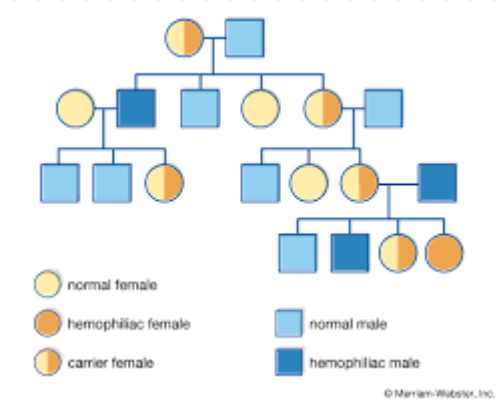
Gene Inheritance and Transmission
Pedigree analysis

Lecture 4

SLE254 Genetics

Chapter 3 Concepts of Genetics (12th edition)

Pages 88-90



Pedigree analysis

- Pedigree analysis follows the inheritance of a trait through a family
  - Used to establish how a trait is inherited
  - Used to determine the risk of having an affected child

- Pedigrees constructed using information from
  - Interviews
  - Medical records
  - Letters
  - Diaries
  - Photographs
  - Family records

Now we have genetic technologies!

Pedigree

- A diagram showing genetic information from a family
- Uses standardised symbols

- Pedigree analysis has two goals

  1) To determine whether the trait has a dominant or a recessive pattern of inheritance

  2) To discover whether the gene in question is located on a sex chromosome (X or Y) or on an autosome

Are inheritance patterns important?

- Pattern of inheritance can be used to predict genetic risk
  - Pregnancy outcomes
  - Adult-onset disorders
  - Recurrence risk of future offspring

Symbols used in pedigrees

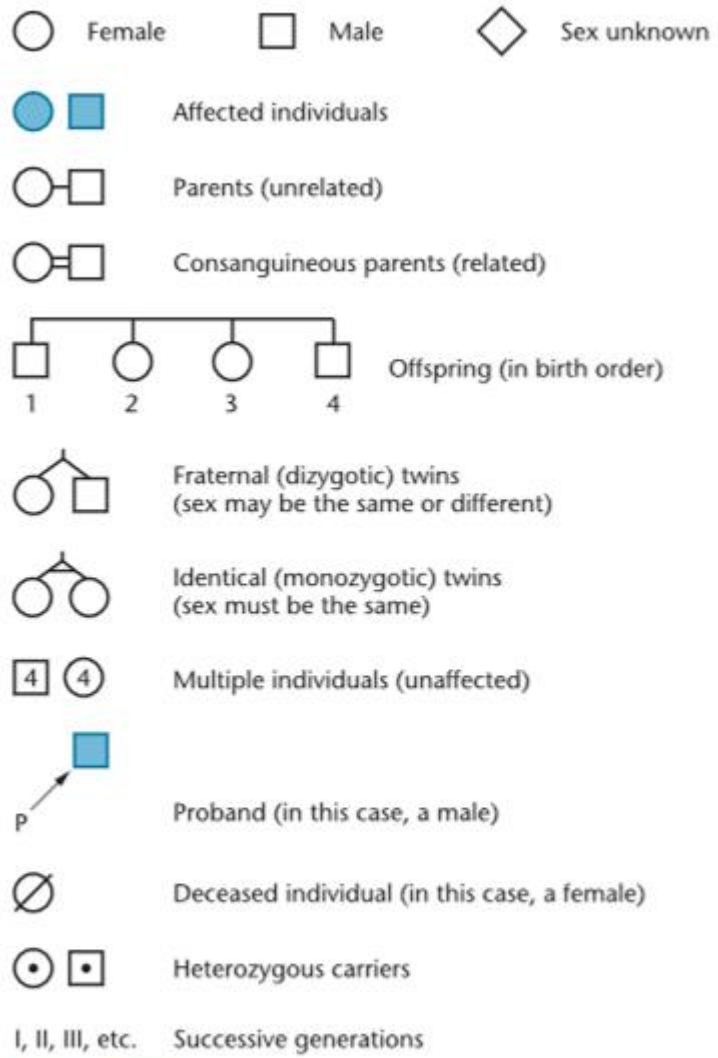
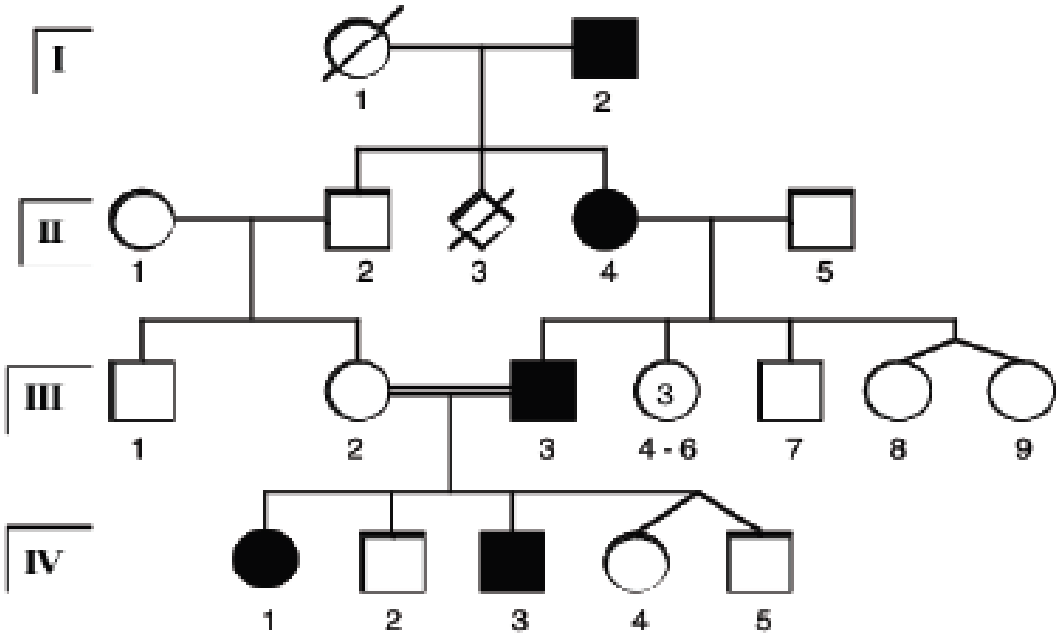


FIGURE 3.12 Conventions commonly encountered in human pedigrees.

You need to know these symbols

Symbols used in pedigrees



You need to know these symbols

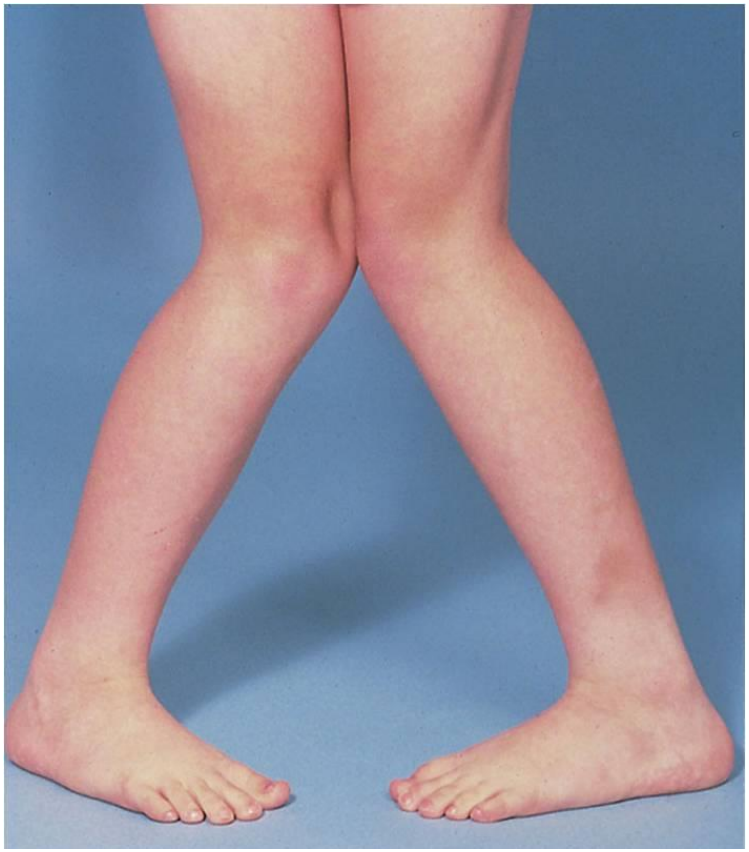
Patterns of inheritance

- Patterns in the pedigree are used to determine how a trait is inherited
  - Autosomal recessive inheritance
  - Autosomal dominant inheritance
  - X-linked dominant inheritance
  - X-linked recessive inheritance
  - Y-linked inheritance

  - Also non-Mendelian pattern of inheritance observed in traits controlled by mitochondrial genes

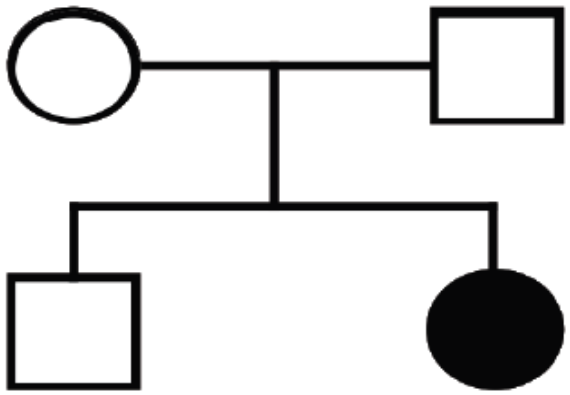
Careful – not always one pattern

- Genetic disorders can be inherited in a number of different ways
  - Ehler's Danlos syndrome can be inherited *as-autosomal dominant*
    autosomal recessive,
    or X-linked recessive
  - The common AD form have highly elastic skin
- **Multiple genes for the same disorder**



Autosomal recessive

- Characteristics of autosomal recessive traits
  - For rare traits, most affected individuals have unaffected parents
  - All children of affected parents are affected
  - The risk of an affected child with heterozygous parents is 25%

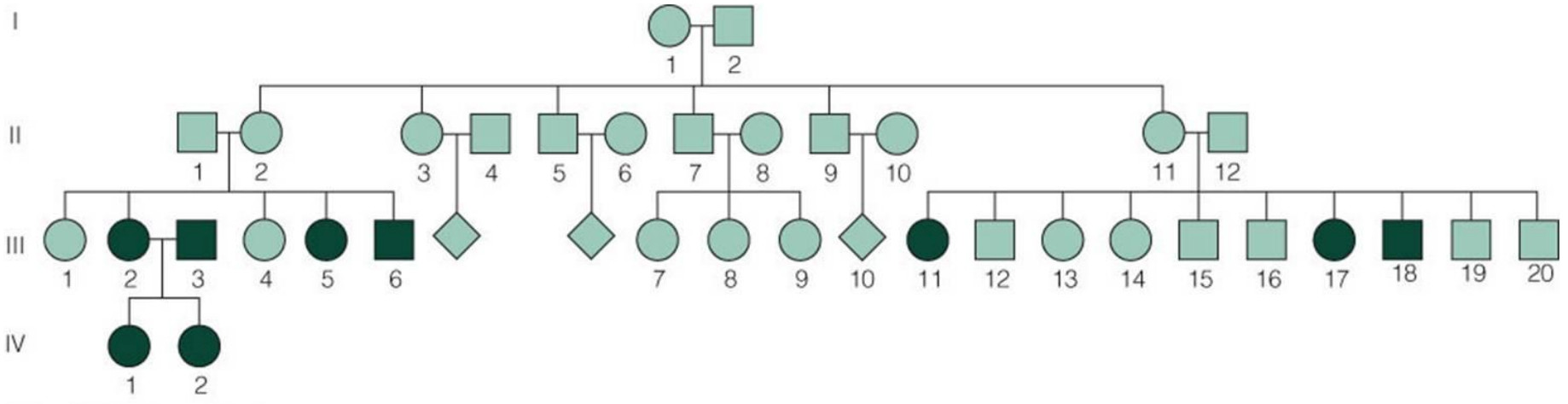


Autosomal recessive trait

Recessive **because two non-affected parents have an affected child**

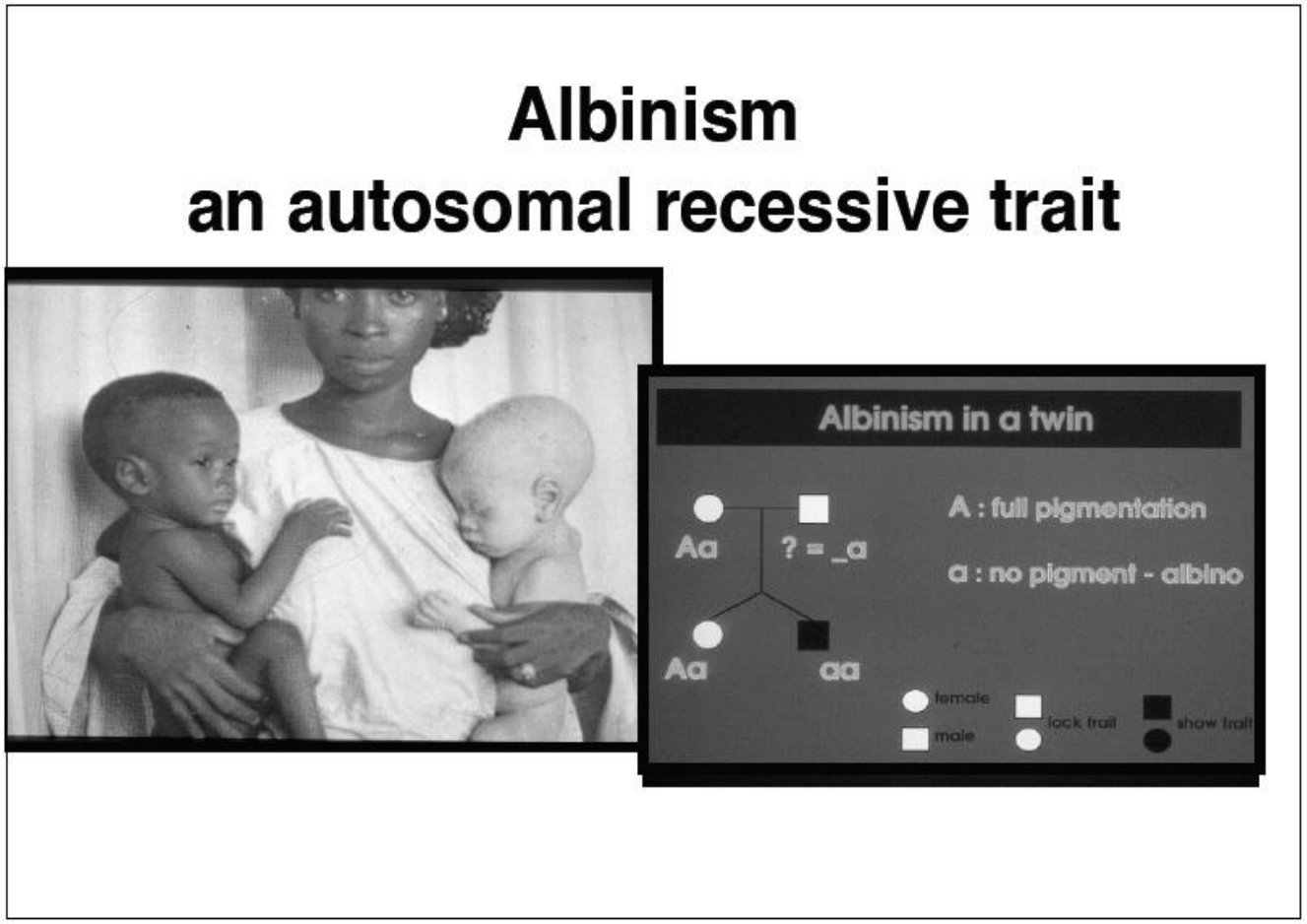
Autosomal **because father must also show the trait if it were X-linked**

Autosomal recessive pedigree



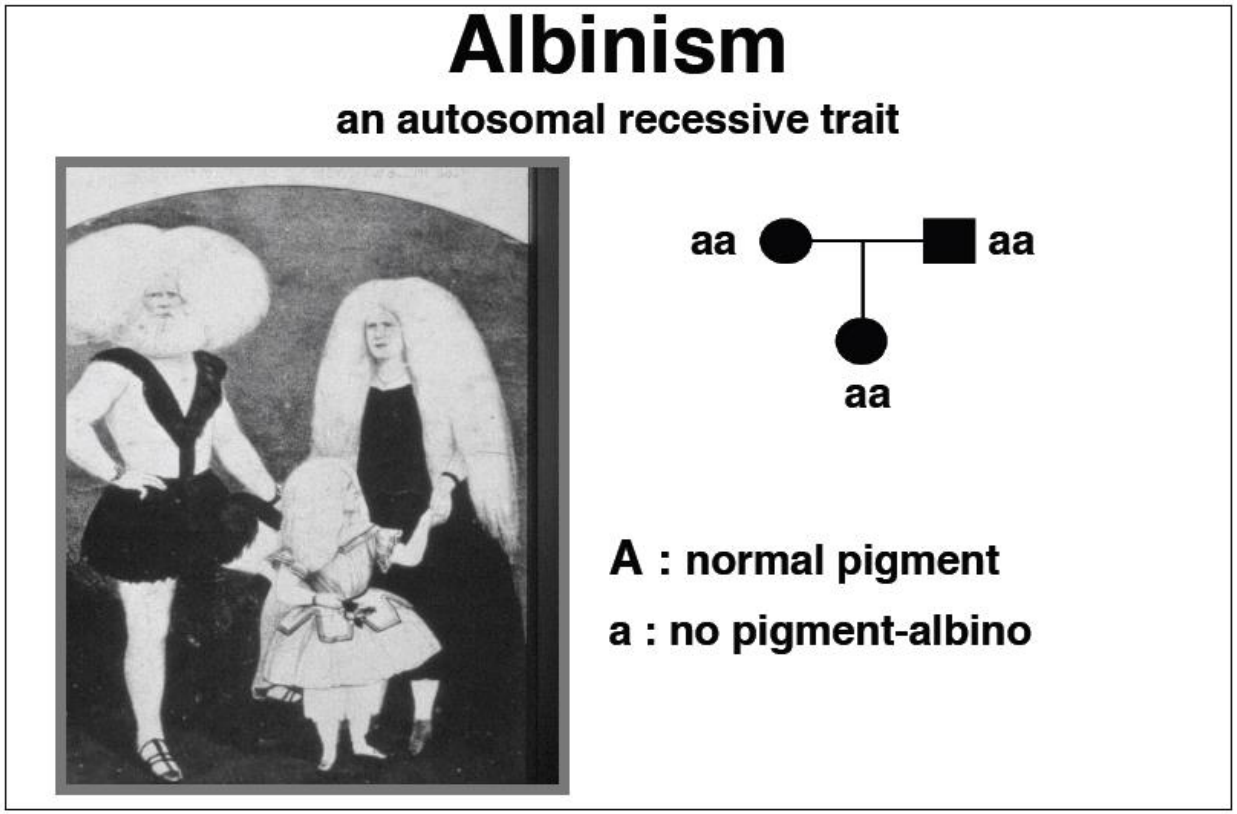
- Most affected individuals have unaffected parents
- About ¼ children in large affected families show the trait
- Both sexes affected in approximately equal numbers
- Affected parents have only affected children

Autosomal recessive pedigree



- What is the father's genotype?

Autosomal recessive pedigree

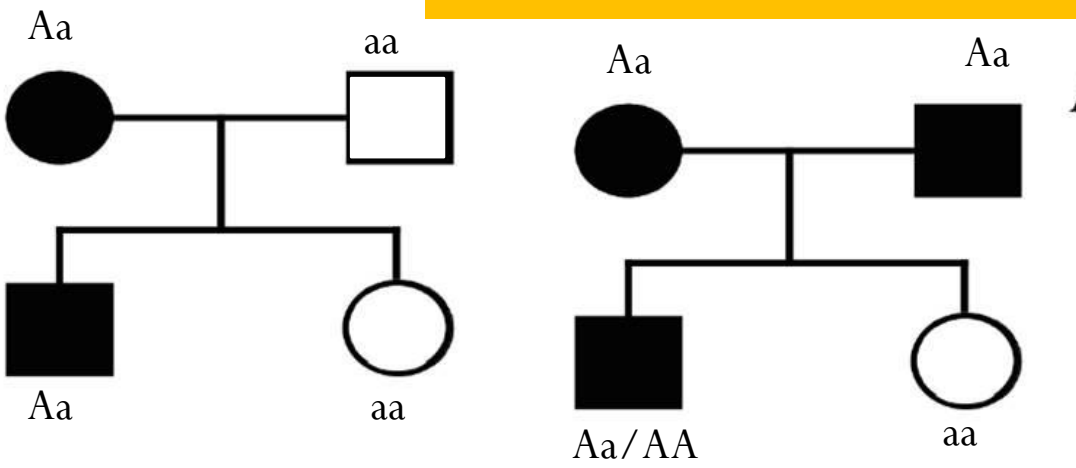


- What is the probability that the next child will be albino?

Autosomal dominant

- **Characteristics of autosomal dominant traits**
  - Every affected individual has at least one affected parent (except in traits with high mutation rates or incomplete penetrance)
  - If an affected individual is heterozygous and has an unaffected mate, each child has a 50% chance of being affected
  - Two affected individuals can have an unaffected child

Can an AA × Aa have unaffected children??

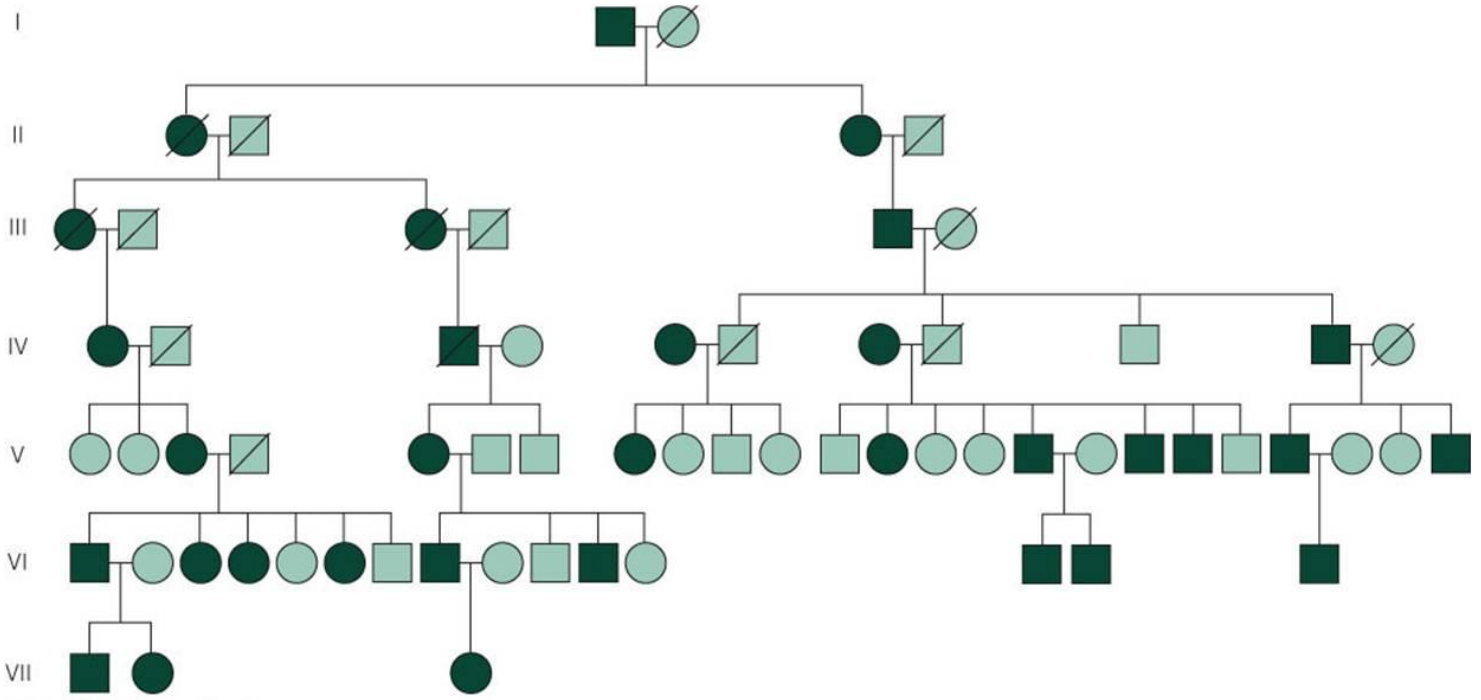


Autosomal dominant trait

Dominant **because two affected parents have a non-affected child**

Autosomal **because daughter must also show the trait if it was X-linked**

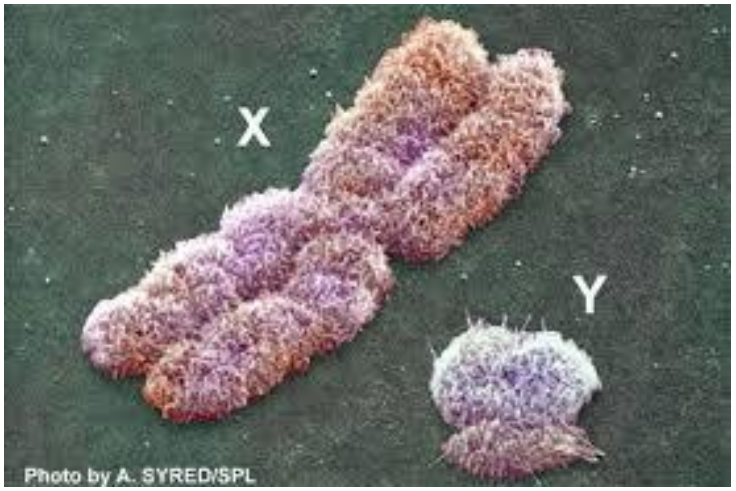
Autosomal dominant pedigree



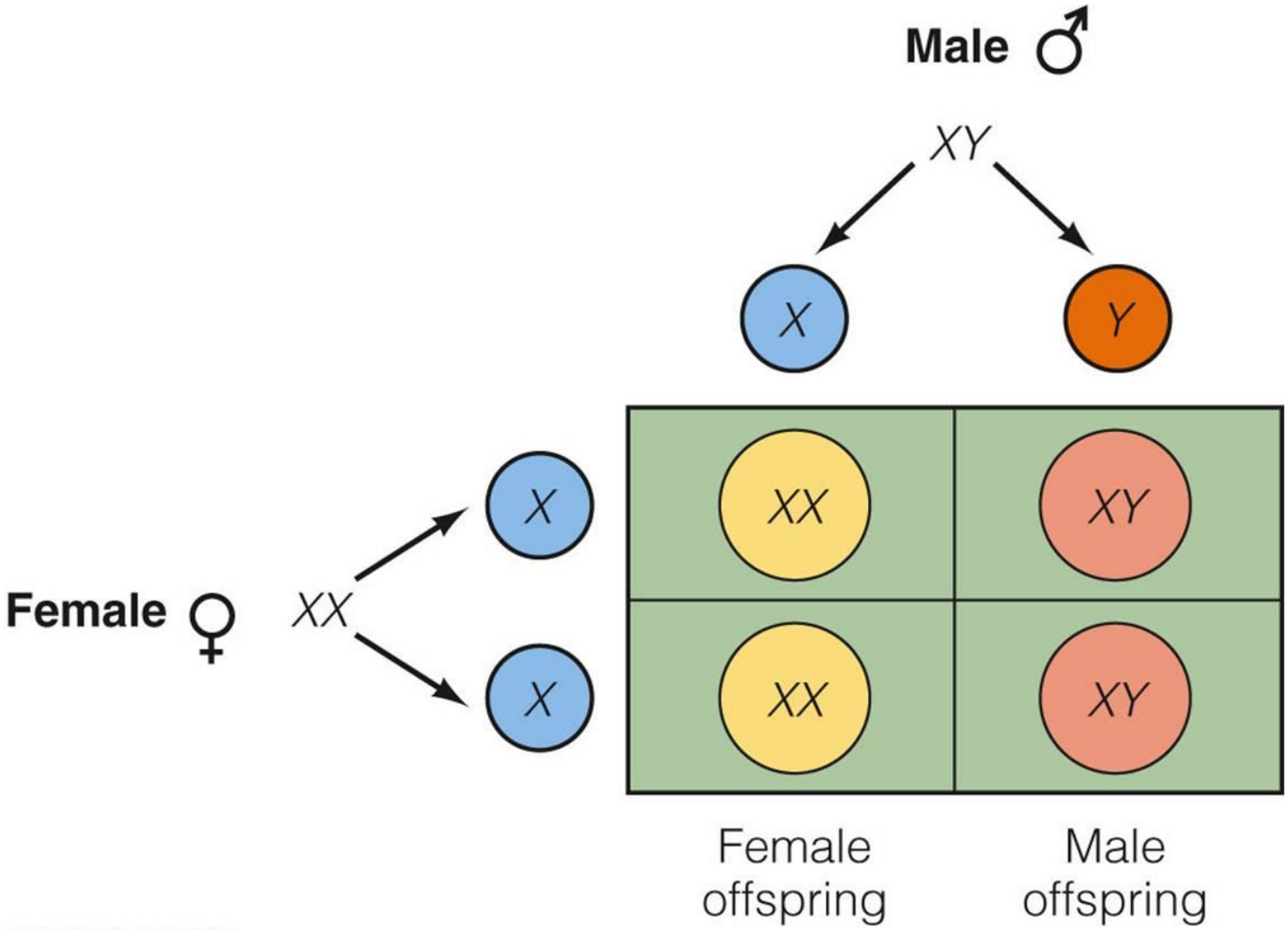
- Affected individuals have at least one affected parent
- About ½ of children of an affected parent are affected
- Both sexes equally affected
- Affected parents can have an unaffected child

Sex-linked inheritance

- Genes on sex chromosomes have a distinct pattern of inheritance
- Males pass an X chromosome to all of their daughters but none of their sons
- Females pass an X chromosome to all of their children
- Most genes on the X chromosome are not on the Y chromosome



Sex-linked inheritance



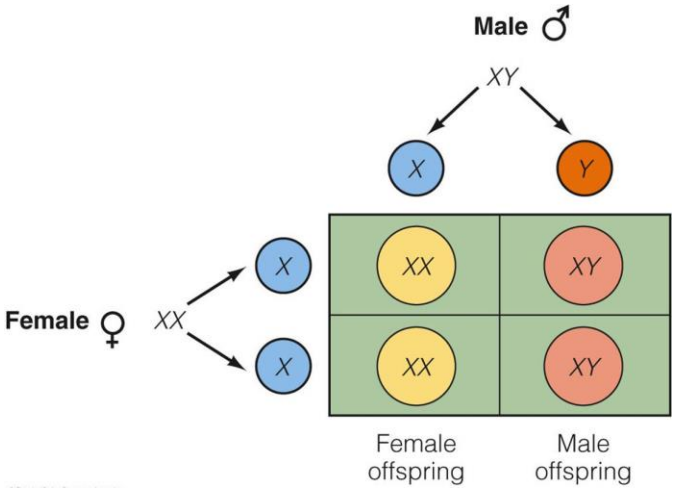
Sex-linked inheritance

- X-linked
  - Pattern of inheritance that results from genes located on the X chromosome

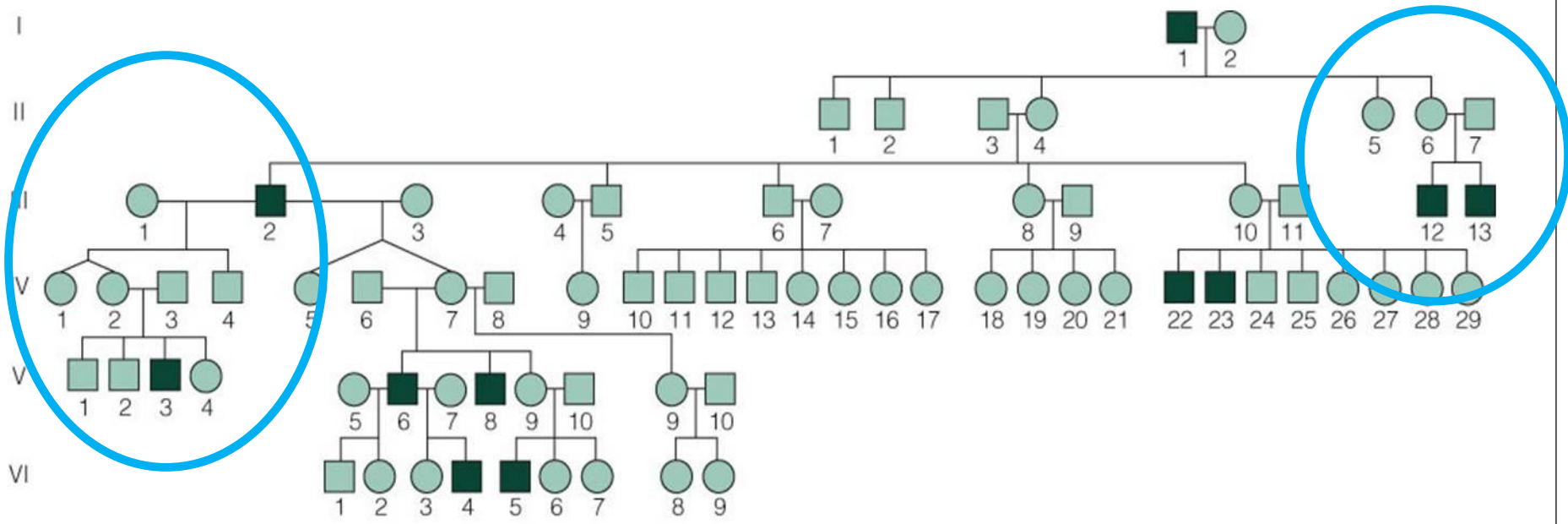
- Y-linked
  - Pattern of inheritance that results from genes located only on the Y chromosome

X-linked recessive

- Characteristics of X-linked recessive traits
  - Affected males receive the mutant allele from their mother and transmit it to all of their daughters, **but not to their sons**
  - Daughters of affected males are usually heterozygous
  - Sons of heterozygous females have a 50% chance of being affected

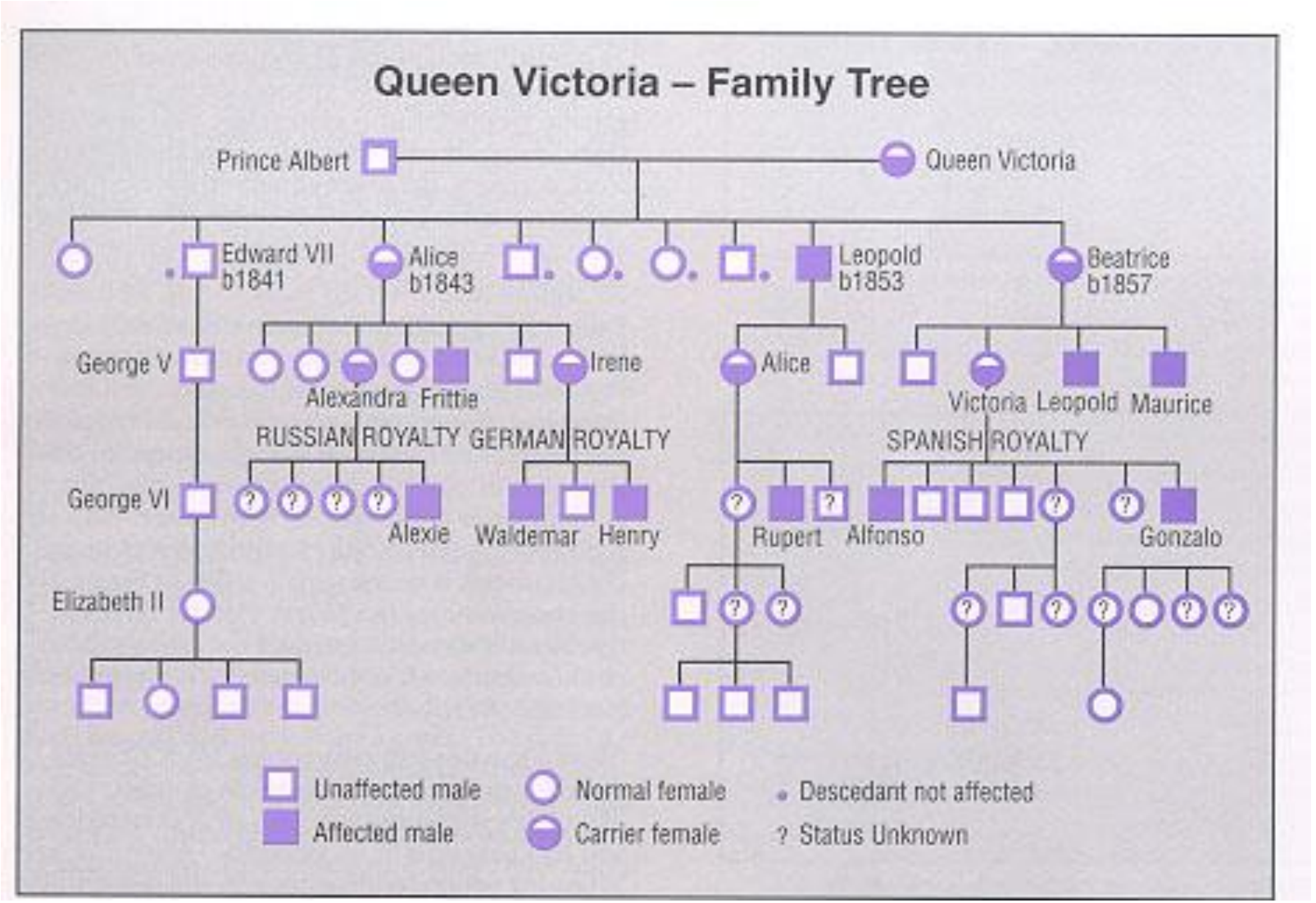


X-linked recessive pedigree



- Hemizygous males are affected and transmit the mutant allele to all their daughters who become carriers
- Phenotypic expression much more common in males

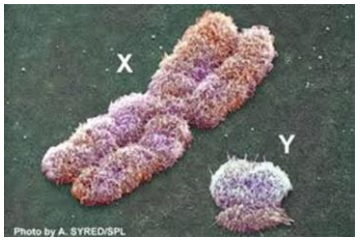
Haemophilia in European royalty



Males have hemizygous genes

- X-linked recessive traits affect males more than females because males are hemizygous for genes on the X chromosome
- A gene present on the X chromosome that is expressed in males in both the recessive and dominant condition

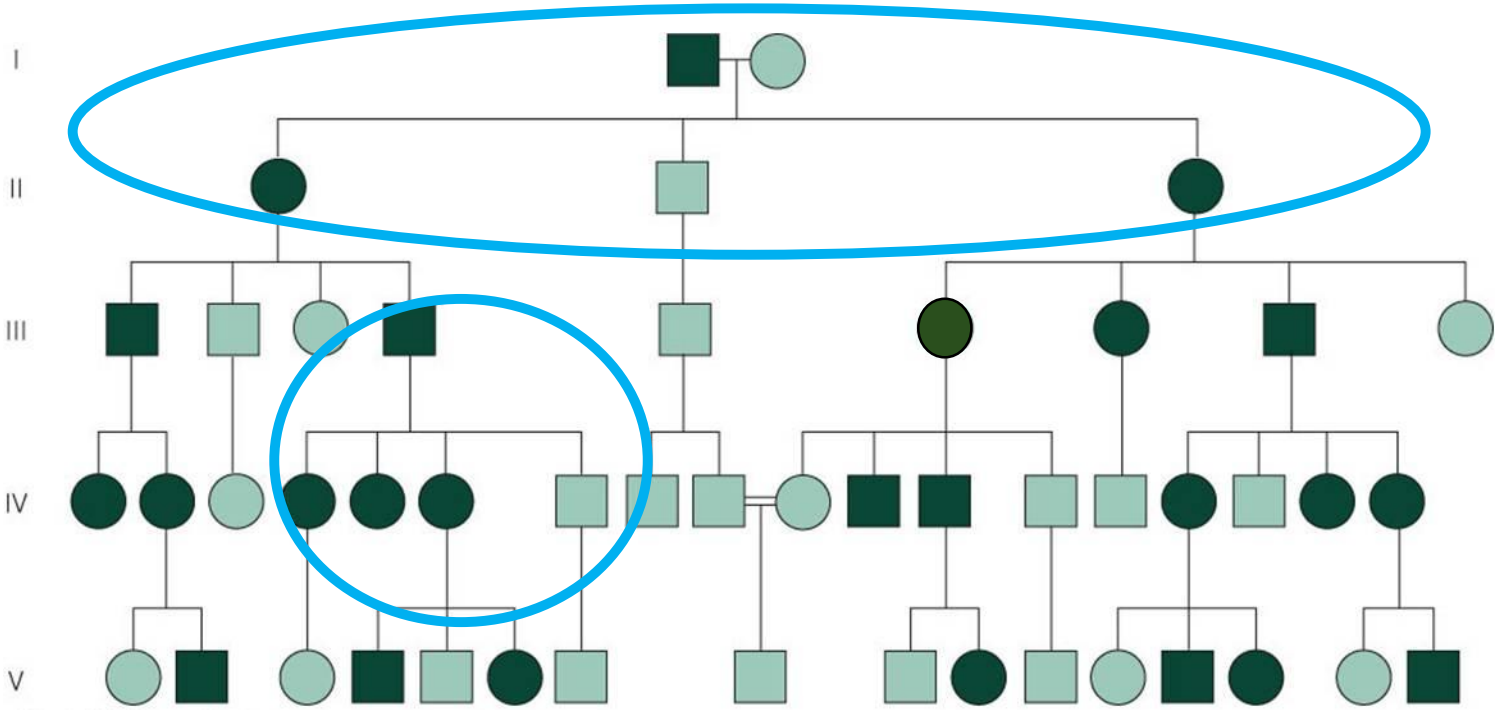
- Or a gene present only in one copy in a diploid organism, e.g. most of the X chromosome genes in a male human.



X-Linked dominant

- Characteristics of X-linked dominant traits
  - Affected males produce all **affected daughters** and no affected sons
  - A heterozygous affected female will transmit the trait to half of her children
    - Her sons and daughters are equally affected
  - On average, twice as many daughters as sons are affected- **WHY?**

X-linked dominant pedigree



- **Affected males produce all affected daughters and no affected sons.**
- Affected females transmit the trait to about half their children.
- About twice as many females affected as males.

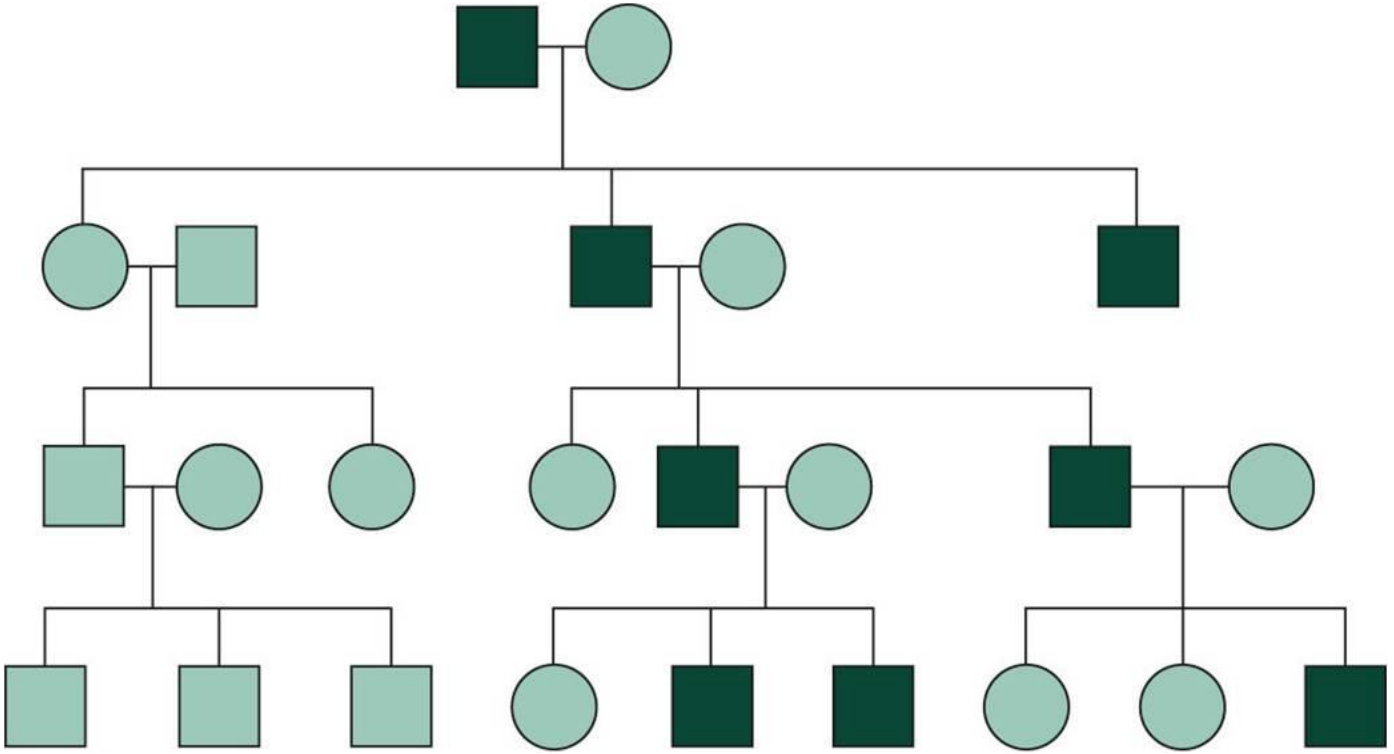
Paternal inheritance: Y Chromosome

- Only males have Y chromosomes
- Genes on the Y chromosome are passed directly from father to son

- All Y-linked genes are expressed
- Males are **hemizygous** for genes on the Y chromosome

- Extremely rare- mutations can become lethal because of the few crucial genes expressed on the Y

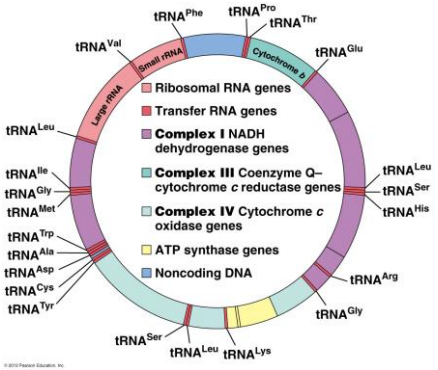
Y-linked pedigree



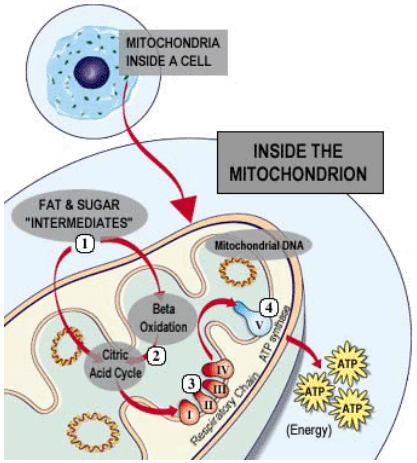
- All sons of affected males are affected

Maternal inheritance: mitochondrial genes

- **Mitochondria**
  - Cytoplasmic organelles that convert energy from food into ATP (ATP powers cellular functions)
  - Carry DNA for 37 mitochondrial genes

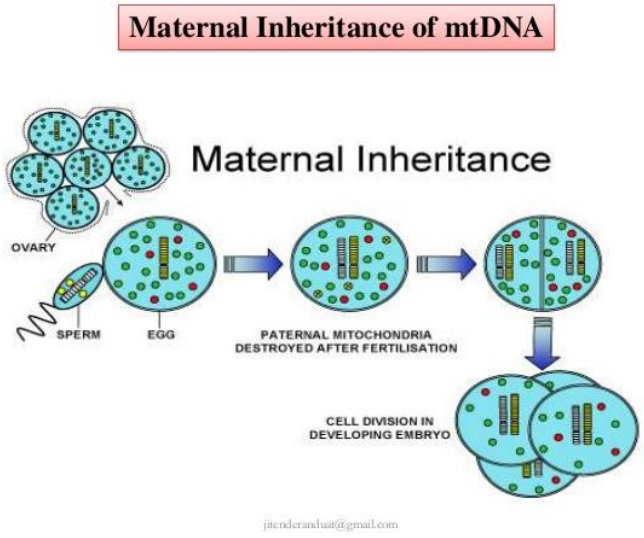


- Genetic disorders in mitochondrial DNA are associated with defects in energy conversion

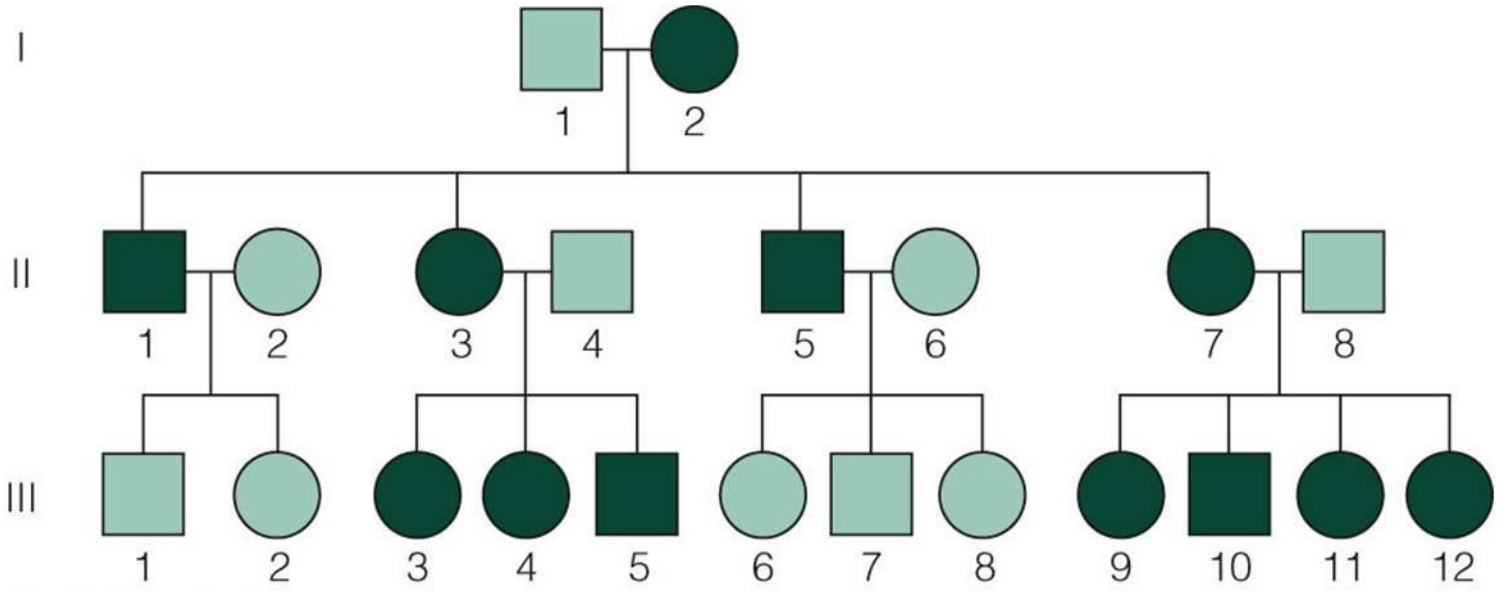


Maternal inheritance: mitochondrial genes

- **The egg provides all the mitochondria to the zygote.**
  The sperm does not pass on any mitochondria
  - Hence we all have our mother's mitochondrial DNA
  - All siblings, male and female, in a family will have the same mitochondrial DNA
  - Used in forensic science to establish identities



Mitochondrial gene pedigree

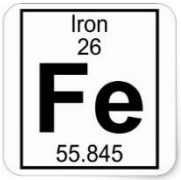


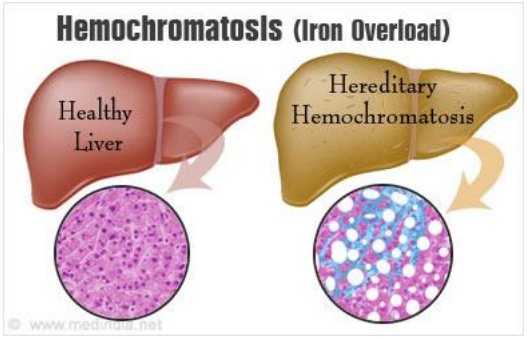
- Mitochondria (and genetic disorders caused by mutations in mitochondrial genes) are maternally inherited
- Both males and females can be affected, but **only affected females** pass on the trait.
- How many mitochondrial genotypes?

Added complexity: Variations in gene expression

- Variations in gene expression affect pedigree analysis and assignment of genotypes to members of the pedigree

- Genotypes can be **masked** because of:
- Factors can affect gene expression
  - Interactions with other genes in the genotype
  - Interactions between genes and the environment





Added complexity: Age-related phenotypic expression

- **Huntington disease**
  - An autosomal dominant disorder associated with progressive neural degeneration and dementia
  - Adult onset is followed by death in 10 to 15 years

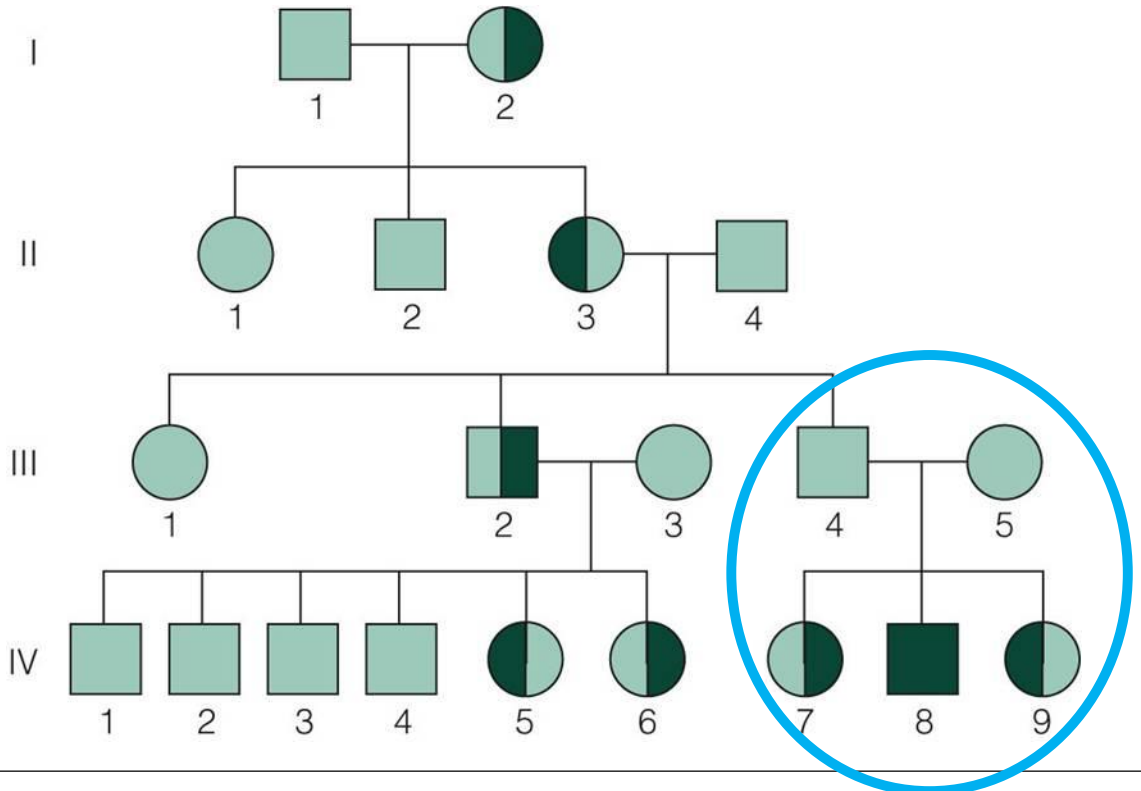
- **Porphyria**
  - An autosomal dominant disorder that leads to intermittent attacks of pain and dementia
  - Symptoms first appear in adulthood

Added complexity: Two aspects of phenotypic variation

- **Penetrance**
  - The probability that a disease phenotype will appear when a disease-related genotype is present
- **Expressivity**
  - The range of phenotypic variation associated with a given phenotype

Incomplete penetrance

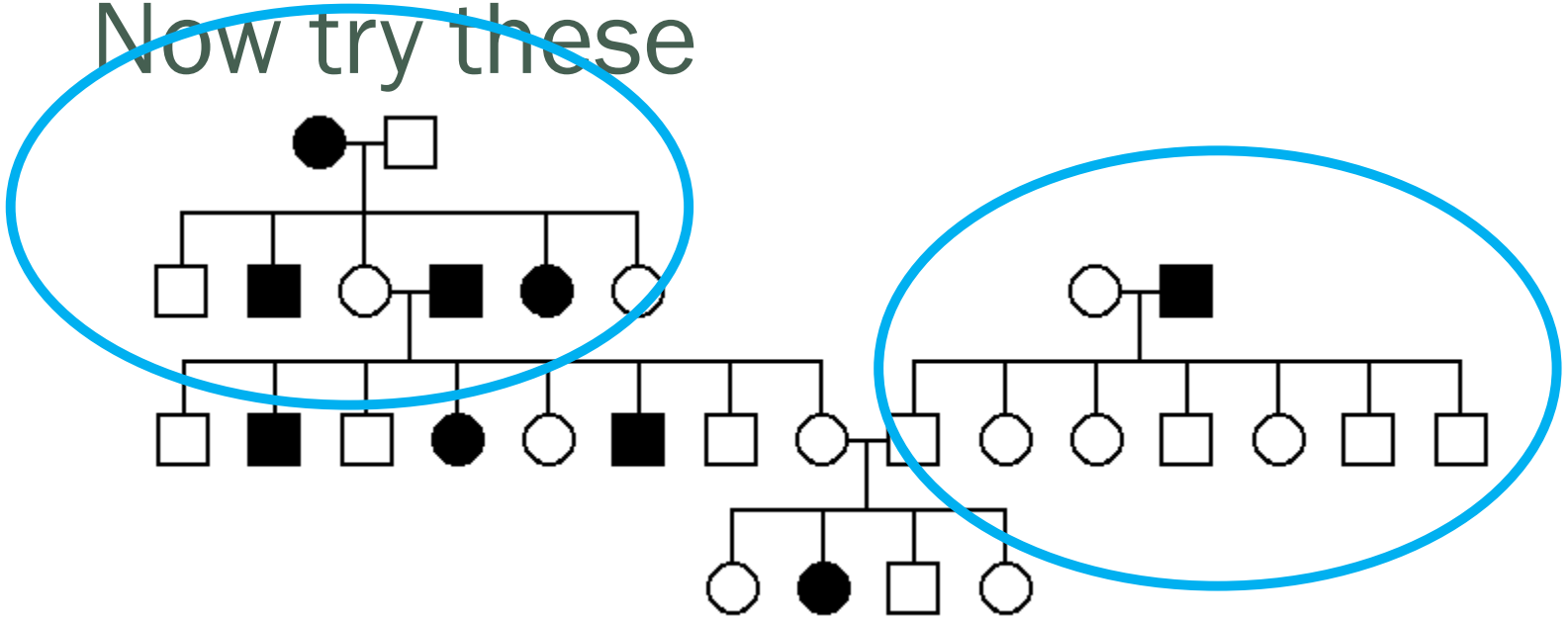
- Camptodactyly (campto-dacty-ly)
  - A dominant trait (immobile, bent little fingers) with **variable expression and incomplete penetrance**



Fully shaded symbols indicate people with both hands affected, left shading only left hand affected, right shading only right hand affected.

III-4 is likely a carrier with incomplete penetrance as children affected

Now try these



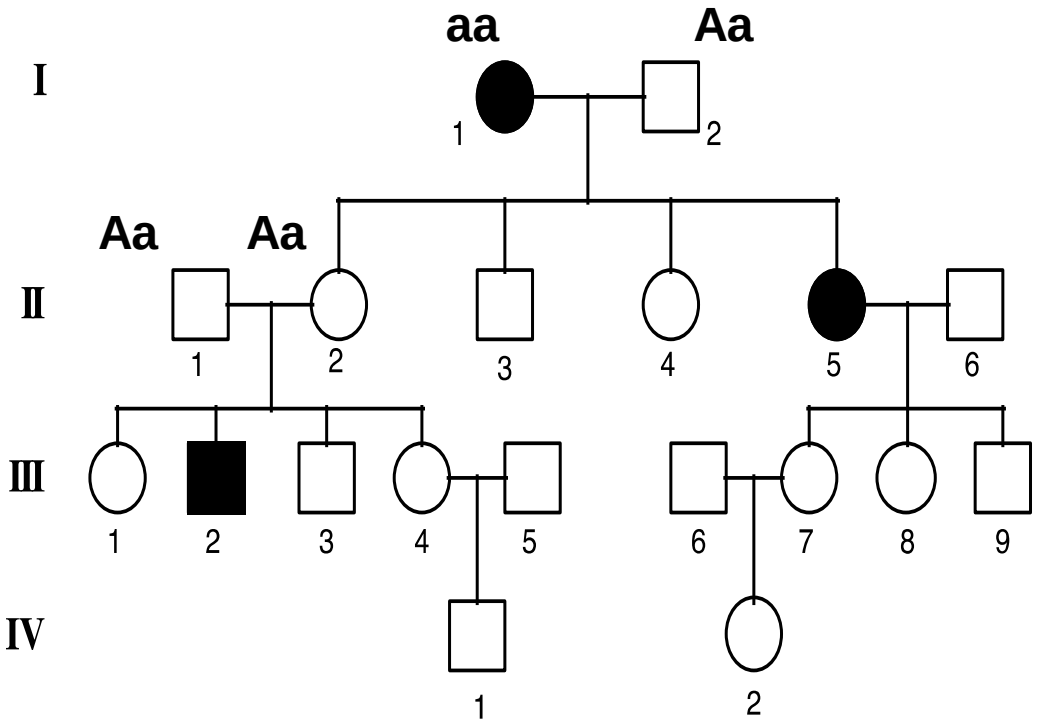
- Which best describes the genetics of the afflicting allele in the pedigree?

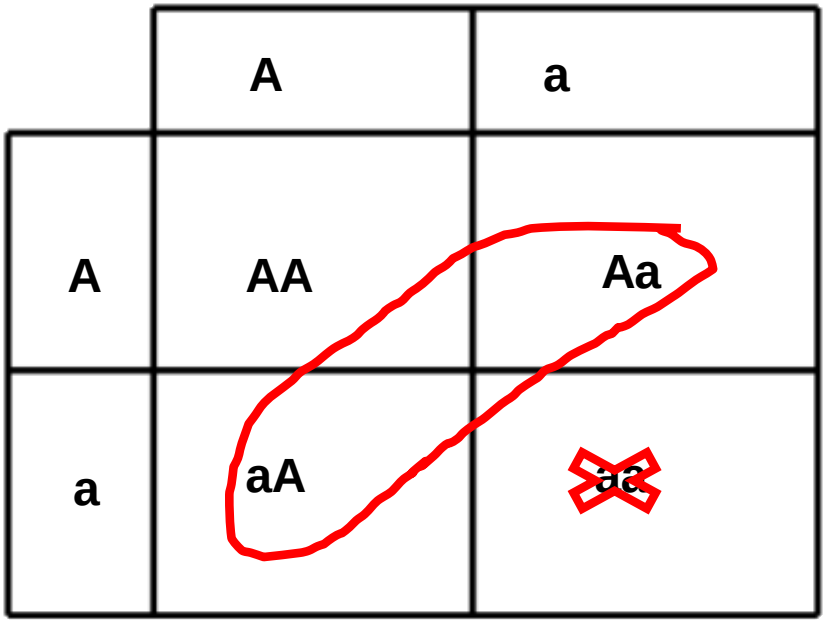
- autosomal dominant
- autosomal recessive
- X-linked dominant
- X-linked recessive
- Y-linked dominant
- Y-linked recessive

- Alkaptonuria (al-kapto-nuria) is a autosomal recessive condition in which an affected person produces urine containing a substance that causes the urine to turn black on exposure to air. The shaded individuals in the following pedigree have alkaptonuria.

The probability of the indicated individual being a heterozygote for alkaptonuria is

A. 2/3 for II-2.
B. ½ for II-1.
C. 2/3 for III-4.
D. ½ for III-7.





4 possible genotypes

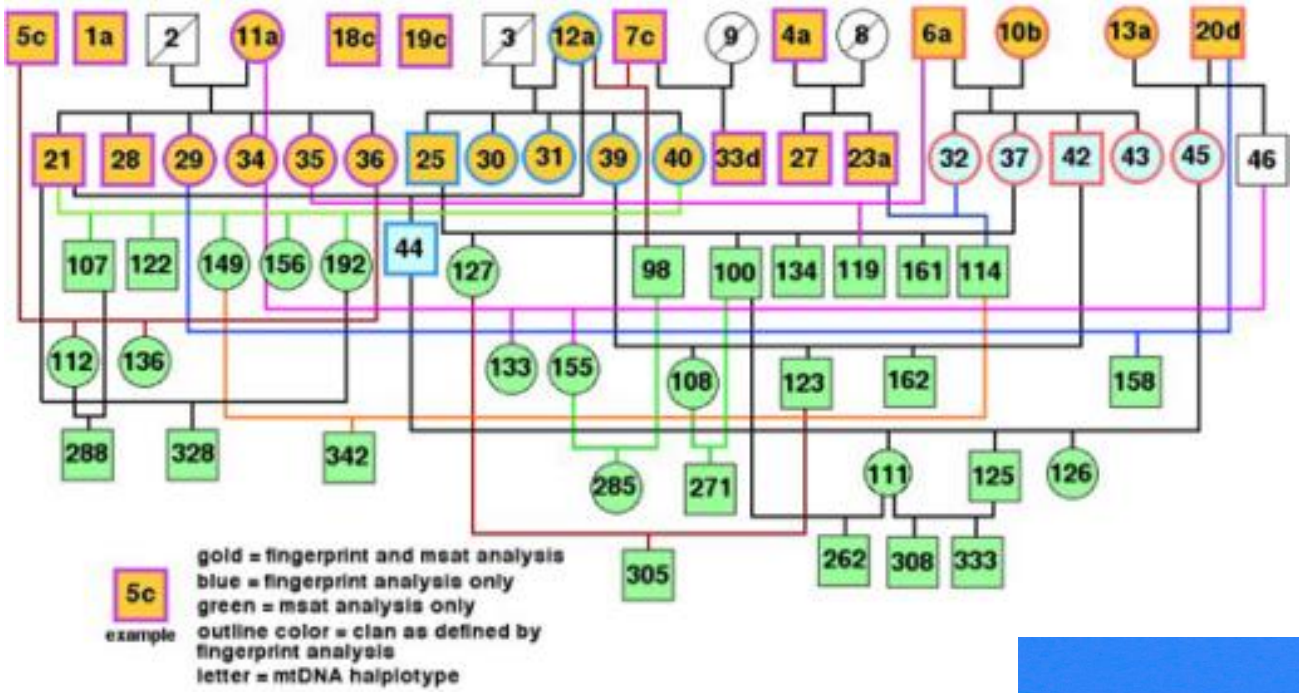
But: individual III-4 is not affected

A catalogue of human genetic traits

- OMIM- https://www.omim.org/
- Genetic traits are described, catalogued, and numbered in a database called
  - Online Mendelian Inheritance in Man (OMIM)
- OMIM is updated daily and contains information about all known human genetic traits

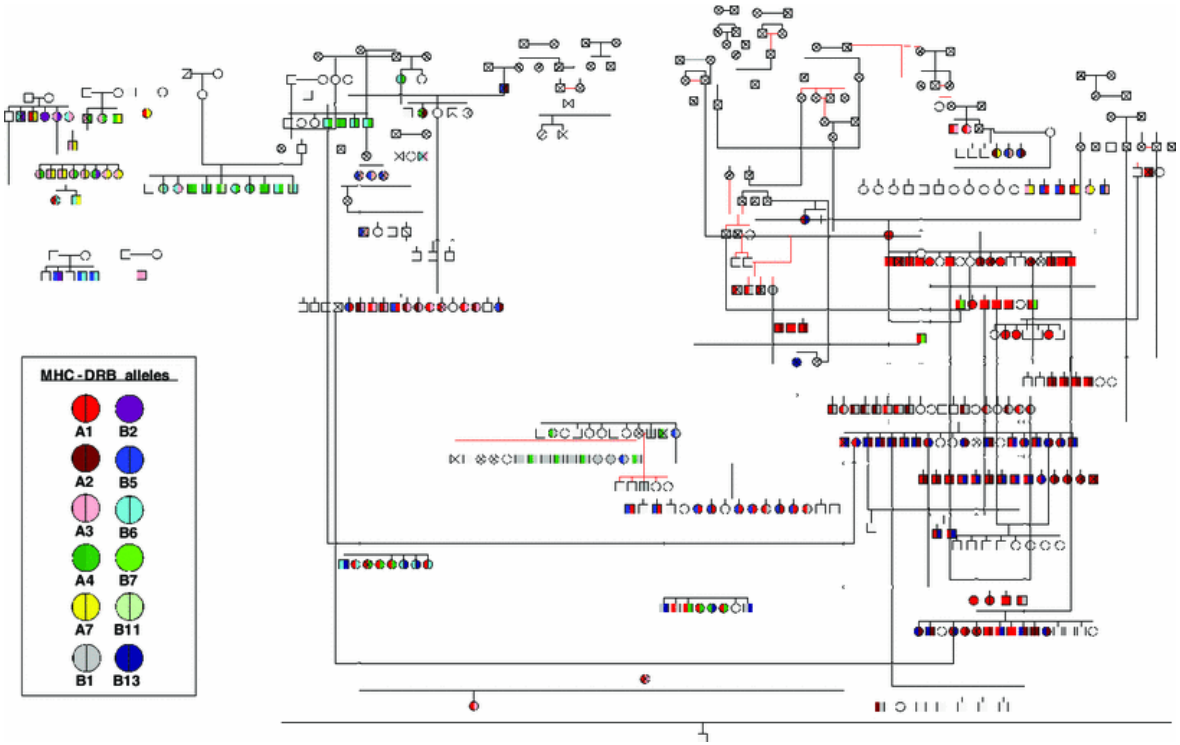
OMIM www.omim.org

Captive breeding of the Californian Condor



Romanov MN, et al. (2009) . The value of avian genomics to the conservation of wildlife BMC Genomics . doi: 10.1186/1471-2164-10-S2-S10.

Current African wild dog pedigree (European captive breeding program



Red lines indicate close inbreeding events. Colours indicate MHC genotypes

8,000 left in the wild, 636 in captivity world wide