

Genetic Introduction

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Types of Referral



Pre-conceptual



Antenatal



Paediatric



Post mortem



**Adult-onset
conditions**



Carrier testing

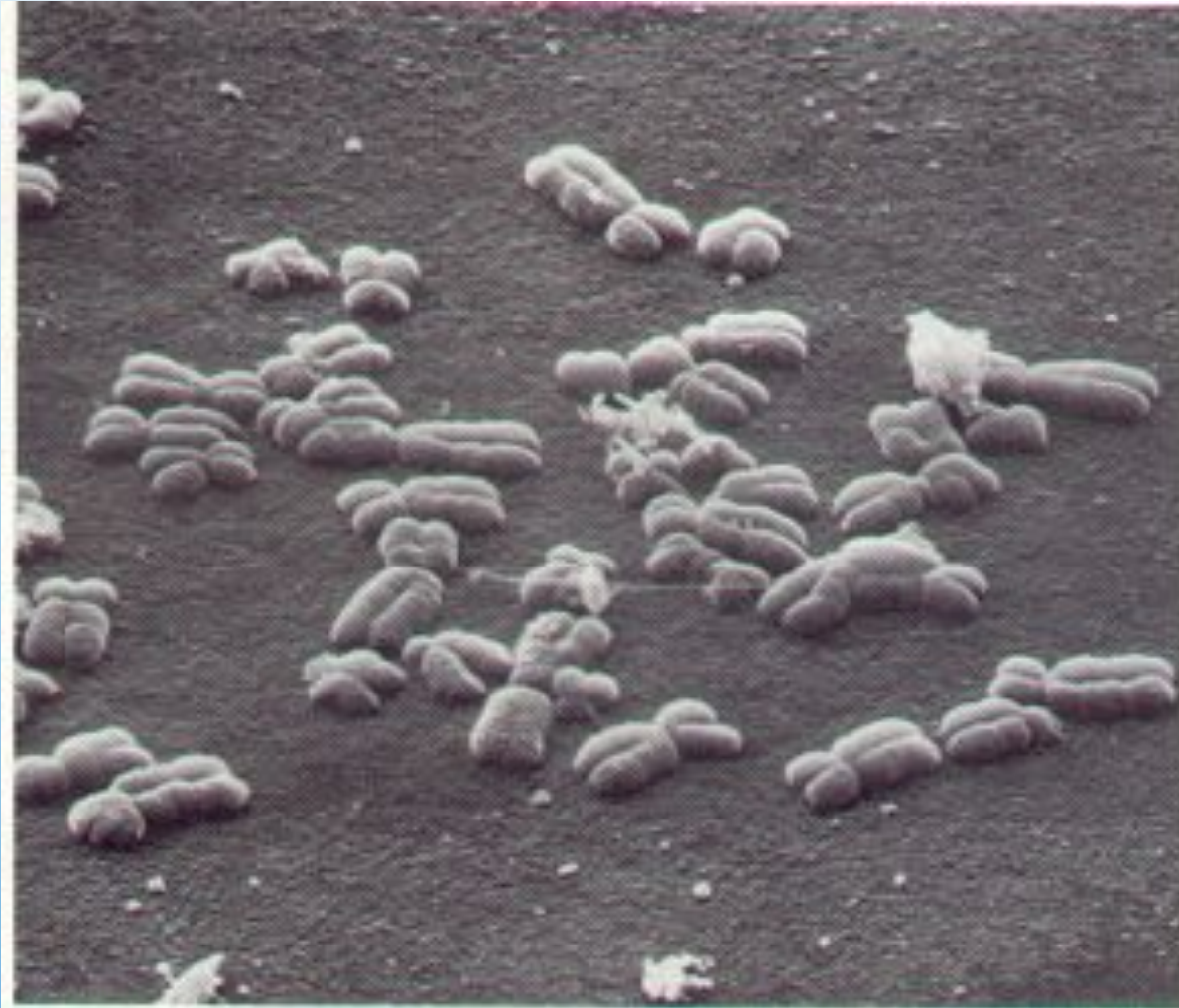


Categories of Genetic Disorders

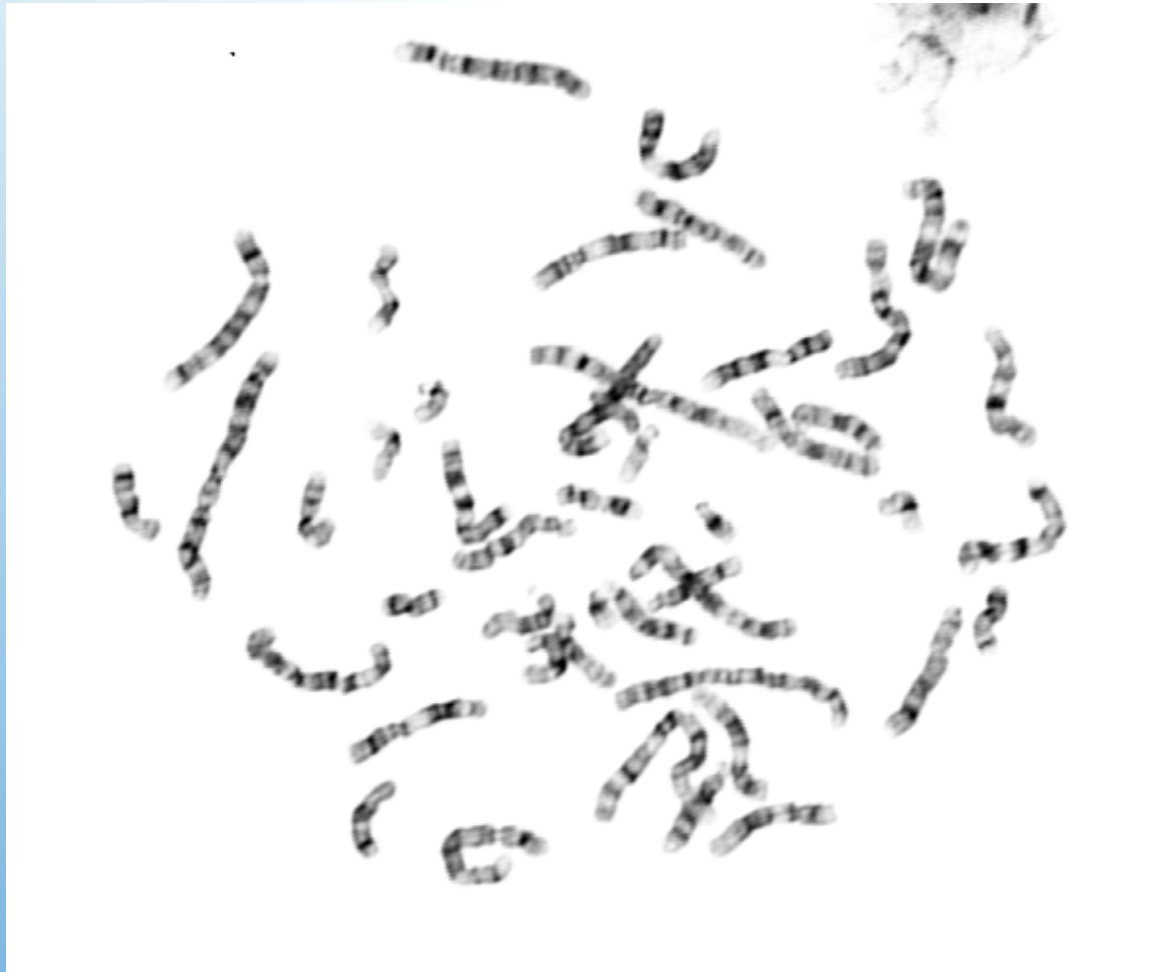
- **Chromosome abnormalities**
- Single gene disorders
- Multi-factorial and polygenic disorders e.g. spina bifida, cleft lip and palate



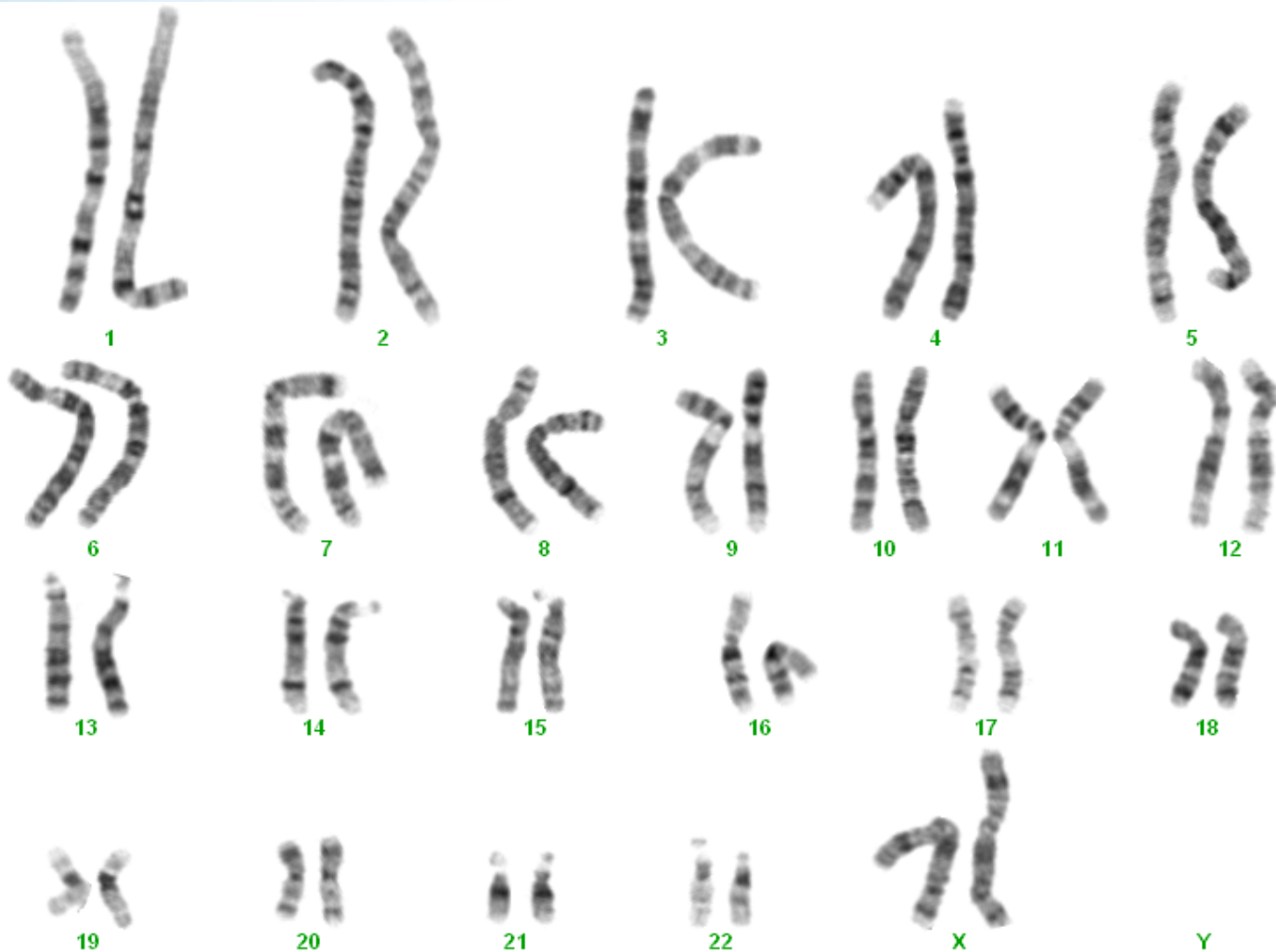
Human Chromosomes



Metaphase Spread



Karyotype



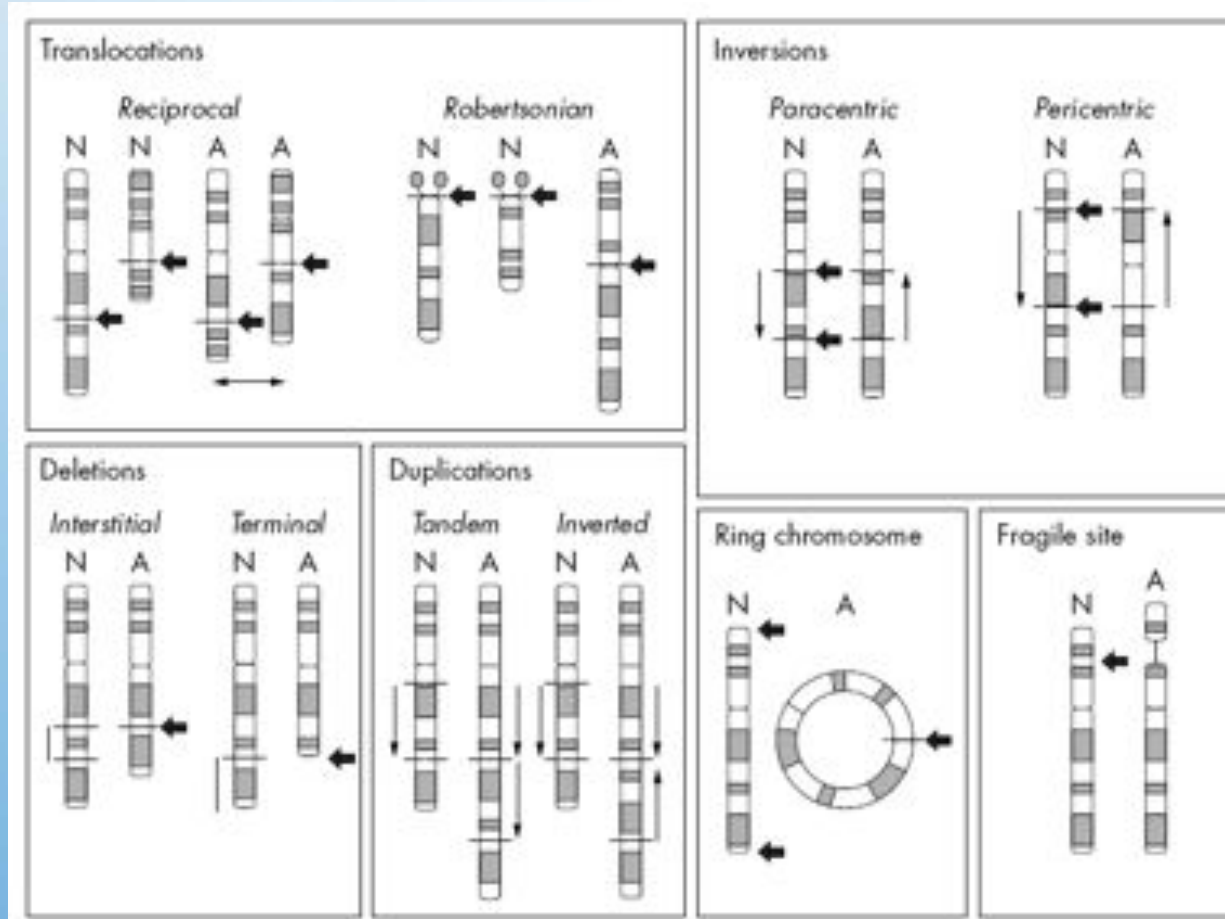
NORMAL FEMALE 46,XX



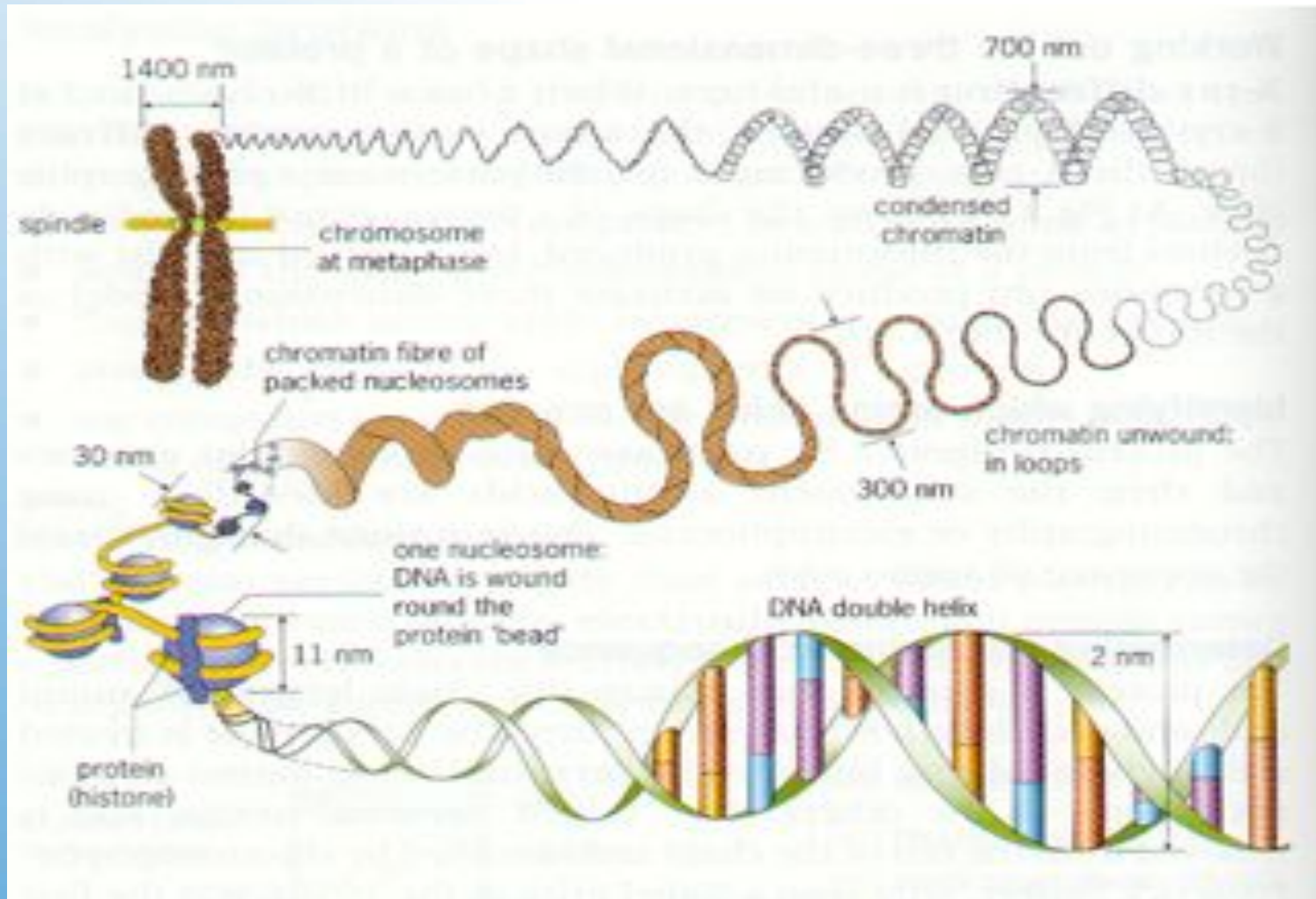
The Power of an Image



Common Structural Anomalies in Clinical Cytogenetics



DNA Packaging



Mendelian Inheritance

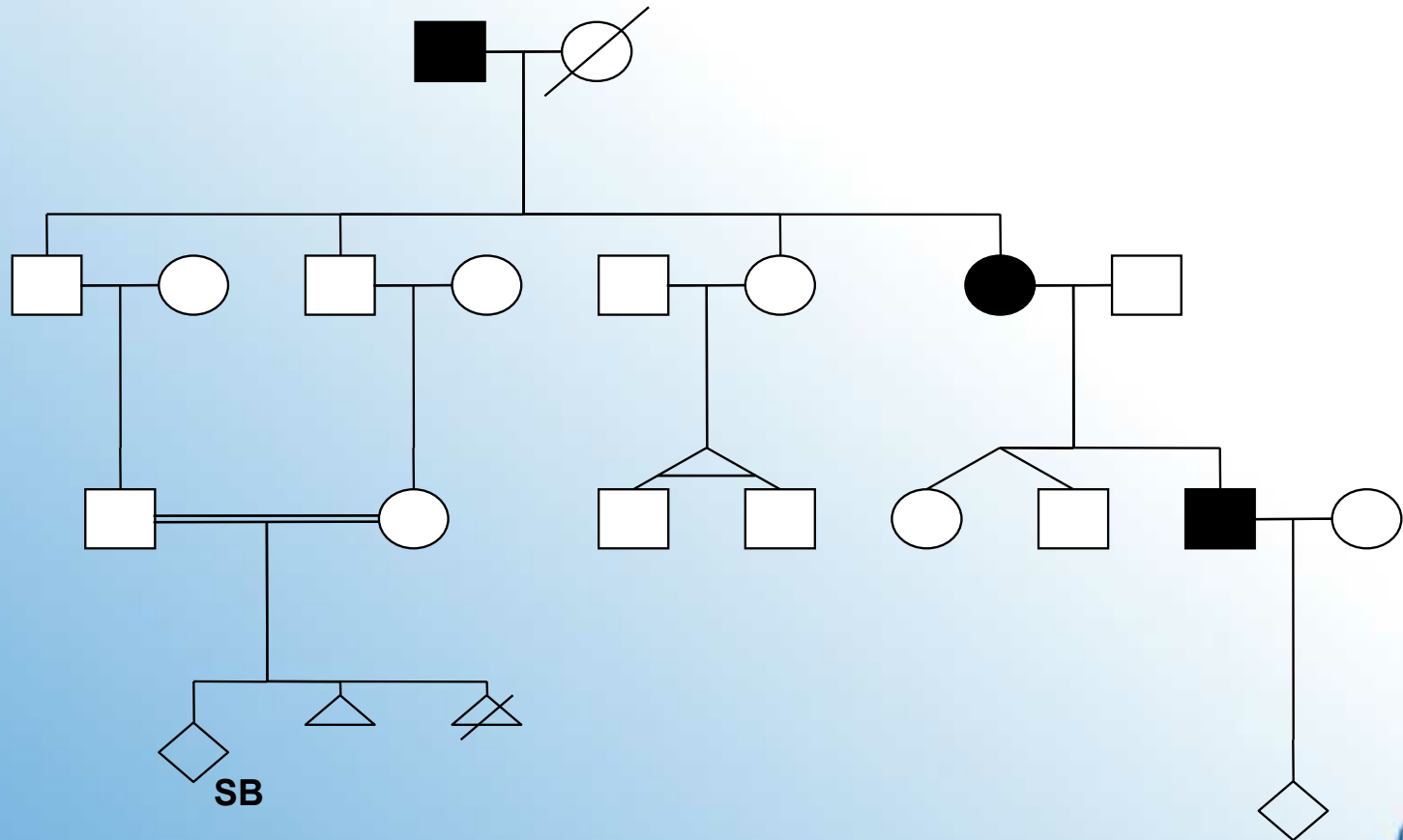
- Autosomal vs. sex-linked
- Dominant vs. recessive

Non-Mendelian Inheritance

- Imprinting
- Mitochondrial inheritance
- Multifactorial
- (Mosaicism)



Pedigree Drawing



Genetic Testing

- What is the condition?
- Can a diagnosis be made clinically?
- Is a genetic test available?
 - gap between research & service
 - not all genes are known!
- What type of test
 - diagnostic, carrier or predictive
- Is consent full & informed
 - who else does the result affect?
 - testing children & adults with learning difficulties
- Any other implications?
- employment, insurance etc.
- Who's paying?



Technology Timeline

Watson & Crick described DNA	1953
Down syndrome (& other aneuploidies)	1959
1 st inherited deletion syndrome (Cri-du-chat)	1963
Chromosome banding	1969
FISH applied to human chromosomes	1982
Dystrophin gene identified	1985
Contiguous gene syndromes	1986
Southern blotting for Fragile-X	1991
CMT duplication	1991
Human Genome project “finished”	2004
Recognition of scale of human genomic variation	2004
Microarrays	2005
Next Generation Sequencing	2012' ish



Pick-up Rates

Standard karyotype

$<1\%$

Fragile-X

$<<1\%$

Microarrays

$\approx 15\%$



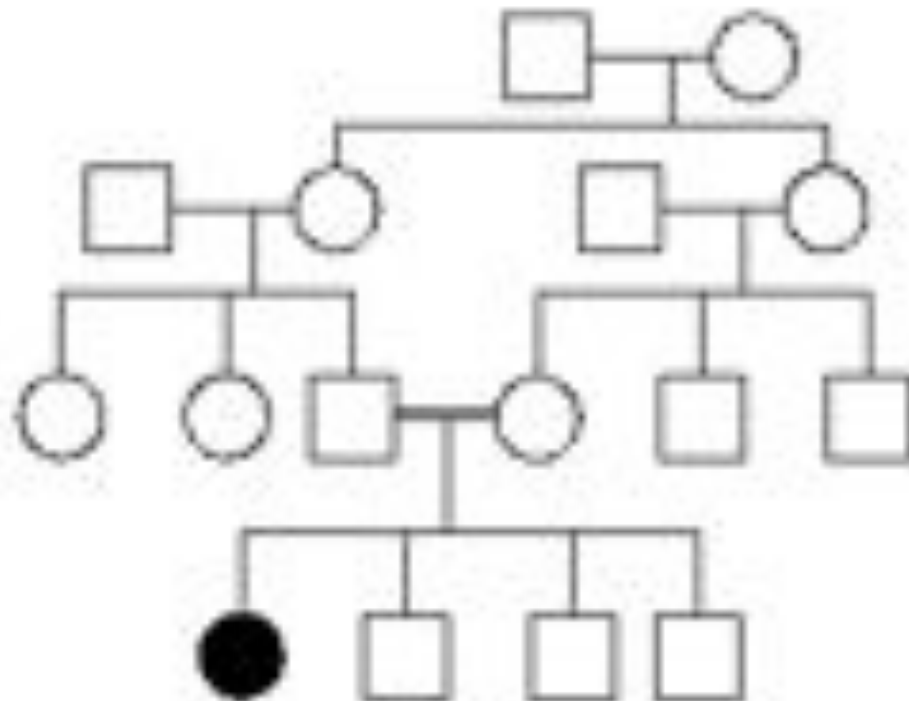
Categories of Genetic Disorders

- Chromosome abnormalities
- **Single gene disorders**
- Multi-factorial and polygenic disorders e.g. spina bifida, cleft lip and palate



What is the Mode of Inheritance Here?

b)



Autosomal Recessive Inheritance

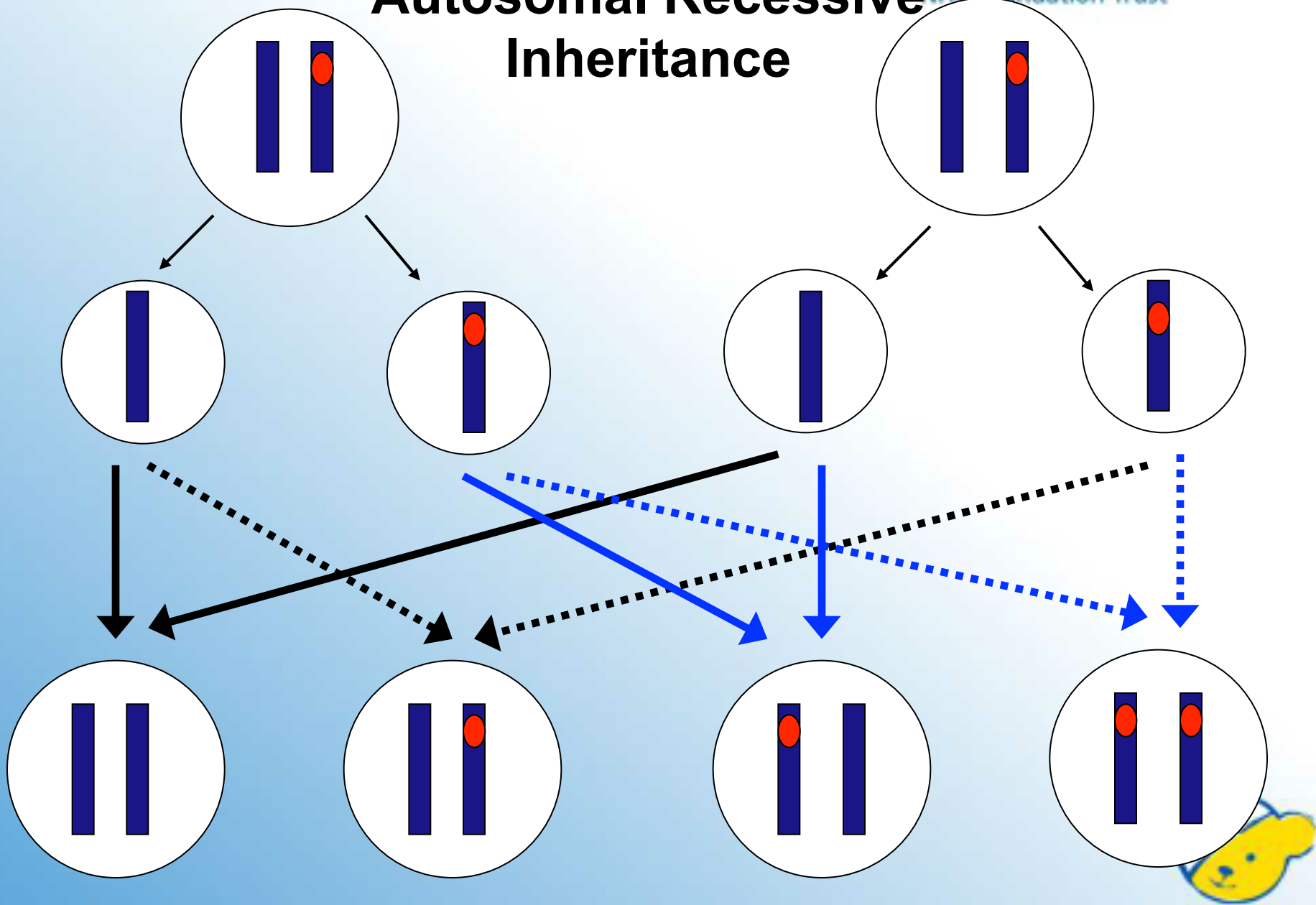
Disease manifest in the homozygous state, i.e. “double-dose” of affected allele(s).

Typical features:

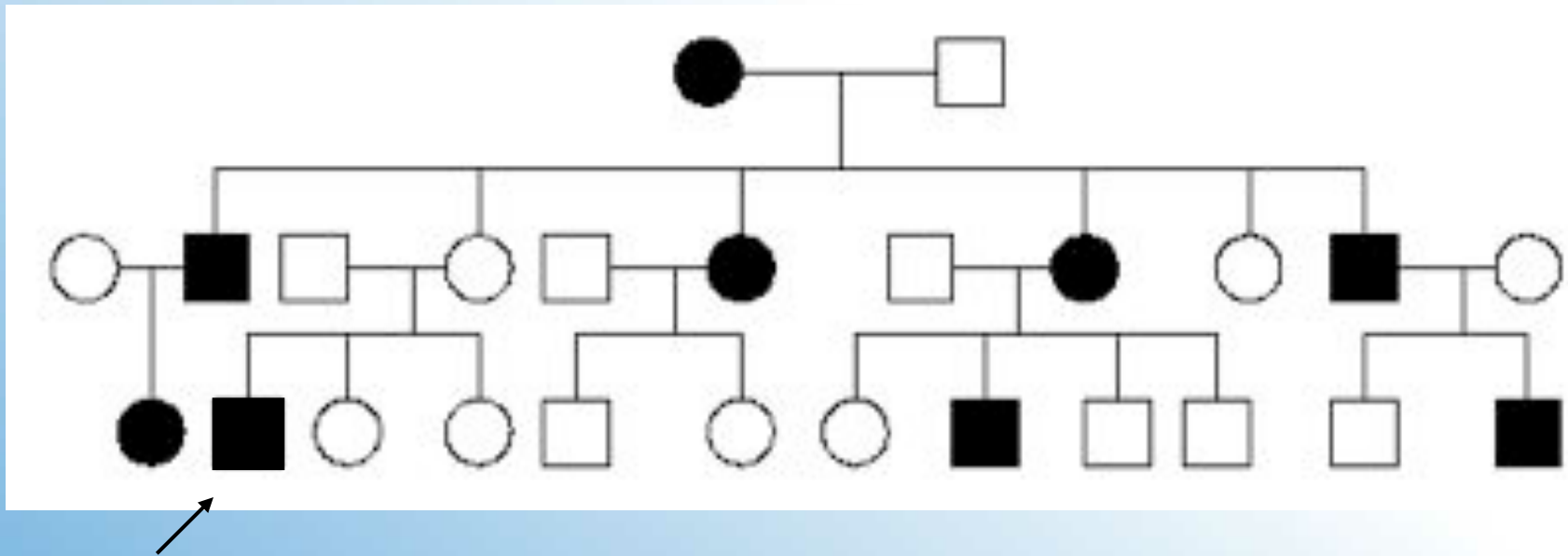
- Male and females affected in equal proportions
- Affected individuals only in a single generation
- Parents can be related, i.e. consanguineous



Autosomal Recessive Inheritance



What is the Mode of Inheritance Here?



Autosomal Dominant Inheritance

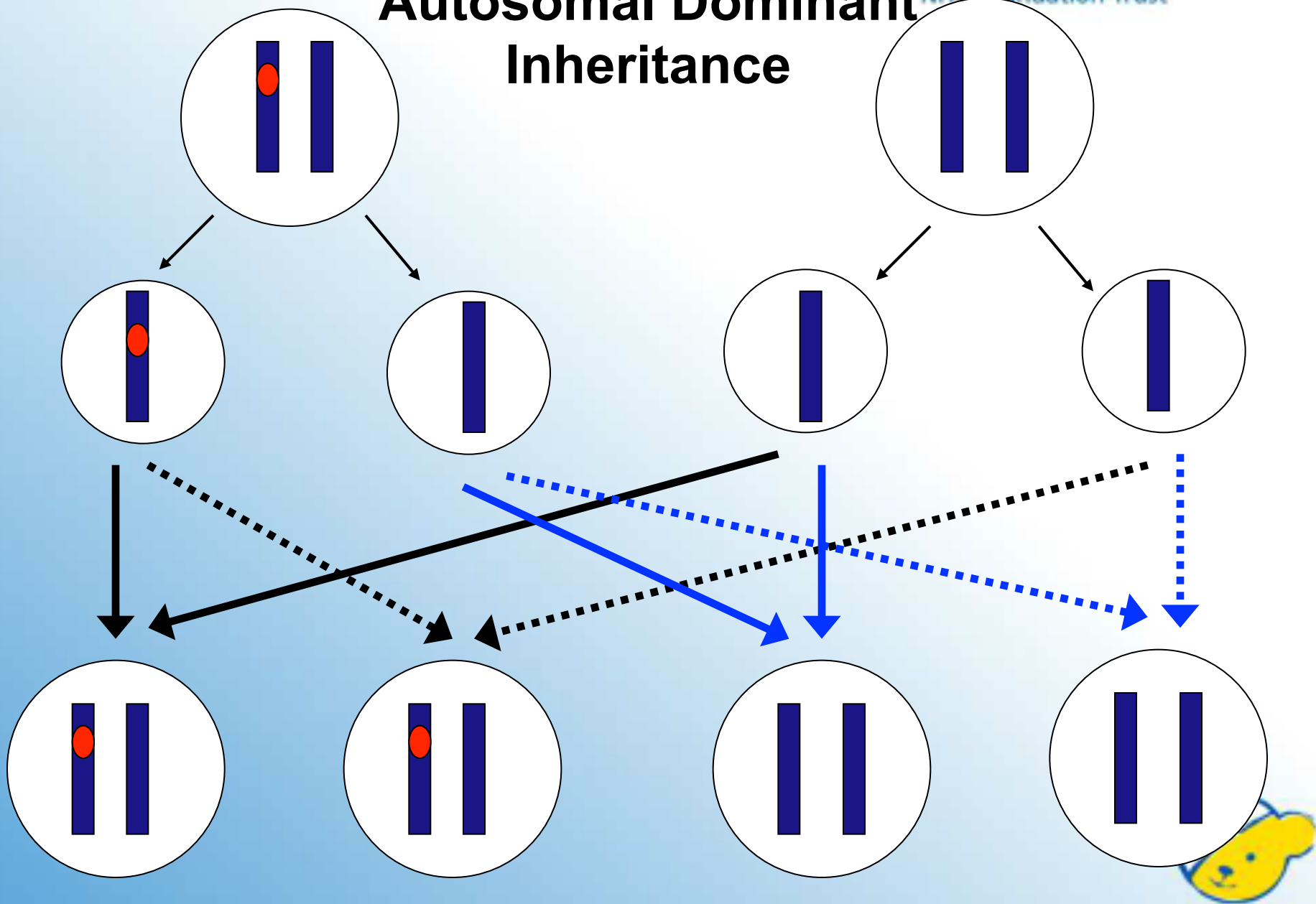
Disease manifest in the heterozygous state,
i.e. only one affected gene needed

Typical features:

- Male and females affected in equal proportions
- Affected individuals in multiple generations
- Transmission by individuals of both sexes, to both sexes
- But don't forget penetrance & variability!



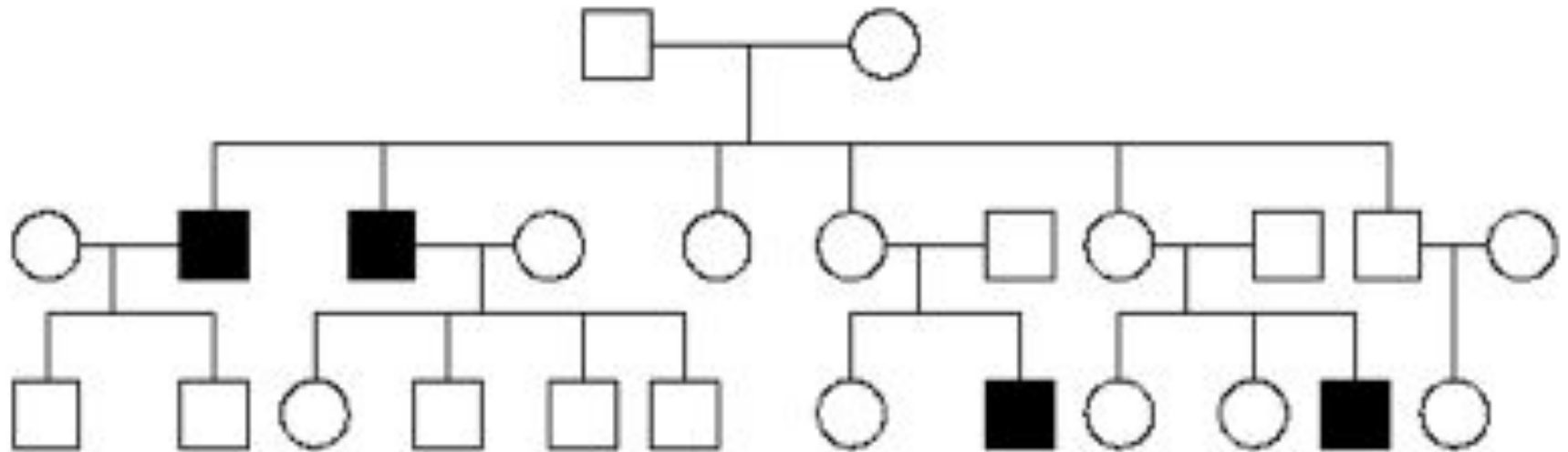
Autosomal Dominant Inheritance



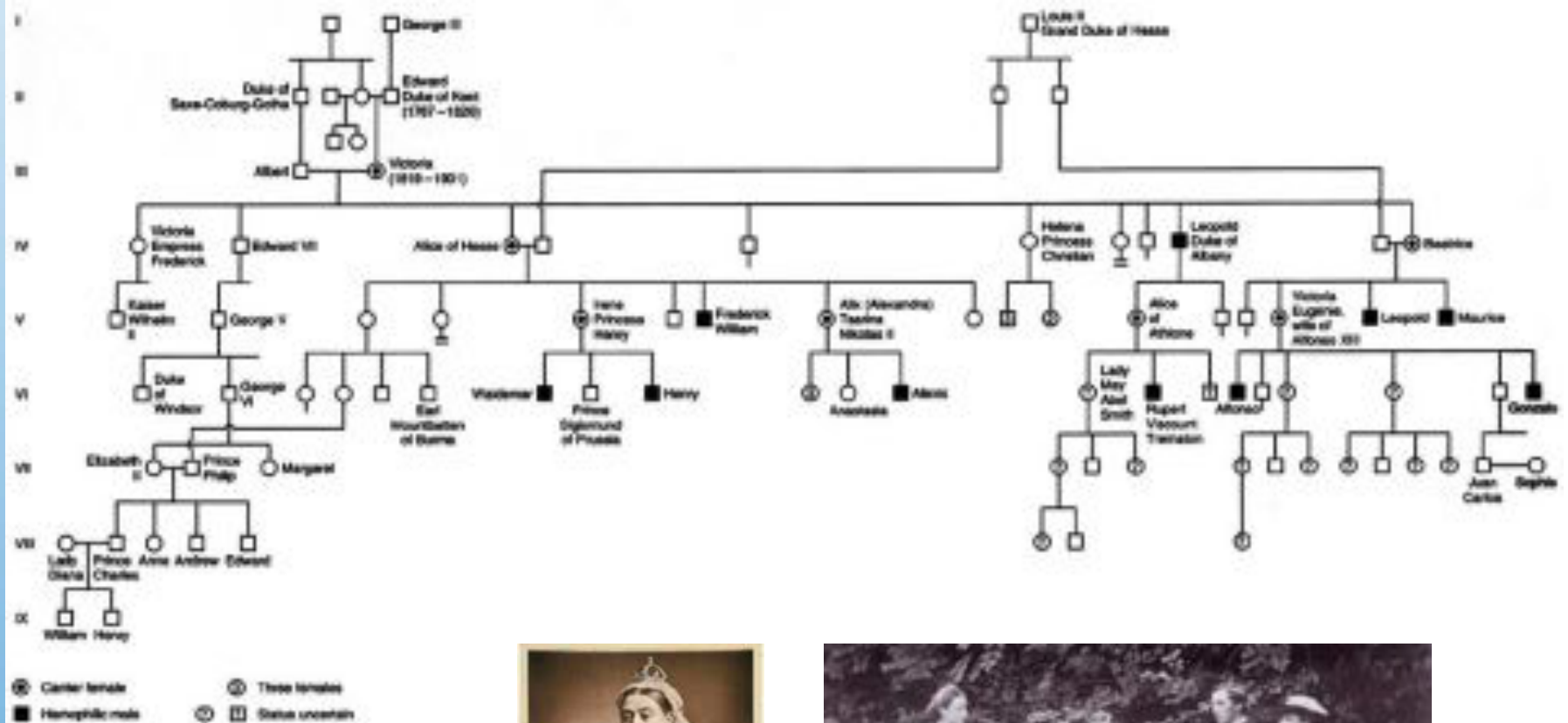
Variable Expression



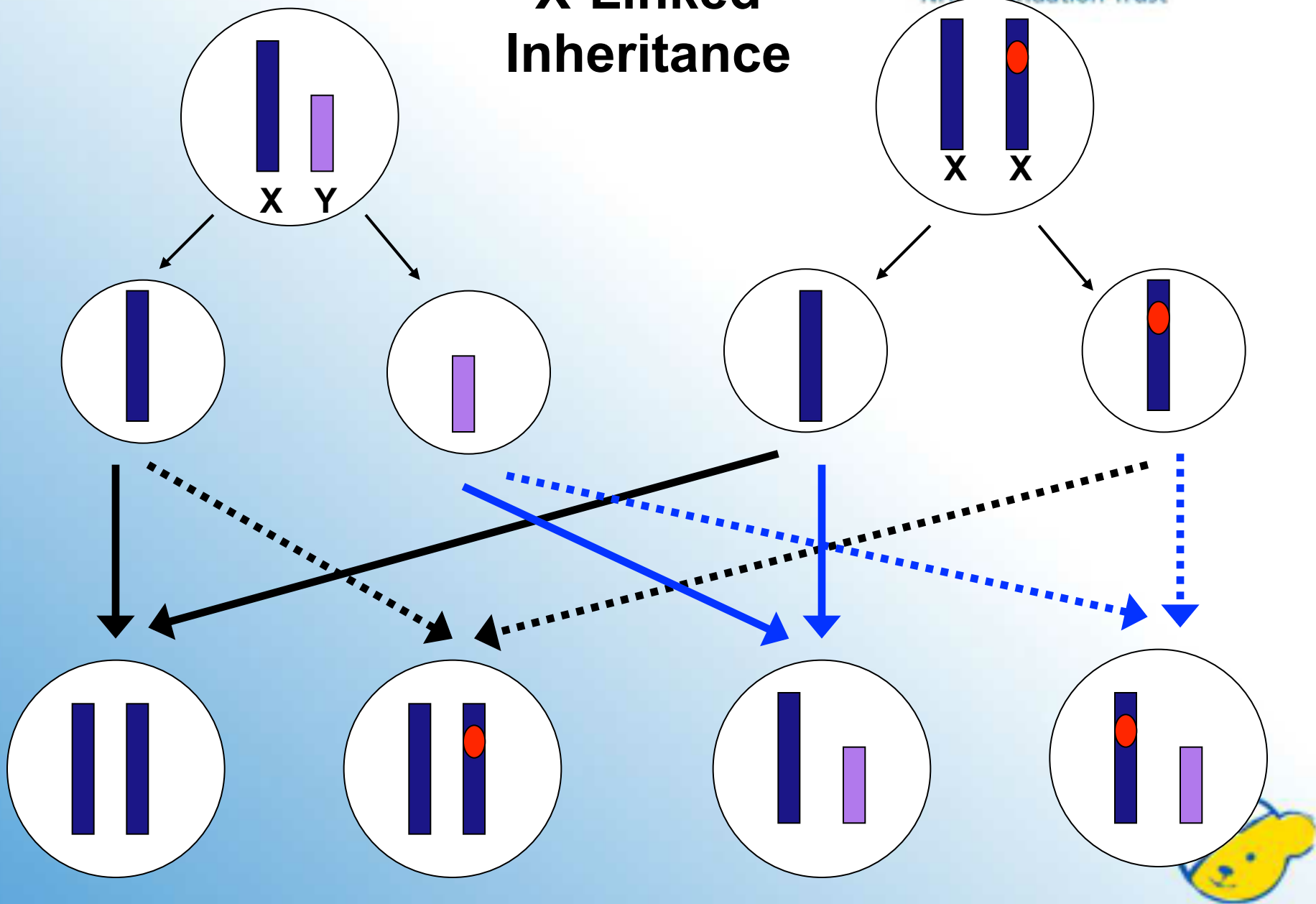
What is the Mode of Inheritance Here?



Haemophilia



X-Linked Inheritance



X-linked Inheritance

Genes carried on X chromosome

Typical features:

- Usually only males affected
- Transmitted (usually) through unaffected females
- No male-to-male transmission



Mendelian Inheritance

- Autosomal vs. sex-linked
- Dominant vs. recessive

Non-Mendelian Inheritance

- Imprinting
- Mitochondrial inheritance
- Multifactorial
- (Mosaicism)

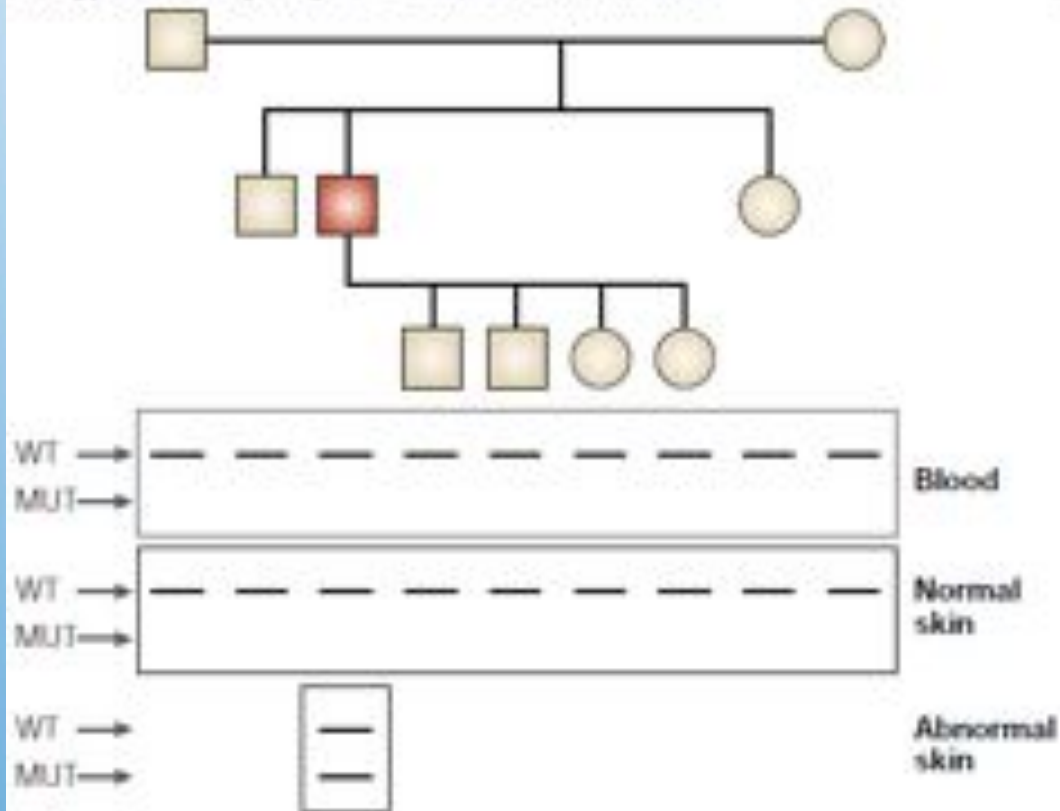


Imprinting

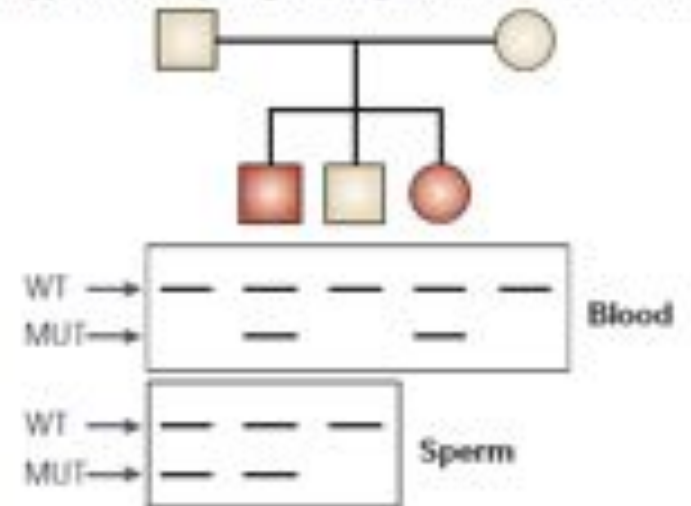


Mosaicism

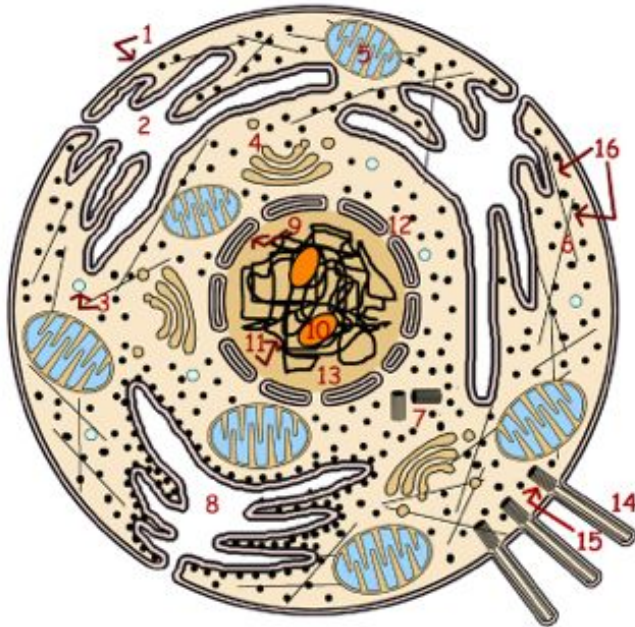
a Hypothetical pedigree of somatic mosaicism



b Hypothetical pedigree of germ-line mosaicism

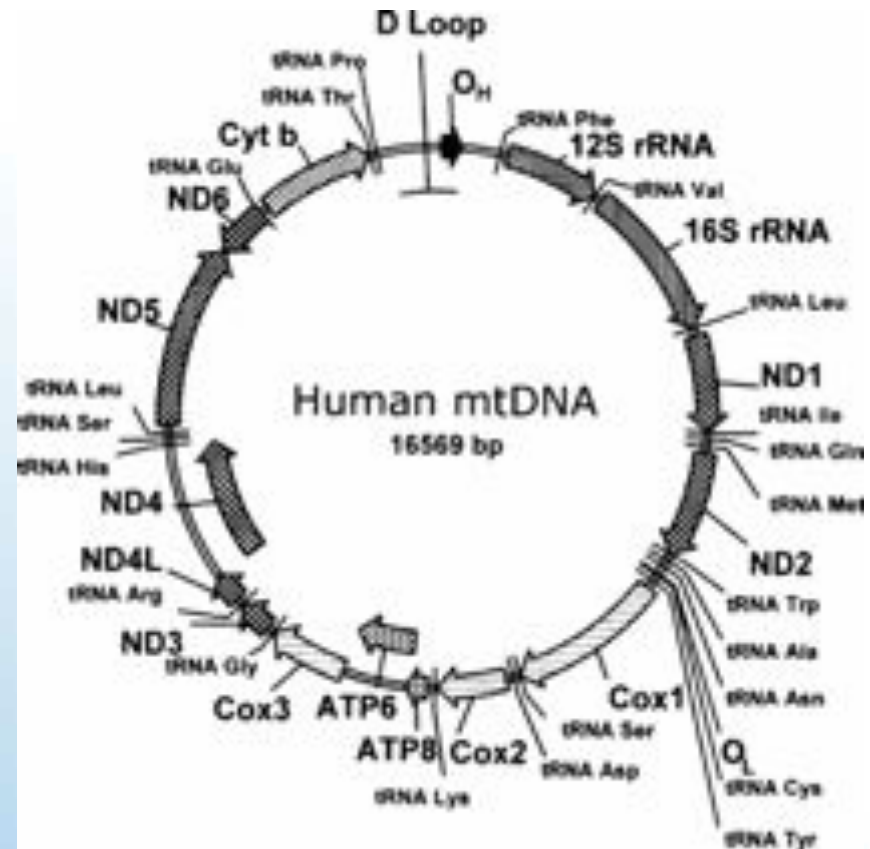


mtDNA



Animal (Eukaryotic) Cell

- | | |
|--------------------------------|----------------------------|
| 1-Plasma Membrane | 9-Double Nuclear Envelope |
| 2-Smooth Endoplasmic Reticulum | 10-Nucleolus |
| 3-Vacuole | 11-Chromosomes (Chromatin) |
| 4-Golgi Body with Vesicles | 12-Nuclear Pore |
| 5-Mitochondrion | 13-Nucleoplasm |
| 6-Ribosomes | 14-Cilium |
| 7-Centrioles | 15-Basal Body |
| 8-Rough Endoplasmic Reticulum | 16-Cytoskeleton |



Thank you for your attention!

Any Questions?

