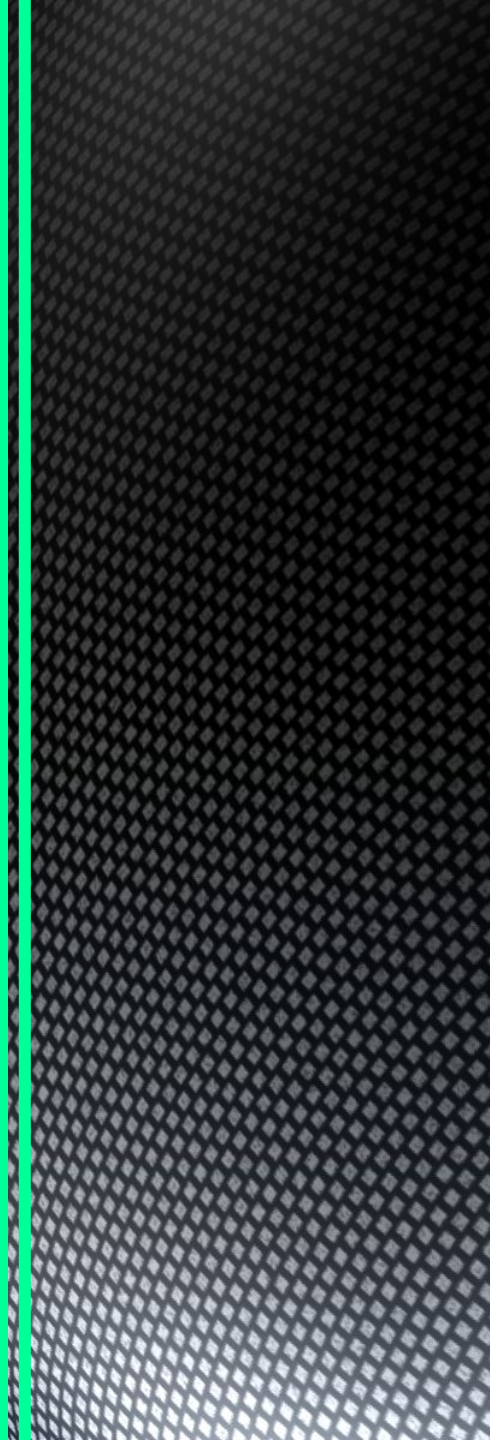
Methods in behavioral genetics

How genes can be altered?



Hereditary or genotypic variability in biology is the process by which the genome of the organism changes. Thanks to it, the individual acquires signs that were previously uncharacteristic of its organism.
According to Charles Darwin theory, hereditary variability is the main engine of evolution.

Types of hereditary variability

- combinative
  - cross-over exchanges
  - free chromosome combinations
- mutational
  - gene
  - chromosomal
  - genome
  - cytoplasmic

Mutations: The Potential Power of a Small Change

https://www.youtube.com/watch?v=GieZ3pk9YVo

The term '**mutation**' was introduced by Hugo De Vries, a Dutch botanist and also rediscovered of Mendel's laws of heredity.

For all mutations, the following properties are characteristic:

- they arise suddenly;
- passed by inheritance;
- they do not have any direction;
- occur in individual individuals, that is, individual;
- by their manifestation, mutations can be recessive or dominant;
- the same mutation can be repeated.

Each mutation is caused by certain causes.
In most cases, it is not possible to accurately determine it.
Under the experimental conditions, a directional factor of the external environment - radiation exposure and the like - is used to obtain mutations.

Causes of mutations

Induced mutations are caused by mutagenic agents like X-ray, UV rays, mustard gas, extreme temperatures, aggressive chemicals such as formaldehyde, caffeine, phenol, some medicines and infection agents etc.
In contrast to them **spontaneous mutations** are the result of mistakes in cell processes.

gene mutations

replacement, loss or insertion
fragment of gene in DNA
transcription mutations
or in RNA
translation mutation

changing the meaning of one
codon and
one amino acid in a protein

change in the structural properties of the protein; disabling gene

The most common type of gene mutations are point ones: replacement or loss of 'a point' – nucleobase pair in DNA or single base in RNA.

Sense mutations

A **nonsense mutation** occurs when one nucleotide is substituted and this leads to the formation of a stop codon instead of a codon that codes for an amino acid. A stop codon a certain sequence of bases (TAG, TAA, or TGA in DNA, and UAG, UAA, or UGA in RNA) that stops the production of the amino acid chain.

It is always found at the end of the mRNA sequence when a protein is being produced, but if a substitution causes it to appear in another place, it will prematurely terminate the amino acid sequence and prevent the correct protein from being produced.

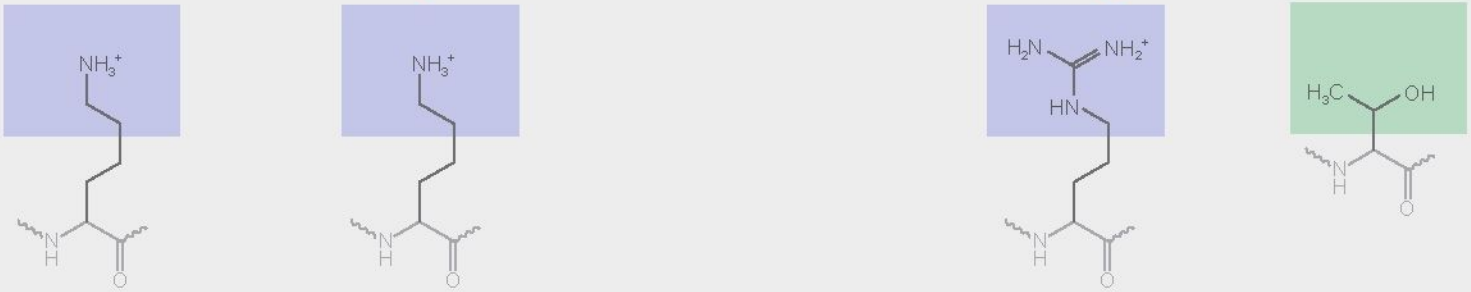
Like a nonsense mutation, a **missense mutation** occurs when one nucleotide is substituted and a different codon is formed; but this time, the codon that forms is not a stop codon. Instead, the codon produces a different amino acid in the sequence of amino acids. For example, if a missense substitution changes a codon from AAG to AGG, the amino acid arginine will be produced instead of lysine.

A missense mutation is considered **conservative** if the amino acid formed via the mutation has similar properties to the one that was supposed to be formed instead.

It is called **non-conservative** if the amino acid has different properties that structure and function of a protein.

Types of point mutations

	No mutation	Point mutations			
		Silent	Nonsense	Missense	
				conservative	non-conservative
DNA level	TTC	TTT	ATC	TCC	TGC
mRNA level	AAG	AAA	UAG	AGG	ACG
protein level	**Lys**	**Lys**	**STOP**	**Arg**	**Thr**



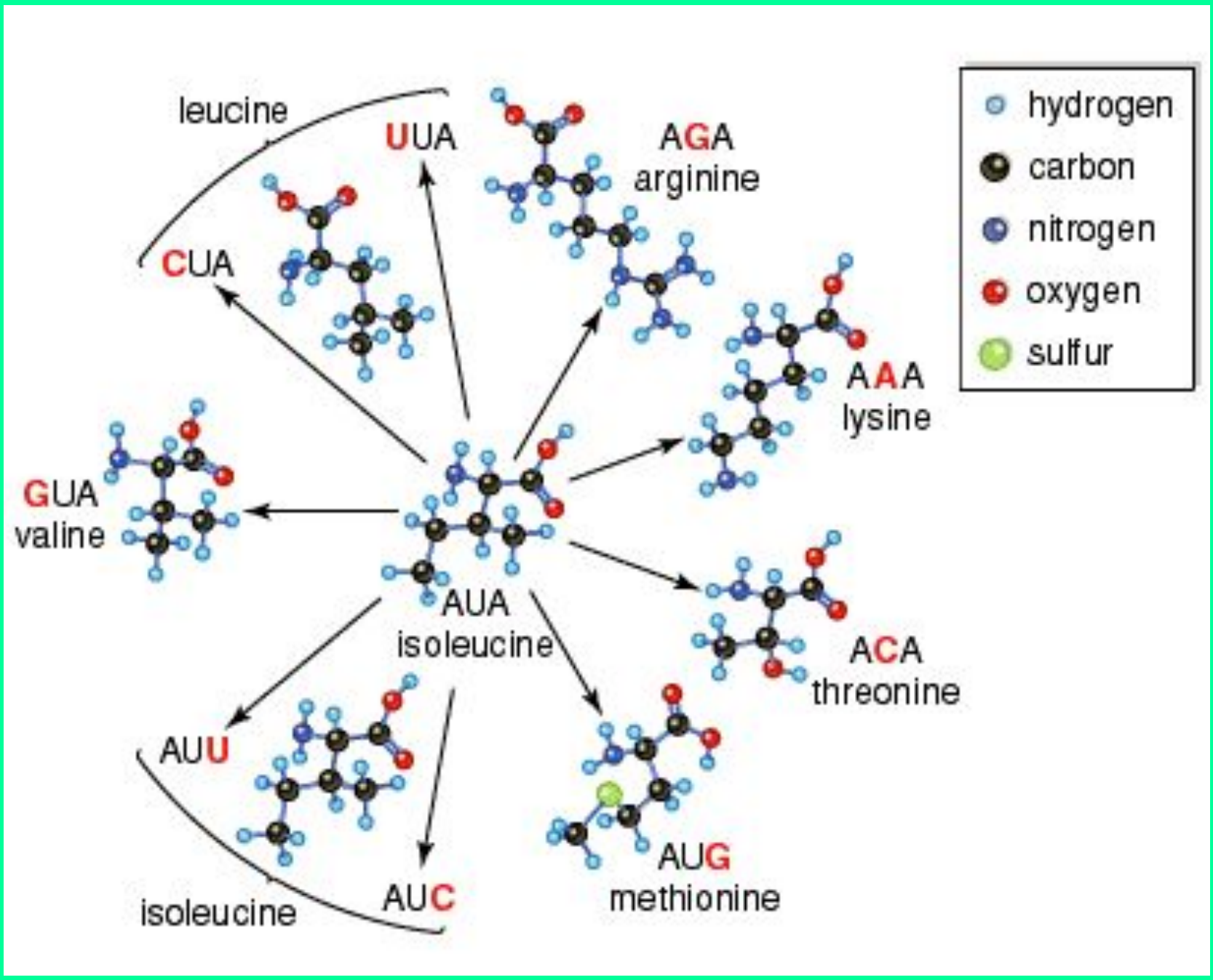
In a **silent mutation**, a nucleotide is substituted but the same amino acid is produced anyway. This can occur because multiple codons can code for the same amino acid. For example, *AAG* and *AAA* both code for lysine, so if the *G* is changed to an *A*, the same amino acid will form and the protein will not be affected.

Insertion and Deletion

An **insertion mutation** occurs when an extra base pair is added to a sequence of bases.

A **deletion mutation** is the opposite; it occurs when a base pair is deleted from a sequence. These two types of point mutations are grouped together because both of them can drastically affect the sequence of amino acids produced.

With one or two bases added or deleted, all of the three-base codons change. This is called a **frameshift mutation**. For example, if a sequence of codons in DNA is normally CCT ATG TTT and an extra A is added between the two cytosine bases, the sequence will instead read CAC TAT GTT T. This completely changes the amino acids that would be produced, which in turn changes the structure and function of the resulting protein and can render it useless. Similarly, if one base was deleted, the sequence would also shift.

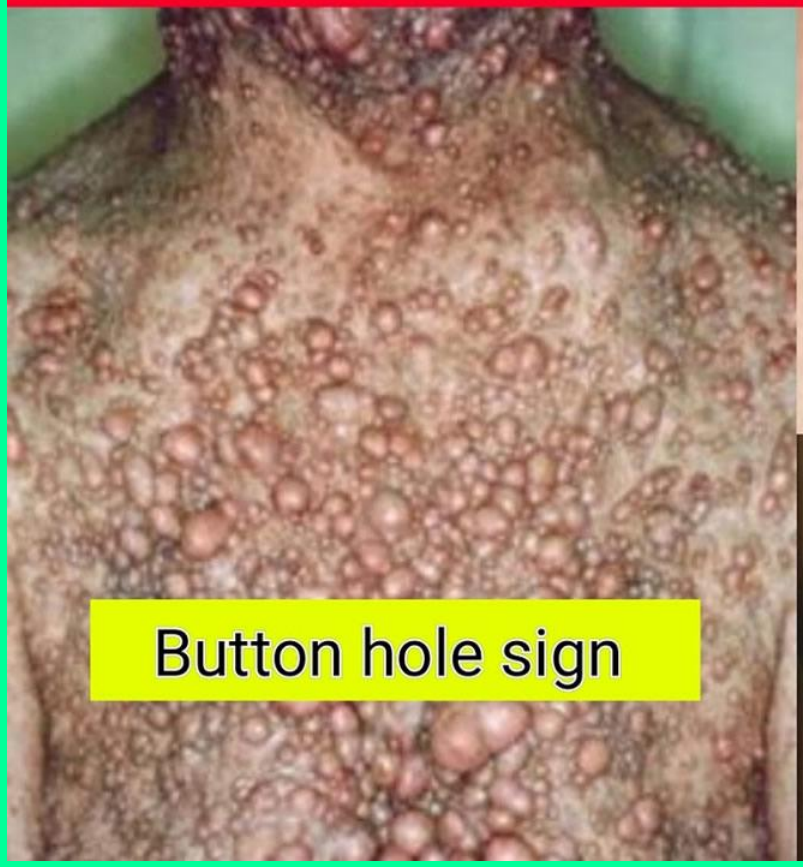

leucine
UUA
AGA
arginine
CUA
AAA
lysine
GUA
valine
AUA
isoleucine
ACA
threonine
AUU
AUG
methionine
AUC
isoleucine
hydrogen
carbon
nitrogen
oxygen
sulfur

Examples of gene mutations in humans

Recklinghausen's disease or neurofibromatosis

This is one of the most common genetic disease that cause tumors to grow along human nerves (neurofibromas) and less frequently, in the brain and spinal cord, and produce other abnormalities such as skin changes and bone deformities, wherever there are nerve cells in the body.
This is a type of nerve tumor that forms soft bumps on or under the skin.
The tumors begin in the supporting cells that make up the nerves and the myelin sheath – the thin membrane that envelops and protects the nerves.
In addition to benign tumors to growing on nerves, neurofibromatosis also affects the development of other systems and tissues including; the cardiovascular system, bones, skin, brain, eyes, respiratory system, gastrointestinal tract and hormonal system.
Treatment may include surgery, focused radiation, or chemotherapy.

NEUROFIBROMATOSIS



Androgen insensitivity syndrome (AIS) or Morris' syndrome

This is a syndrome when a person who is genetically male (46, XY) is resistant to male hormones (**androgens**). As a result they may have mostly female external sex characteristics or signs of both male and female sexual development.

People with **complete AIS** have the external sex characteristics of females, but do not have a internal woman structures and therefore do not menstruate and are unable to conceive a child (**infertile**). They are typically raised as females and have a female gender identity.

Affected individuals have male internal sex organs (**testicles**) that are abnormally located in the pelvis or abdomen which may probably be a cause of becoming cancerous later in life if they are not surgically removed. People with complete AIS also have sparse or absent hair in the pubic area and under the arms.

The frequency of the complete form of AIS is as many as 1 in 20,000 live births.

People with **partial AIS** can have genitalia that look typically female, genitalia that have both male and female characteristics, or genitalia that look typically male. They may be raised as males or as females and may have a male or a female gender identity.

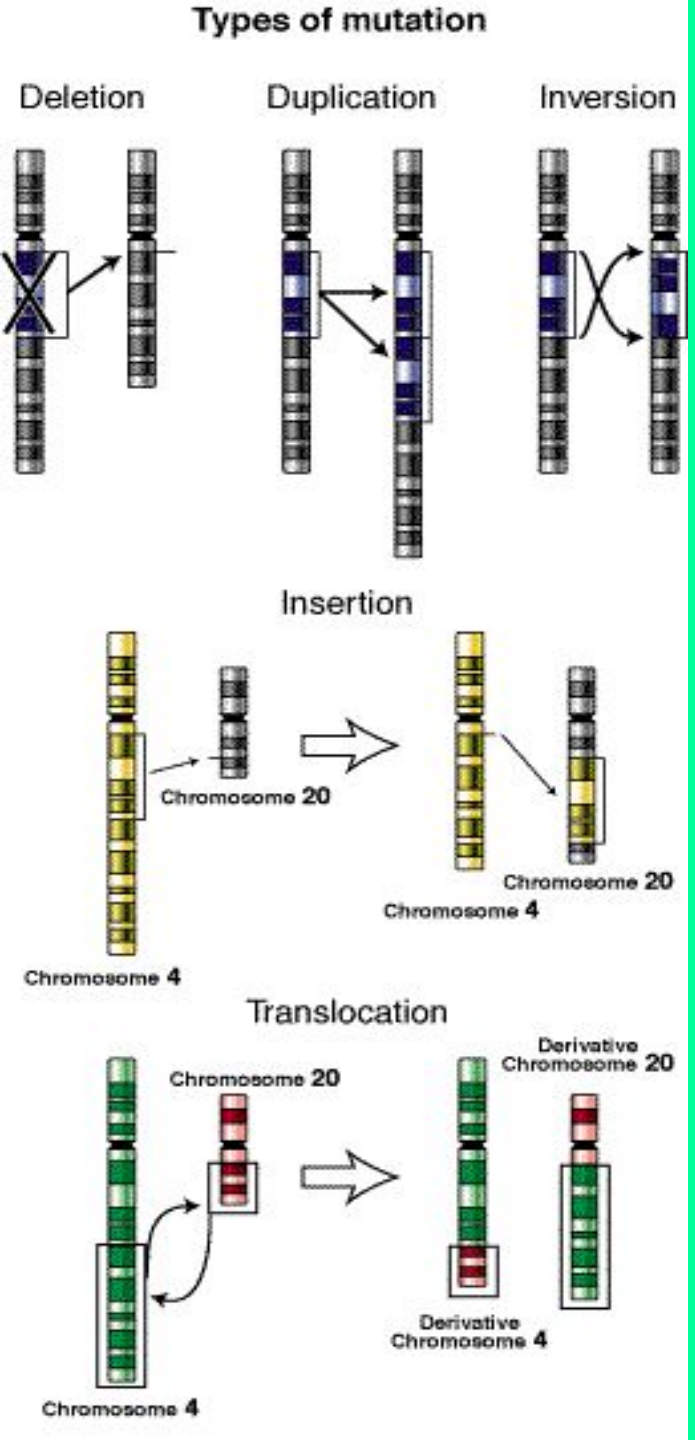
People with **mild AIS** are born with male sex characteristics, but they are often infertile and tend to breast enlargement at puberty.

chromosome mutations

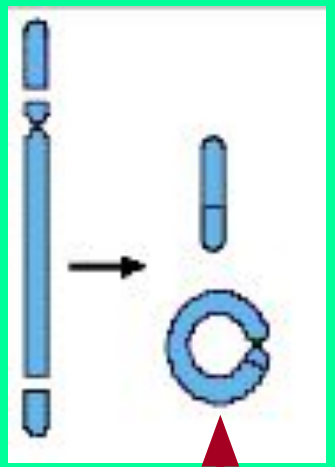
replacement, loss or insertion
DNA or RNA site

changing the order and
number of genes

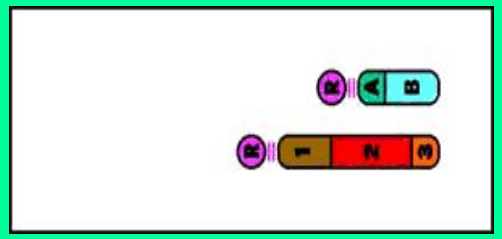
changing the location and number of genes;
changing regulatory and functional
protein and RNA properties;
termination of recombinant gene exchange
in a pair of chromosomes



Chromosome mutations



ringed chromosome

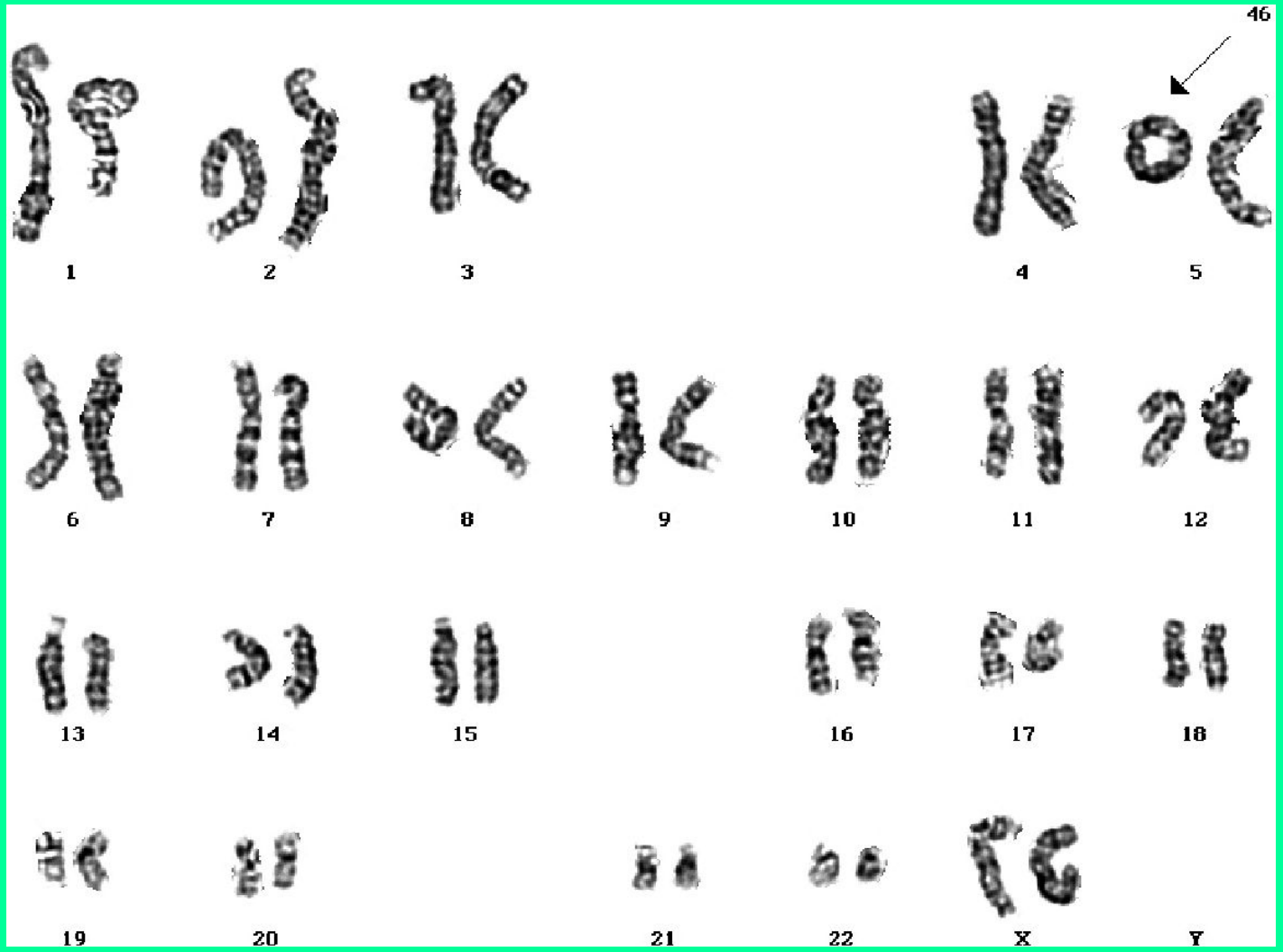


Robertsonian translocation

gene family

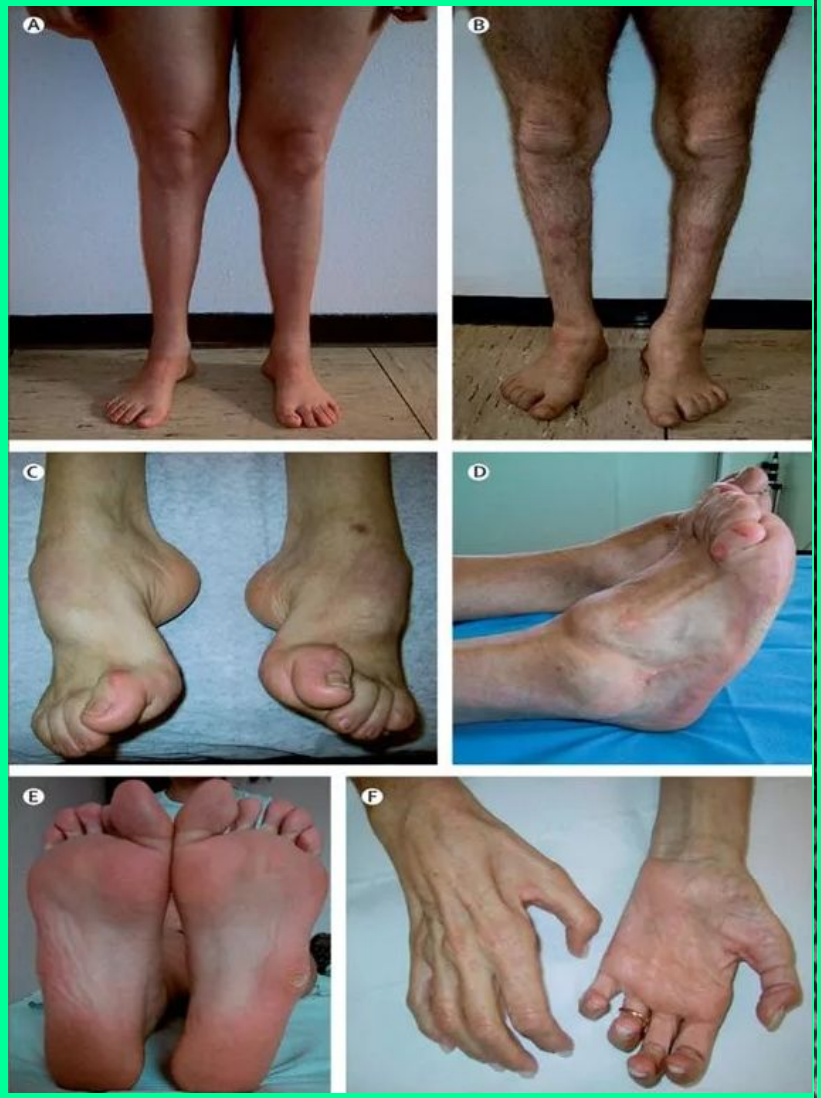
theredcatatethefatrat
theredcatatethefatfatrat
theredcatatethefatfatrat
theredcatatethefatfatfitfitrat
theredcatatethefatfatfitfitbat
theredcatatethefatfatfitfitbatbat

Human karyotype with a ringed 5th chromosome



Examples of chromosome mutations in humans

(**CMT**) is a kind of the hereditary motor and sensory neuropathy, a group of varied inherited disorders of the peripheral nervous system characterized by progressive loss of muscle tissue and touch sensation across various parts of the body.
Loss of touch sensation in the feet, ankles, and legs, as well as in the hands, wrists, and arms occurs with various types of the disease.
The cause of the disease are mutations that lead to defects in neuronal proteins.
The 70–80% of the cases of CMT is the result of the duplication of a large region on the short arm of chromosome 17.
Currently incurable, this disease is the most commonly inherited neurological disorder, and affects about one in 2,500 people.



Swyer syndrome, or **XY gonadal dysgenesis**

This is a type of hypogonadism in a person whose karyotype is 46, XY. The cause of the disorder are defects of SRY (Sex-determining Region on Y-chromosome), which encodes the factor of testis forming.
The person is externally female with streak gonads, and if left untreated, will not experience puberty.
A baby who is apparently a girl is born and is normal in most anatomic respects except that the child has nonfunctional streak gonads instead of ovaries or testes.
As girls' ovaries normally produce no important body changes before puberty, a defect of the reproductive system typically remains unsuspected until puberty fails to occur in people with Swyer syndrome. They appear to be normal girls and are generally considered so.

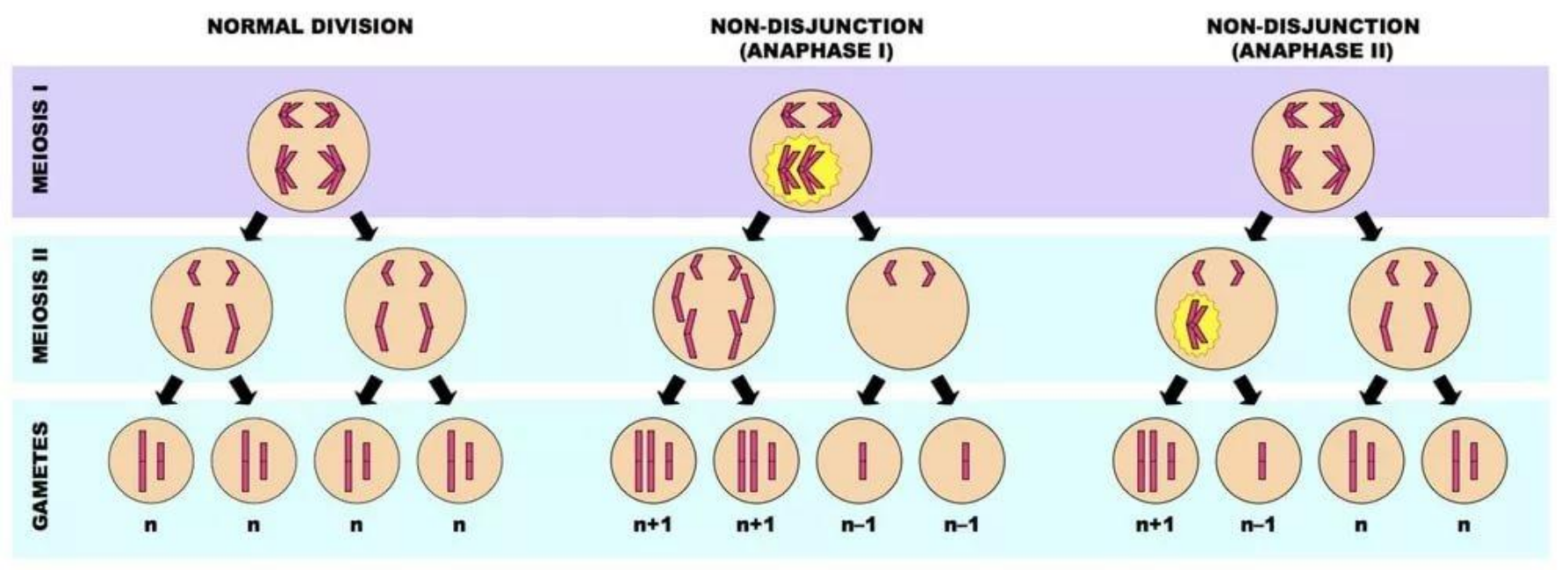
genomic mutations

multiple increase in the haploid number of all chromosomes (polyploidy = euploidy),
loss or addition of one chromosome from a pair (aneuploidy)

change in the number of complexes
structural and functional genes

changing the properties of the body
(viability, gender, etc)

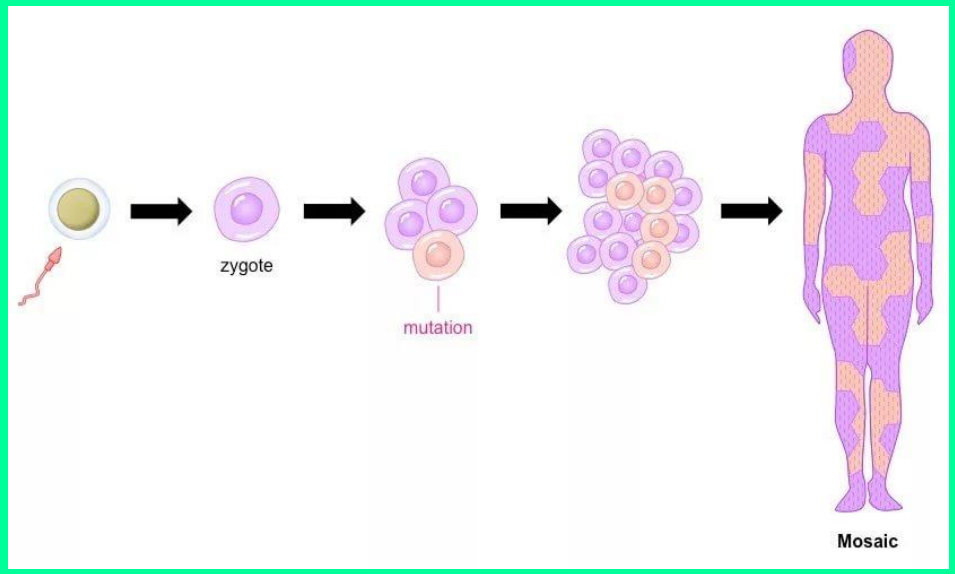
Alteration of chromosome number

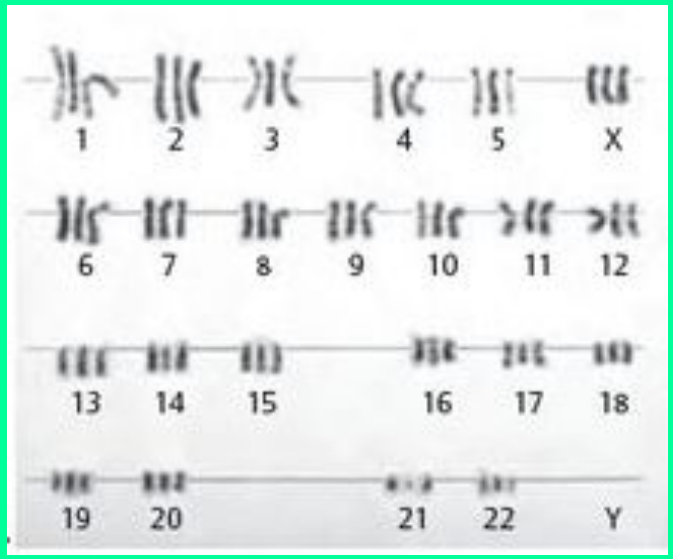


Nondisjunction
is a failure either of two homologous chromosomes to pass to separate cells during the first meiotic division, or of the two chromatids of a chromosome to pass to separate cells during mitosis or during the second meiotic division.
As a result, one daughter cell has two chromosomes or two chromatids, and the other has none. If this happens during meiosis, an **aneuploid** individual (for example, a child with Down syndrome) may develop following fertilization.

Examples of genomic mutations in humans

Triploid syndrome, also called **triploidy**, is a genomic disorder in which a fetus has three copies of every chromosome instead of the normal two.
Triploidy can result from either two sperm fertilizing one egg cell (60%) or from one sperm fertilizing an egg with two copies of every chromosome (40%).
If this occurs in only some cells, it is called **mosaic triploidy** and is less severe.





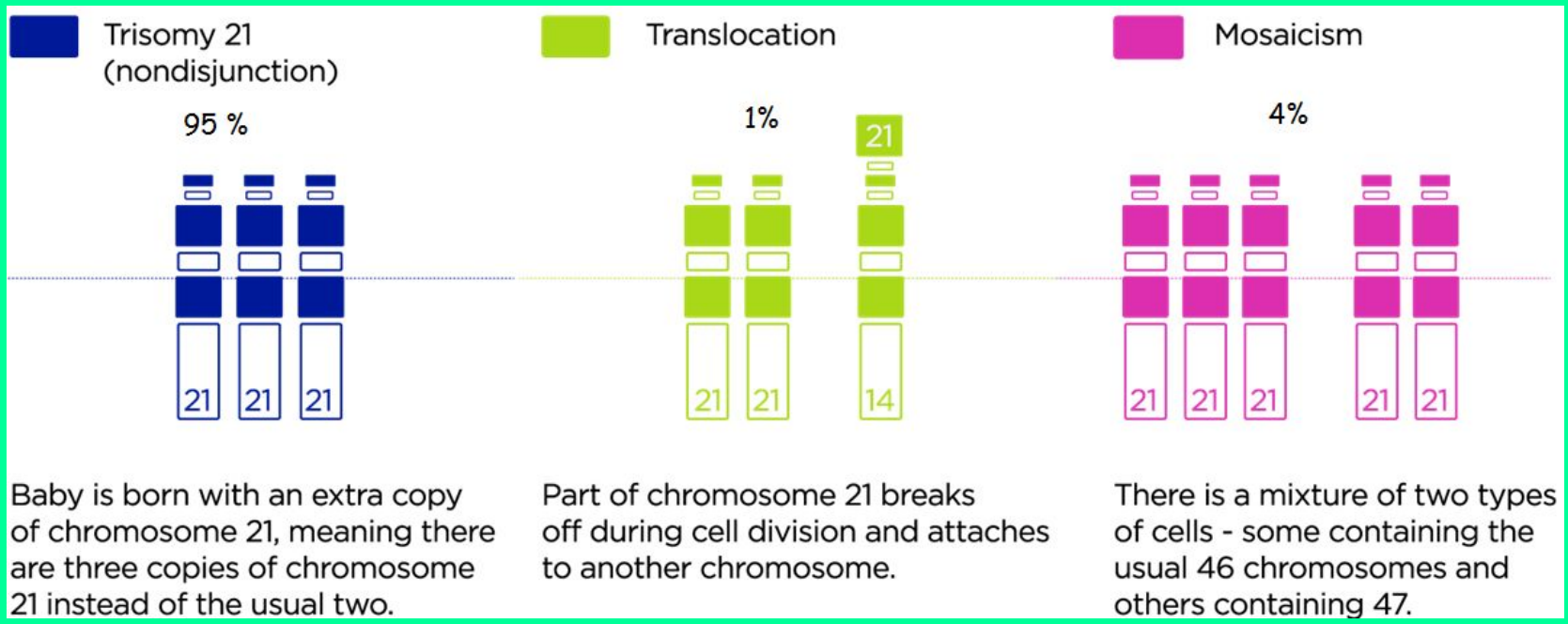
Triploidy is a frequent chromosomal abnormality found in 12% of all spontaneous first trimester abortions.

Down's Syndrome or trisomy 21

This is a condition in which a child is born with triple copy of their 21st chromosome, which causes physical and mental developmental delays and disabilities.

Many of the disabilities are lifelong, and they can also shorten life expectancy. However, people with Down syndrome can live healthy and fulfilling lives.

There are three types of the syndrome:



Recent medical advances, as well as cultural and institutional support for people with Down syndrome and their families, provides many opportunities to help overcome the challenges of this condition.

Klinefelter syndrome

The syndrome is a genetic condition that affects males physical, behavioral, and cognitive development and functioning. Boys and men are born with an extra X chromosome are still genetically male and often will not realize they have this extra X chromosome (47, XXY), but occasionally it can cause problems that may require treatment, problems such as a small penis, small testes and infertility. The features of Klinefelter syndrome (47, XXY) are typically associated with decreased testosterone level and elevated gonadotropin levels.

Some affected people have conditions known as "variants of Klinefelter syndrome" where there is more than one extra sex chromosome in each cell (48,XXXY, 48,XXYY and 49,XXXXY). Most these variants are much rarer, occurring in 1 in 50,000 to 1 in 85,000 or fewer newborns.

Common physical features may include tall stature, reduced muscle tone, small testes (**hypogonadism**), delayed pubertal development and lack of secondary male sex characteristics such as decreased facial and body hair and increased breast growth (**gynecomastia**) in late puberty.

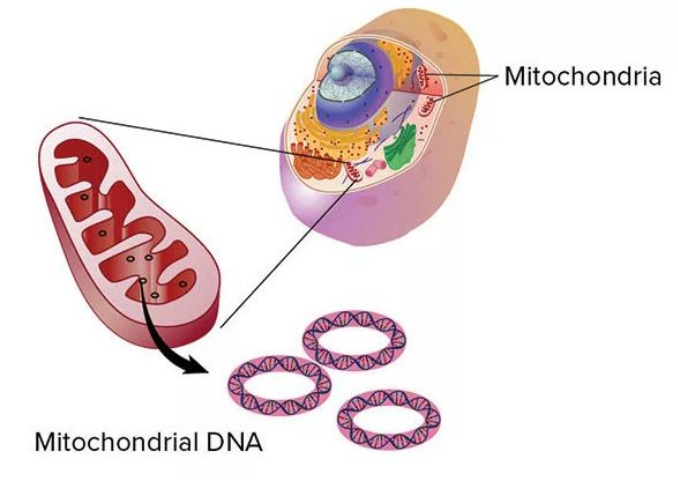
Common cognitive and behavioral features may include speech and language delays, ADHD (**attention deficit hyperactivity disorder**), and emotional and social functioning challenges.

Klinefelter syndrome is quite common, affecting around 1 in every 500 to 1,000 newborn males.

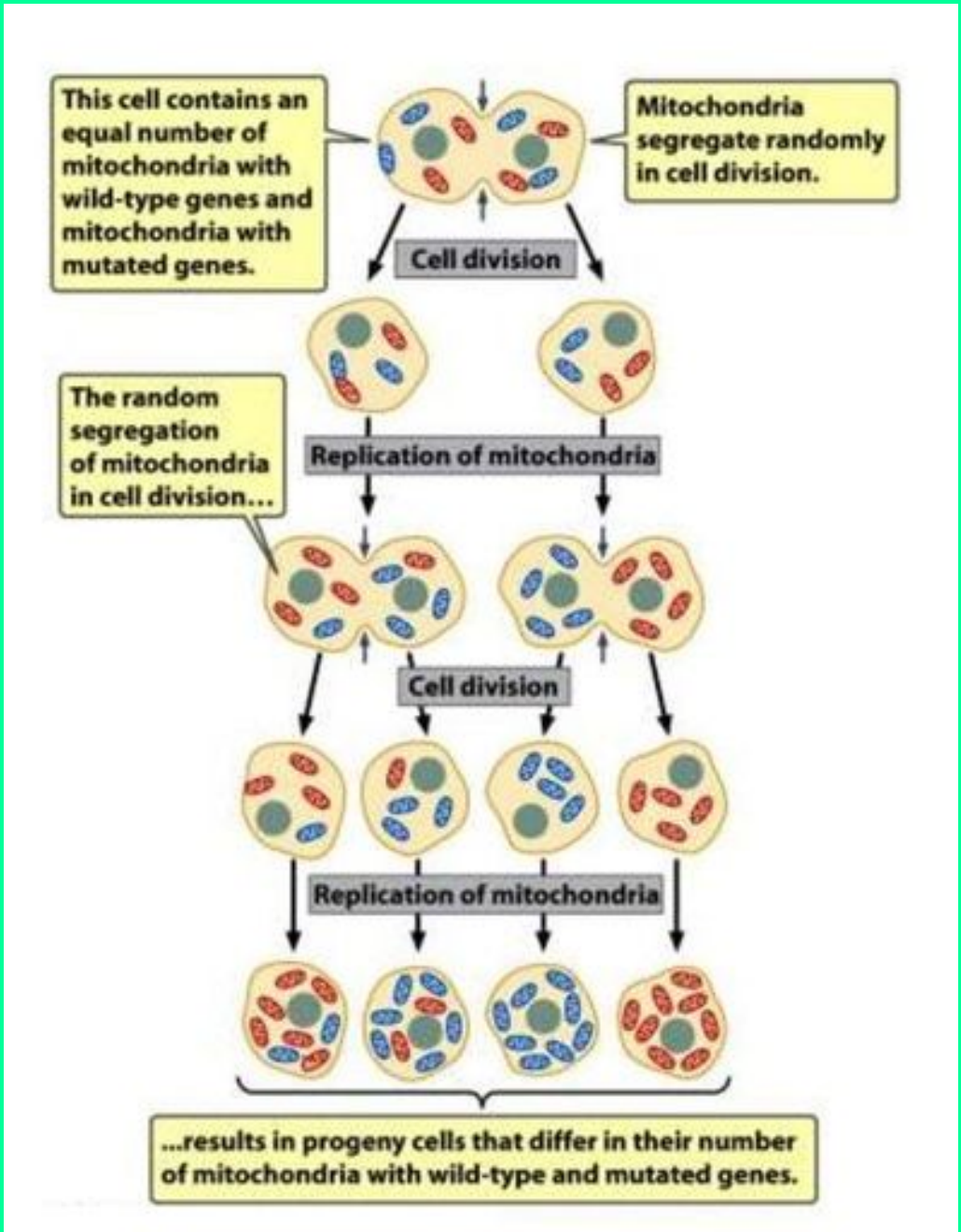
Cytoplasmic mutations

Cytoplasmic mutations are associated with changes in the cytoplasmic structures of cells containing DNA molecules, such as mitochondria.

These mutations are transmitted along the maternal line, since the zygote receives the entire cytoplasm from the maternal ovule.

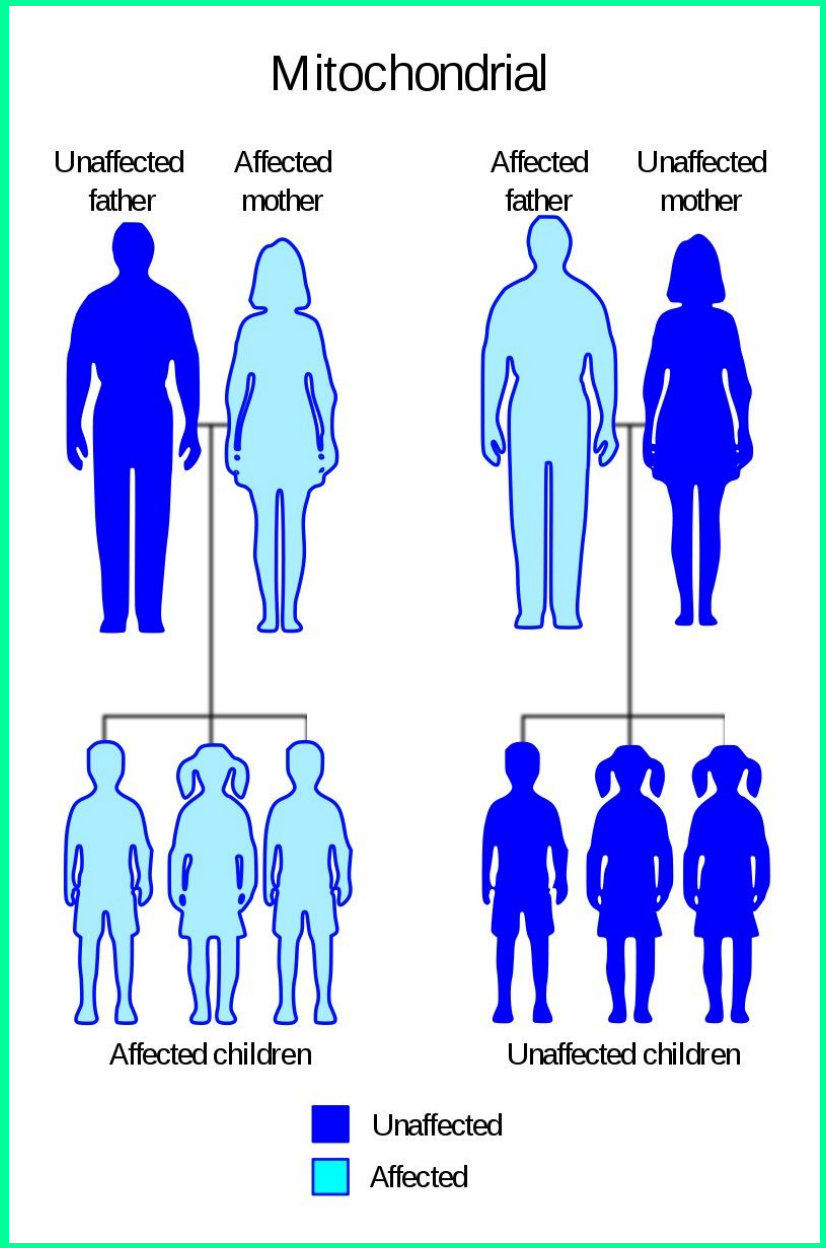


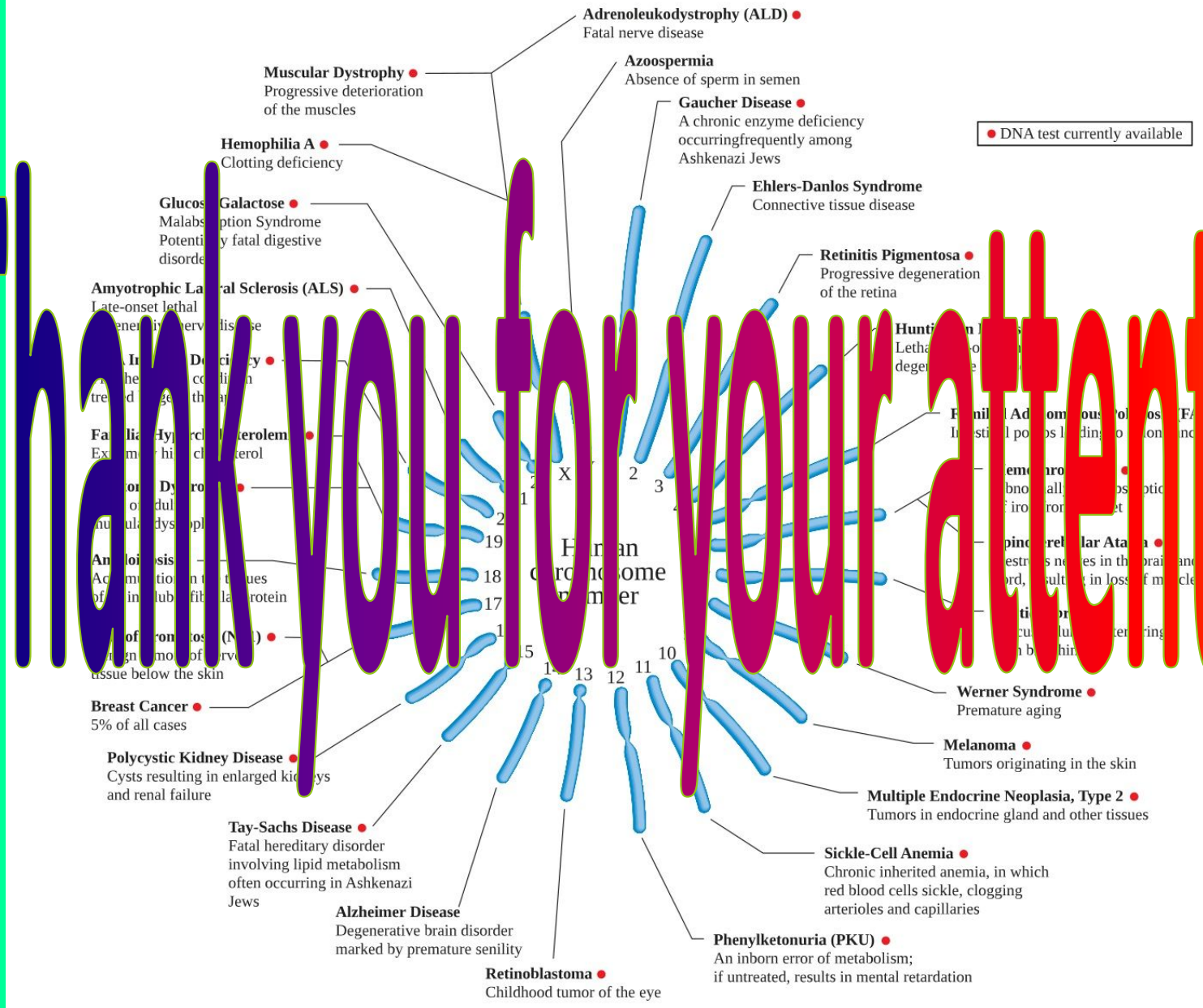
Human mitochondrial DNA includes 37 genes.



Examples of mitochondrial effects in humans

MERRF syndrome - myoclonic epilepsy and ragged redfibers.
The disease is a multisystem disorder indicating dysfunction of the mitochondrial respiratory chain, that is due in about 80% of cases to a A > G mutation at nucleotide 8344.
Patients with the syndrome will primarily display myoclonus (brief convulsions of the body), seizures, cerebellar ataxia and myopathy.
Secondary features include dementia, optic atrophy, bilateral deafness, peripheral neuropathy, spasticity, or lipomatosis.
Due to the multiple symptoms presented by the individual, the severity of the syndrome is very difficult to evaluate.
Mitochondrial disorders, including MERRF, may present at any age.





Thank you for your attention

Pedigrees
https://www.youtube.com/watch?v=Gd09V2AkZv4

Genetic Drift
https://www.youtube.com/watch?v=W0TM4LQmoZY