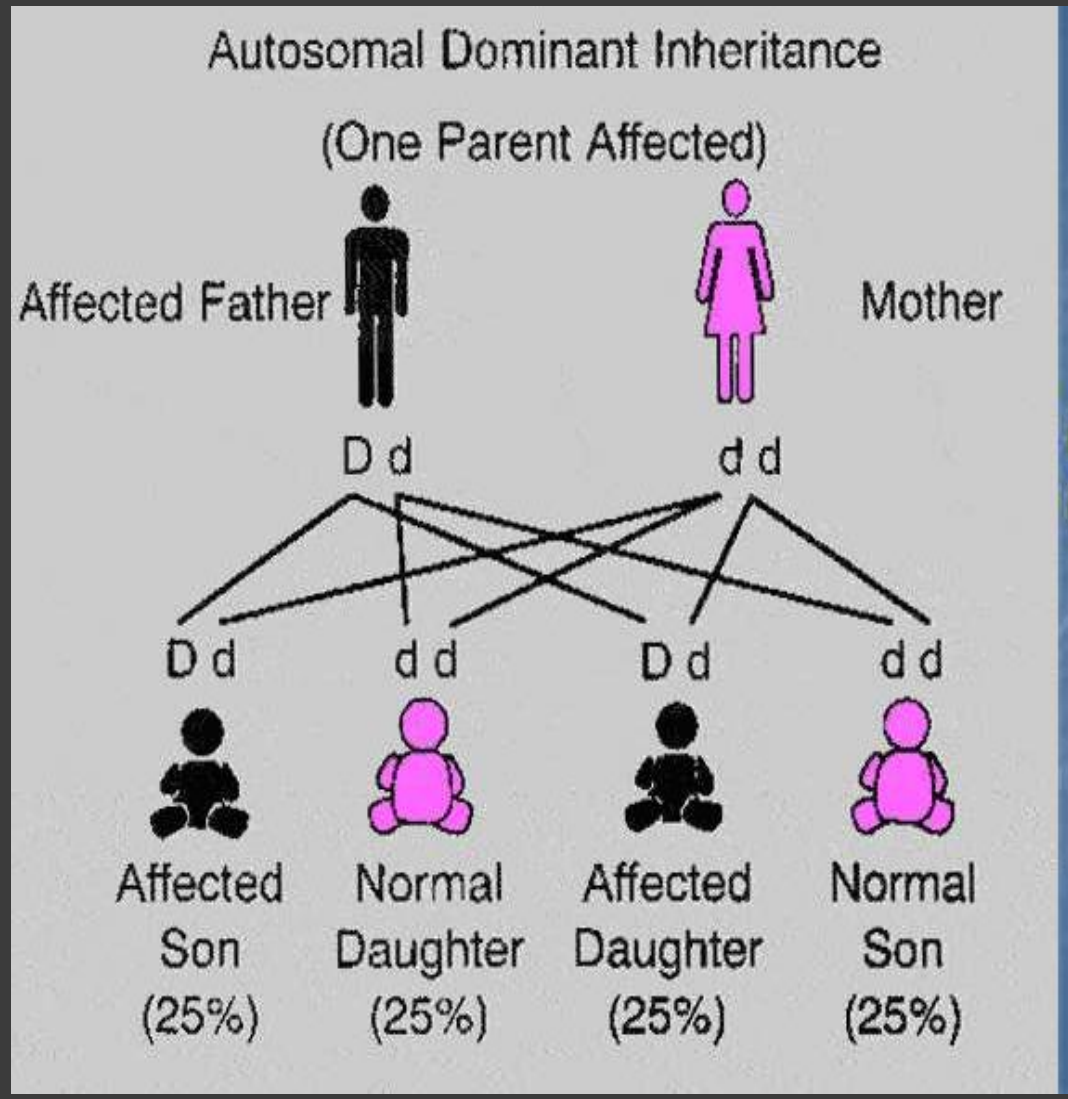
SINGLE-GENE DISORDERS

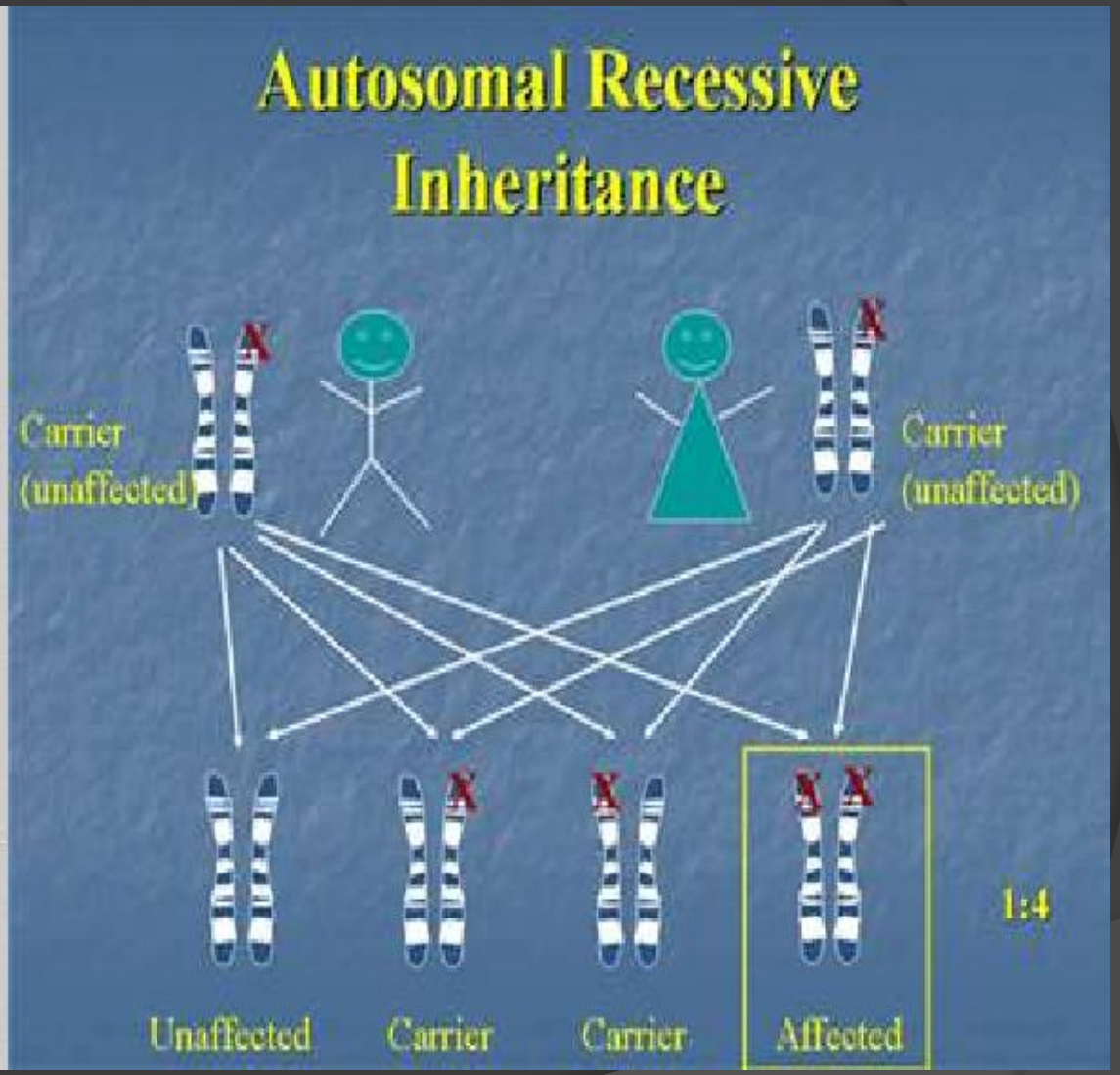
- Over 10,000 human disorders are caused by a change, known as a mutation, in a single gene. These are known as single gene disorders
- When a certain gene is known to cause a disease, we refer to it as a single gene disorder or a Mendelian disorder. OR A genetic disorder in which only one gene are affected is called single gene disorder.
- Individually, single gene disorders are each very rare, but as a whole, they affect about one percent of the population
- Since only a single gene is involved, these disorders can be easily tracked through families and the risk of them occuring in later generations can be predicted.
- Single gene disorders can be divided into different categories: dominant, recessive, and X-linked
- For example, you may have heard of cystic fibrosis, sickle cell disease, Fragile X syndrome, muscular dystrophy, or Huntington disease. These are all examples of single gene disorders.

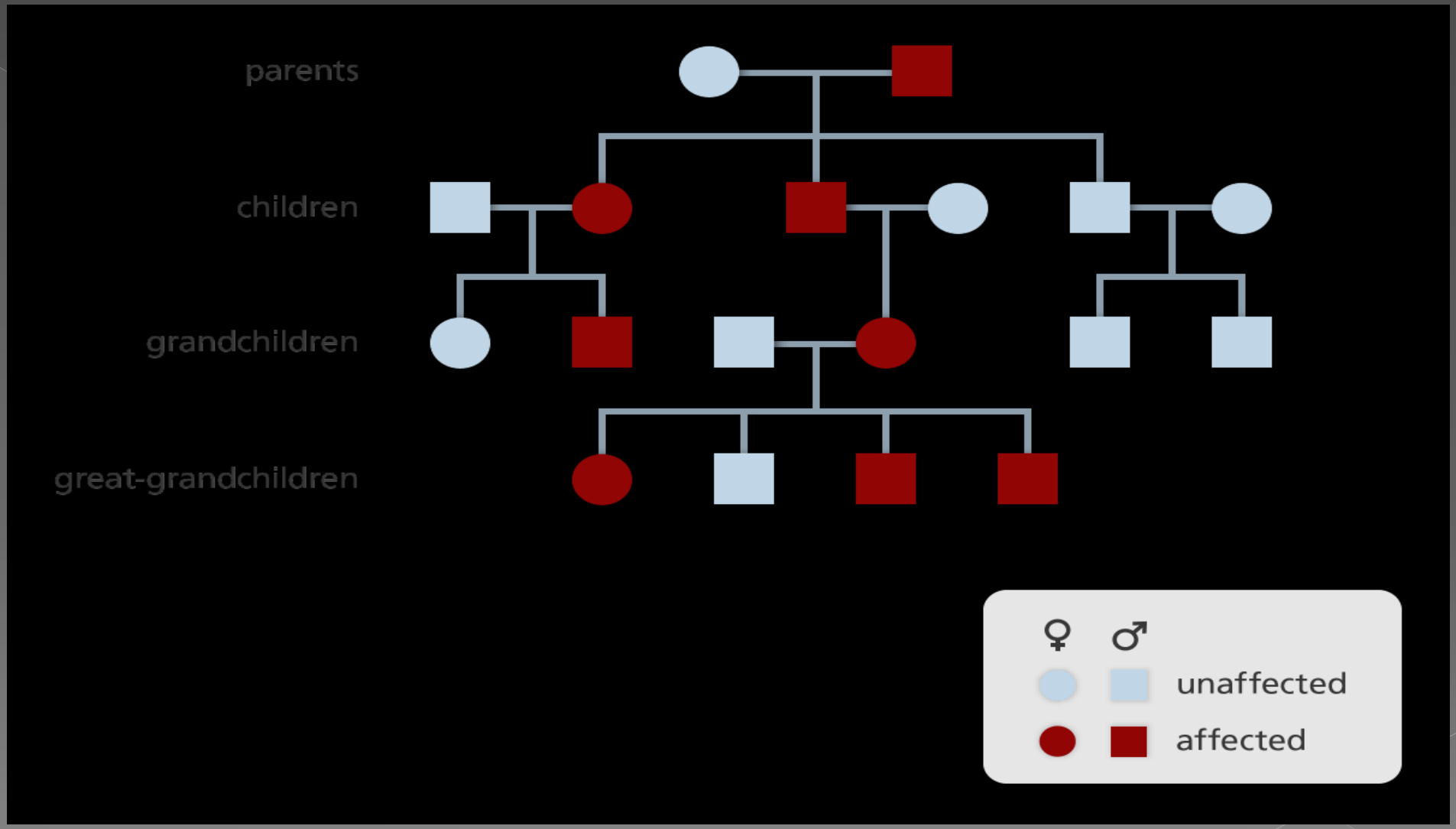
CONT...

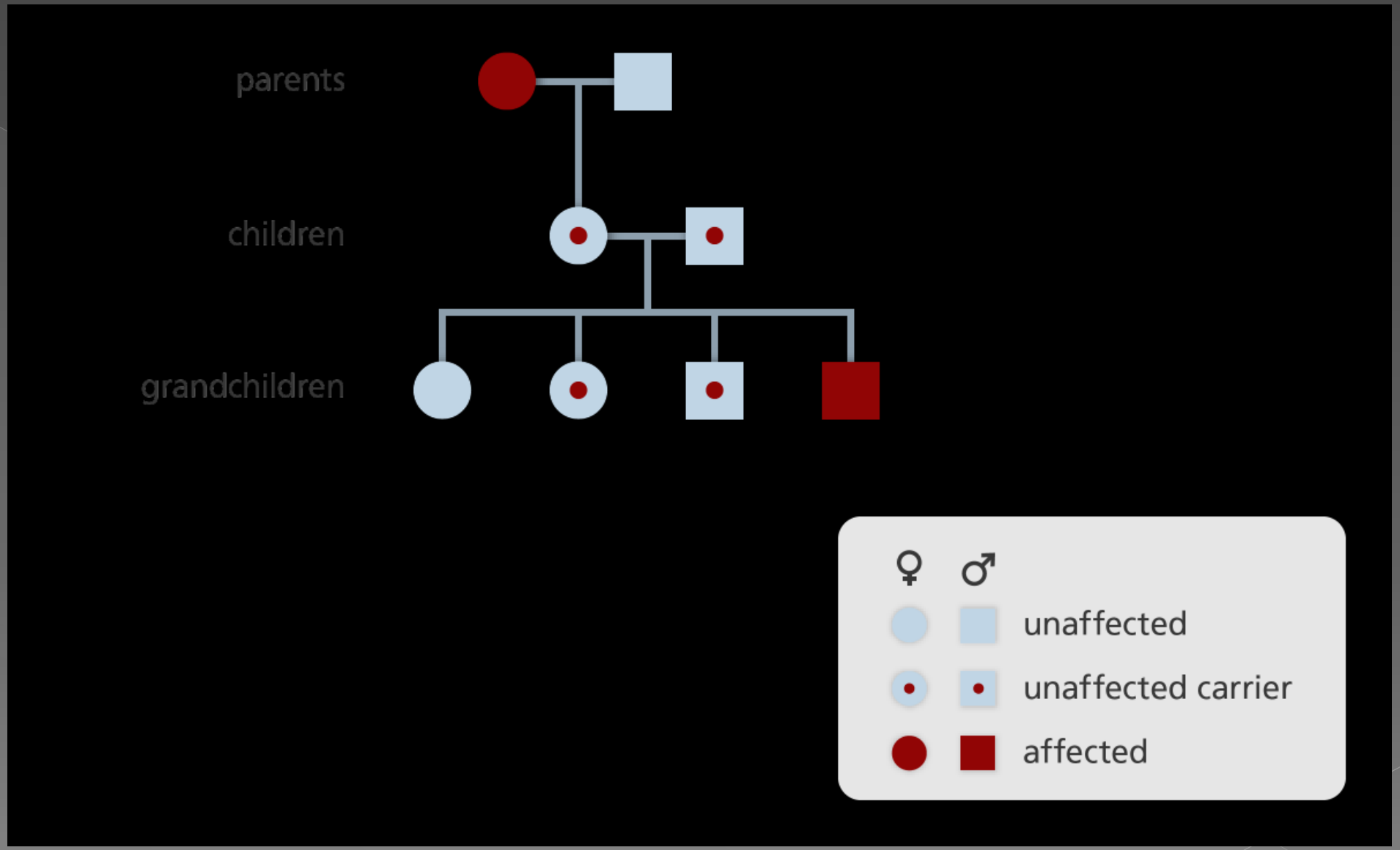
- Autosomal dominant means that a person only needs one copy of the changed gene (genetic difference) in order to have the disorder. Usually, the changed gene is inherited from a parent who also has the disorder and every generation in the family may have members with the disorder.

- Autosomal recessive means that it is necessary to have two copies of the changed gene to have the disorder. Each parent contributes one changed copy of the gene to the child who has the disorder.


Autosomal Dominant Inheritance
(One Parent Affected)
Affected Father
Mother
D d
d d
D d
d d
D d
d d
Affected Son (25%)
Normal Daughter (25%)
Affected Daughter (25%)
Normal Son (25%)


Autosomal Recessive Inheritance
Carrier (unaffected)
Carrier (unaffected)
Unaffected
Carrier
Carrier
Affected
1:4


parents
children
grandchildren
great-grandchildren
♀
♂
unaffected
affected

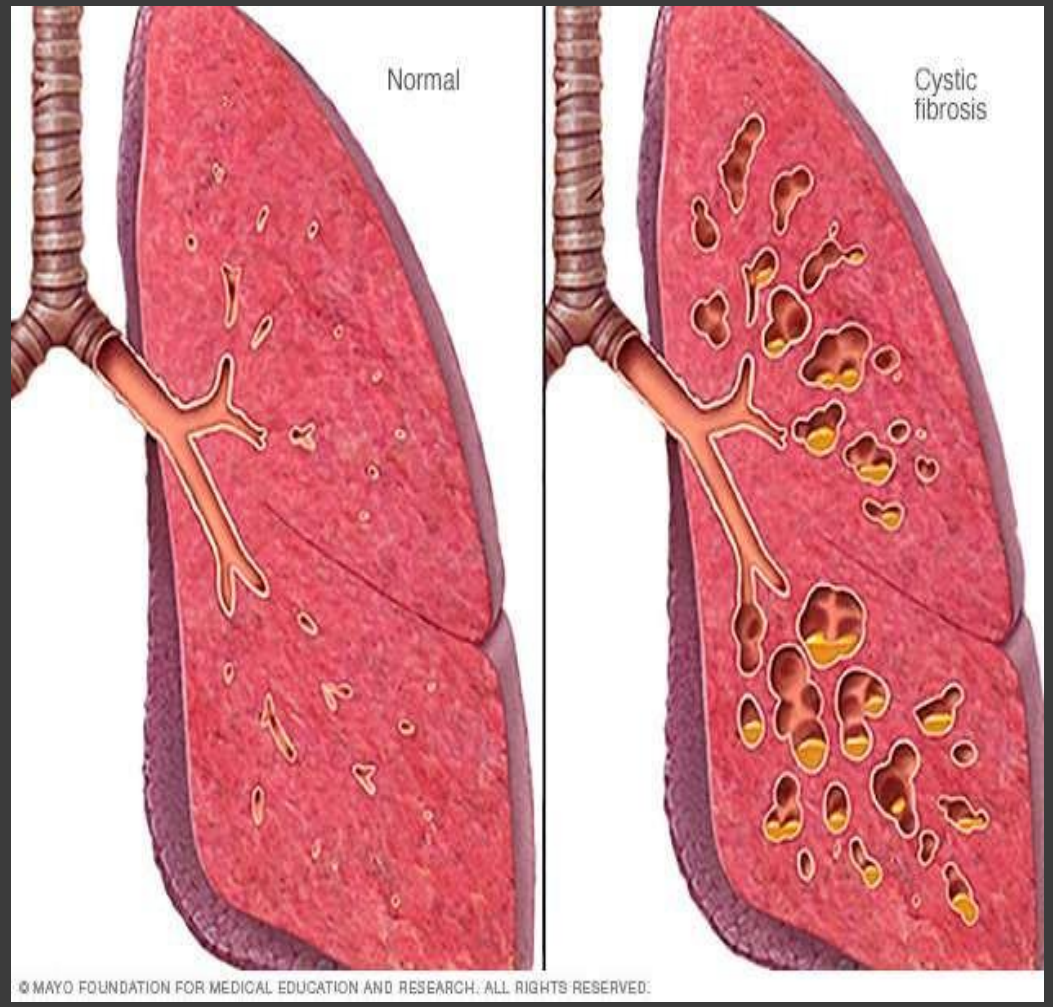

parents
children
grandchildren
♀
♂
unaffected
unaffected carrier
affected

X- linked diseases

- X- linked disorders are single gene disorders that result from the presence of a mutated gene on the X- chromosome.
- Because females have two copies of X chromosome (XX) but males (XY) only have one copy, X- linked disorders are more common in males. If a male’s single copy on the X chromosome is mutated he has no healthy copy to restore healthy function
- The inheritance patters of X linked diseases are simplified by the fact that males always pass their X chromosome to their daughters but never to their sons.
- Eg: Haemophilia, Muscular dystrophy

(1) CYSTIC FIBROSIS

- Mutations in the CFTR gene cause the CFTR **protein** to malfunction or not be made at all, leading to a buildup of thick mucus, which in turn leads to persistent lung infections, destruction of the pancreas, and complications in other organs. Cystic fibrosis is an example of a recessive disease.
- Cystic fibrosis is an inherited disorder that causes severe damage to the lungs, digestive system and other organs in the body.
- A hereditary disorder affecting the exocrine glands. It causes the production of abnormally thick mucus, leading to the blockage of the pancreatic ducts, intestines, and bronchi and often resulting in respiratory infection.
- Cystic fibrosis affects the cells that produce mucus, sweat and digestive juices. These secreted fluids are normally thin and slippery.
- But in people with cystic fibrosis, a defective gene causes the secretions to become sticky and thick. Instead of acting as a lubricant, the secretions plug up tubes, ducts and passageways, especially in the lungs and pancreas


Normal
Cystic fibrosis
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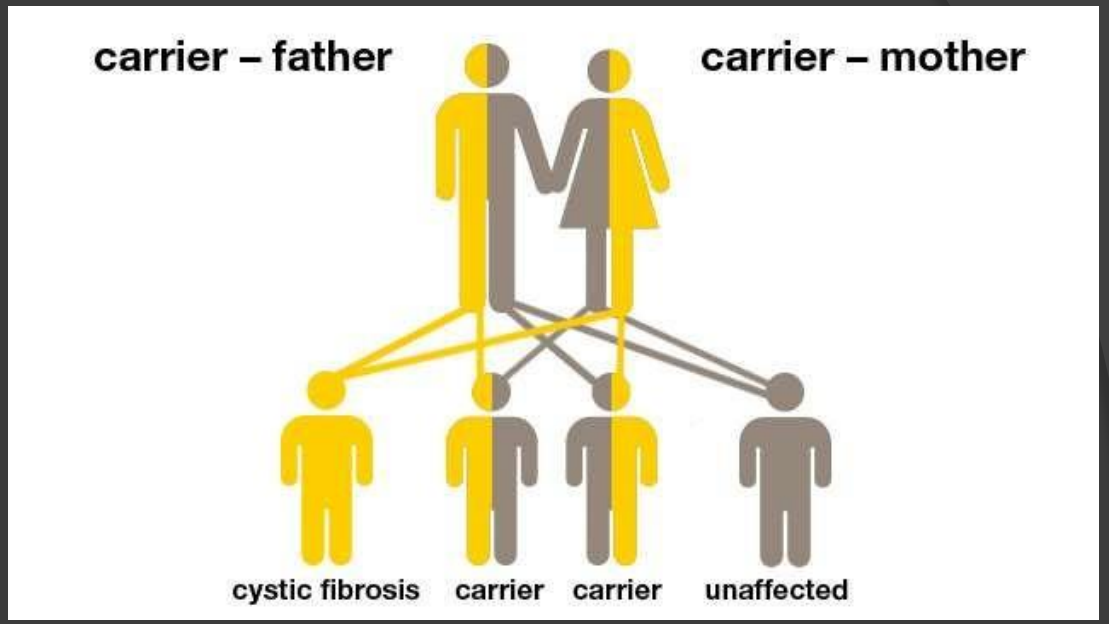
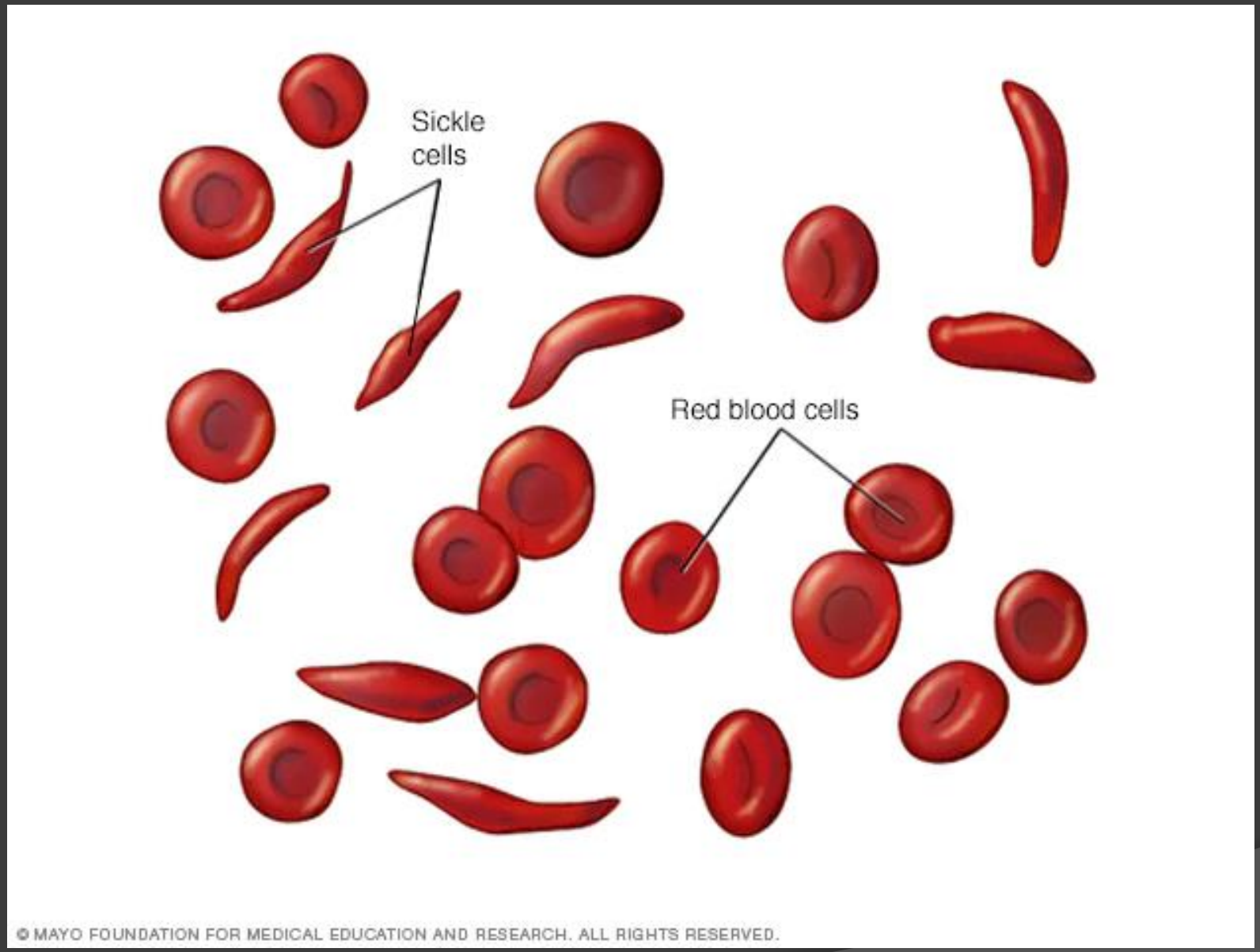

carrier – father
carrier – mother
cystic fibrosis
carrier
carrier
unaffected

(2) SICKLE CELL ANEMIA

- **Sickle cell disease** is **caused** by a mutation in the hemoglobin-Beta **gene** found on chromosome 11.
- A severe hereditary form of anemia in which a mutated form of hemoglobin distorts the red blood cells into a crescent shape at low oxygen levels.
- Sickle cell disease is a group of disorders that affects hemoglobin, the molecule in red blood cells that delivers oxygen to cells throughout the body.
- People with this disorder have atypical hemoglobin molecules called hemoglobin S, which can distort red blood cells into a sickle, or crescent, shape.

SIGNS AND SYMPTOMS

- Begin in early childhood. Characteristic features of this disorder include a low number of red blood cells anemia. The signs and symptoms of sickle cell disease are caused by the sickling of red blood cells.
- When red blood cells sickle, they break down prematurely, which can lead to anemia. Anemia can cause shortness of breath, fatigue, and delayed growth and development in children. The rapid breakdown of red blood cells may also cause yellowing of the eyes and skin, which are signs of jaundice.
- This condition is inherited in an **autosomal recessive pattern**, which means both copies of the gene in each cell have mutations.



(3) FRAGILE X SYNDROME

- Mutations in the FMR1 (**fragile X** mental retardation 1) **gene cause fragile X syndrome**. The FMR1 **gene** provides instructions for making a protein called FMRP. This protein helps regulate the production of other proteins and plays a role in the development of synapses, which are specialized connections between nerve cells. This **protein**, most commonly found in the brain, is essential for normal cognitive development and female reproductive function.
- Fragile X syndrome (FXS) is an inherited genetic condition. It's also known at Martin-Bell syndrome.
- FXS can cause learning disabilities, developmental delays, and social or behavioral problems. Disabilities vary in severity.
- When babies miss developmental milestones it can be can symptom of FXS. There are also notable physical features, like large head circumference or an elongated face

- FXS is the most common hereditary cause of mental disability in boys.
- People with FXS usually experience a range of developmental and learning problems.
- The disease is a chronic or lifelong condition. Only some people with FXS are able to live independently.

FRAGILE X SYNDROME

Broad forehead
Elongated face
Large prominent ears
Strabismus (crossed eyes)
Highly arched palette

Hyperextensible Joints
Hand calluses
Pectus Excavatum
(indentation of chest)
Mitral valve prolapse

Hypotonia (low muscle tone)
Soft, fleshy skin
Enlarged testicles
Flat feet
Seizures in 10%

(4) WHAT IS HUNTINGTON'S DISEASE?

- **Huntington's disease** is a progressive brain **disorder caused** by a single **defective gene** on chromosome 4 — one of the 23 human chromosomes that carry a person's entire **genetic** code. This **defect** is "dominant," meaning that anyone who inherits it from a parent with **Huntington's** will eventually develop the **disease**.
- Huntington's disease (HD) is a fatal genetic disorder that causes the progressive breakdown of nerve cells in the brain. It deteriorates a person's physical and mental abilities during their prime working years and has no cure. HD is known as the quintessential family disease because every child of a parent with HD has a 50/50 chance of carrying the faulty gene.

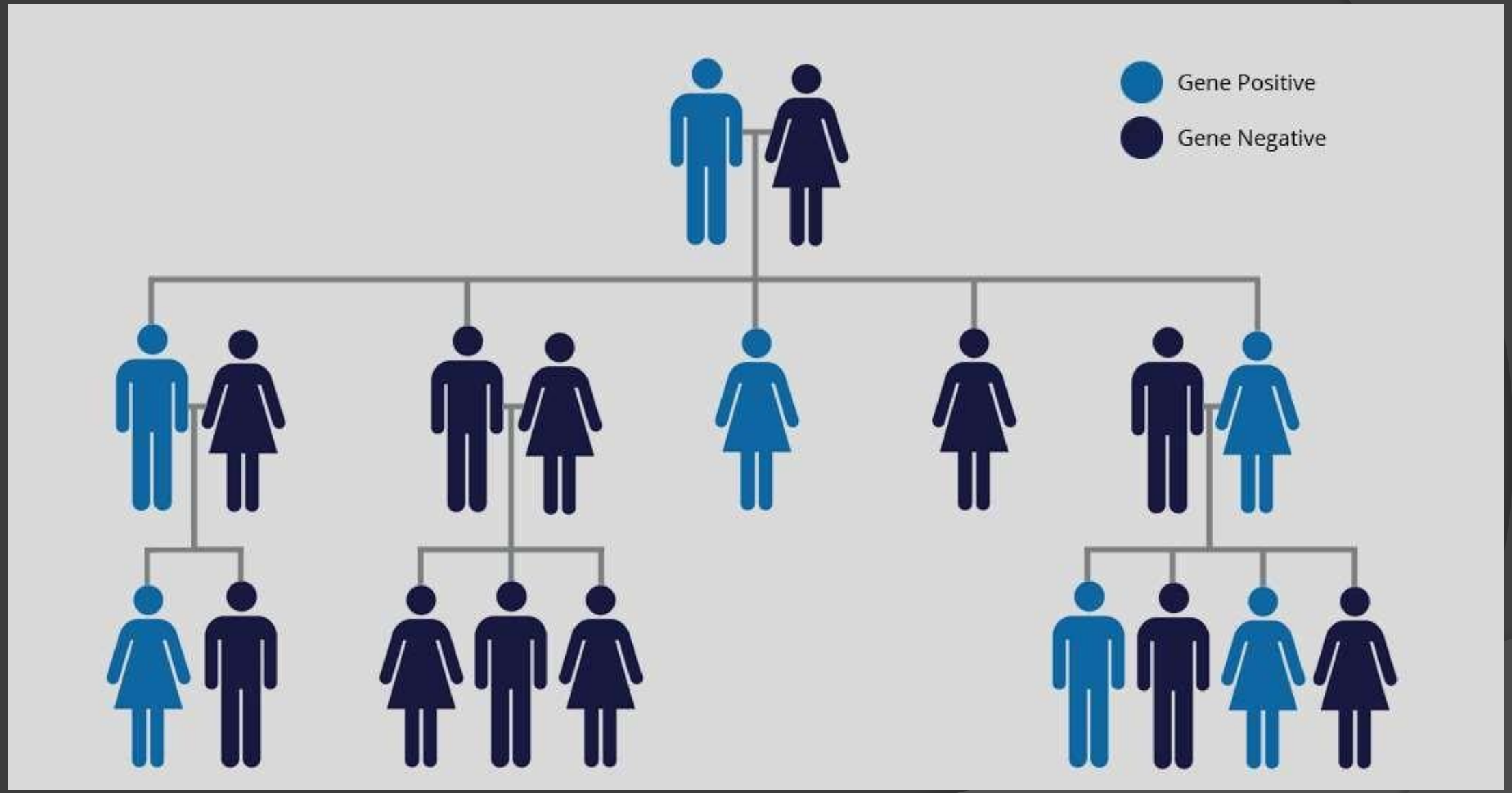
SYMPTOMS

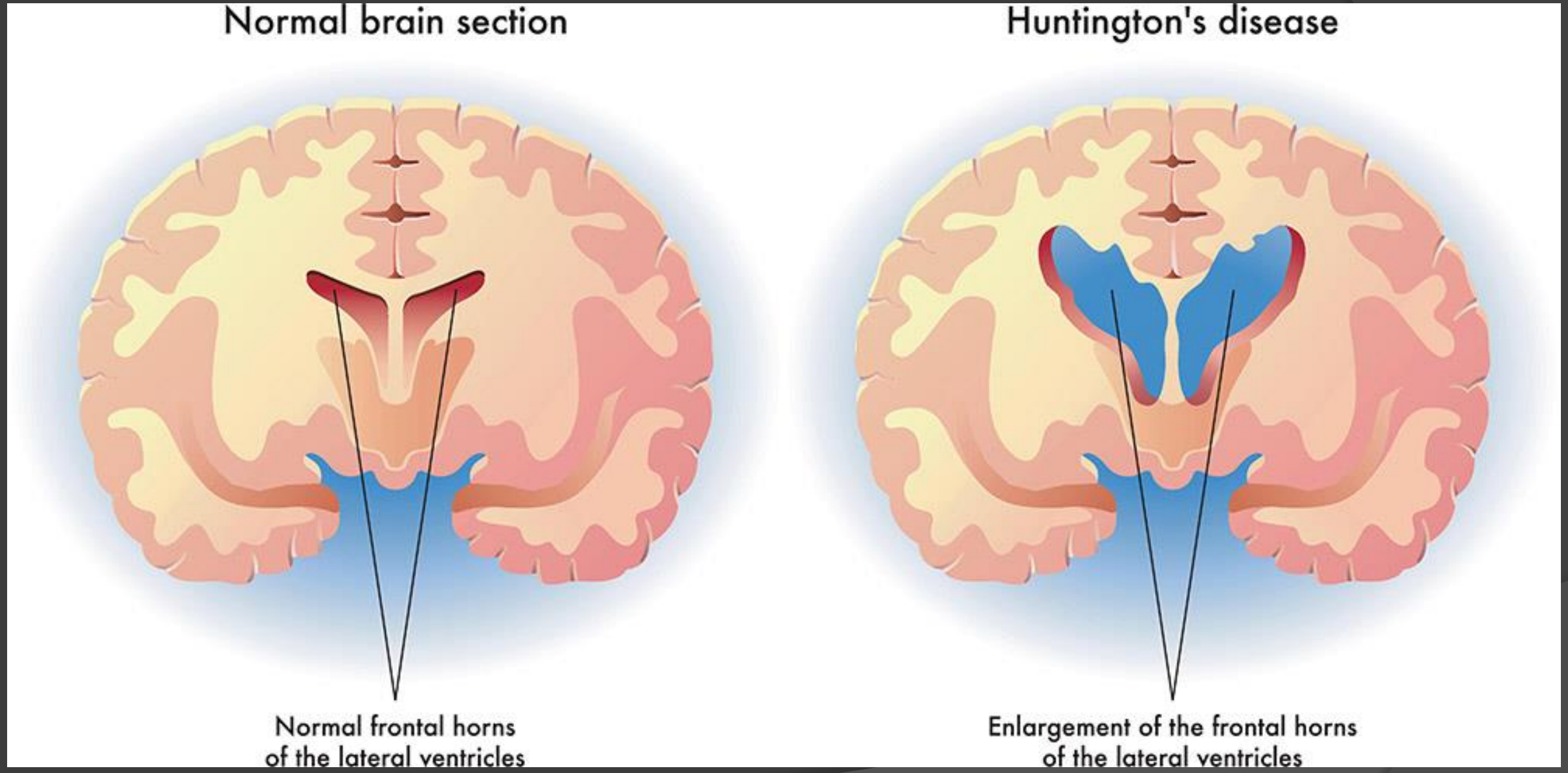
- Many describe the symptoms of HD as having Parkinson's and Alzheimer's
- Symptoms usually appear between the ages of 30 to 50, and worsen over a 10 to 25 year period. Ultimately, the weakened individual succumbs to pneumonia, heart failure or other complications.
- Everyone has the gene that causes HD, but only those that inherit the expansion of the gene will develop HD and perhaps pass it on to each of their children.
- Every person who inherits the expanded HD gene will eventually develop the disease.

  Over time, HD affects the individual's ability to reason, walk and speak.

Include:

- Personality changes, mood swings & depression
- Forgetfulness & impaired judgment
- Unsteady gait & involuntary movements (chorea)
- Slurred speech, difficulty in swallowing & significant weight loss


Gene Positive
Gene Negative


Normal brain section
Huntington's disease
Normal frontal horns
of the lateral ventricles
Enlargement of the frontal horns
of the lateral ventricles

(5) MUSCULAR DYSTROPHY

- **Mutations** in the DMD **gene cause** the Duchenne and Becker forms of **muscular dystrophy**. The DMD **gene** provides instructions for making a protein called **dystrophin** . This protein is located primarily in skeletal and cardiac **muscle**, where it helps stabilize and protect **muscle** fibers.
- Muscular dystrophy is a group of diseases that cause progressive weakness and loss of muscle mass. In muscular dystrophy, abnormal genes (mutations) interfere with the production of proteins needed to form healthy muscle.
- However, it often occurs in people without a known family history of the condition. The condition most often affects boys due to the way the disease is inherited.
- Some people who have muscular dystrophy will eventually lose the ability to walk. Some may have trouble breathing or swallowing.
- There is no cure for muscular dystrophy. But medications and therapy can help manage symptoms and slow the course of the disease.

SIGNS AND SYMPTOMS

- The main sign of muscular dystrophy is progressive muscle weakness. Specific signs and symptoms begin at different ages and in different muscle groups, depending on the type of muscular dystrophy.

- Typically appear between the ages of 2 and 3, and may include:

  Frequent falls, Difficulty getting up from a lying or sitting position, Trouble running and jumping, Waddling gait, Walking on the toes, Large calf muscles, Muscle pain and stiffness, Learning disabilities.

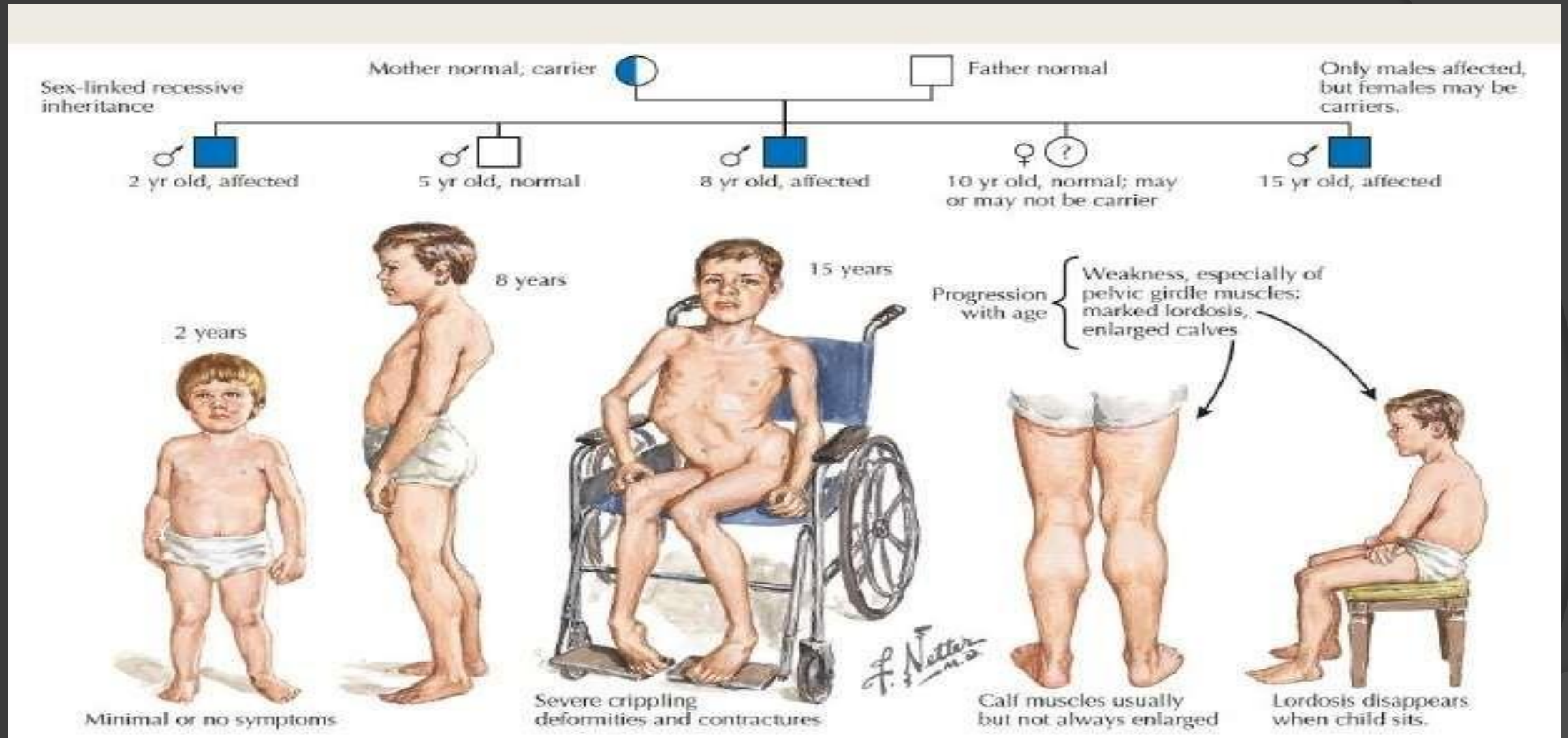
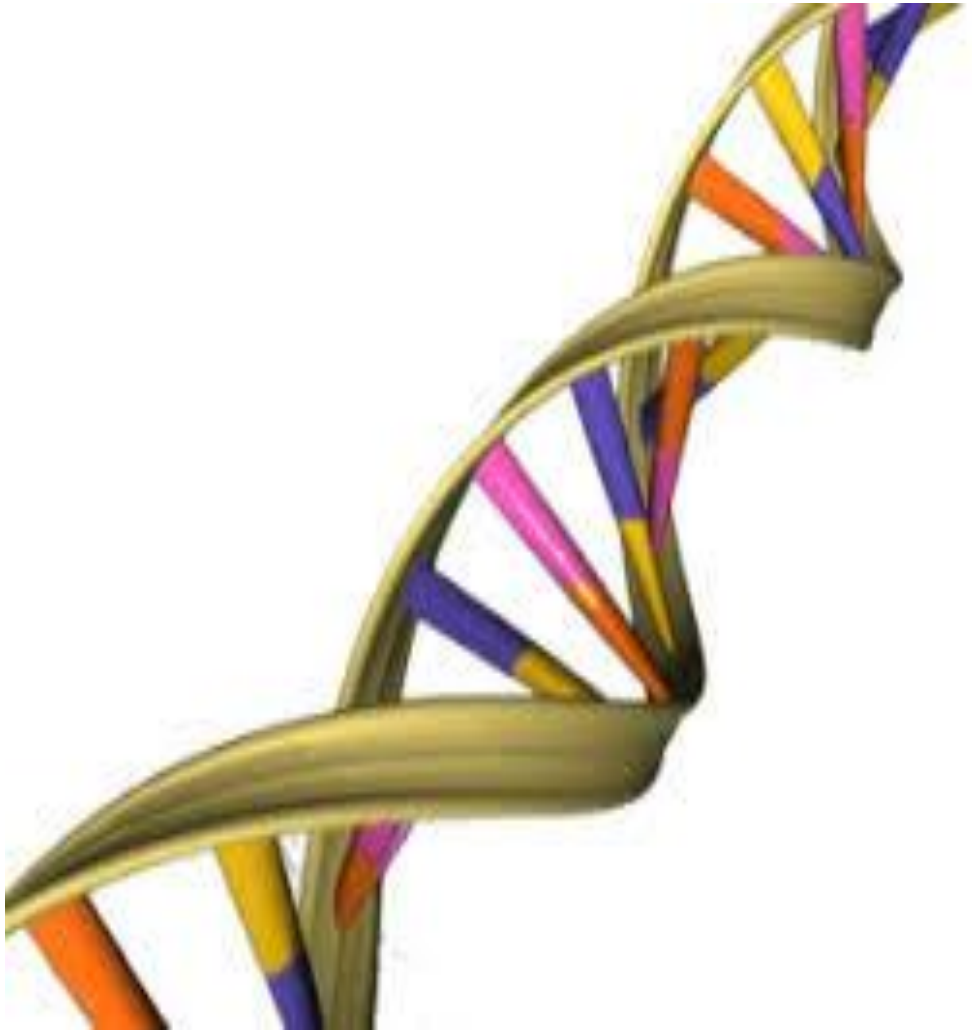


Figure 75-11 Duchenne Muscular Dystrophy.

Mendel’s laws



Genetics

- Passing of characters from parents to offsprings

What is genetics?

- Genetics is a branch of biology concerned with the study of genes, genetic variation, and heredity in organisms.

What is a gene?

- A distinct sequence of nucleotides forming part of a chromosome. A unit of heredity which is transferred from a parent to offspring and is held to determine some characteristic of the offspring.

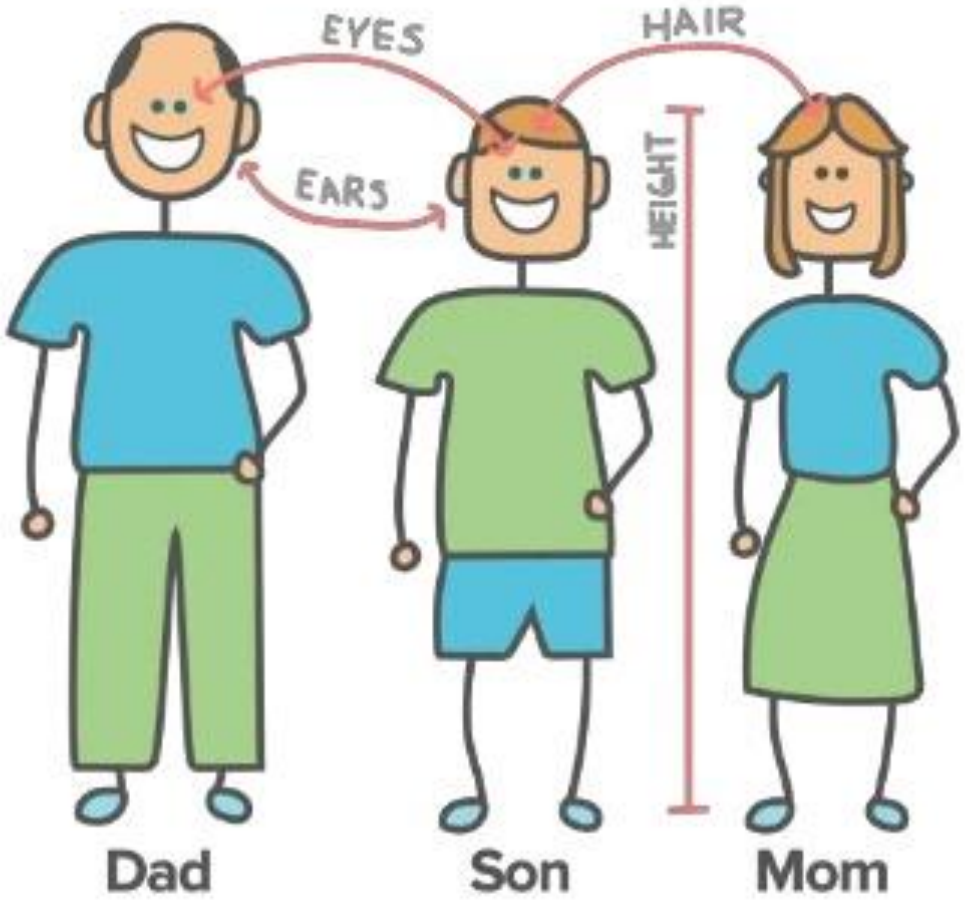
Genetic variations?

- Genetic variation is the difference in DNA among individuals or the differences between populations.

Heredity?

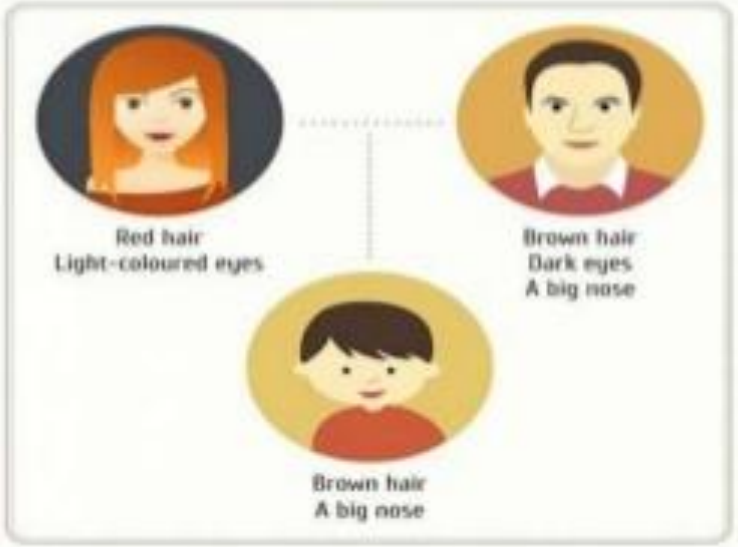
- Heredity, also called inheritance or biological inheritance, is the passing on of traits from parents to their offspring; either through asexual reproduction or sexual reproduction, the offspring cells or organisms acquire the genetic information of their parents.

- **Heredity** is the passing on of ***traits*** from parents to their offspring



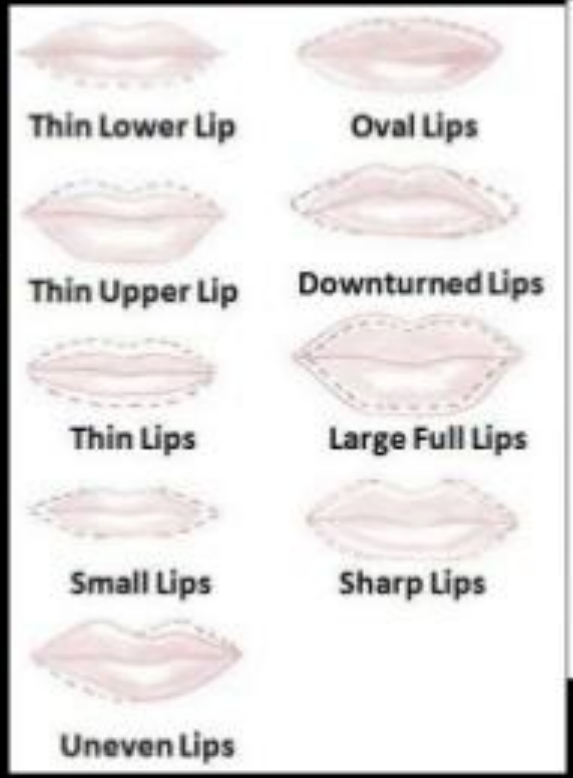
What are Traits

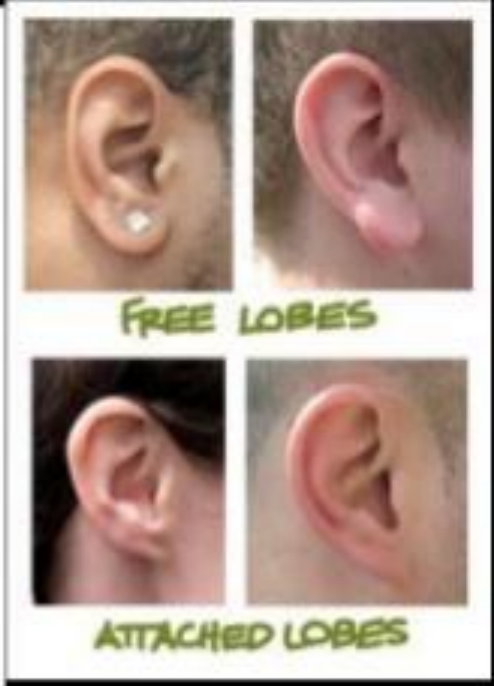
- Eye Colour
- Hair Colour
- Height
- Body Structure
- Facial Features
- Skin Colour

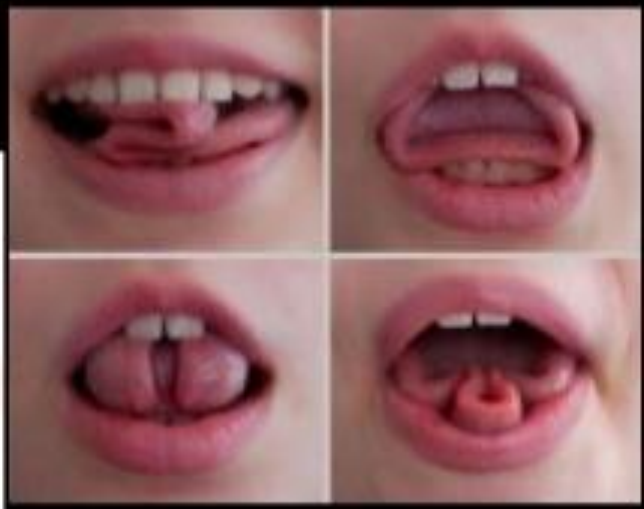


Other inherited traits include:

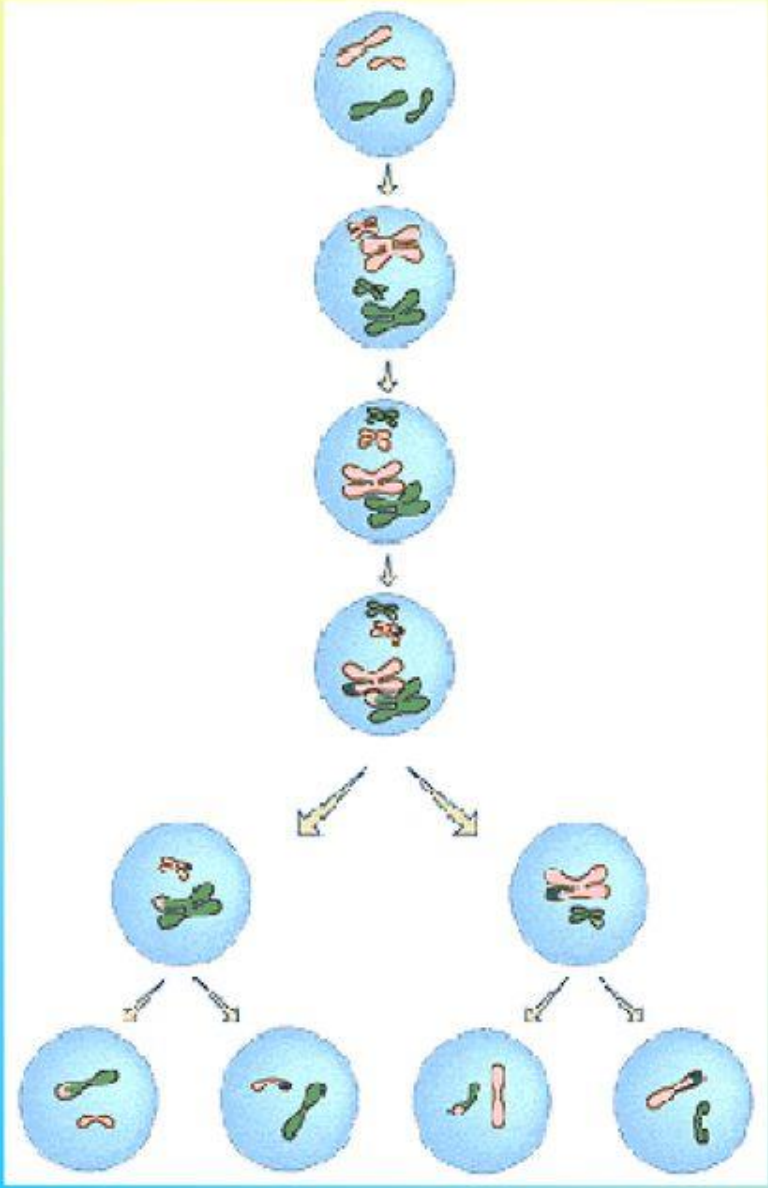
a) Free and attached airlobe
b) Straight or the bent thumb
c) Tongue rolling
d) Color of eyes
e) Shape of lips
f) Color of hair
g) Blood type
h) Diabetes
i) Texture of the hair







Where do we get our genes from?



- $\frac{1}{2}$ comes from mother
  - 23 single chromosomes in the egg cell
- $\frac{1}{2}$ comes from father
  - 23 single chromosomes in sperm cell

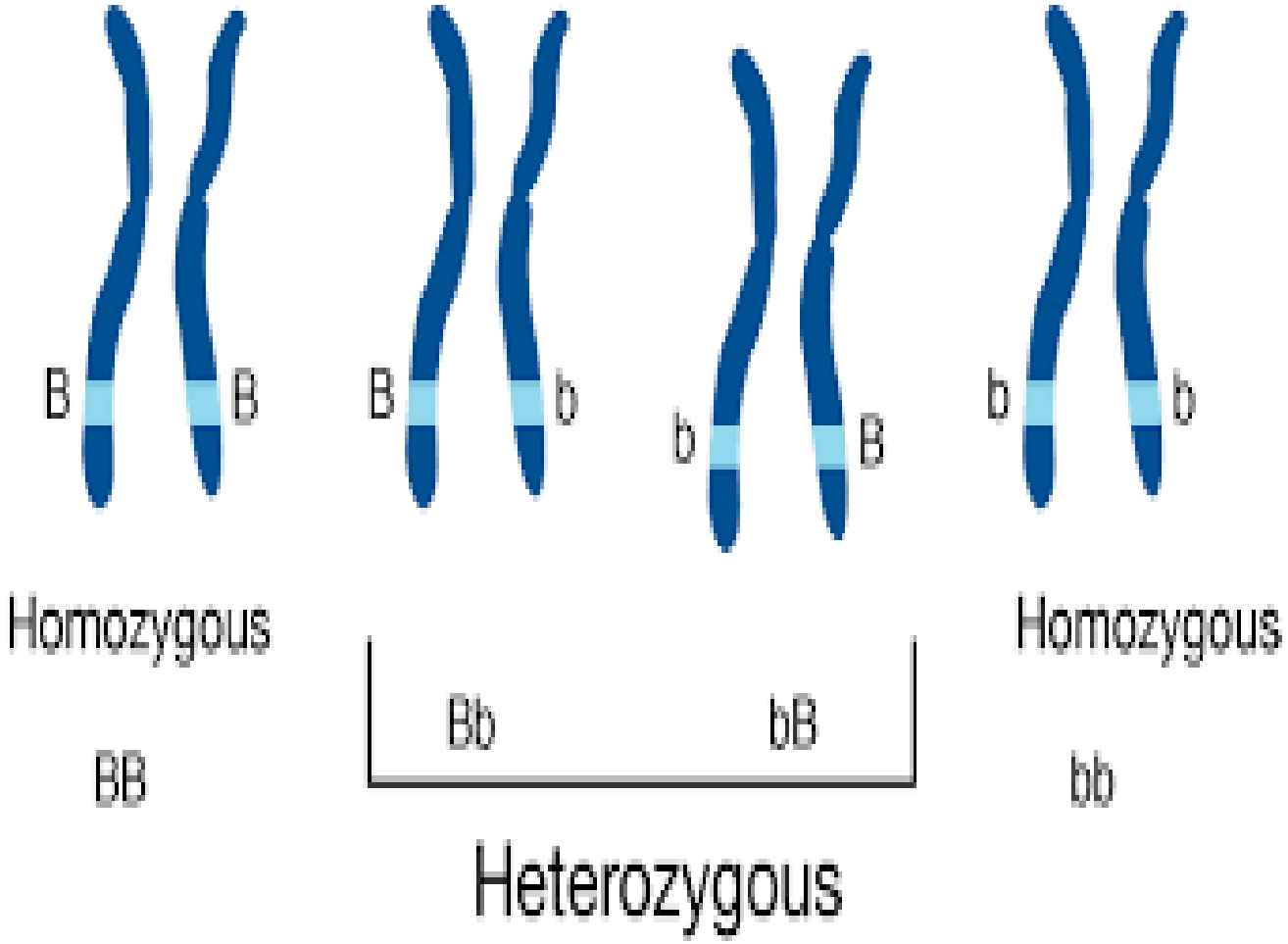
Allele?

- An **allele** is a variant form of a gene. Some genes have a variety of different forms, which are located at the same position, or genetic locus, on a chromosome. Humans are called diploid organisms because they have two **alleles** at each genetic locus, with one **allele** inherited from each parent**.**

Homozygous vs. Heterozygous

- **Homozygous**: inherits two similar alleles from the parents for a particular gene
  - Ex: tall allele and tall allele, written as TT
  - Ex: short allele and short allele written as tt

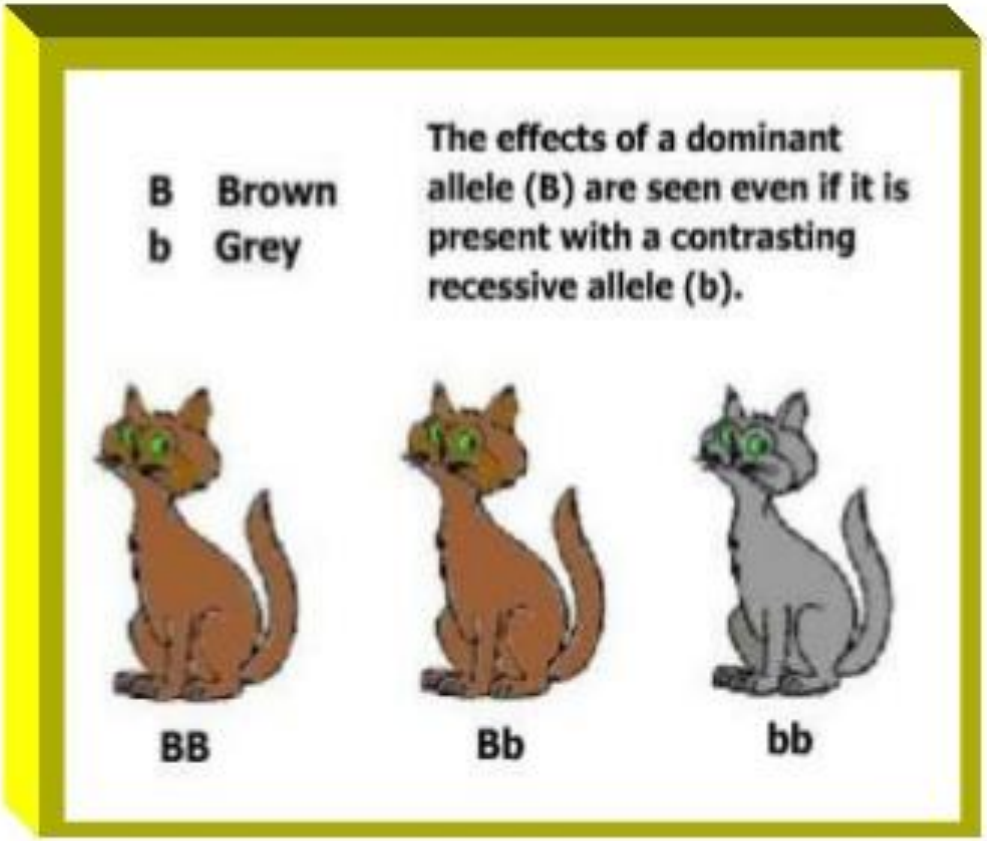
- **Heterozygous**: inherits two different alleles from the parents for a particular gene
  - Ex: tall allele and short allele, written as Tt


B
B
B
b
b
B
b
b
Homozygous
BB
Bb
bB
Heterozygous
Homozygous
bb

Dominant vs. Recessive

- A ***dominant*** allele is expressed even if it is paired with a recessive allele.

- A ***recessive*** allele is only visible when paired with another recessive allele.



Homozygous Dominant

A	A

Heterozygous

A	a

Homozygous Recessive

a	a

Genotype vs. Phenotype

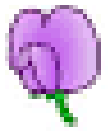
Genotype

- The entire genetic makeup of an organism; the combination of genes for one or more specific traits
- The combination of alleles inherited from parents
- The actual **GENES**
- Ex) **GG** (one "G" from each parent) = green pea pod

Phenotype

- An organism's appearance or other detectable appearance
- Observable traits
- **PHYSICAL** appearance
- Ex) GG = **Green pea pod** (observable trait; based on genotype)

Genotype vs. Phenotype

Genotype	Phenotype
BB Homozygous dominant	
Bb Heterozygous	
bb Homozygous recessive	

Gregor Mendel (1822-1884)

Responsible for the Laws governing Inheritance of Traits

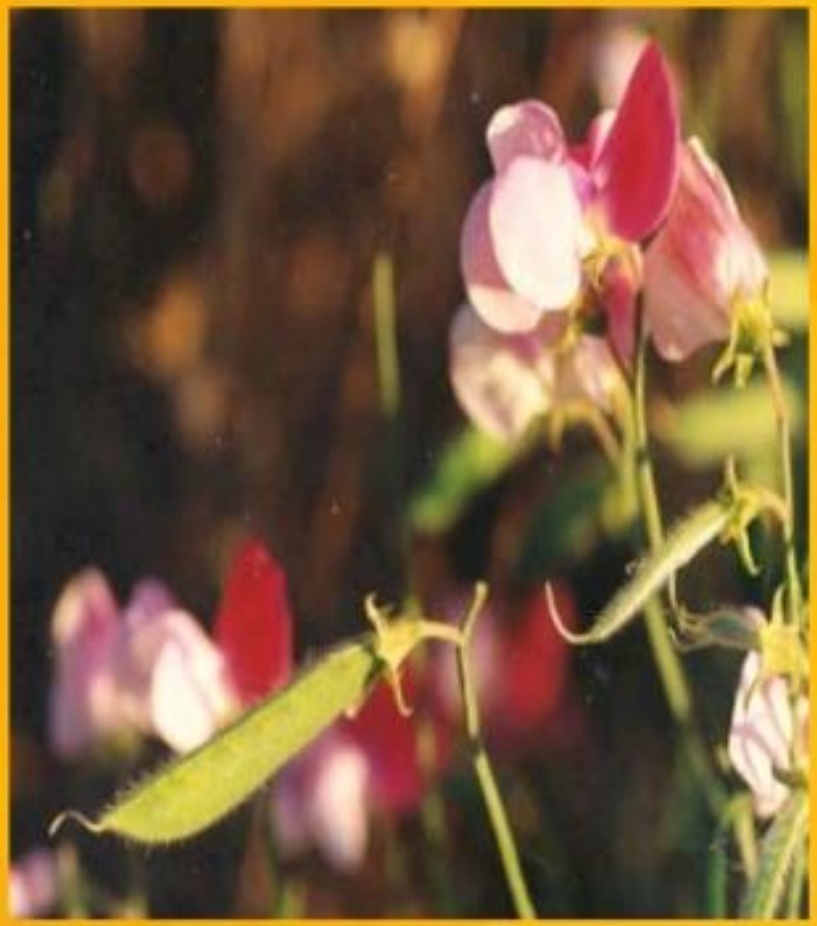
Gregor Johann Mendel

- Austrian monk
- Studied the inheritance of traits in pea plants
- Developed the laws of inheritance
- Mendel's work was not recognized until the turn of the 20th century

Mendel's Pea Plant Experiments

Why peas, *Pisum sativum*?

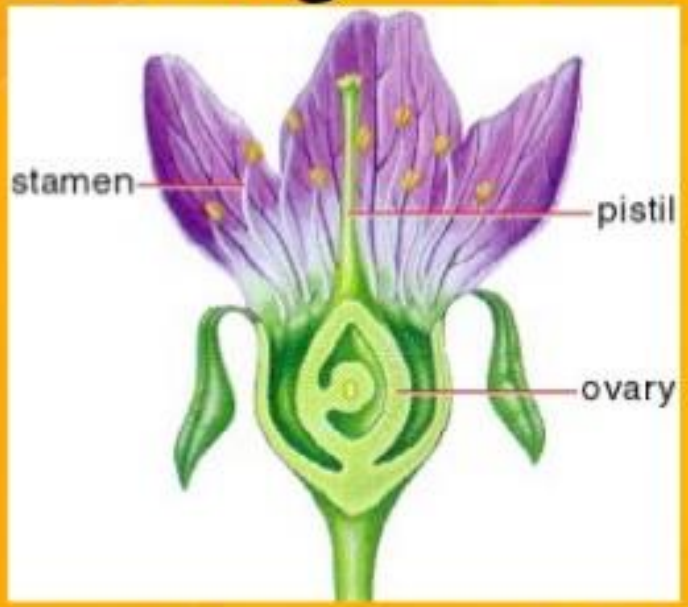
- Can be grown in a small area
- Produce lots of offspring
- Produce pure plants when allowed to self-pollinate several generations
- Can be artificially cross-



Reproduction in Flowering Plants

Pollen contains sperm
- Produced by the stamen

Ovary contains eggs
- Found inside the



Pollen carries sperm to the eggs for fertilization
- *Self-fertilization* can occur in the same flower
- *Cross-fertilization* can occur between flowers

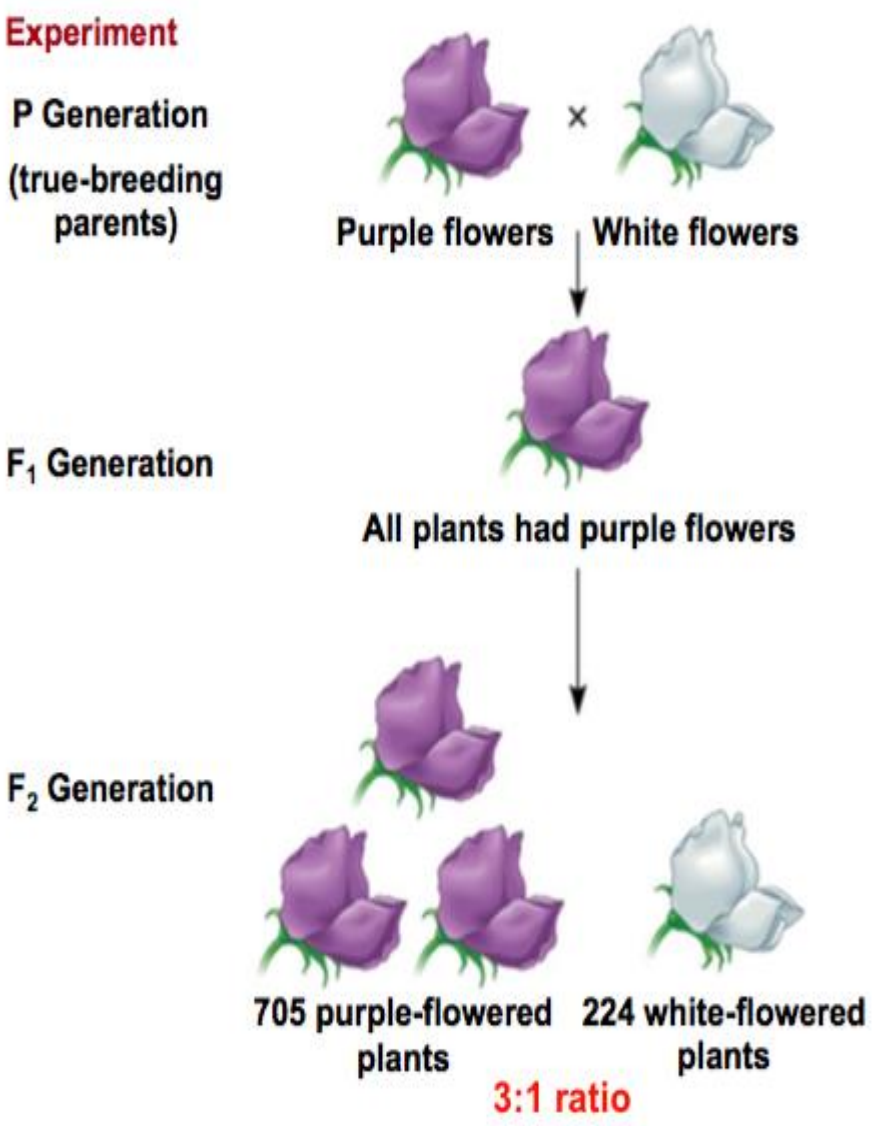
Mendel's Experimental Methods

Mendel hand-pollinated flowers using a paintbrush

- He could snip the stamens to prevent self-pollination
- Covered each flower with a cloth bag

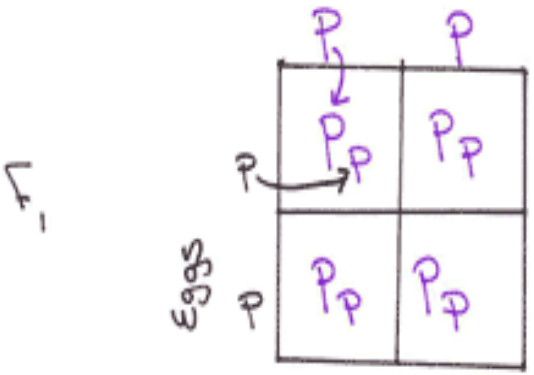
He traced traits through the several generations

	Flower Colour	Plant Height	Seed Color	Seed Shape	Pod Colour	Pod Shape	Flower Position
Dominant Trait	 Purple	 Tall	 Yellow	 Round	 Green	 Inflated (full)	 Axial
Recessive Trait	 White	 Short	 Green	 Wrinkled	 Yellow	 Constricted (flat)	 Terminal


Experiment
P Generation
(true-breeding parents)
×
Purple flowers
White flowers
F1 Generation
All plants had purple flowers
F2 Generation
705 purple-flowered plants
224 white-flowered plants
3:1 ratio

Monohybrid Cross

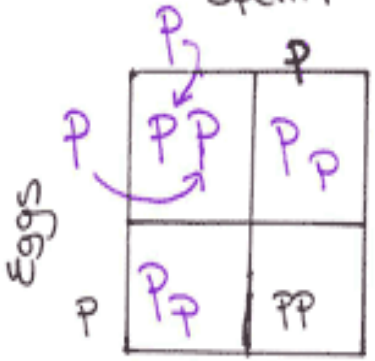
P Generation Pp (purple) × pp (white)



Offspring, F_1, are 100% Pp genotype.

100% purple flower phenotype

$F_1 \times F_1$ $(Pp \times Pp)$



F_2 are

1 : 2 : 1

PP : Pp : pp

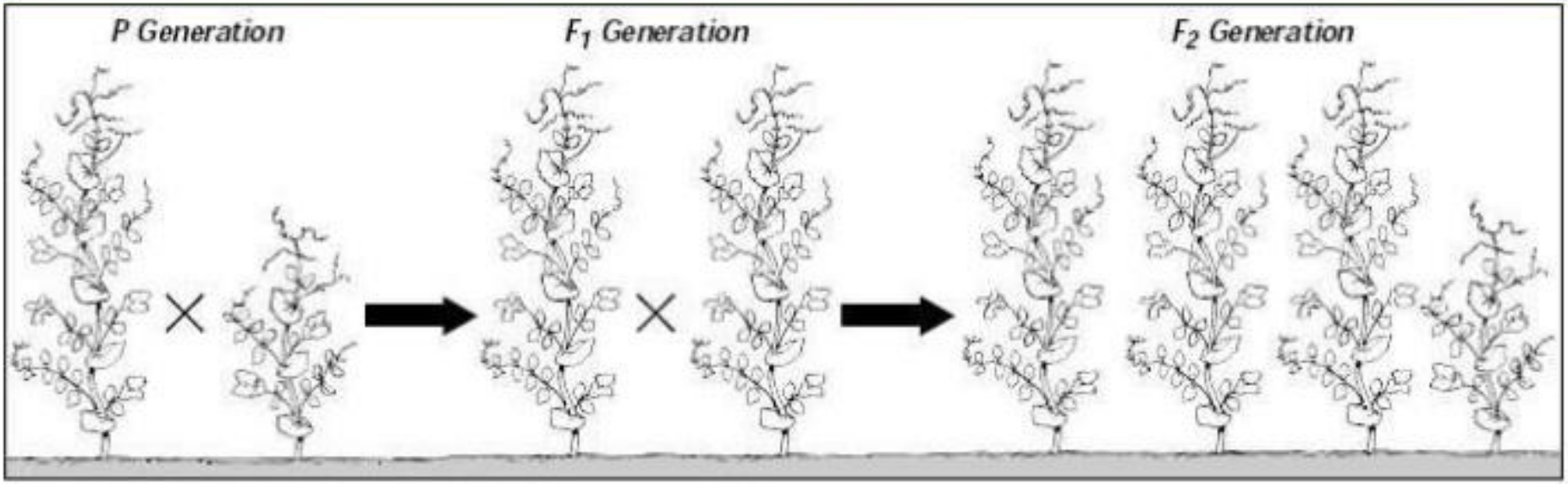
Genotype

3 : 1

Purple : white

Phenotype

Following the Generations



Cross 2 Pure Plants

TT x tt

Results in all Hybrids

Tt

Cross 2 Hybrids get 3 Tall & 1 Short

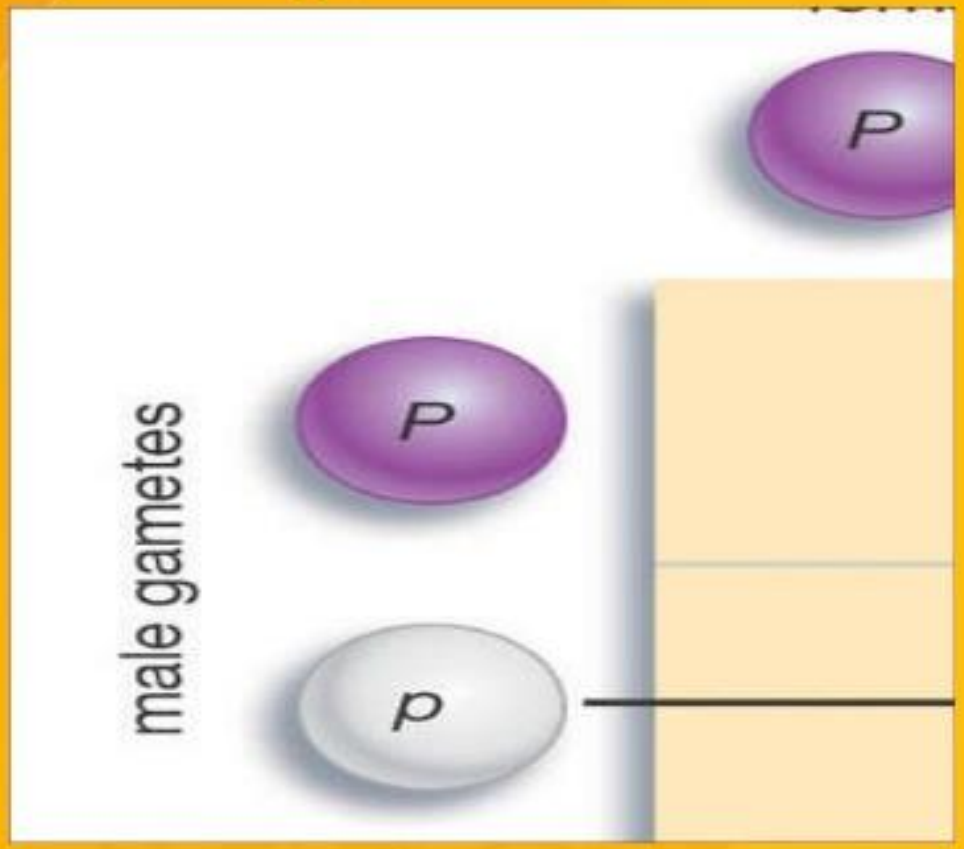
TT, Tt, tt

Types of Genetic Crosses

- **Monohybrid cross** - cross involving a single trait
  e.g. flower color
- **Dihybrid cross** - cross involving two traits
  e.g. flower color & plant height

Punnett Square

Used to help solve genetics problems



P_1 Monohybrid Cross

Trait: Seed Shape

Alleles: R - Round r - Wrinkled

Cross: Round seeds x Wrinkled seeds

RR x rr

	r	r
R	Rr	Rr
R	Rr	Rr

Genotype: Rr

Phenotype: Round

Genotypic Ratio: All alike

Phenotypic Ratio: All alike

F_1 Monohybrid Cross Review

- Heterozygous x heterozygous
- Offspring:
  25% Homozygous dominant RR
  50% Heterozygous Rr
  25% Homozygous Recessive rr
- Offspring called F_2 generation
- Genotypic ratio is 1:2:1
- Phenotypic Ratio is 3:1

What Do the Peas Look Like?

F_2 Monohybrid Cross (2nd)

Trait: Seed Shape

Alleles: R - Round r - Wrinkled

Cross: Wrinkled seeds x Round seeds

rr x Rr

	R	r
r	Rr	rr
r	Rr	rr

Genotype: Rr, rr

Phenotype: Round & Wrinkled

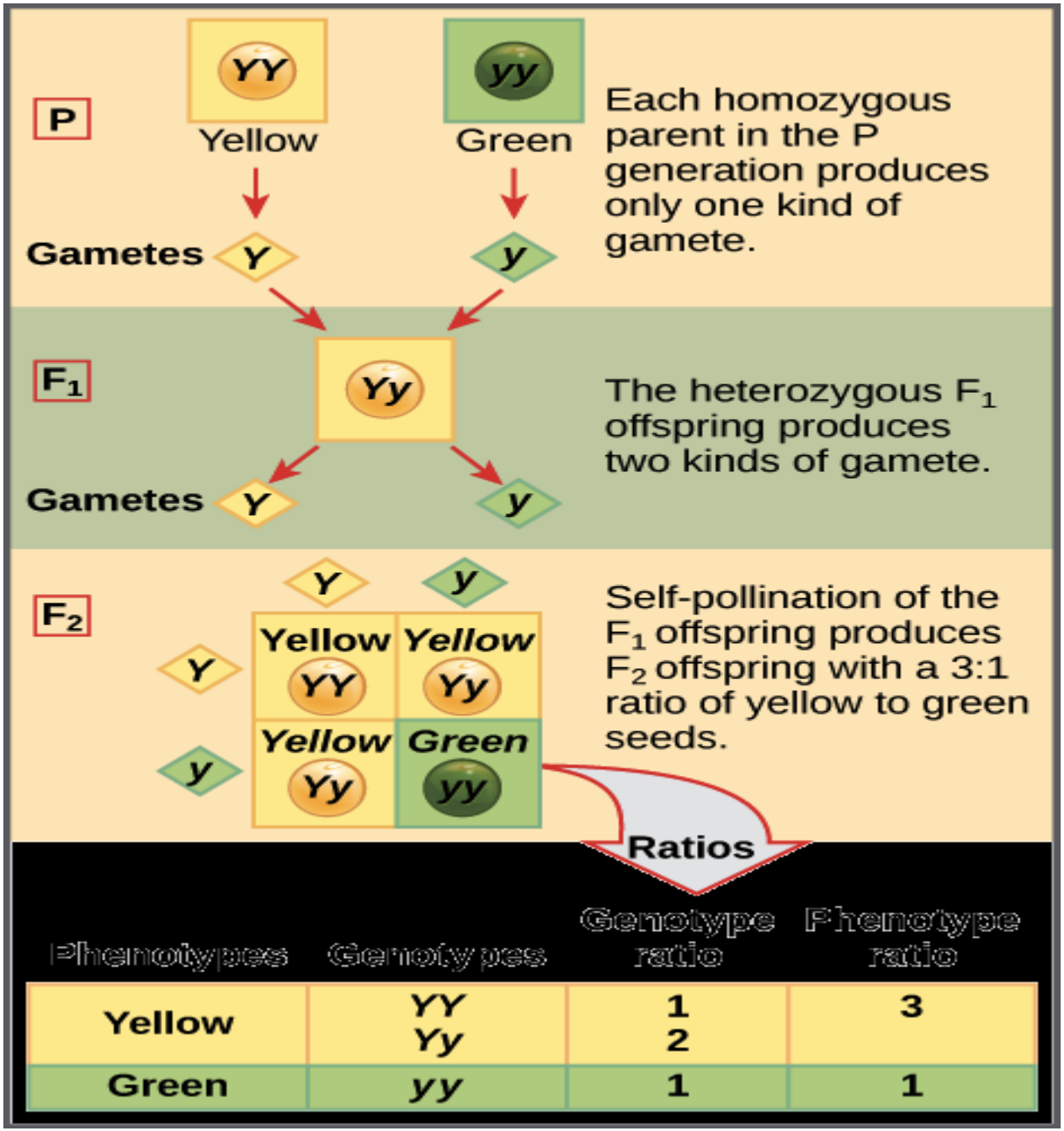
G. Ratio: 1:1

P.Ratio: 1:1

Laws of genetics by Mendel

Law of segregation

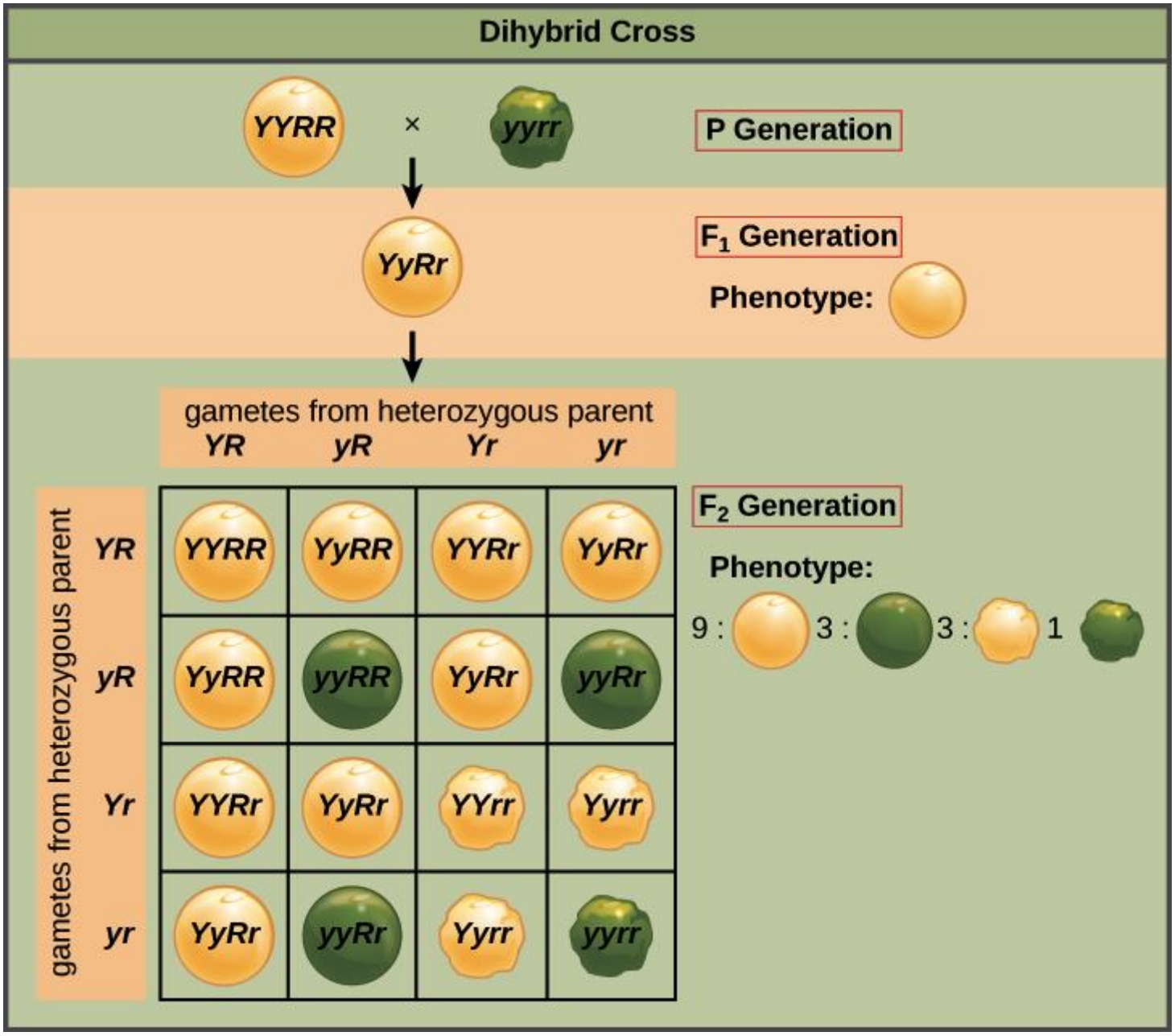
- According to the **law of segregation**, During gamete formation the alleles for each gene segregate from each other such that each gamete formed carries only one allele for each gene. The diagram below illustrates this idea:



Phenotypes	Genotypes	Genotype ratio	Phenotype ratio
Yellow	YY Yy	1 2	3
Green	yy	1	1

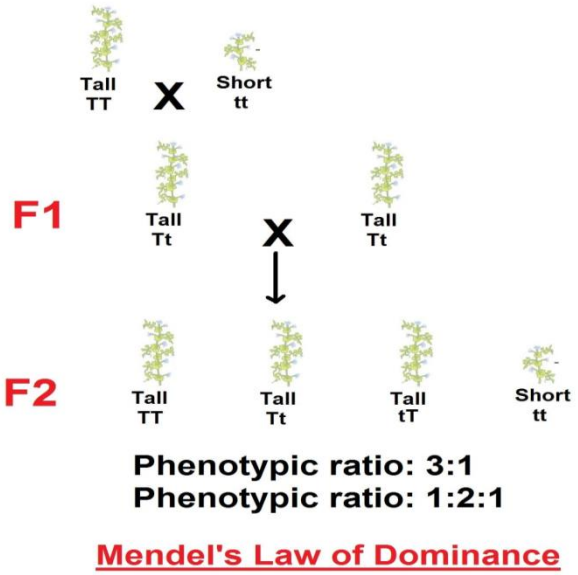
- **What is the law of independent assortment?**
- Mendel's **law of independent assortment** states that the alleles of two (or more) different genes get sorted into gametes independently of one another. In other words, the allele a gamete receives for one gene does not influence the allele received for another gene.

- **Example: Pea color and pea shape genes**
- Let's look at a concrete example of the law of independent assortment. Imagine that we cross two pure-breeding pea plants: one with yellow, round seeds (*YYRR*) and one with green, wrinkled seeds (*yyrr*).


Dihybrid Cross
YYRR
×
yyrr
P Generation
YyRr
F1 Generation
Phenotype:
gametes from heterozygous parent
YR yR Yr yr
gametes from heterozygous parent
YR yR Yr yr
YYRR YyRR YYRr YyRr
YyRR yyRR YyRr yyRr
YYRr YyRr YYrr Yyrr
YyRr yyRr Yyrr yyrr
F2 Generation
Phenotype:
9 : 3 : 3 : 1

Law of Dominance

- It states that “some alleles are dominant while others are recessive. An organism with at least one dominant allele displays the effect irrespective of the presence of the recessive one”

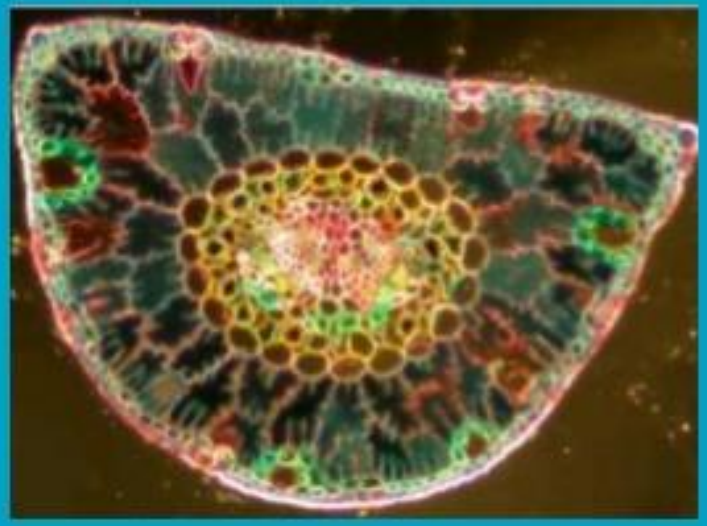


Cell division

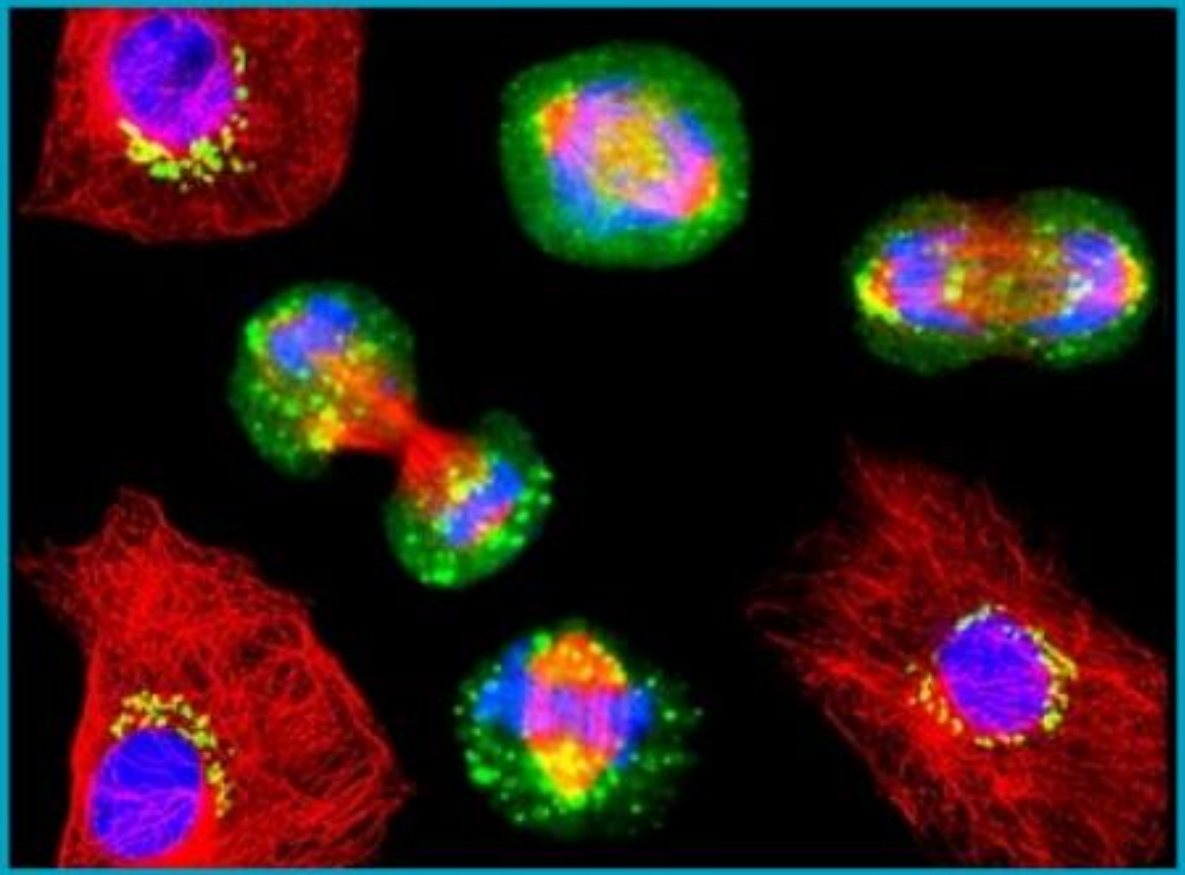
Why Is Cell Division Important?

1. All Living Things are made of Cells

2. The Cell is the basic unit of Structure and Function in Living Things.



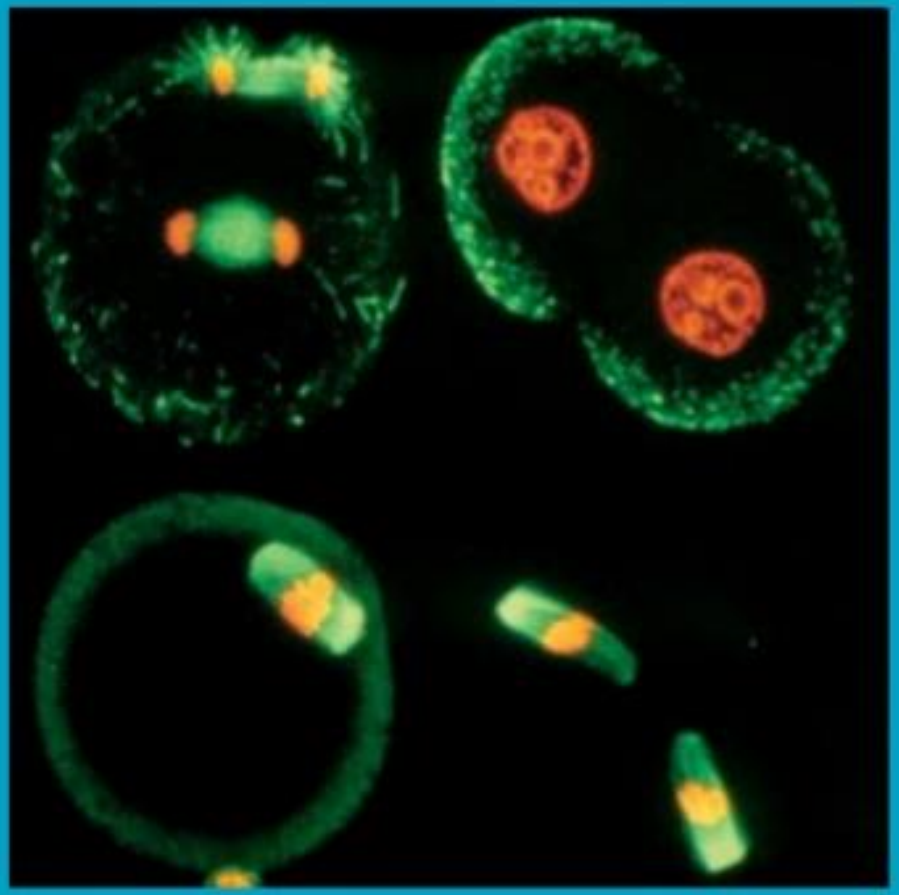
3. All Cells come from pre existing Cells



You are a living organism, made of cells.

In order to keep living, your cells must stay alive.

In order for cells to keep living, they must divide and multiply

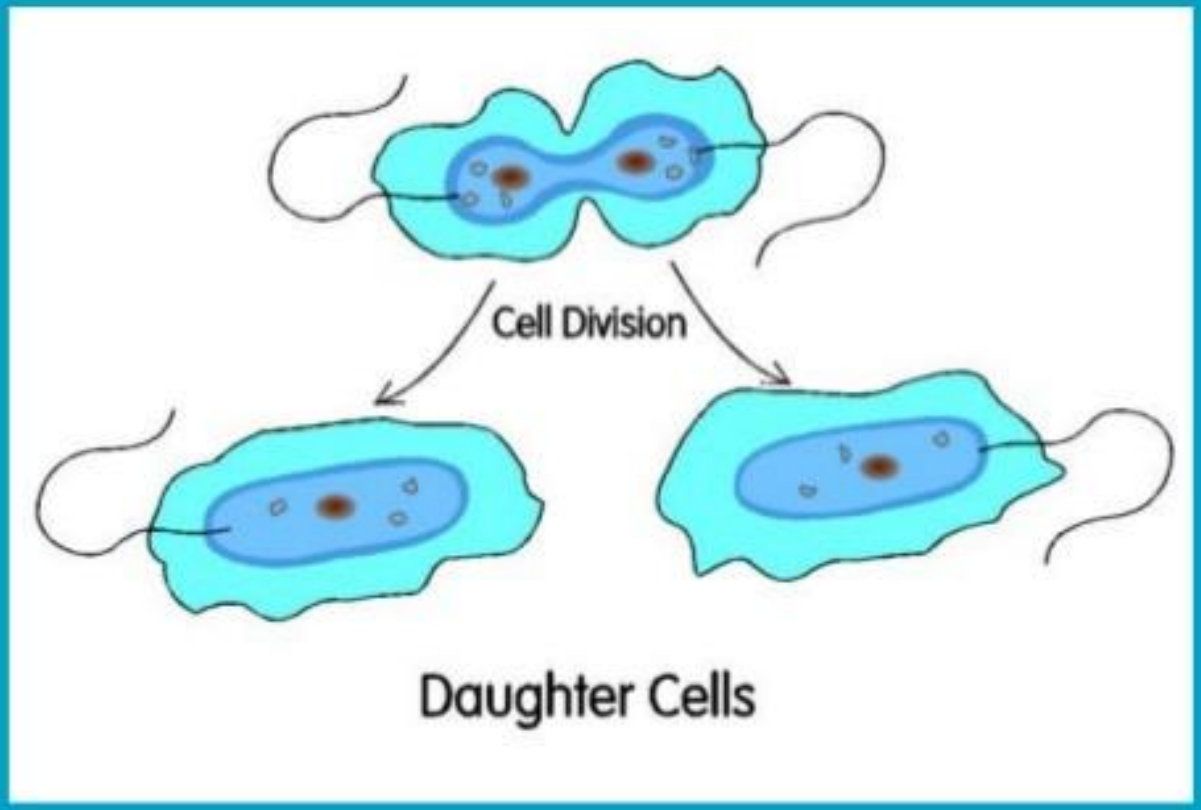


Cell Division

What is it?

Why do Cells do it?

Why is it important to me?

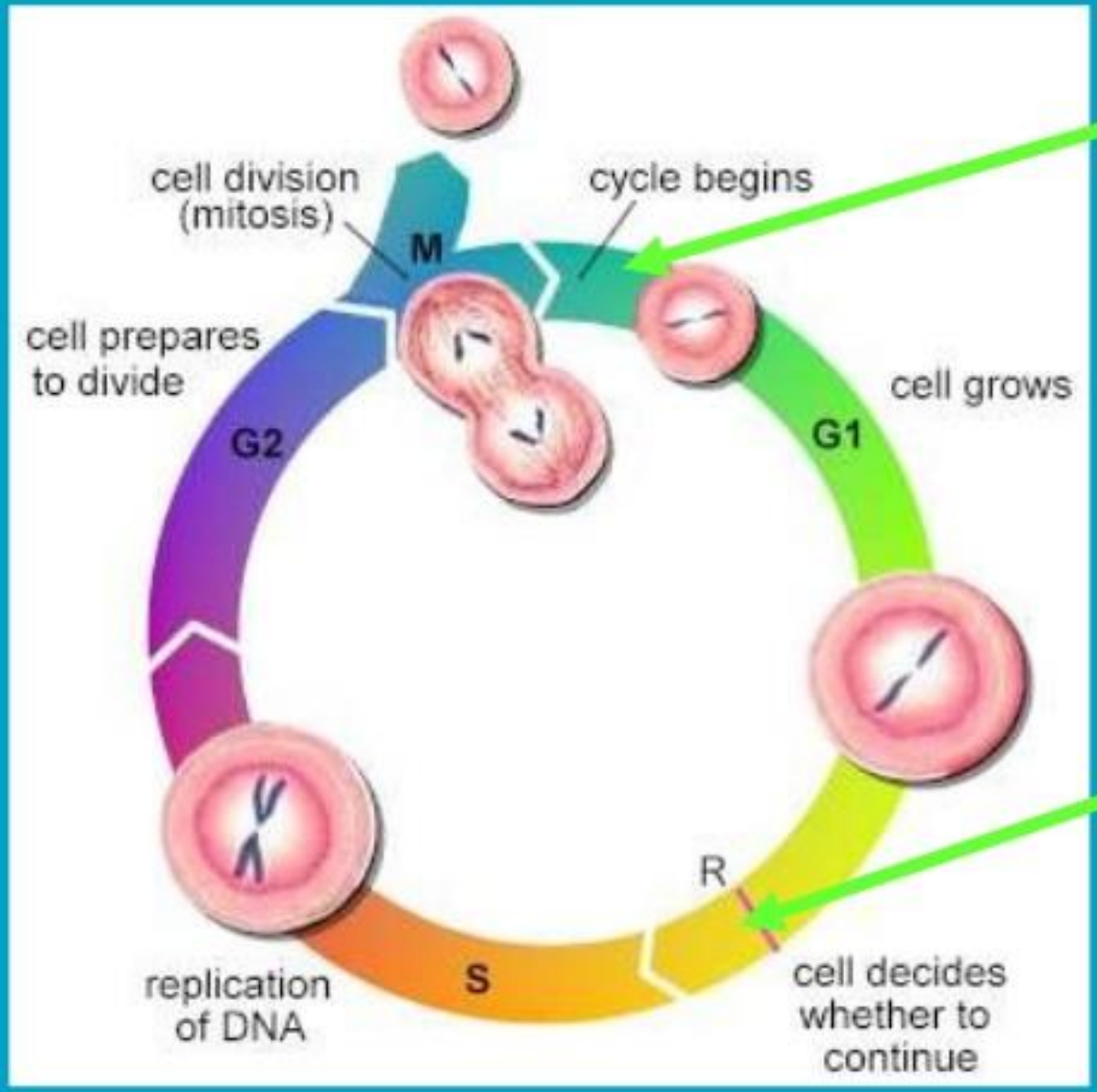


Cell Division

Also known as
Mitosis

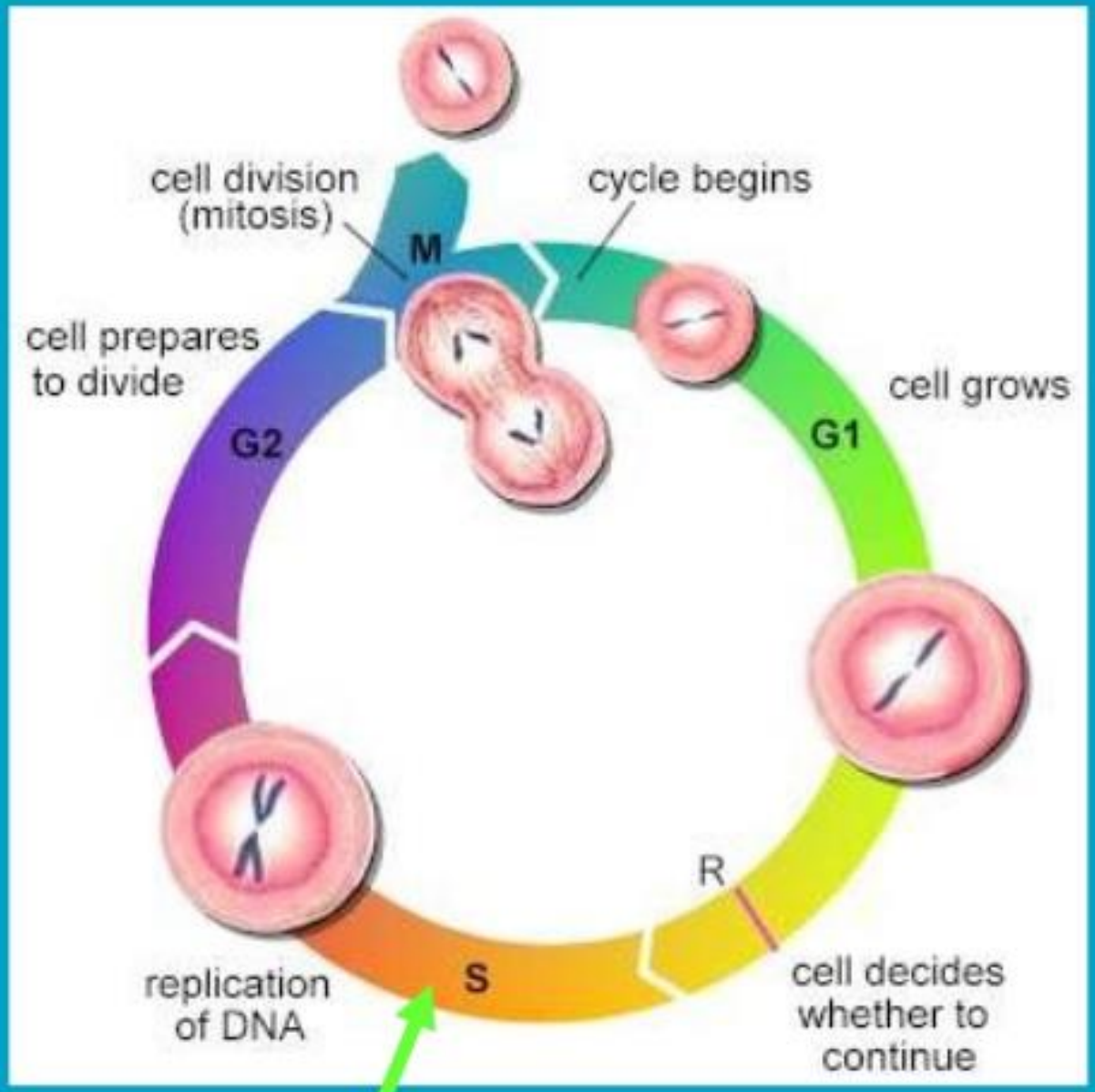
Takes place in
Regular Body Cells

Keeps Cells Living
and Growing



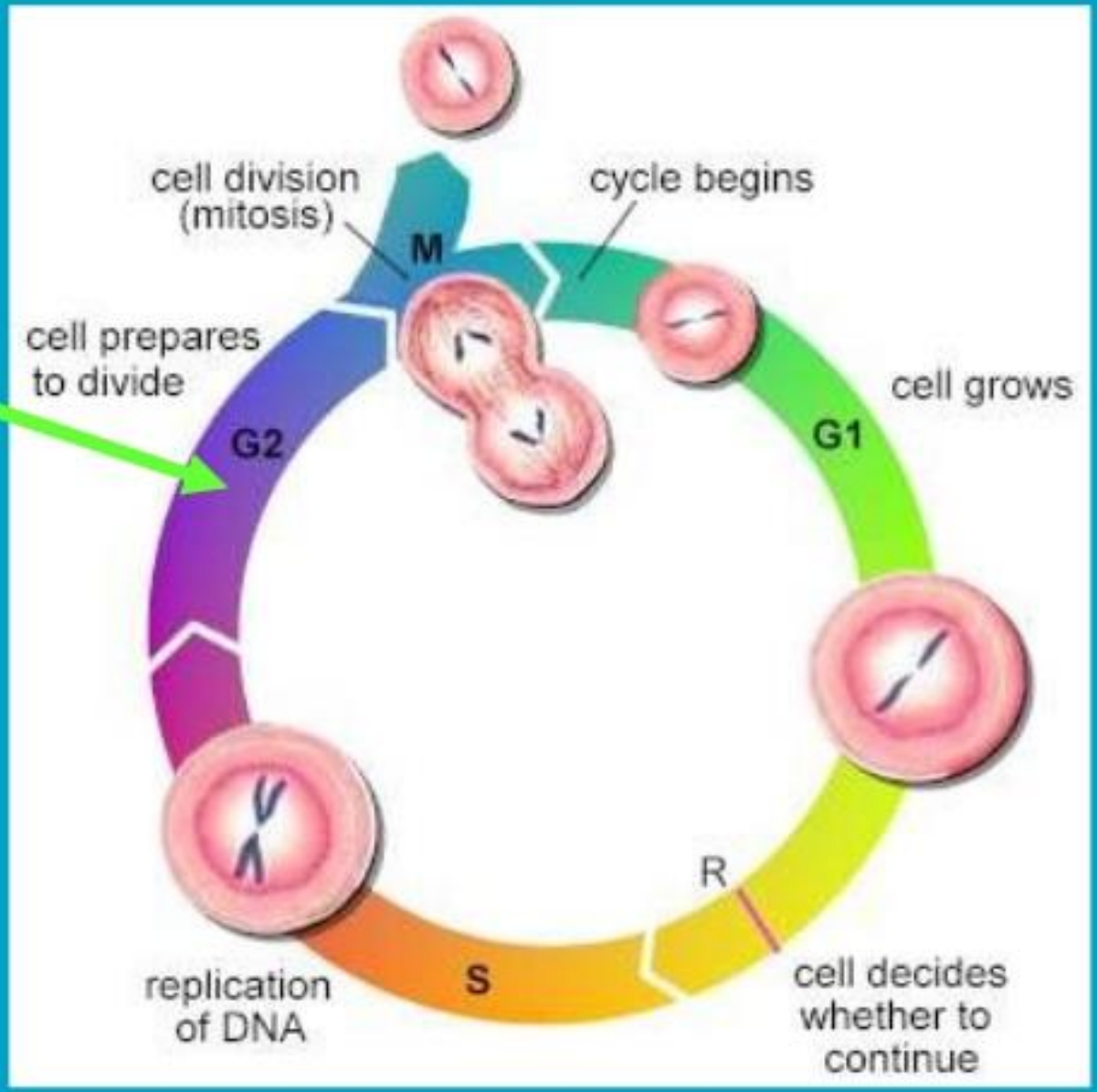
Part of Interphase is also known as the G1 Phase of the Cell Cycle

(Growth Phase)



The Second part of Interphase is known as the S Phase of the Cell Cycle

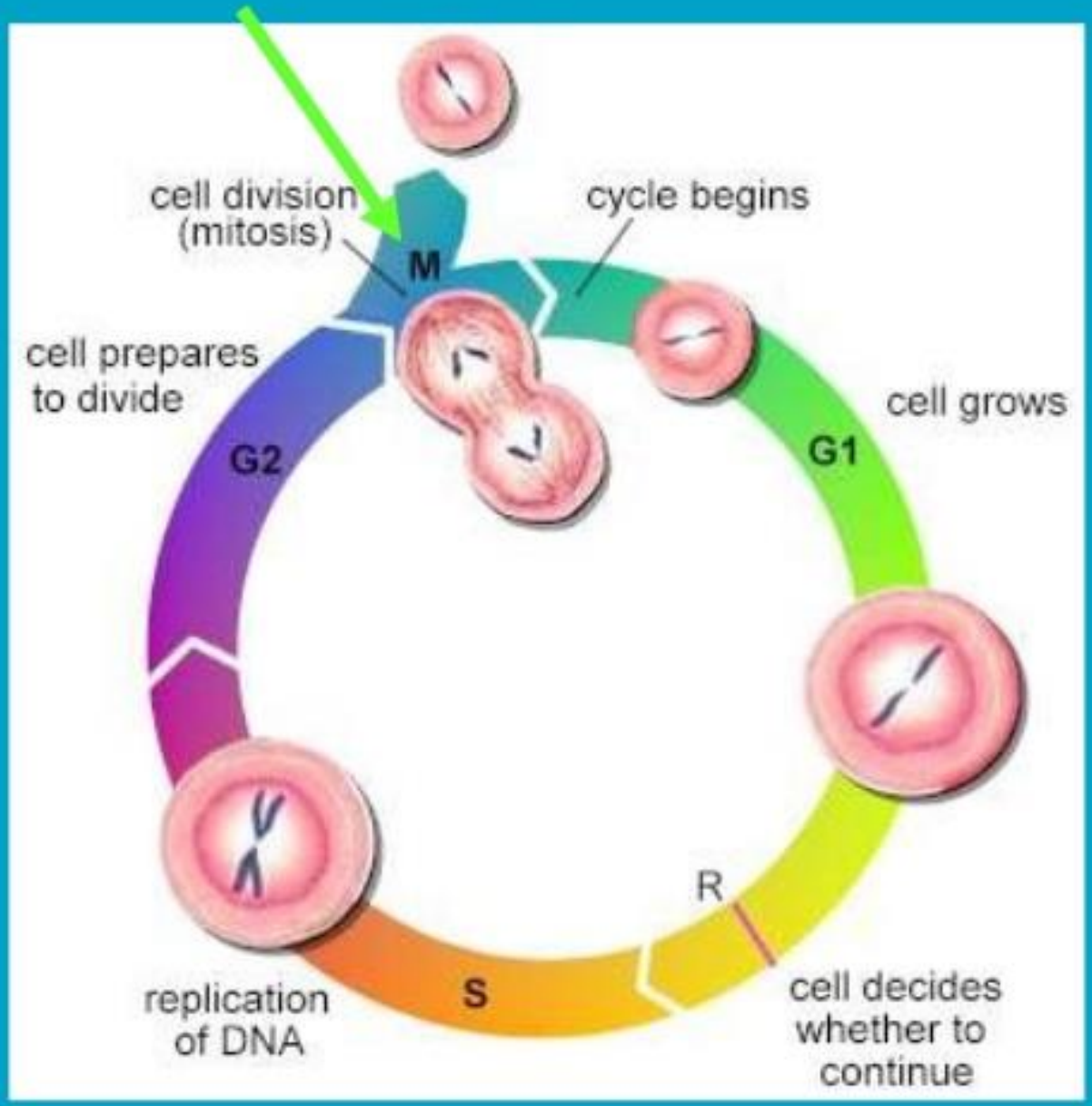
(Synthesis Phase – when DNA duplicates)



The third part of the Cell Cycle, G2, is just a checkpoint to make sure the DNA is correct.

Next step –

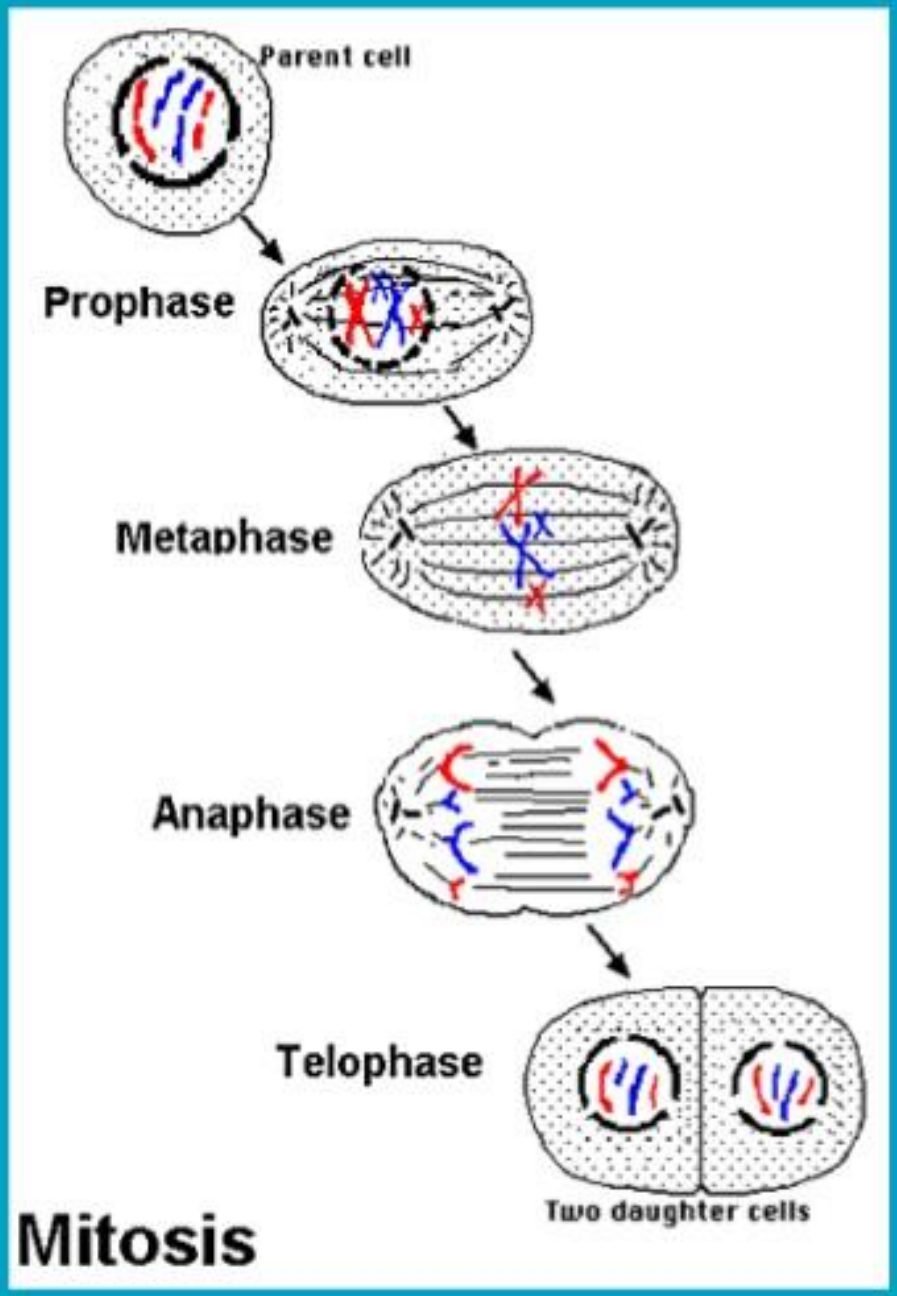
Mitosis



Mitosis:

Cell Division

The last part of the Cell Cycle is called Mitosis and has 4 phases during which the cell divides into 2 cells

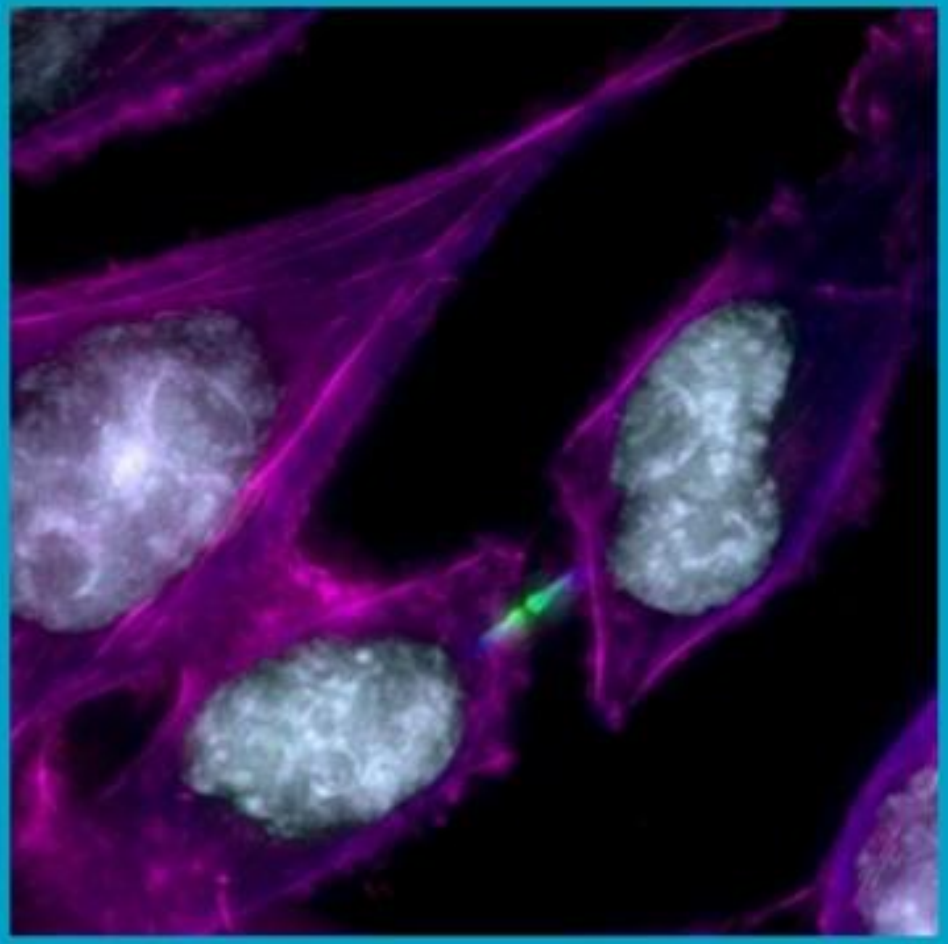


Mitosis

The Basic Phases of a Cell's Life:

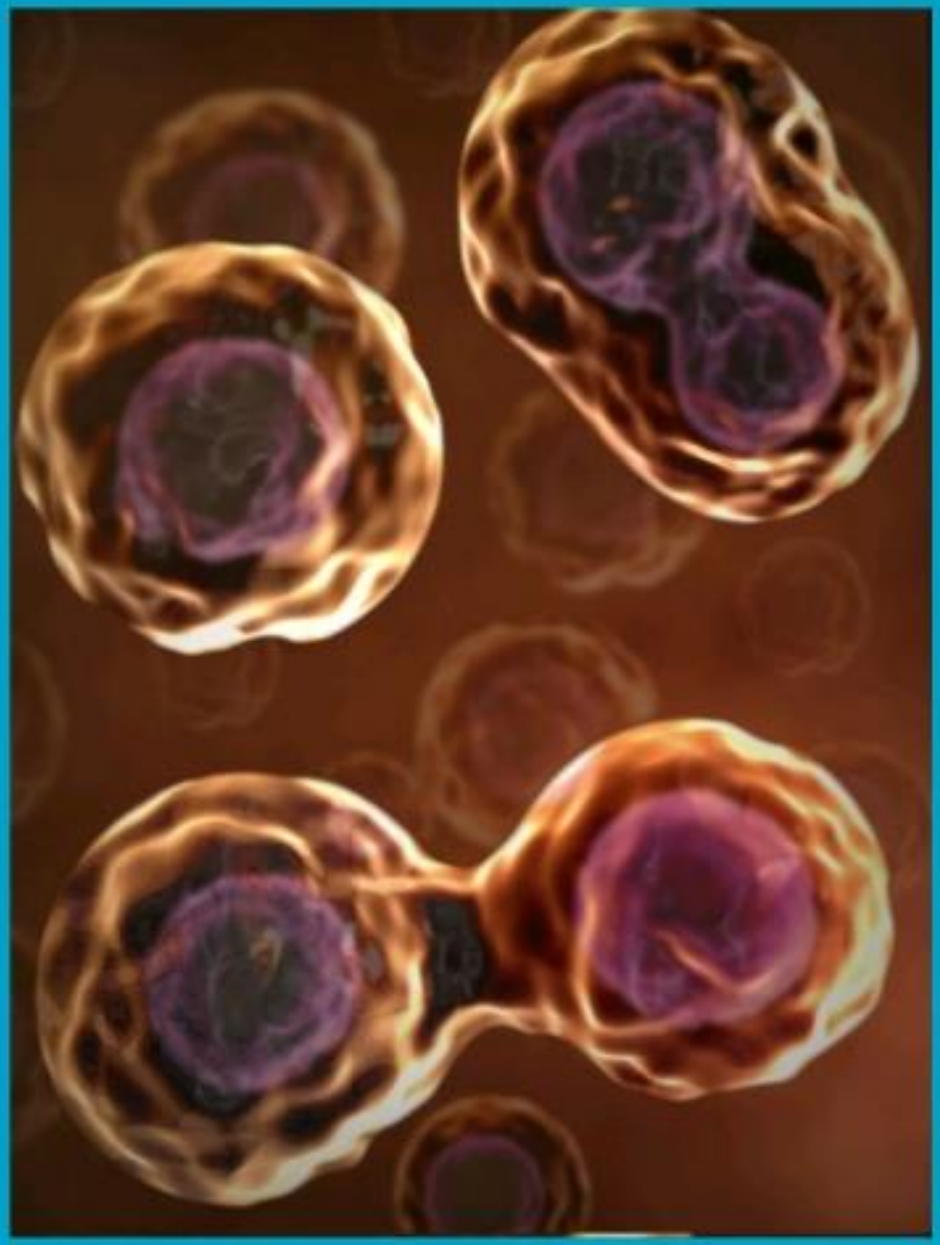
- Interphase
- Prophase
- Metaphase
- Anaphase
- Telophase
- Cytokinesis

Why Do Cells Divide?



The larger a cell becomes, the more demands the cell places on it's DNA.

It also has more trouble moving enough food and wastes across its cell membrane.



So, once cells reach a certain size they must divide in order to continue to function – or they will no longer be able to take in nutrients and eliminate waste.

MEIOSIS

- The process to make cells with half the number of chromosomes for **sexual reproduction**
- Usually humans and most animals and some plants have **diploid** (2n) body cells. Meaning that they have two sets of chromosomes (one from each parent)
- Meiosis occurs in our **germ cells** that produce gametes (Sperm & egg)
- Meiosis results in four cells which are genetically different from parent cell and from each other.
- The end products of Meiosis are 4 **Haploid** (n) cells

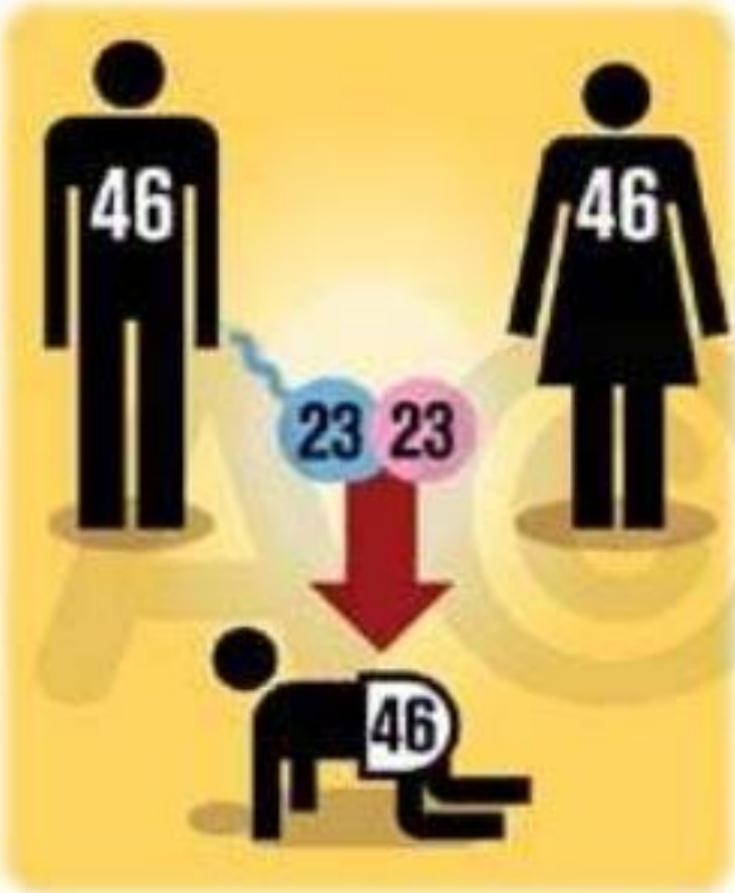
- **Meiosis** is a process that converts **diploid nuclei to haploid nuclei**.
  - **Diploid cells** have **2** sets of chromosomes.
  - **Haploid cells** have **1** set of chromosomes.
  - **Meiosis** occurs in the **sex organs**, producing **gametes**—**sperm** and **eggs.**

- **Fertilization** is the fusion of a sperm and egg cell.

- The **zygote** has a **diploid** chromosome number, **one set from each parent.**

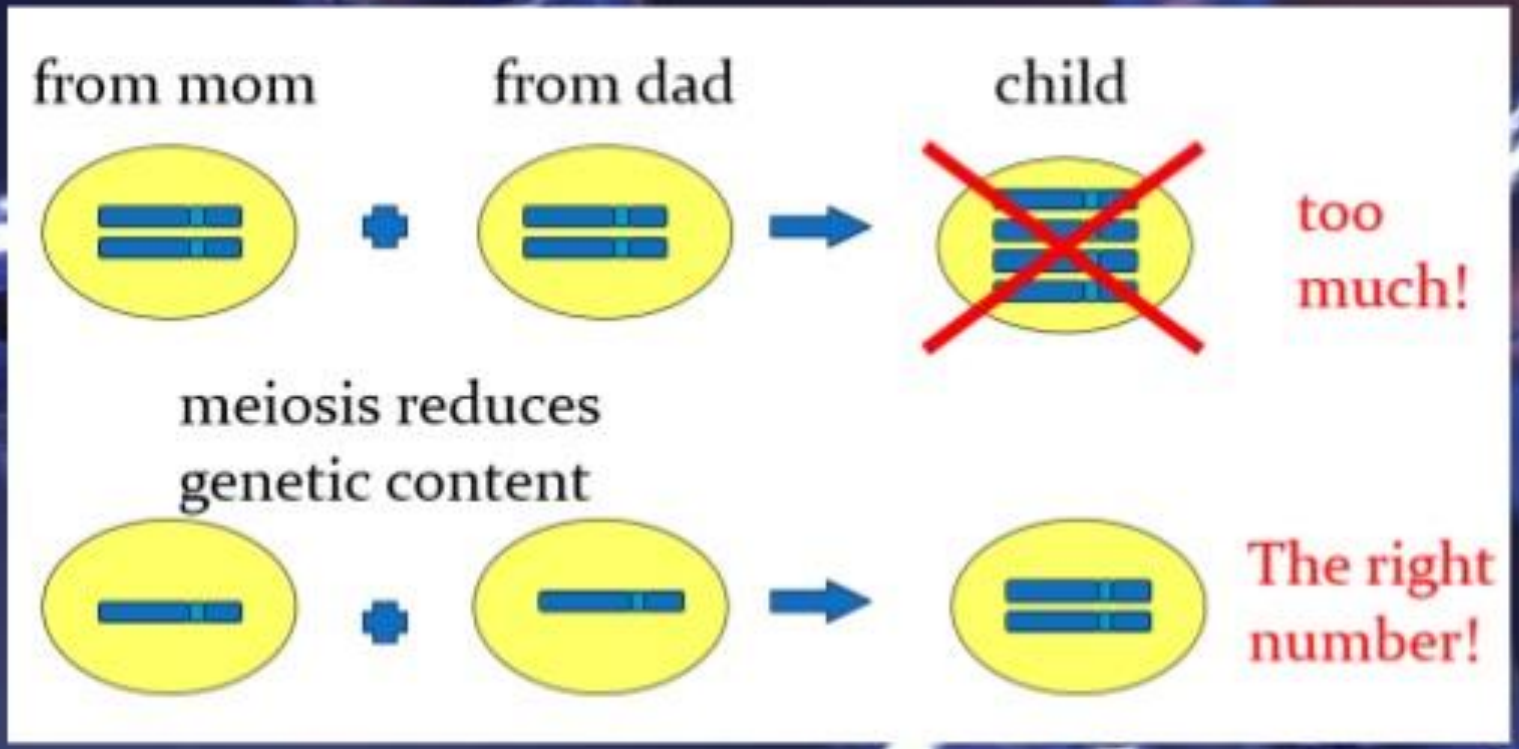
Why do we need Meiosis?

- It is the fundamental basis of sexual reproduction
- Two haploid (n) gametes are brought together through fertilization to form a diploid (2n) zygote
- If egg and sperm had the same number of chromosomes as other body cells then the offspring would have too many chromosomes.

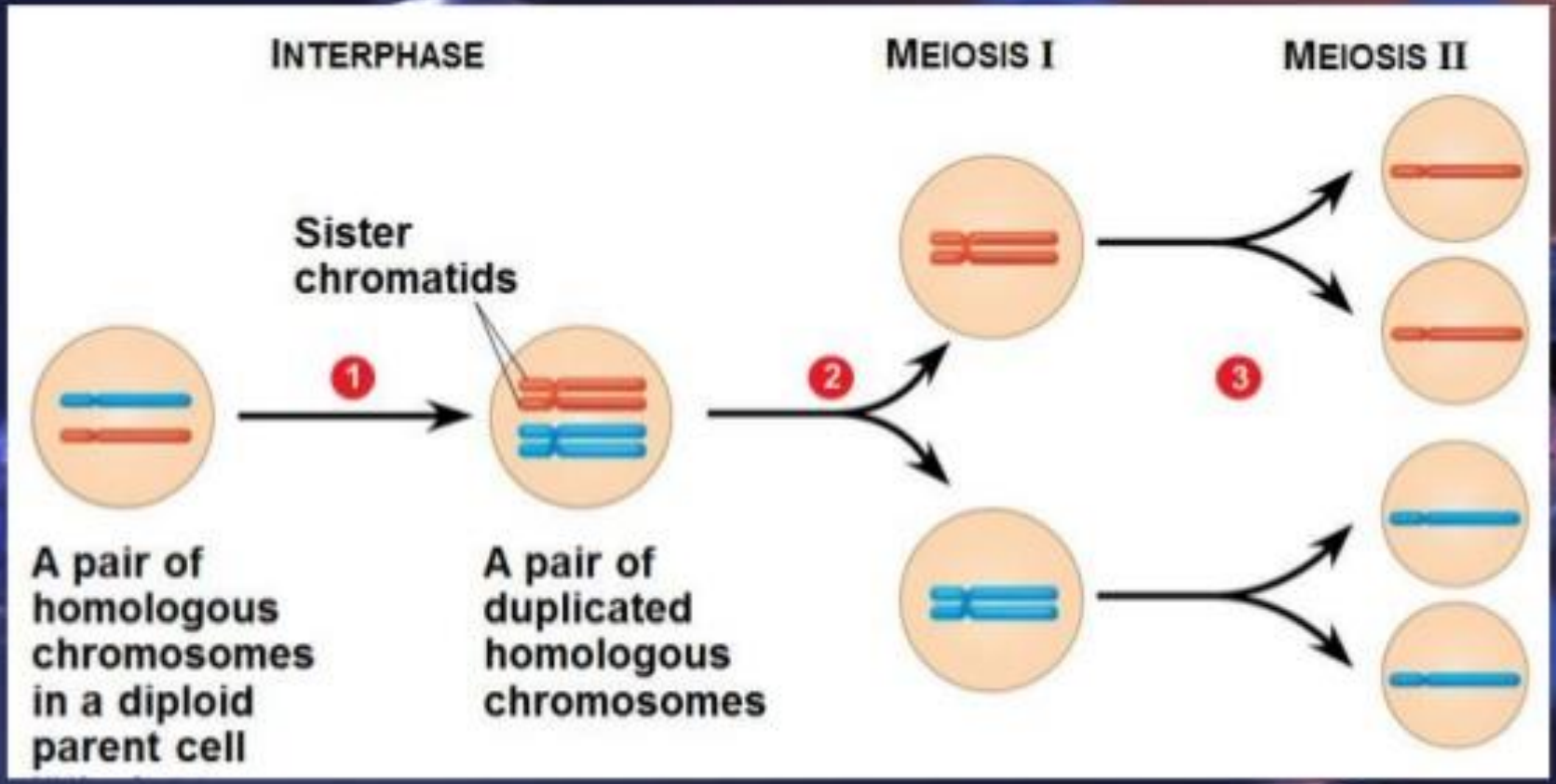


Why do you inherit half of your genes from each parent? In humans, a cell contains two copies of each of 23 different chromosomes, or 46 chromosomes in total. A mother's egg cell has only 23 chromosomes, one copy of each chromosome. So does a father's sperm cell. When a sperm joins an egg, the two sets of chromosomes join, making the normal number of chromosomes (46) in each cell.

- Meiosis **must** reduce the chromosome number by half (n)
- Fertilization then restores the 2n number

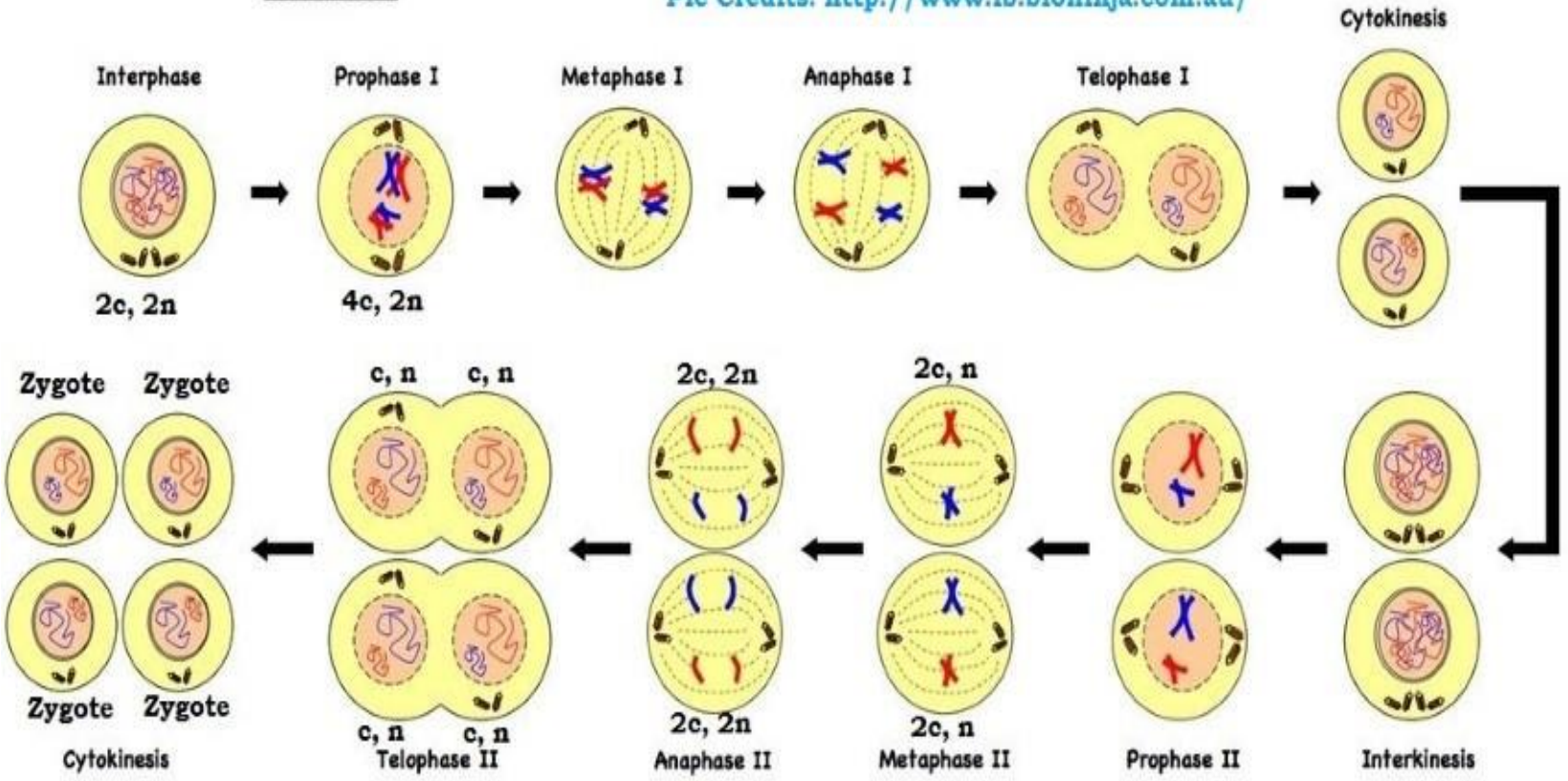


Summary of the Meiotic process



MEIOSIS I

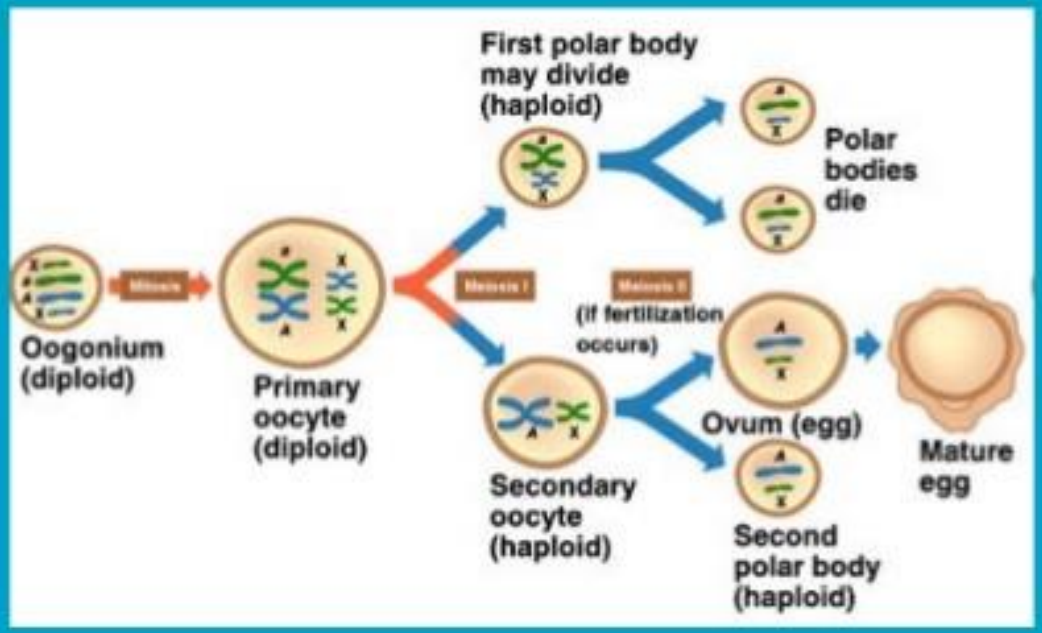
Pic Credits: http://www.ib.bioninja.com.au/



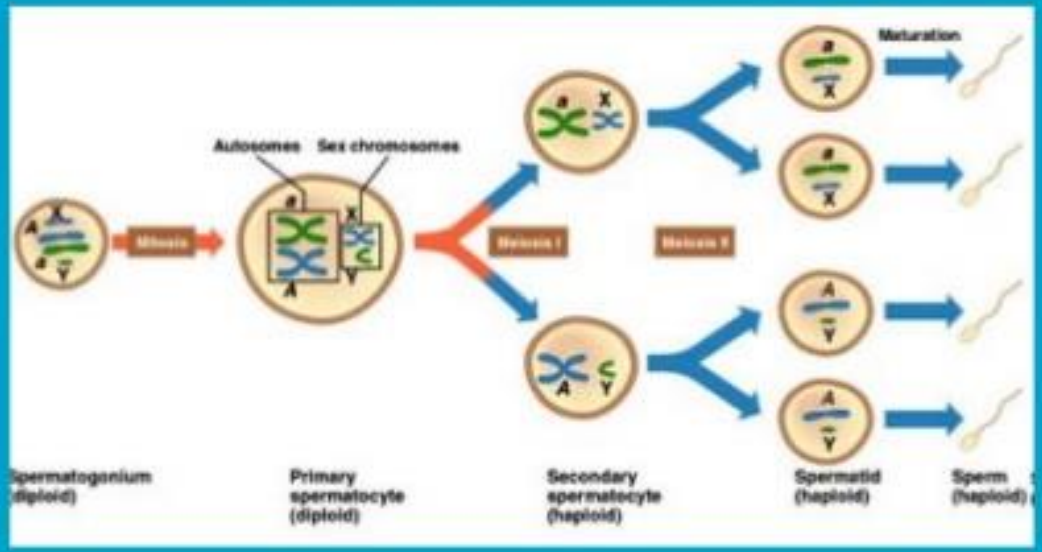
Finally there are 4 haploid cells from a single diploid cell

Unlike Mitosis, meiosis is not a cycle. It's only a cell division.

MEIOSIS II



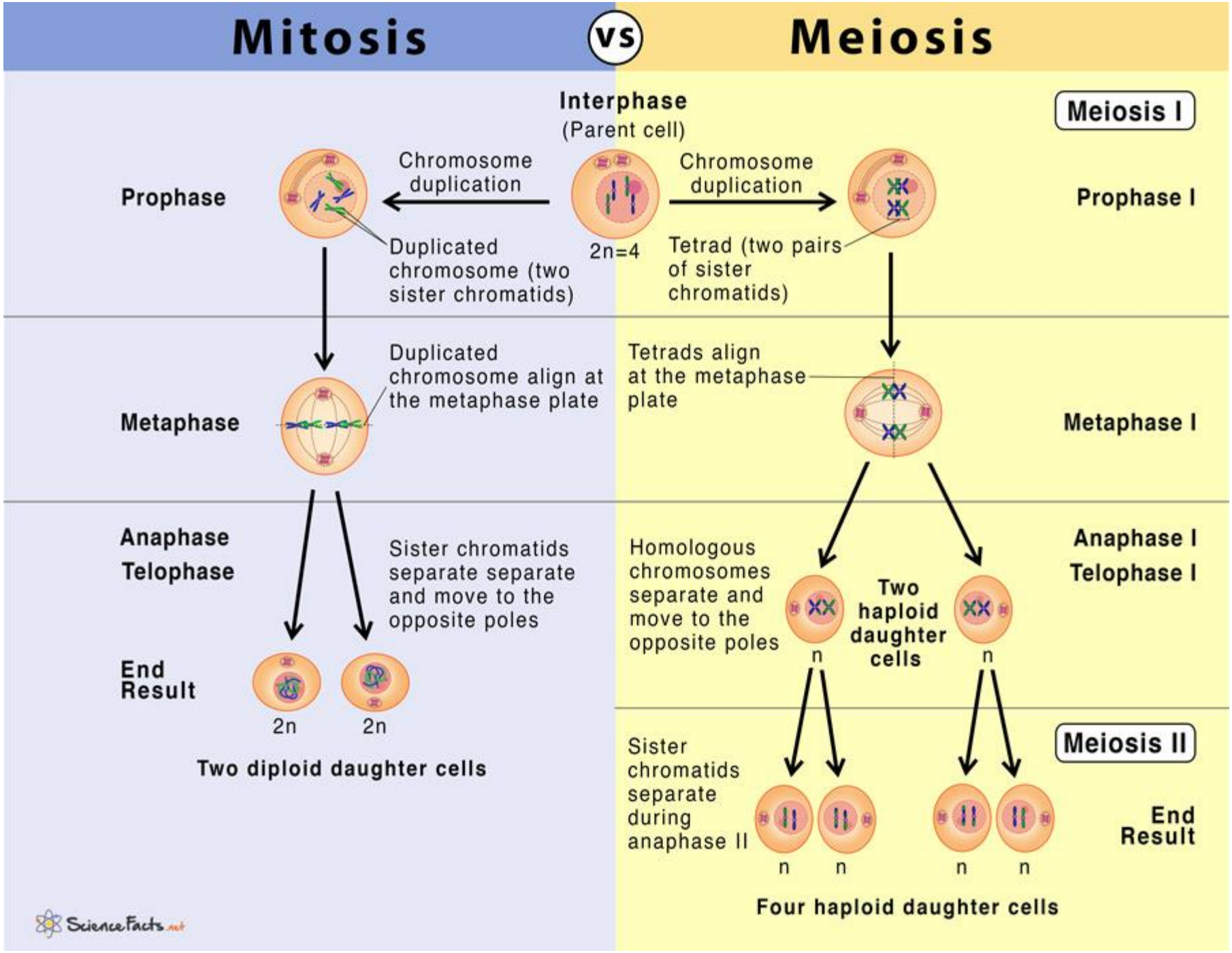
OOGENESIS



SPERMATOGENESIS

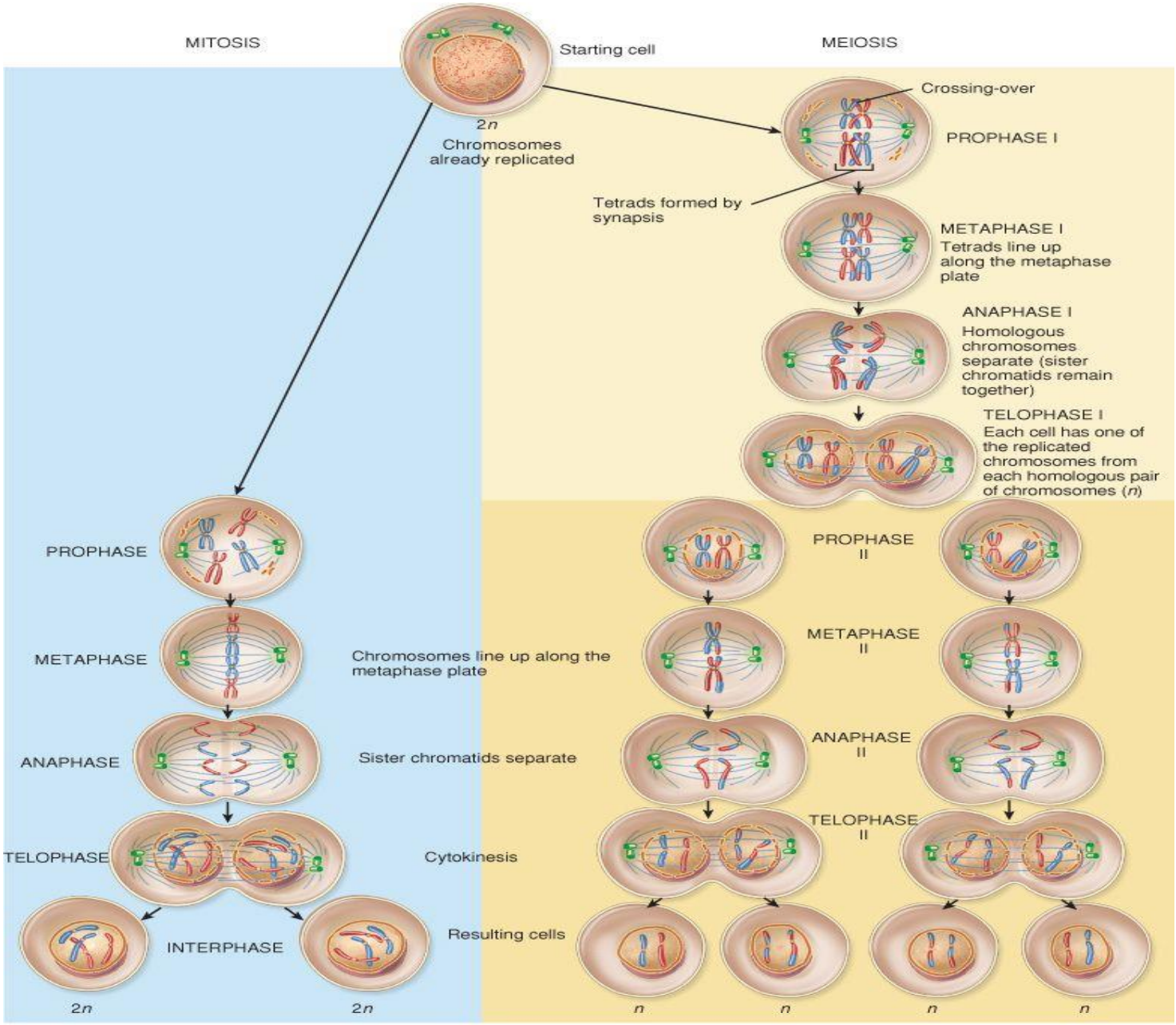
Differences between Mitosis and Meiosis

Mitosis	Meiosis
1. Mitosis occurs continuously in the body or somatic cells.	1. Meiosis occurs in the germ cells during the process of gametogenesis.
2. The whole process complete in one sequence or phase after one round of DNA replication.	2. The whole process completes in two successive divisions which occur one after the other.
3.The prophase is of short duration and does not include any sub stage.	3. The prophase is of longer duration and it complete in six successive stages.
4. The homologous chromosomes duplicate into two chromatids ,the chromatids separate and form new chromosomes.	4. Out of the two homologous chromosomes only one type of chromosome either maternal or paternal moves to the daughter cells.
5. No pairing or synapsis takes place between the homologous chromosomes.	5. Pairing or synapsis occurs between the homologous chromosomes.
6. Duplication of chromosomes takes place in the early prophase.	6. Duplication or splitting of chromosomes takes place in late prophase.
7. No chiasma formation or crossing over takes place.	7. Chiasma formation or crossing over takes place during meiosis.
8. The exchange of the genetic material between the homologous chromosomes does not occur.	8. The exchange of genetic material takes place between the chromatids of homologous chromosomes.
9. The chromosome number remains the same in the newly formed daughter cells.	9. Chromosome number is reduced into half in the newly formed daughter cells.
10. Two daughter cells are formed.	10. Four daughter cells are formed.


Mitosis
vs
Meiosis
Interphase
(Parent cell)
2n=4
Chromosome duplication
Chromosome duplication
Meiosis I
Prophase
Prophase I
Duplicated chromosome (two sister chromatids)
Tetrad (two pairs of sister chromatids)
Metaphase
Duplicated chromosome align at the metaphase plate
Tetrads align at the metaphase plate
Metaphase I
Anaphase
Telophase
Sister chromatids separate separate and move to the opposite poles
Homologous chromosomes separate and move to the opposite poles
Two haploid daughter cells
Anaphase I
Telophase I
End Result
2n
2n
n
n
Two diploid daughter cells
Sister chromatids separate during anaphase II
Meiosis II
End Result
n
n
n
n
Four haploid daughter cells
ScienceFacts.net

Differences Between Mitosis and Meiosis

3	Mitosis	Meiosis
	1. General	
01	The division occurs in **somatic cells.**	It occurs in **reproductive cells.**
02	Mitosis takes place throughout the life of a multicellular organism.	Meiosis takes place only at the time of **sexual reproduction.**
03	It may happen **innumerable times** in the life cycle of an organism.	Meiosis happens only once in the life cycle of an organism.
04	**Both diploid & haploid cells** show mitosis.	Meiosis is found only in **diploid cells.**
05	It is a **single division.**	It is a **double division.**
06	All divisions are **similar.**	The two divisions are **different.**
07	The daughter cells **resemble** each other as well as their mother cell.	The daughter cells **neither resemble** one another nor their mother cell.
08	**Chromosome number** the same	Chromosome number is **halved.**
09	Replication of chromosomes occurs **before every mitotic division.**	Replication of chromosomes occurs only once before Meiosis-I.
10	It **does not introduce variations.**	Meiosis **introduces variations.**
11	Mitosis is **required for growth, repair and healing.**	Meiosis has **no such function.**
12	Mitosis is involved in **vegetative and asexual reproduction.**	It is involved in **sexual reproduction.**
13	It occurs in both **sexually and asexually reproducing organisms.**	Meiosis is found in only **sexually reproducing organisms.**


MITOSIS
Starting cell
MEIOSIS
2n
Chromosomes already replicated
Crossing-over
PROPHASE I
Tetrads formed by synapsis
METAPHASE I
Tetrads line up along the metaphase plate
ANAPHASE I
Homologous chromosomes separate (sister chromatids remain together)
TELOPHASE I
Each cell has one of the replicated chromosomes from each homologous pair of chromosomes (n)
PROPHASE
METAPHASE
Chromosomes line up along the metaphase plate
ANAPHASE
Sister chromatids separate
TELOPHASE
Cytokinesis
INTERPHASE
Resulting cells
2n
2n
PROPHASE II
METAPHASE II
ANAPHASE II
TELOPHASE II
n
n
n
n
Somatic cells with diploid number of chromosomes (not replicated)
Gametes with haploid number of chromosomes (not replicated)

Introduction

- Gene mapping means the mapping of genes to specific locations on chromosomes.
- It is very important in the understanding of genetic diseases.
- Such maps indicates the positions of genes in the genome and also distance between them.

Types Of Gene Mapping

- Genetic mapping
  - Based on the use of genetic techniques to construct maps.
  - These maps show the positions of genes and other sequence features on a genome.
  - Also helps to determine the relative position between two genes on a chromosome.
- Physical mapping
  - Uses molecular biology techniques to examine DNA molecules directly.
  - Based on these techniques map construction is done.
  - These maps show the positions of sequence features , including genes.

Commonly Used DNA Markers

- **RFLPs**, or **restriction fragment length polymorphisms**, were among the first developed DNA markers. RFLPs are defined by the presence or absence of a specific site, called a restriction site, for a bacterial restriction enzyme. This enzyme breaks apart strands of DNA wherever they contain a certain nucleotide sequence.

- **VNTRs**, or **variable number of tandem repeat polymorphisms**, occur in non-coding regions of DNA. This type of marker is defined by the presence of a nucleotide sequence that is repeated several times. In each case, the number of times a sequence is repeated may vary.

- **Microsatellite polymorphisms** are defined by a variable number of repetitions of a very small number of base pairs within a sequence. Oftentimes, these repeats consist of the nucleotides, or bases, cytosine and adenosine. The number of repeats for a given microsatellite may differ between individuals, hence the term **polymorphism**--the existence of different forms within a population.

- **SNPs**, or **single nucleotide polymorphisms**, are individual point mutations, or substitutions of a single nucleotide, that do not change the overall length of the DNA sequence in that region. SNPs occur throughout an individual's genome.

Gene linkage

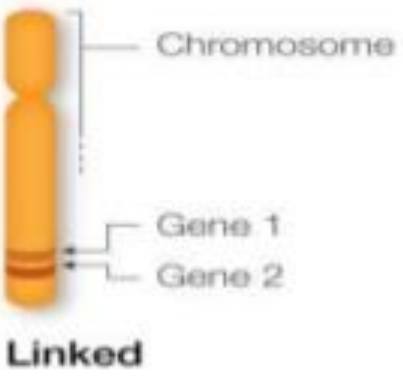
- **Genetic linkage** is the tendency of alleles that are close together on a chromosome to be inherited together during the meiosis phase of sexual reproduction.

Linkage

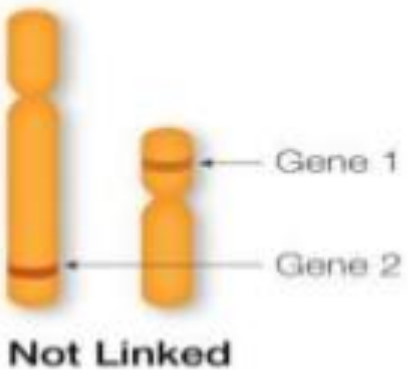
A recombination frequency of 50% means that genes are unlinked. There are two ways in which genes maybe unlinked:

They may be on separate chromosomes.

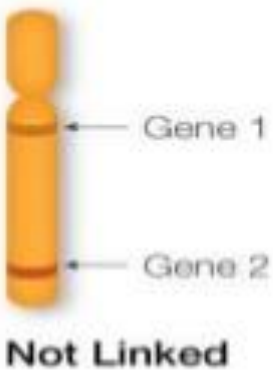
They may be far apart on the same chromosome.



Linked



Not Linked



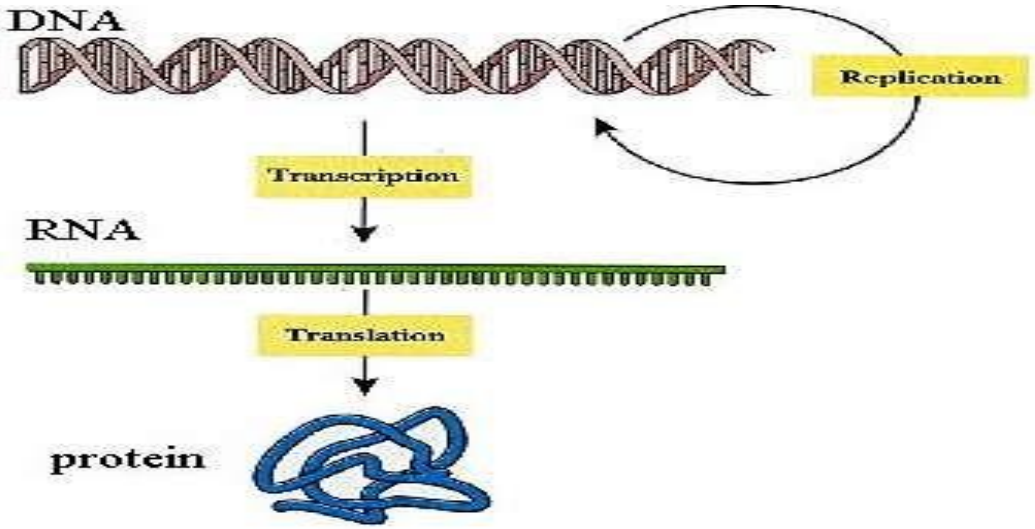
Not Linked

Uses of Gene mapping

- ❑ Identify genes responsible for diseases
- Heritable diseases
- Cancer
- ❑ Identify genes responsible for traits
- Plants or animals
- Disease resistance
- Meat or milk production

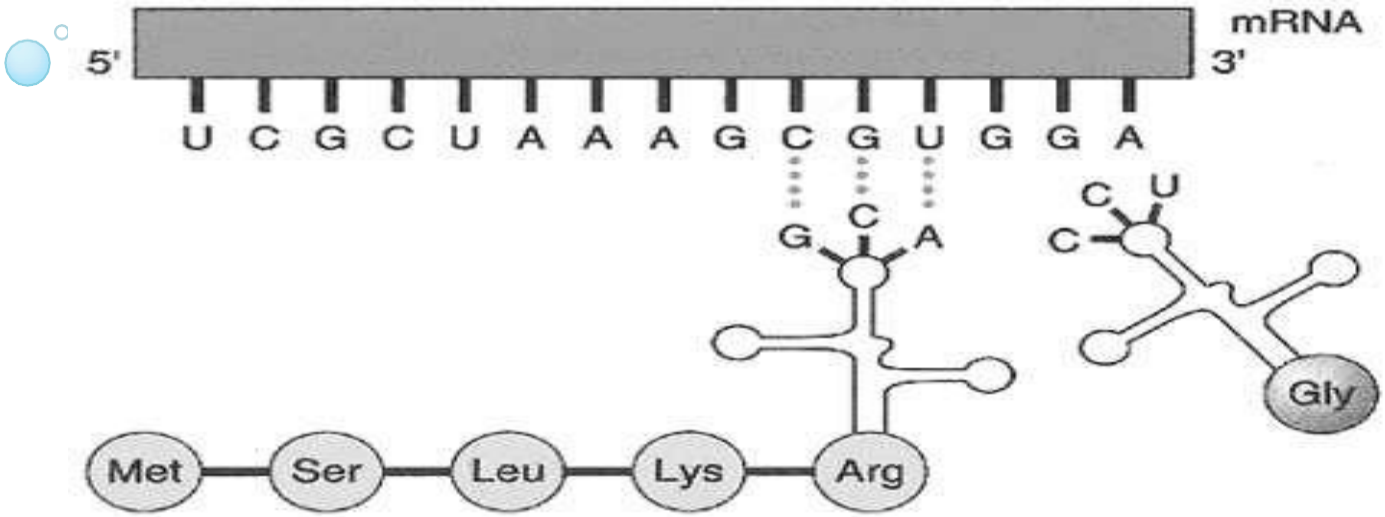
Genetic code and its characteristics

Flow of genetic information



The central dogma of molecular biology describes the two-step process, transcription and translation, by which the information in genes flows into proteins: DNA → RNA → protein.

Introduction

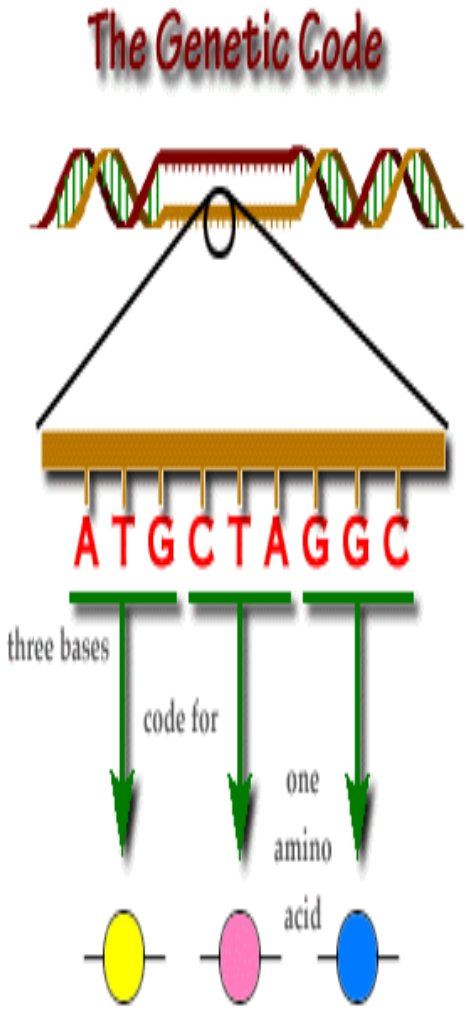


The pathway of protein synthesis is called Translation because the language of nucleotide sequence on mRNA is translated in to the language of an amino acid sequence. The process of Translation requires a Genetic code, through which the information contained in nucleic acid sequence is expressed to produce a specific sequence of amino acids.

Introduction – Genetic Code

The letters A, G, T and C correspond to the nucleotides found in DNA. They are organized into codons.
The collection of codons is called Genetic code.

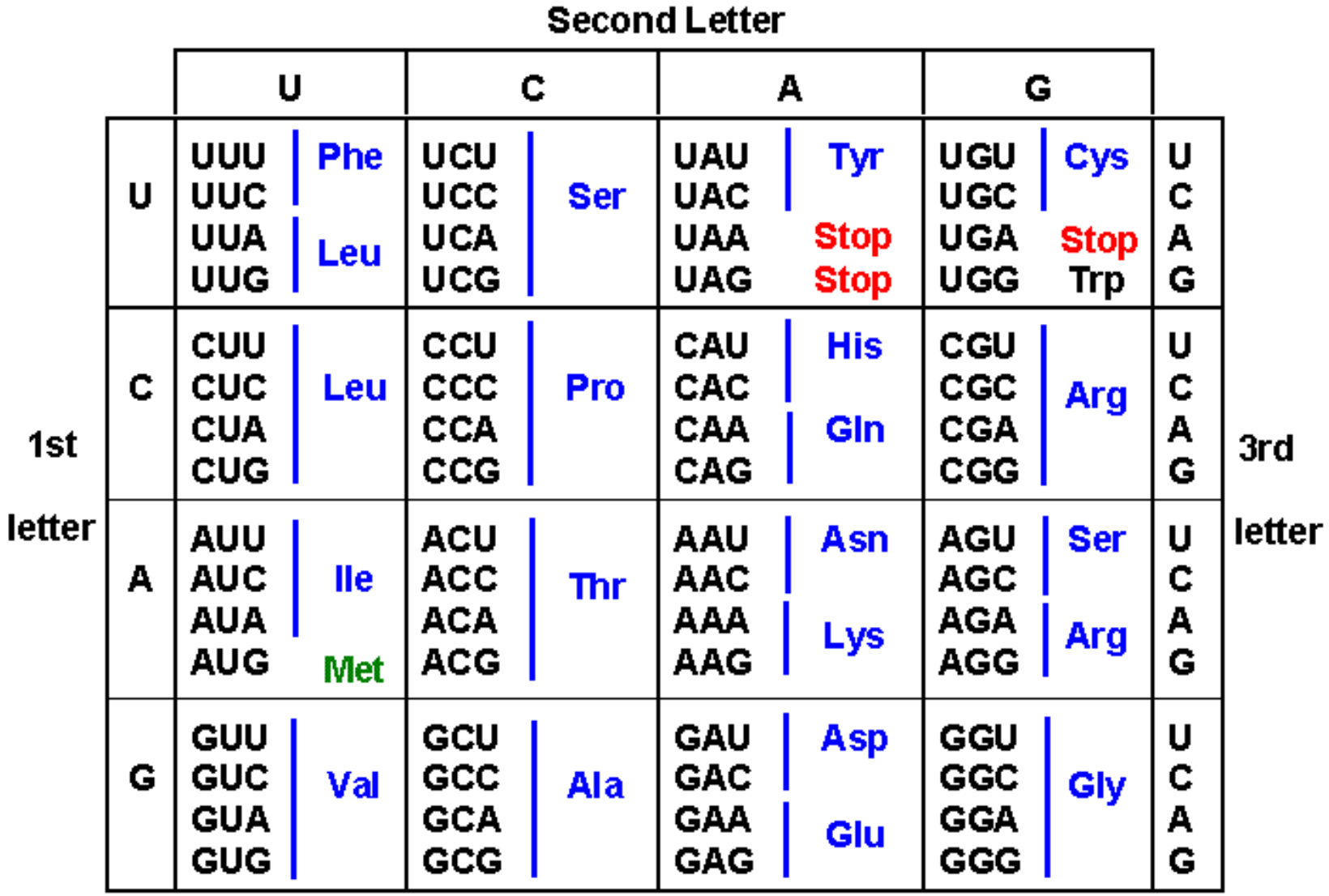
For 20 amino acids there should be 20 codons.
Each codon should have 3 nucleotides to impart specificity to each of the amino acid for a specific codon
1 Nucleotide- 4 combinations
2 Nucleotides 16 combinations
3 Nucleotides- 64 combinations (Most suited for 20 amino acids)



Genetic Code

- Genetic code is a dictionary that corresponds with sequence of nucleotides and sequence of Amino Acids.
- Words in dictionary are in the form of codons
- Each codon is a triplet of nucleotides
- 64 codons in total and three out of these are Non Sense codons.
- 61 codons for 20 amino acids

Genetic Code - Table



Genetic Code - Characteristics

- **Specificity-** Genetic code is specific (Unambiguous)
- A specific codon always codes for the same amino acid.
- e.g. UUU codes for Phenyl Alanine, it can not code for any other amino acid.

Genetic Code-Universal

- **Universal-** In all living organism Genetic code is the same.

- The exception to universality is found in mitochondrial codons where AUA codes for methionine and UGA for tryptophan, instead of isoleucine and termination codon respectively of cytoplasmic protein synthesizing machinery.
- AGA and AGG code for Arginine in cytoplasm but in mitochondria they are termination codons.

Genetic Code - Redundant

Redundant- Genetic code is Redundant, also called Degenerate.

Although each codon corresponds to a single amino acid but a single amino acid can have multiple codons. Except Tryptophan and Methionine each amino acid has multiple codons.

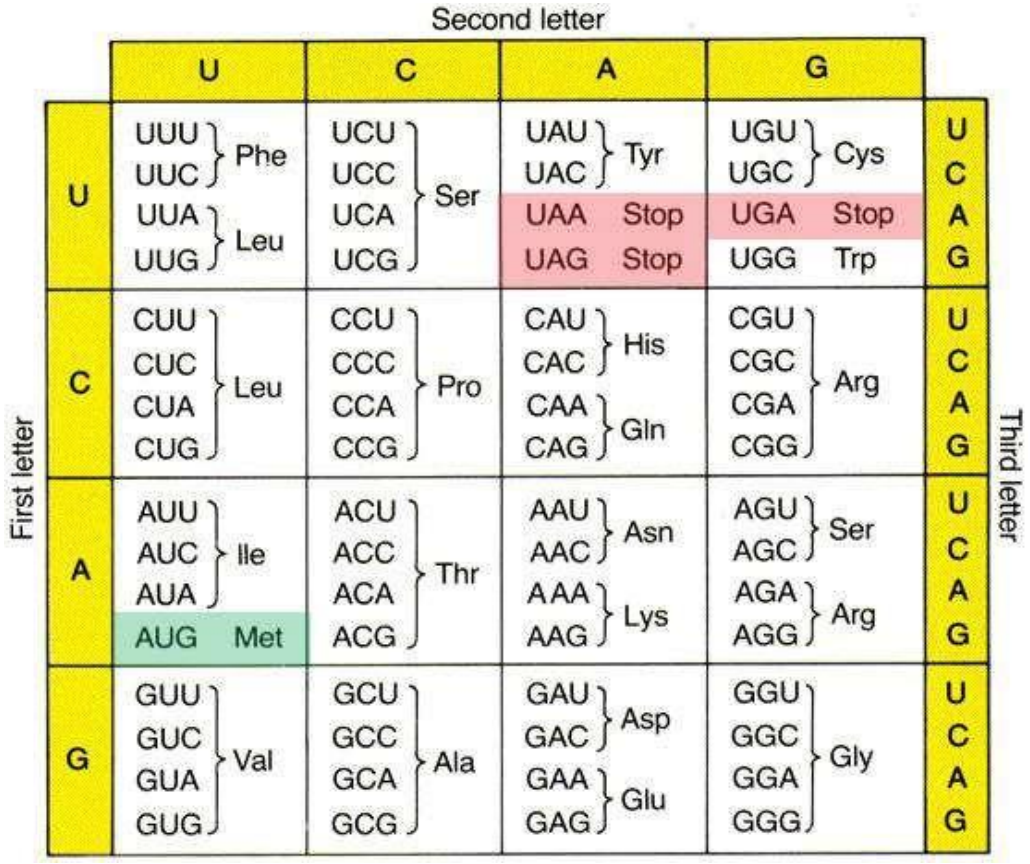
	U	C	A	G
U	UUU, UUC — Phe UUA, UUG — Leu	UCU, UCC, UCA, UCG — Ser	UAU, UAC — Tyr UAA, UAG — *Stop*	UGU, UGC — Cys UGA — *Stop* UGG — Trp
C	CUU, CUC, CUA, CUG — Leu	CCU, CCC, CCA, CCG — Pro	CAU, CAC — His CAA, CAG — Gln	CGU, CGC, CGA, CGG — Arg
A	AUU, AUC, AUA — Ile AUG — Met	ACU, ACC, ACA, ACG — Thr	AAU, AAC — Asn AAA, AAG — Lys	AGU, AGC — Ser AGA, AGG — Arg
G	GUU, GUC, GUA, GUG — Val	GCU, GCC, GCA, GCG — Ala	GAU, GAC — Asp GAA, GAG — Glu	GGU, GGC, GGA, GGG — Gly

Genetic Code- Non Overlapping and Non Punctuated

- All codons are independent sets of 3 bases.
- There is no overlapping ,
- Codon is read from a fixed starting point as a continuous sequence of bases, taken three at a time.
- The starting point is extremely important and this is called Reading frame.

Non Sense Codons

- There are 3 codons out of 64 in genetic code which do not encode for any Amino Acid.
- These are called **termination codons or stop codons** or nonsense codons. The stop codons are UAA, UAG, and UGA. They encode no amino acid. The ribosome pauses and falls off the mRNA.



Initiator codon

- AUG is the initiator codon in majority of proteins-
- In a few cases GUG may be the initiator codon
- Methionine is the only amino acid specified by just one codon, AUG.

Clinical Significance

Mutations can be well explained using the genetic code.

A) Point Mutations

1) Silent

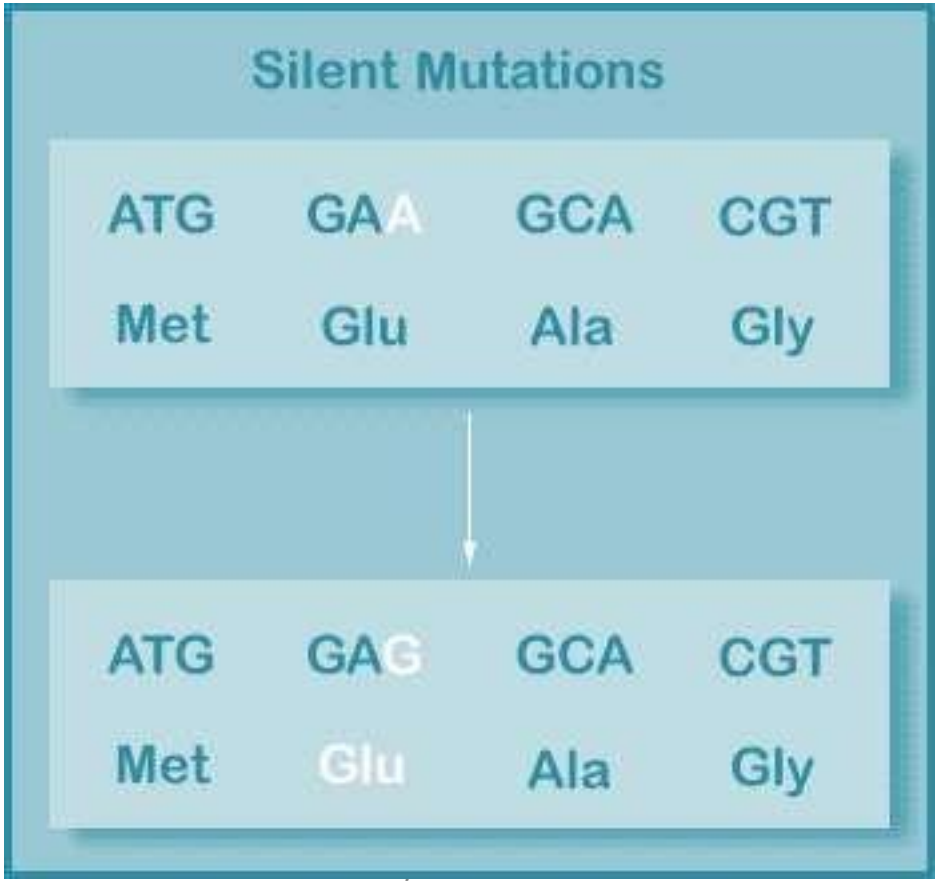
2) Misense

3) Nonsense

B) Frame shift mutations

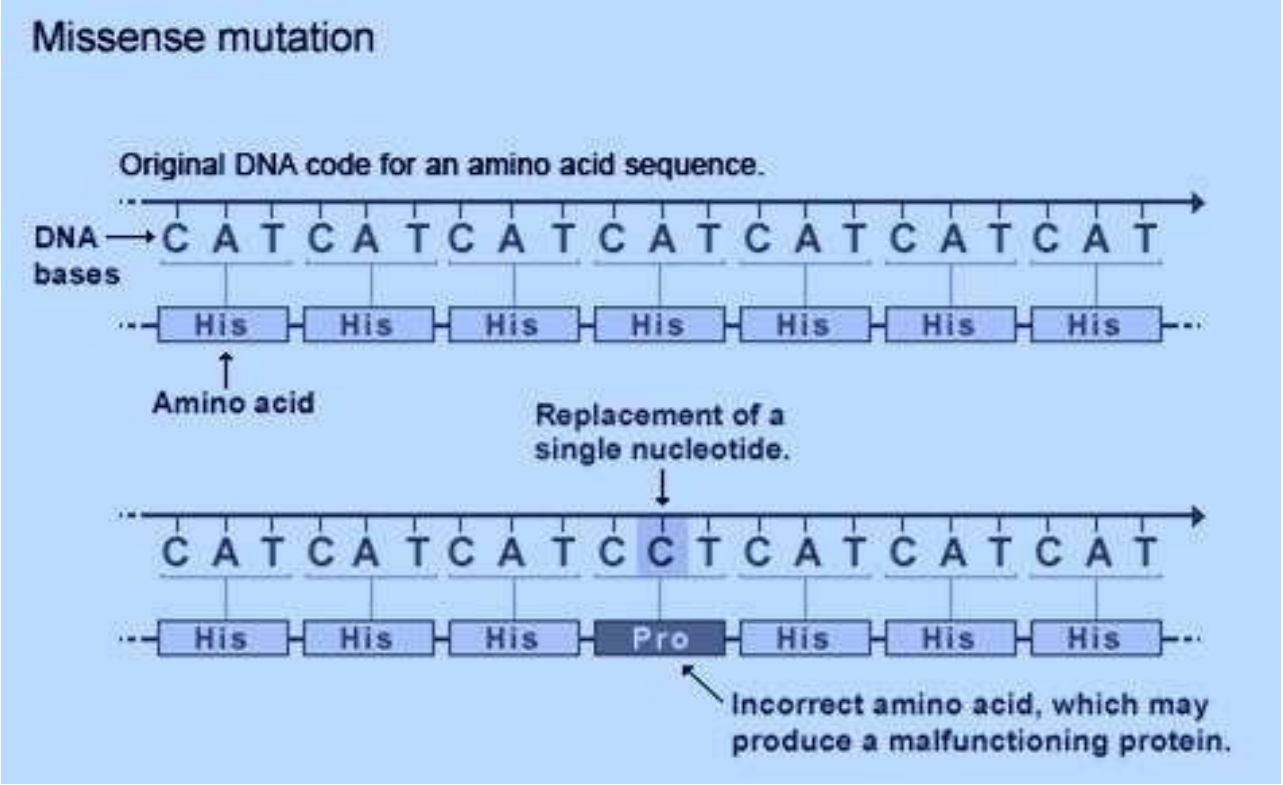
Silent Mutations

Single nucleotide change-A to G, same amino acid is incorporated. Mutation goes unnoticed.



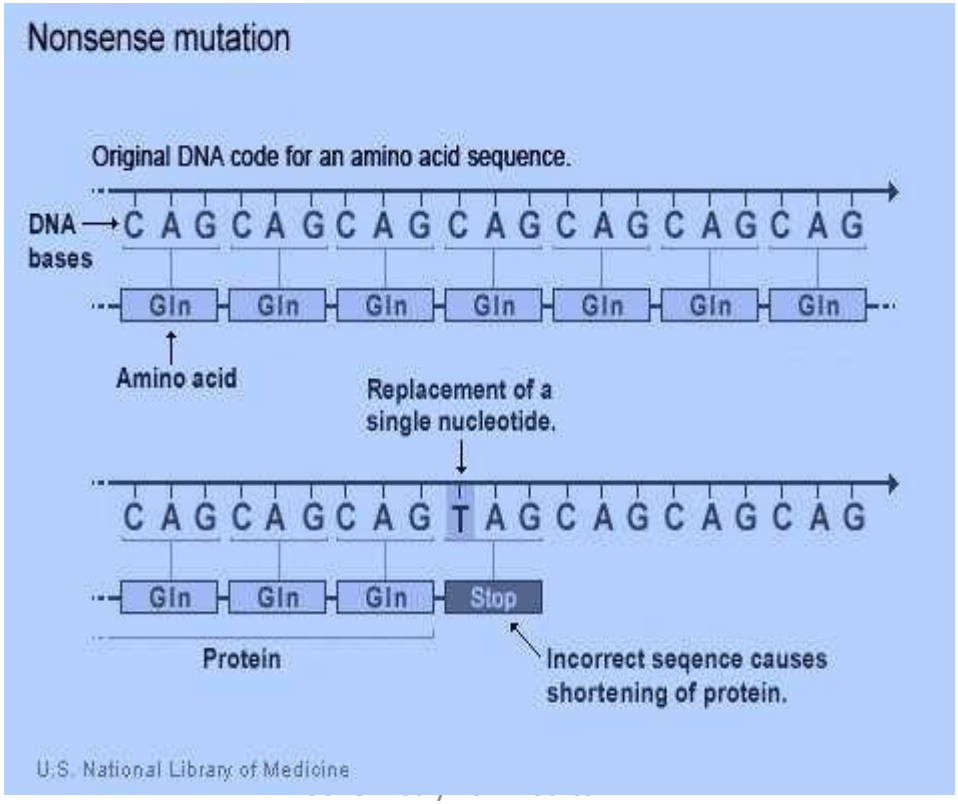
Missense mutations

Single nucleotide change A to C – different amino acid incorporated. Loss of functional capacity of protein.



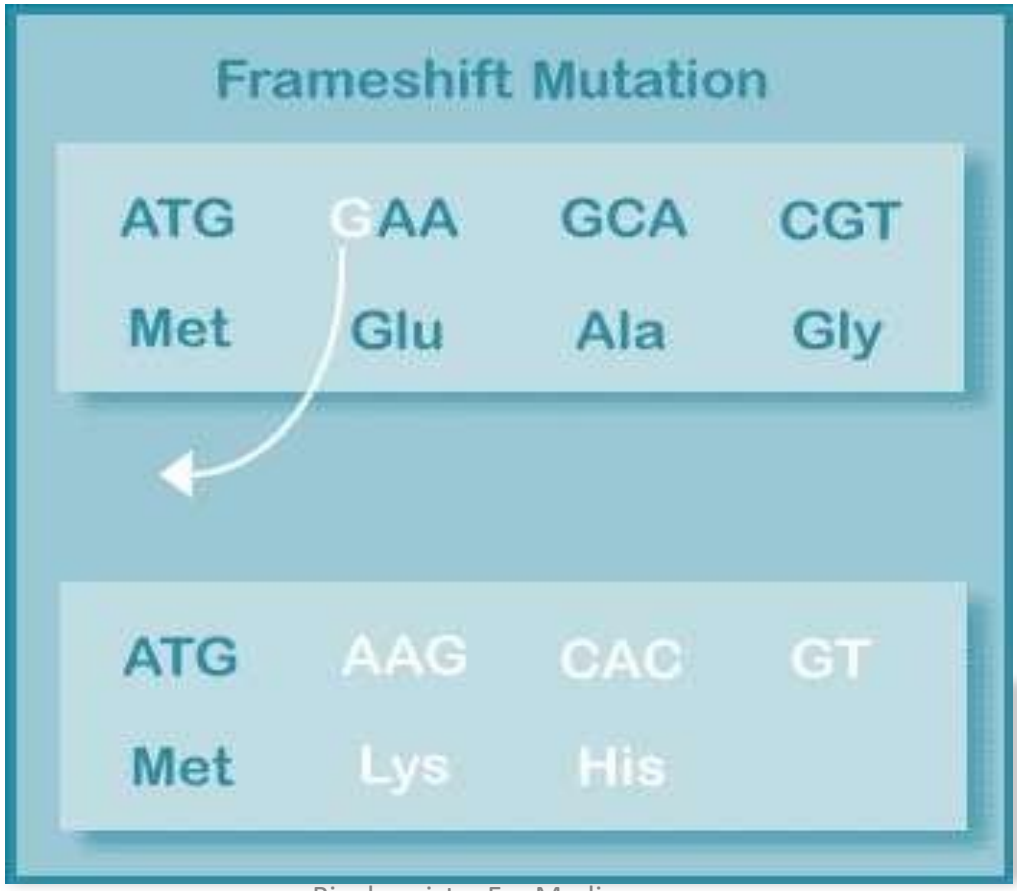
Non sense Mutation

Single nucleotide change from C to T, stop codon is generated (In m RNA represented by UAG), premature termination of chain, may be incompatible with life.



Frame sift Mutations

- Insertion or removal of a base/bases can alter the reading frame with the resultant incorporation of different amino acids



Genetic code- Summary

- Genetic code is unambiguous, universal, degenerate, commaless and non overlapping.
- UAG, UGA and UAA are termination codons .
- AUG is the start codon
- Mutations can be well described using genetic code