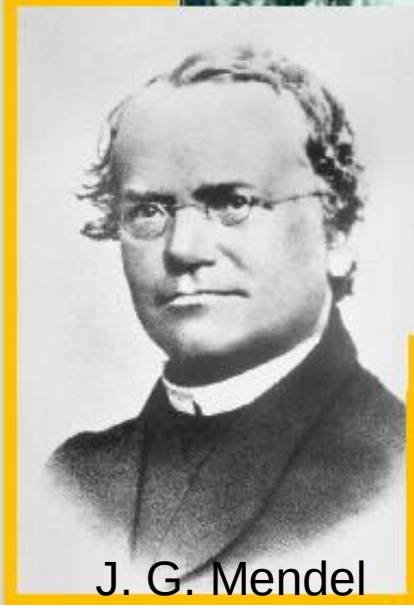
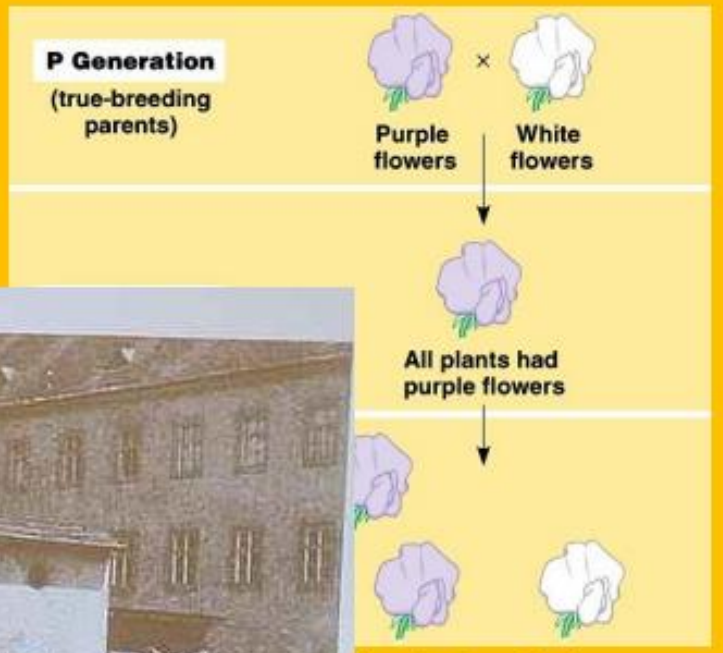
BASIC CELL GENETICS





ted why first
d second
Pea Plant have
eredity

J. G. Mendel
Augustinian friar and abbot
of St. Thomas' Abbey in Brno

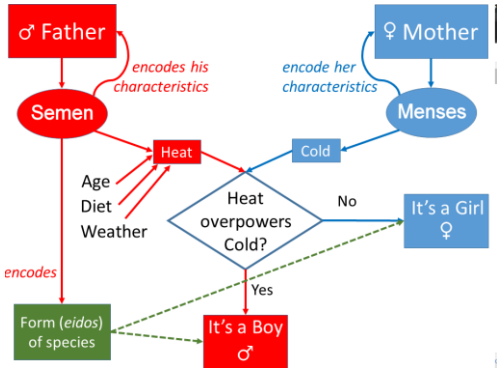
Historical photo
of original green house of
Mendel Abbey in Brno

- Mendel was the first scienceman creating inheritance theory? No. Since ages of faraons and antical states, there were some archaic (less or more mistake) theory:

- Aristotel (384 B.C.)

Opinion without any microscope

He did know anything bout X adn Y chromosome

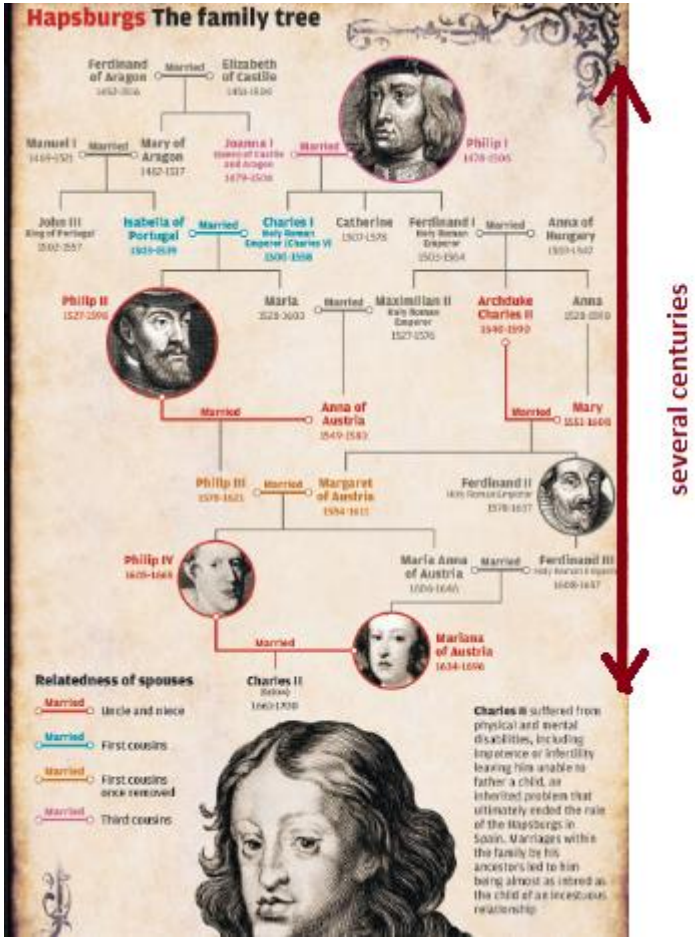


Leevuenhoek (1632)

Idea after see „ miniatur person in sperm!“

- Why Mendel and other scienceman and doctors see the basic law of heredity in last centuries and not erly?

Human life was very short to see the phenotype of parents and first generation and second generation. However if scienceman use to good model organism, it si possible to see to many generation in one year and make a idea about heredity.



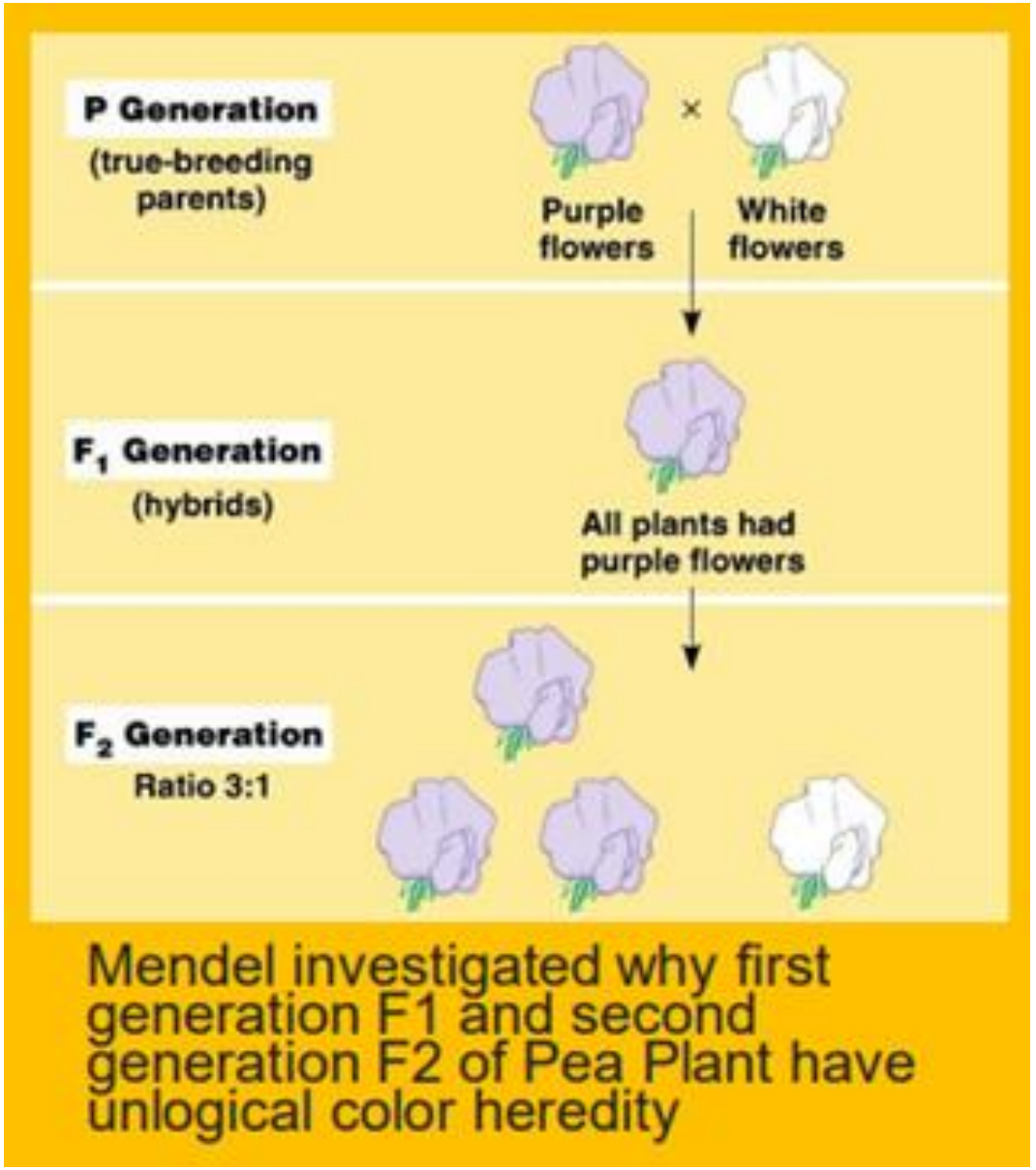
several centuries

weeks or days

DEFINITION: **Heredity, also called inheritance or biological inheritance**,

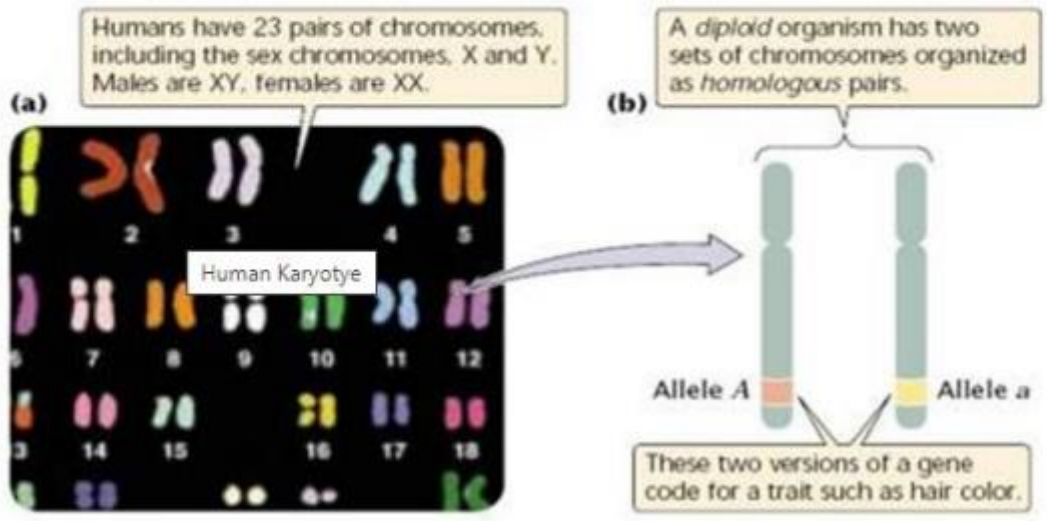
is the passing on of traits from parents to their offspring; either through asexual reproduction or sexual reproduction,


PEA

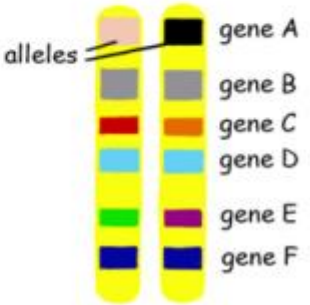

P Generation
(true-breeding parents)
Purple flowers
×
White flowers
F1 Generation
(hybrids)
All plants had purple flowers
F2 Generation
Ratio 3:1
Mendel investigated why first generation F1 and second generation F2 of Pea Plant have unlogical color heredity

BASIC GENETIC FACTS

Actually a diploid organism has two copies of a gene or two sets of chromosomes, one from father's sperm and other from mother's egg. The chromosome of similar size and nature often form pairs during meiotic division and such identical chromosomes are called homologous chromosomes.



Human has many genes (color of eye, gene for hemoglobin structure, ...



- **Mendel's basic conclusions for gene delivery** – MENDEL LAWs

1. **Law of Segregation:** When gametes form, alleles are separated so that each gamete carries only one allele for each gene
2. **Law of Independent Assortment:** The segregation of alleles for one gene occurs independently to that of any other gene*
3. **Law of Dominance:** Recessive alleles will be masked by dominant alleles†

* *The law of independent assortment does not hold true for genes located on the same chromosome (i.e. linked genes)*

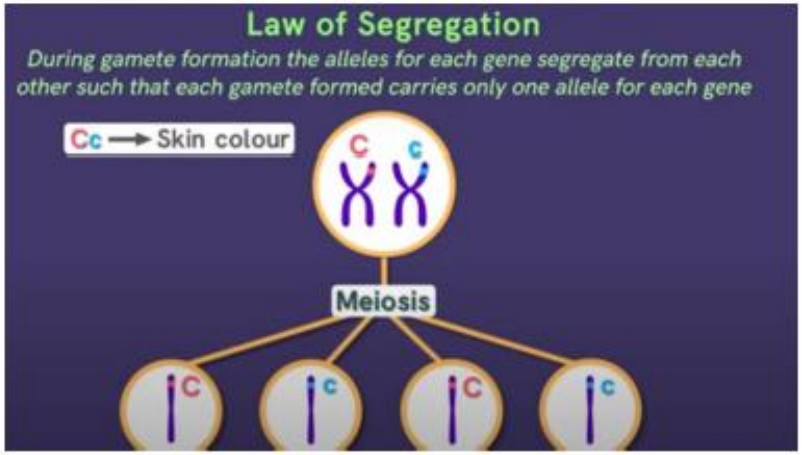
- **Mendel's basic conclusions for gene delivery** – MENDEL LAWs

1. **Law of Segregation**: When gametes form, alleles are separated so that each gamete carries only one allele for each gene

FIRST MENDEL LAW

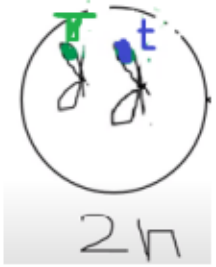
t

- Simple, but not very good illustration :



FIRST MENDEL LAW

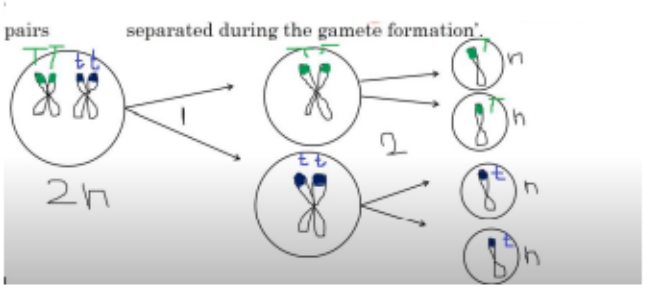
- Better ilustrations:



CELL before MEIOSIS

(T-gene in dominant form

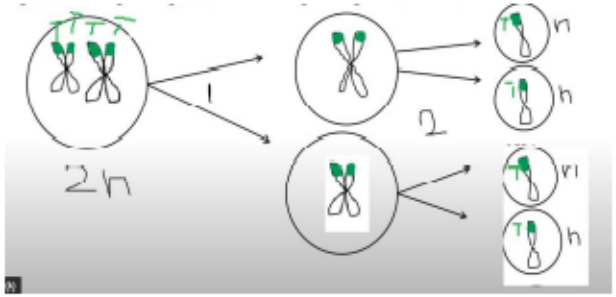
t -gen in recesive form)



After chromoson duplication

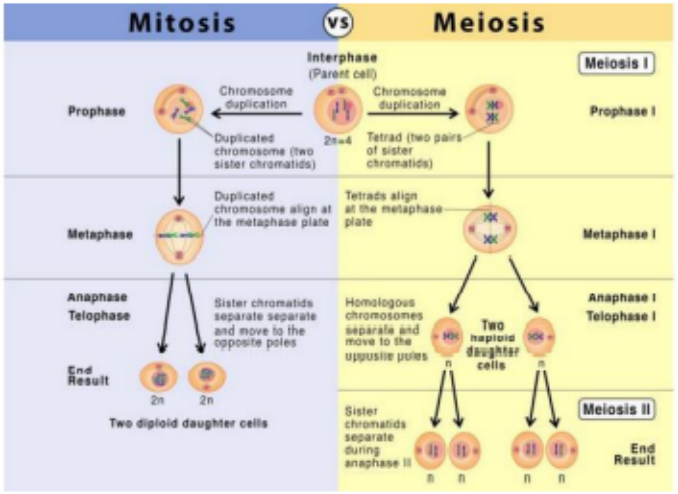
After ANAPHASE I

Delivery of different T or t into Gamets



Why are 4 alelles at final stage from one parentcell??

- Remeber MEIOSIS Prophase scheme in previous lessons :



- Skip …

- **Mendel's basic conclusions for gene delivery** – MENDEL LAWs

1.

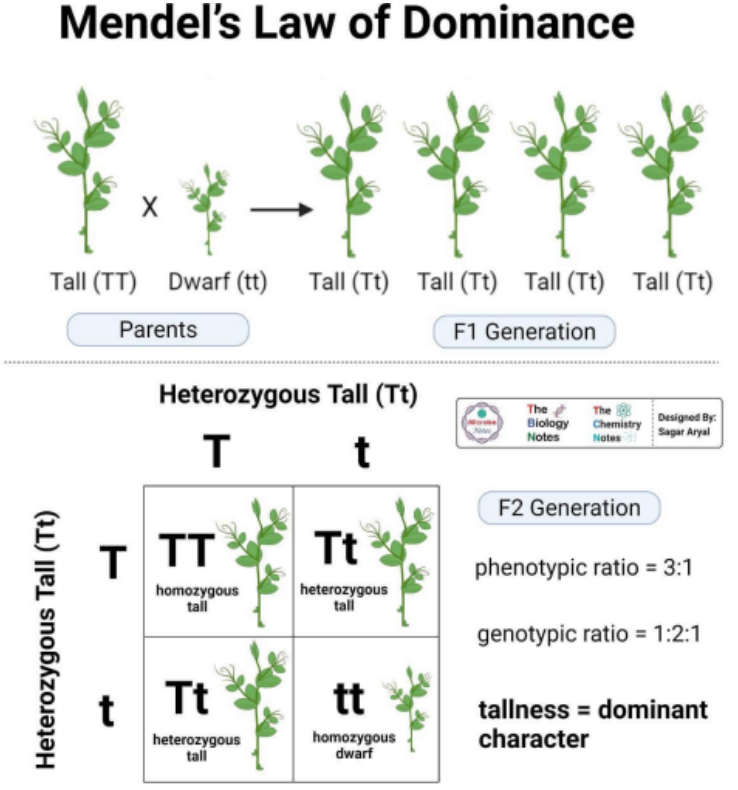
2.

3. **Law of Dominance**: Recessive alleles will be masked by dominant alleles†

THIRD MENDEL LAW
(law of dominance)

•The pair of genes can be homozygous (TT or tt) or heterozygous (Tt) , and in the case of heterozygous pairs, one of the factors dominates the other.

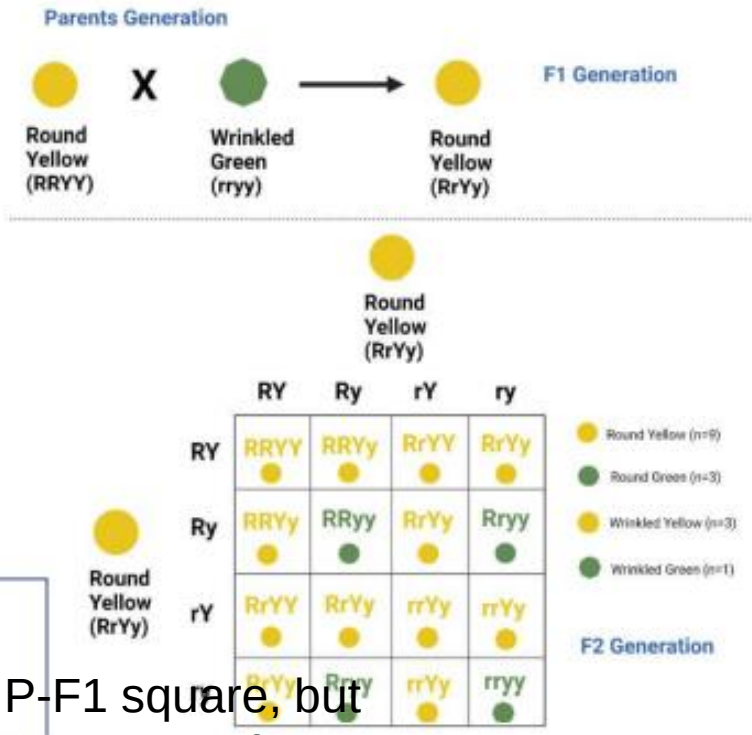
•The character that dominates (T) is called the dominant character, and the one that remains unexpressed (t) is the recessive character.
•The recessive character, even though latent, is transmitted to the offspring in the same way as the dominant character.
•The recessive character is only expressed when the offspring has two copies of the same allele resulting in a homozygous individual.



- Skip back to 2nd law

SECOND MENDEL LAW

Mendel's Law of Independent Assortment

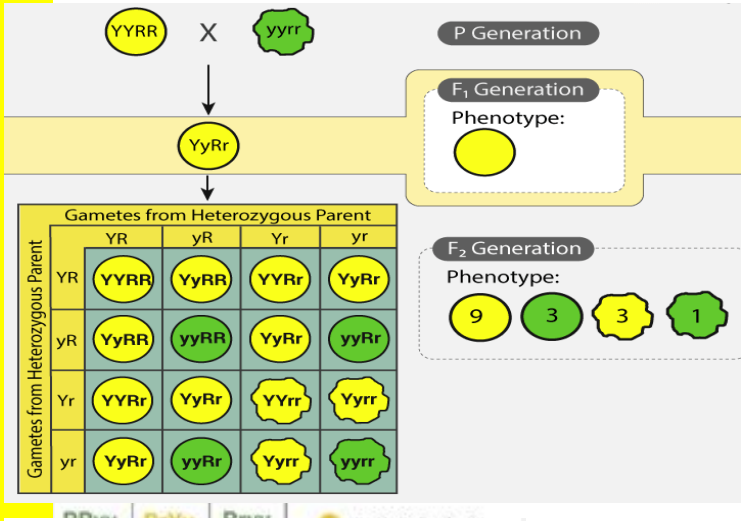


This law is the most complicated.

Sometimes is ilustradet only by this P-F1 square, but **this is not exact definition of basic message** for clincal and biological application!! (it is only the islutration of mendel science experiment which start this hypothesis)

SECOND MENDEL LAW

The law of independent assortment means that separate traits of different alleles are inherited by the zygote independently from each other. Where the random selection of one allele for a certain trait is not connected by any means to the selection of another allele for a different trait.



Independent assortment states that the inheritance of various genes occurs independently of each other. In the law of independent assortment, the combination of genes and their probability is calculated and assumed by multiplying the probabilities of each gene. Probability of having one gene does not influence the probability of having the other.

Summary of Mendel's laws

LAW	PARENT CROSS	OFFSPRING
DOMINANCE	TT x tt tall x short	100% Tt tall
SEGREGATION	Tt x Tt tall x tall	75% tall 25% short
INDEPENDENT ASSORTMENT	RrGg x RrGg round & green x round & green	9/16 round seeds & green pods 3/16 round seeds & yellow pods 3/16 wrinkled seeds & green pods 1/16 wrinkled seeds & yellow pods

- Note important aspect of mendelian genetic:

Phenotype profile vs. Genotype profile

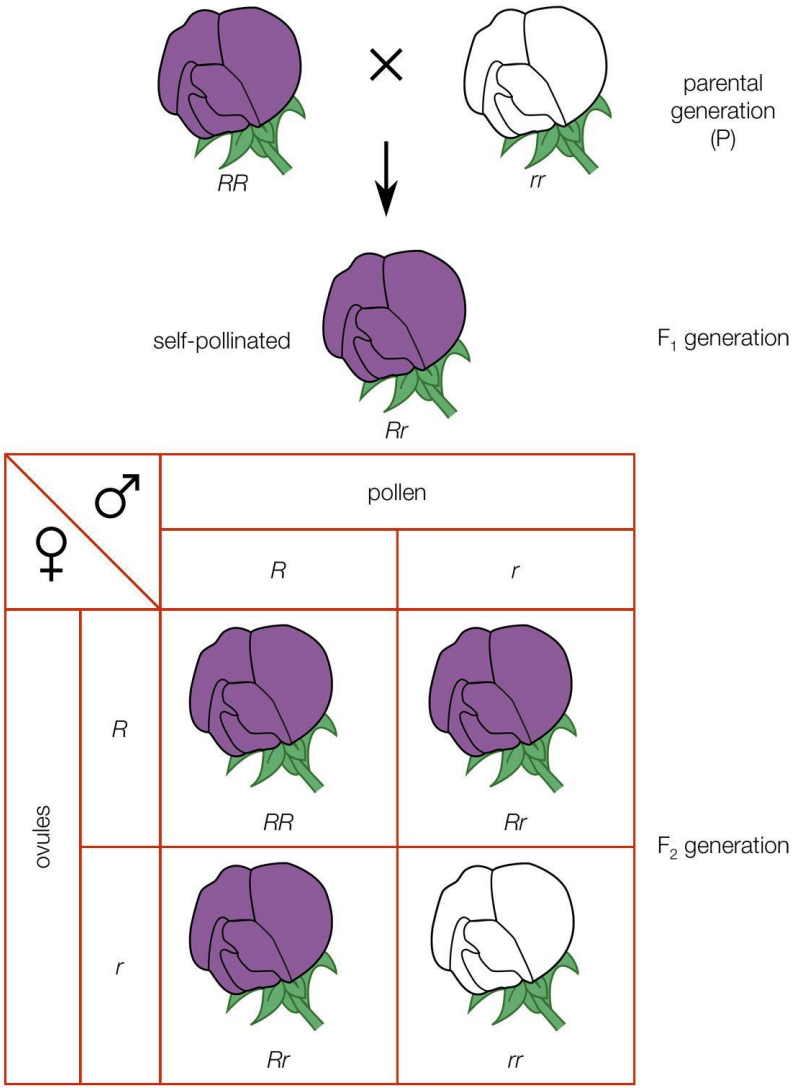
Homozygote

Heterozygote

Dihybrid vs. Monohybrid

MENDEL SQUARES = sometimes are celled as PUNNET SQUARES

Some another typical ilustraion of MENDEL SQUARE for 1 gene
(2 variant of gene: G or g)

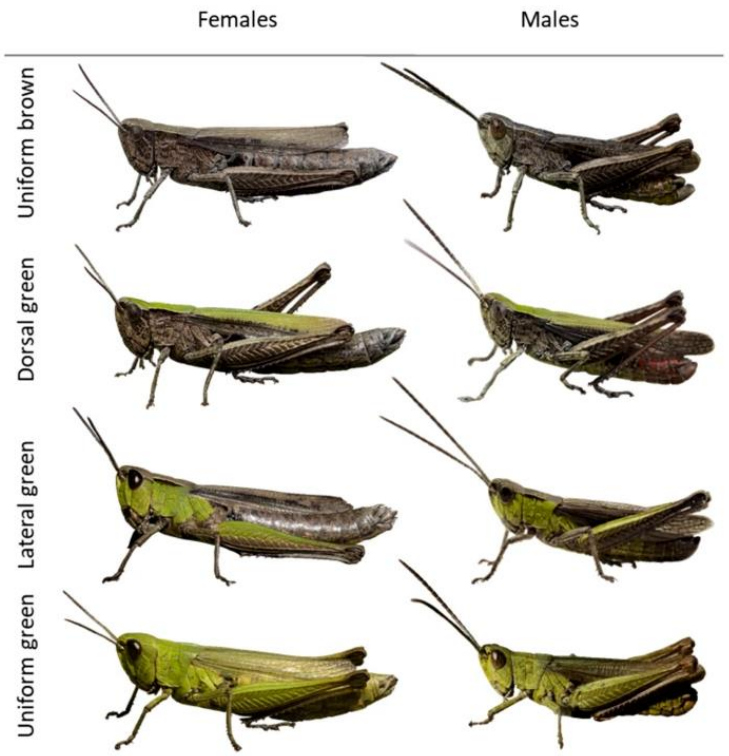


MENDEL SQUARES = sometimes are celled as PUNNET SQUARES

Some another typical ilustraion of MENDEL SQUARE for 3 genes (3 phenotypic marker) (2 variant of all genes)

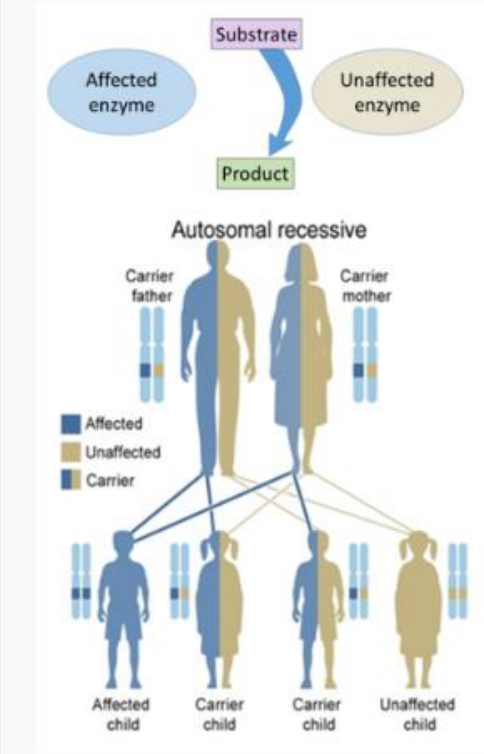
	GDL	GDn	GuL	Gun	bDL	bDn	buL	bun
GDL	GGDDLL	GGDDLn	GGDuLL	GGDuLn	GbDDLL	GbDDLn	GbDuLL	GbDuLn
GDn	GGDDLn	GGDDnn	GGDuLn	GGDunn	GbDDLn	GbDDnn	GbDuLn	GbDunn
GuL	GGDuLL	GGDuLn	GGuuLL	GGuuLn	GbDuLL	GbDuLn	GbuuLL	GbuuLn
Gun	GGDuLn	GGDunn	GGuuLn	GGuunn	GbDuLn	GbDunn	GbuuLn	Gbuunn
bDL	GbDDLL	GbDDLn	GbDuLL	GbDuLn	bbDDLL	bbDDLn	bbDuLL	bbDuLn
bDn	GbDDLn	GbDDnn	GbDuLn	GbDunn	bbDDLn	bbDDnn	bbDuLn	bbDunn
buL	GbDuLL	GbDuLn	GbuuLL	GbuuLn	bbDuLL	bbDuLn	bbuuLL	bbuuLn
bun	GbDuLn	GbDunn	GbuuLn	Gbuunn	bbDuLn	bbDunn	bbuuLn	bbuunn

Uniform brown (B) | Dorsal green (D) | Lateral green (L) | Uniform green (G)



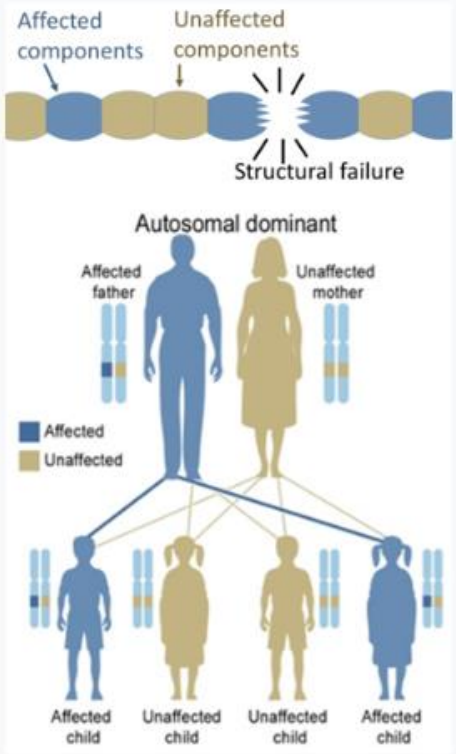
AUTOSOMAL RECESIVE GENES (ILLNESS)
vs.
AUTOSOMAL DOMINANT GENES

RECES.



Hereditary defects in enzymes are generally inherited in an autosomal fashion because there are more non-X chromosomes than X-chromosomes,

DOMINAN.



On the other hand, hereditary defects in structural proteins (such as osteogenesis imperfecta, Marfan's syndrome and many Ehlers–Danlos syndromes)

Reces.

H = healthy h = disorder

Autosomal recessive

- Sufferers must inherit 2 alleles to have the disorder
- Healthy = Dominant
- Disorder = Recessive

	H	h
H	H H Healthy	H h Healthy carrier
h	H h Healthy carrier	h h Disorder

H = Disorder h = Healthy

Autosomal Dominance

- Sufferers must inherit only 1 allele to have the disorder
- Disorder = Dominant
- Healthy = Recessive

	H	h
H	H H Disorder (severe)	H h Disorder (moderate)
h	H h Disorder (moderate)	h h Healthy

Domin.

H = healthy h = disorder

Autosomal recessive

- Man = heterozygous carrier of PKU
- Woman = suffers from PKU

	H	h
h	H h Healthy carrier	h h disorder
h	H h Healthy carrier	h h disorder

H = Disorder h = Healthy

Autosomal Dominance

- Man = healthy

~~HH~~ ~~Hh~~ hh

- Woman = suffers from Huntington's disease

~~HH~~ Hh ~~hh~~

	h	h
H	H h Disorder (moderate)	H h Disorder (moderate)
h	h h Healthy	h h Healthy

Autosomal Dominant vs Autosomal Recessive Disorders

More Information Online WWW.DIFFERENCEBETWEEN.COM

	Autosomal Dominant Disorders	Autosomal Dominant Disorders
DEFINITION	In autosomal dominant disorders, one altered single copy of a gene is enough to cause the disease	In autosomal recessive disorders, both altered copies of the gene are needed to cause the disease
NUMBER OF AFFECTED ALLELES	Only one allele is needed from the maternal or paternal side	Two alleles are needed from both the maternal and paternal side
CARRIER STATE	No carrier status	Carrier state only when one allele is affected
ONSET OF THE DISEASE	Late onset	Early onset
DOMINANT/ RECESSIVE	Mutated copy of the gene (allele) is in dominant state	Mutated copies of the gene (alleles) are in recessive state
CHANCES OF AN AFFECTED CHILD	50% chance of having an affected child	25% chance of having an affected child
PARENT'S STATUS	One parent is affected	Parents are unaffected
EXAMPLES	Huntington disease, tuberous sclerosis, Myotonic dystrophy, and neurofibromatosis	Sickle cell disease and cystic fibrosis

Learn example

Summary of basic mendelian genetic

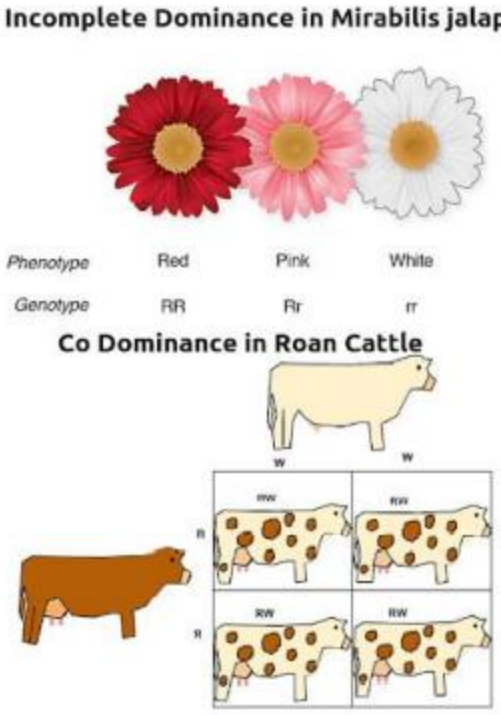
- Mendel was the first, who derived from mathematical result of experiment with P (parent), F1 (firt generation) and F2 (second generation) the opinion, that 2 variant of genetic informatin must be in all parental cell, and only one of this variant is shifted to egg or sperm.

- Mendel never see something like chromosome or DNA. DNA was recognised and structuraly investigatedy more than 100 year later. However these modern microcopic techniq and biochmeistry investigation.

- Mendel law about SEGREGATION and DOMINANCE can be aplied in all modern descripton of inheritance of important marker of all human and most of the animal (pigment, enzyme aktivity, muscle components of patients) and alos in desription of inheritance of many pathology (anemia, schizophremia, some type of cancer, …)

- **NOT ALL INHERITANCE PHENOMENON visible in modern medicine** in specific pathology, **can be described only by 3 MENDEL LAW**. There must be add also some antoher modern laws o genetic: MORGAN LAW, Law of incomplete dominance, Law of codominace and Rules of non-independent genes. (In next lecture material)

Mendel laws have some exception in some organism: example where DOMINANT is not full:



Exceptions to Mendel Law

MEMORIZE some antoher important definiton from basic genetic:

Epistasis

The phenomenon where one gene affects the expression of a second gene

Example: Hairless dogs: genes for color of hair have no effect if not hair is produced. Epistatic interaction seen is albinism in which one gene blocks the genes that produces color

Example: **Bombay phenotype**

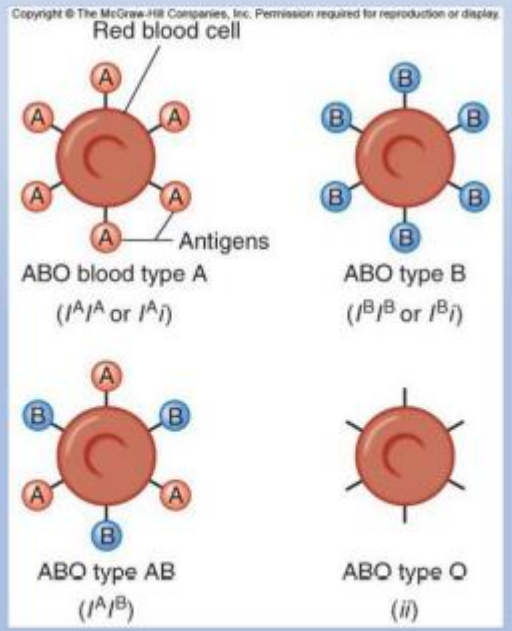
…or some other exception (the case of human surface molecules of erytrocytes)

Mendel's traits showed two distinct forms: either Dominant or recessive

Most genes do not exhibit simple inheritance

Genotypic ratios persist but phenotypic ratios may vary due to "outside-the-gene" influences including

- Multiple alleles
- Other nuclear genes
- Non-nuclear genes
- Gene linkage
- Environment



- Not only one gene caused one function (or disfunction)

Genetic Heterogeneity

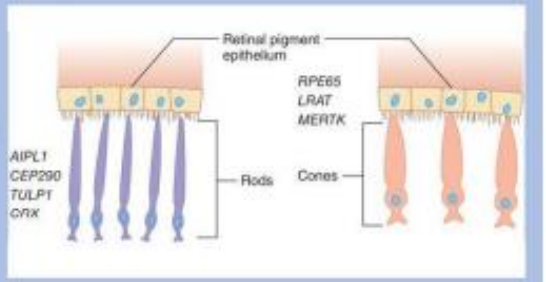
Different genes can produce identical phenotypes

- *Hearing loss* – 132 autosomal recessive forms

- *Osteogenesis imperfecta* – At least two different genes involved. Abnormal collagen causes very brittle bones in children.

- *Alzheimer disease* – At least four different genes involved. Genes may encode enzymes that catalyze the same biochemical pathway, or different proteins that are part of the pathway

- *pathways to blindness* mutations in over 100 genes cause degeneration of the retina resulting in many pathways to blindness



Additive non-mendelian rules

Table 5.1 Factors That Alter Single-Gene Phenotypic Ratios

Phenomenon	Effect on Phenotype	Example
Lethal alleles	A phenotypic class does not survive to reproduce.	Spontaneous abortion
Multiple alleles	Many variants or degrees of a phenotype occur.	Cystic fibrosis
Incomplete dominance	A heterozygote's phenotype is intermediate between those of two homozygotes.	Familial hypercholesterolemia
Codominance	A heterozygote's phenotype is distinct from and not intermediate between those of the two homozygotes.	ABO blood types
Epistasis	One gene masks or otherwise affects another's phenotype.	Bombay phenotype
Penetrance	Some individuals with a particular genotype do not have the associated phenotype.	Polydactyly
Expressivity	A genotype is associated with a phenotype of varying intensity.	Polydactyly
Pleiotropy	The phenotype includes many symptoms, with different subsets in different individuals.	Porphyria variegata
Phenocopy	An environmentally caused condition has symptoms and a recurrence pattern similar to those of a known inherited trait.	Infection
Genetic heterogeneity	Different genotypes are associated with the same phenotype.	Leber congenital amaurosis

Some GENETIC mistakes

from
high school and internet pages

(1) EYE

GENETIC mistakes

Blue and green eye phenotype is somewhere in textbook described as simple Mendel dominant/recesive gen cooperation (on left picture). The reality is little bit different (on right)

Not exact theory
(only for several family):
Some high school textbook

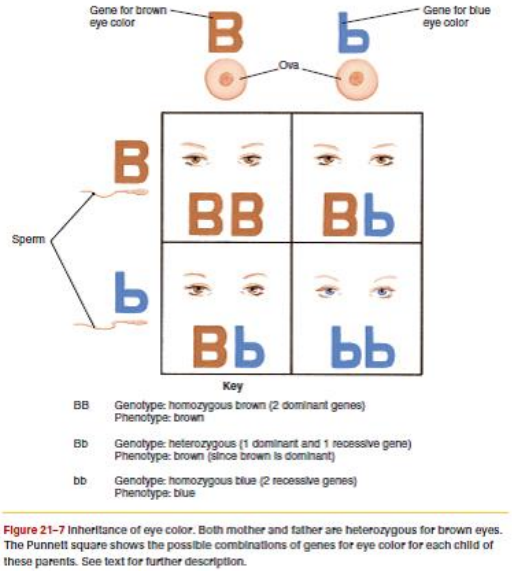
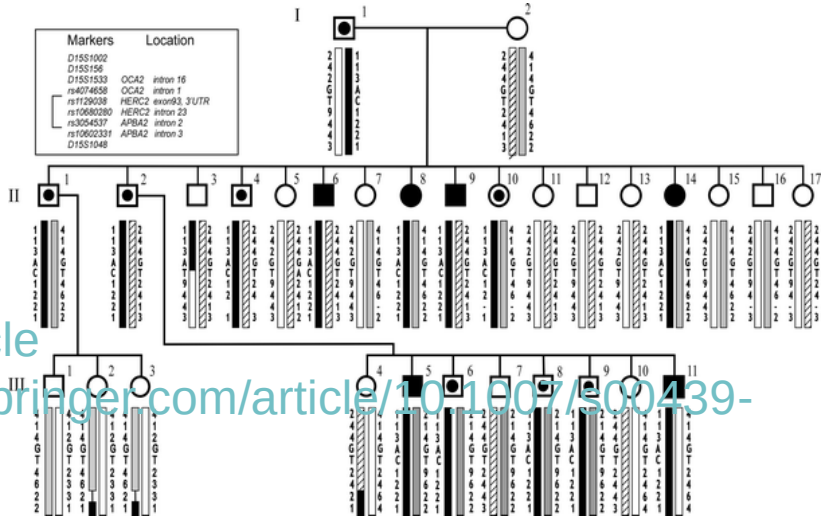


Figure 21–7 Inheritance of eye color. Both mother and father are heterozygous for brown eyes. The Punnett square shows the possible combinations of genes for eye color for each child of these parents. See text for further description.

Reality:
Hans Eiberg --- Human Genetics volume 123, pages177–187 (2008)
The human eye color is a **quantitative trait displaying multifactorial** inheritance. Several studies have shown that the *OCA2* locus is the major contributor to the human eye color variation



See the article
https://link.springer.com/article/10.1007/s00439-007-0460-x

(2) Cancer screening

Women with mutations in either BRCA1 and BRCA2 do have a five-fold increased risk of breast cancer compared with other women. But many did not know that these mutations are rare: far less than one percent of women have them.

Most people also still don't know that the BRCA mutations are only linked to five to 10 percent **of all breast cancer cases.** And that in terms of absolute numbers, many more women with no family history of the disease get diagnosed with breast cancer than do those with a history of breast cancer in the family.

(3) Diabetes type II – has one typical gene? No, there is the set of gene. And also some genetic change in INTRON of genome!!

ARTICLE
https://www.researchgate.net/figure/Major-susceptibility-genes-and-pathogenic-mechanisms-for-type-2-diabetes-identified-so_fig9_41510100

Major susceptibility genes and pathogenic mechanisms for type 2 diabetes identified so far (2008).
SNP = Single-nucleotide polymorphism;
CGA = candidate gene approach;
GWA = genome-wide association;

LSA = large-scale association.