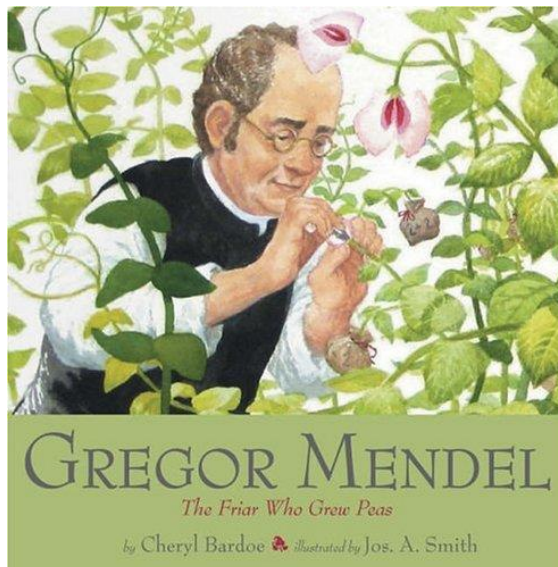


Gregor Johann Mendel

- The Father of Genetics



(1822-1884)

What did Mendel do differently from those who preceded him?

Chapter I

Mendel's Law of Inheritance

I. Mendel's breakthrough

Patterns, particles, and principles of heredity

II. Extension to Mendel's laws

Complexities in relating genotype to phenotype

- 1. Single-gene inheritance**
- 2. Multifactorial inheritance**

Chapters in reference books: [H2-H3](#), [D3](#)

Key Words

law of segregation (分离定律)
law of independent assortment (独立分配定律)

reciprocal cross (反交)
backcross, back cross (回交)
testcross, test cross (测交)

P: parental generation (亲本, 亲代)
F₁: first filial generation (子一代)
F₂: second filial generation (子二代)

Key Words

self-fertilization, selfing (自体受精, 自交)

cross-fertilization (异体受精)

inbreeding, incross (内交, 近交)

outbreeding, outcross (外交, 远交)

pure-breeding (纯系繁育)

true-breeding (纯育)

pure line (纯系)

pure breed, purebred (纯种)

selfing line (自交系)

inbred line, inbred strain (近交系)

Key Words

dominant, dominance (显性)
recessive, recessiveness (隐性)

genotype (基因型)
phenotype (表现型, 表型)

allele (等位基因)
gamete (配子)
zygote (合子)

homozygous (纯合)
heterozygous (杂合)
homozygote (纯合子, 纯合体)
heterozygote (杂合子, 杂合体)

Key Words

product rule (乘法法则, 相乘定律)
sum rule (加法法则, 相加定律)

hybrid (杂种)
monohybrid (单杂种, 单因子杂种)
dihybrid (双因子杂种, 双因子杂合子)
multihybrid (多基因杂种)

Punnett square (Punnett 棋盘式方格)
branched-line diagram (分支图)

pedigree (系谱, 家谱)
consanguineous mating (近亲交配)
sibling (同胞)

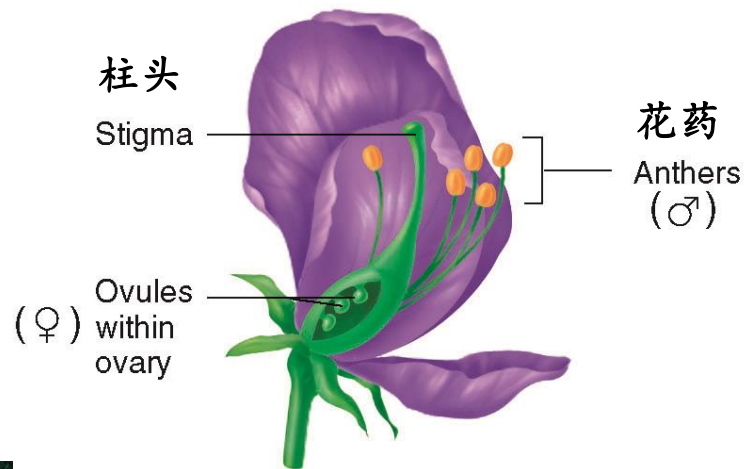
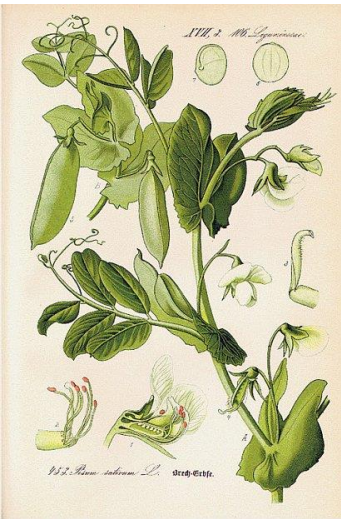
How to make a scientific breakthrough?

Breakthrough vs. Discovery

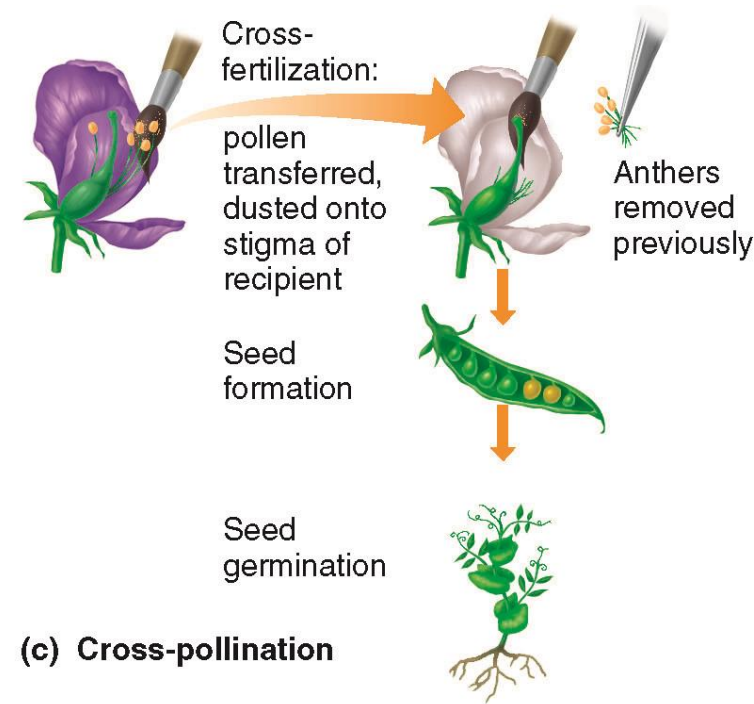
1. To address a **BIG** scientific question;
2. To use a **suitable** experimental material;
3. To employ strong assays and **unique** technique;
4. To perform **black and white** experiments (easy to analyze; easy to repeat)
5. To rigorously analyze **systematically** recorded information;
6. To make **verifiable** predictions

Mendel's Experimental Material

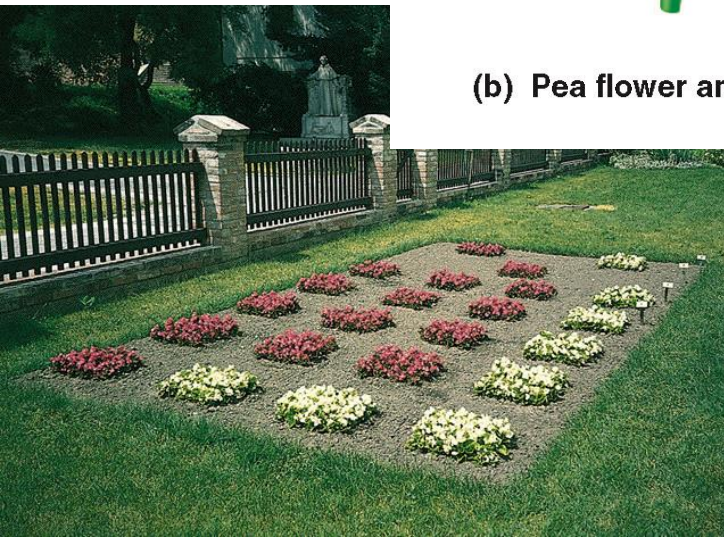
Garden pea (*Pisum sativum*)



(b) Pea flower anatomy



(c) Cross-pollination



self-fertilization, selfing (自体受精, 自交)
cross-fertilization (异体受精)

What is an ideal experimental organism?

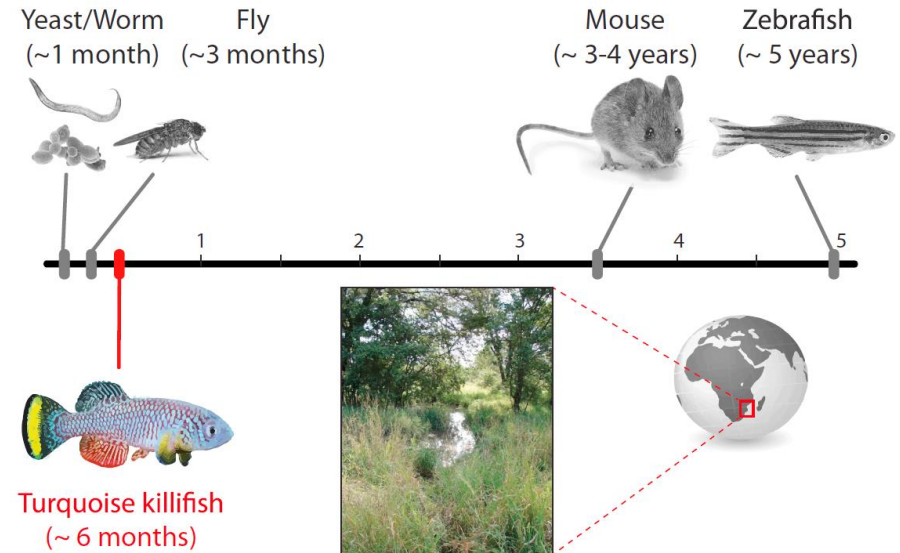
Aging and longevity research



African Turquoise killifish

非洲青鳉鱼

A Vertebrate and non-vertebrate genetic aging models



Shortest-lived vertebrate species bred in the lab

The life span of the tiny fish can be measured in months, not years, and it does everything quickly: hatch, mature, breed and even age.

- Due to very short duration of the rain season

What is an ideal experimental organism?



Cancer and aging research



Naked mole rat

裸鼹鼠



Rarely get cancer (very active DNA repair; error-free translation; high levels of chaperones; early contact inhibition)

Resistant to some types of pain

Can survive up to 18 minutes without oxygen

Do not age – “At advanced ages, their mortality rate remains lower than any other mammal that has been documented.”

Fertility does not drop as they age.

Mendel's Experimental Material

Antagonistic Pairs Appearance of Hybrid
(dominant trait)

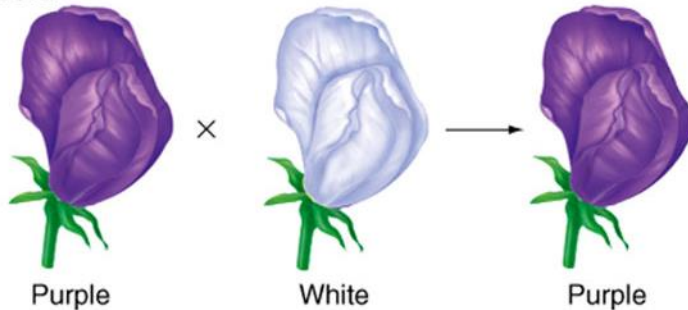
Seed color (interior)



Seed shape



Flower color



Antagonistic Pairs

Appearance of Hybrid
(dominant trait)

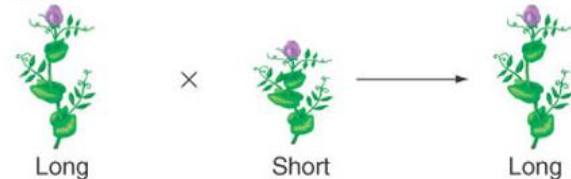
Pod color (unripe)



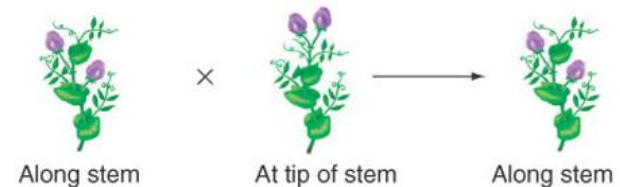
Pod shape (ripe)



Stem length

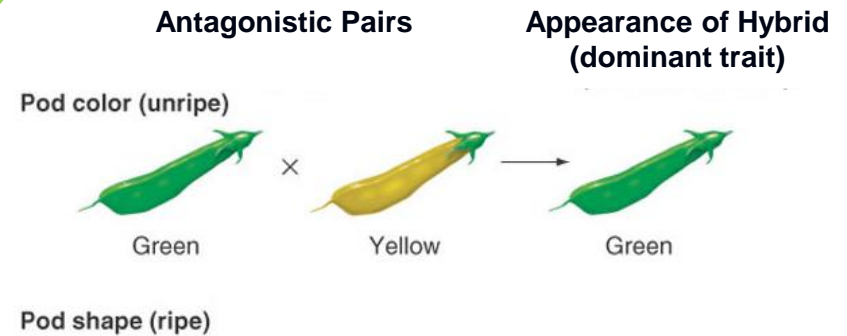


Flower position



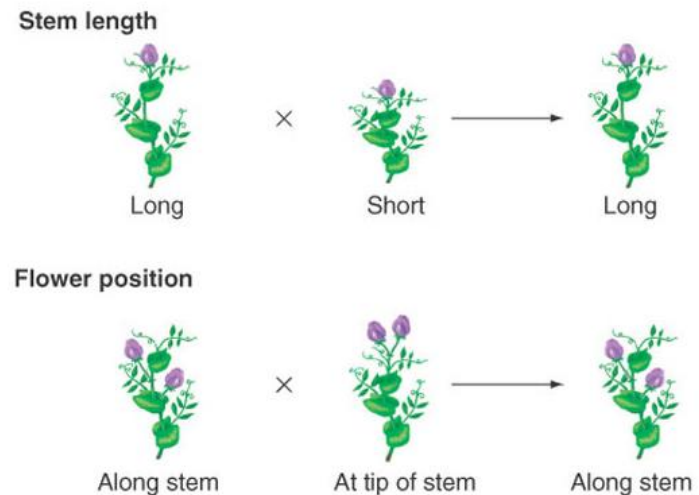
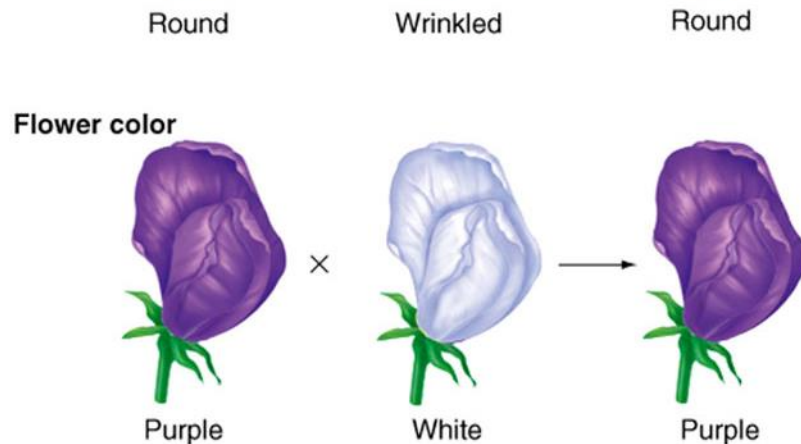
Pure breeding lines produce offspring carrying specific parental traits that **remain constant** from generation to generation.

Mendel's Experimental Material



Seed shape

2 years of trial experiments
– observed his pure-breeding lines for up to **8** generations



Pure breeding: produce offspring carrying specific parental traits that remain **constant** from generation to generation.

Monohybrid crosses reveal units of inheritance and Law of Segregation

1854

Generation

Parental (P)
(pure-breeding)



First filial (F₁)

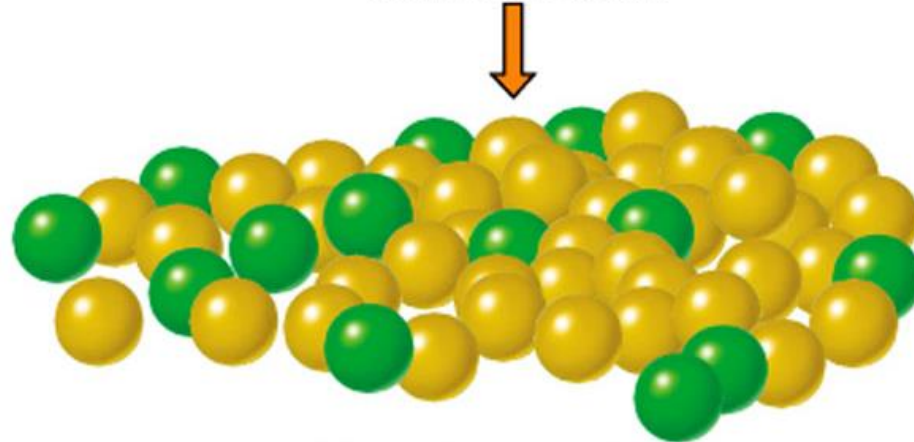


Disappeared entirely or hidden?

Self-fertilization

Large number of plants
Numerical analysis

Second filial (F₂)



6022 yellow : 2001 green

3 : 1

Keys to Mendel's Success!

What did Mendel do differently from those who preceded him?

1. Mendel chose **an ideal experimental organism**
 - Vigorously grow
 - Self-fertilize
 - Easy to cross-fertilize
 - Produce large number of offspring each generation
2. Mendel established **pure-breeding** lines to conduct his experiments (2-year **trial experiments**) 磨刀不误砍柴工
3. Mendel analyzed traits with discrete **alternative** forms
 - yellow vs. green peas
 - round vs. wrinkled seeds

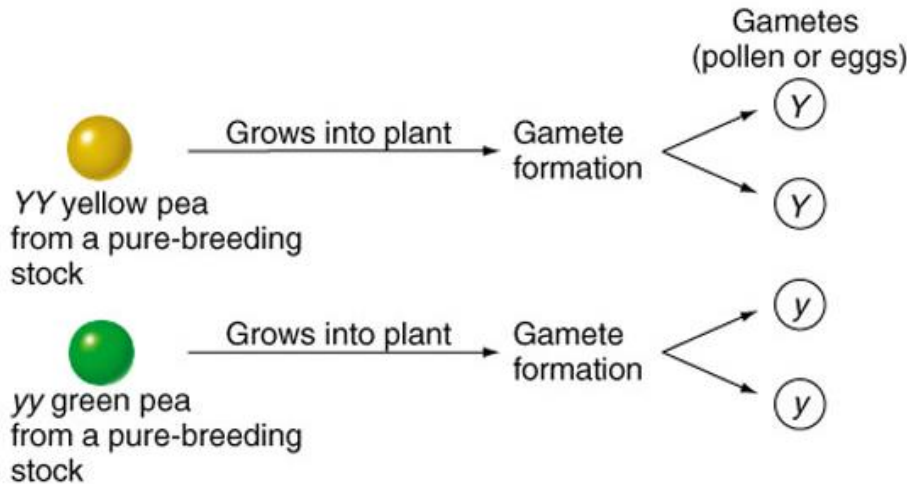
Black-and-white experiment
4. Mendel used **numerical analysis** to study inheritance (big N)

Traits have dominant and recessive forms

- Disappearance of traits in F_1 generation and **reappearance** in the F_2 generation disproves the hypothesis that traits blend
- Trait must have two forms that can each **breed true**
- One form must be hidden when plants with each trait are interbred
- Trait that appears in F_1 is **dominant (显性)**
- Trait that is hidden in F_1 is **recessive (隐性)**
- Each trait carries two copies of a unit of inheritance, one inherited from the mother and the other from the father
- Alternative forms of traits are called **alleles (等位基因)**

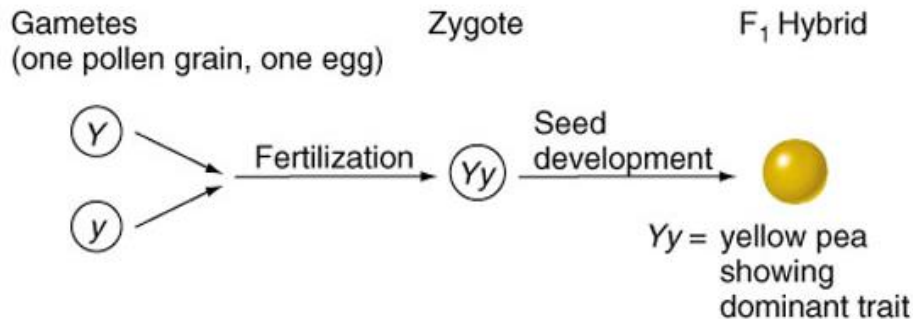
Law of Segregation (分离定律)

(a) The two alleles for each trait separate during gamete formation.



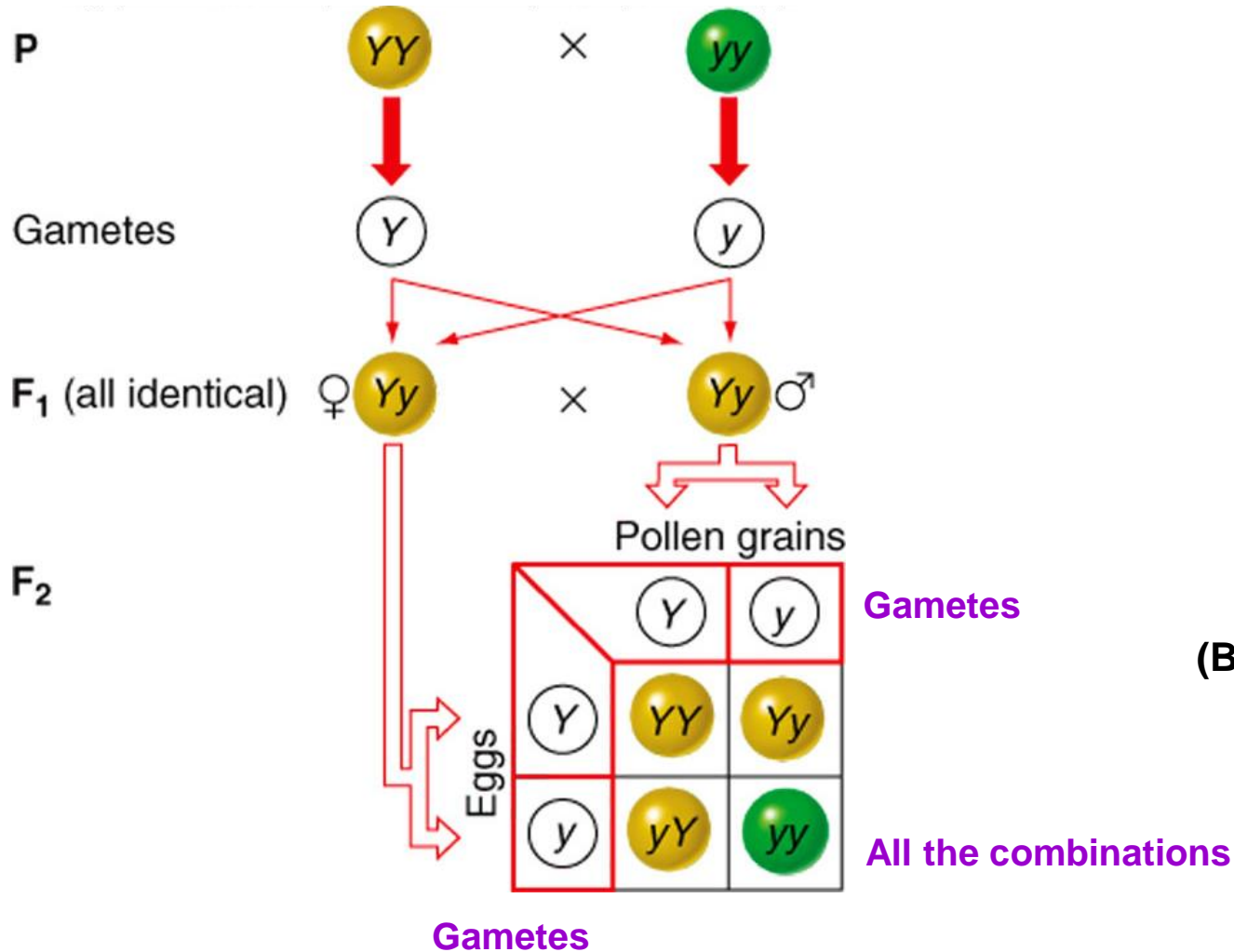
Two **alleles** for each trait separate (**segregate**) during gamete formation, and then unite **at random**, one from each parent, at fertilization.

(b) Two gametes, one from each parent, unite at random at fertilization.



Y = yellow-determining allele of pea color gene
y = green-determining allele of pea color gene

The Punnett Square (Punnett 棋盘式方格)



Reginald Punnett
(British mathematician)

Rules of Probability

Independent events

probability of two events occurring together - **product rule**
(乘法法则, 相乘定律)

What is the probability that both A and B will occur?

Solution = determine the probability of each and multiply them together.

Mutually exclusive events

probability of one or another event occurring - **sum rule**
(加法法则, 相加定律)

What is the probability of either A or B occurring?

Solution = determine the probability of each and add them together.



Probability and Mendel's Results



Cross $Yy \times Yy$ pea plants

Chance of Y sperm uniting with a Y egg (YY offspring)

$\frac{1}{2}$ chance of sperm with Y allele

$\frac{1}{2}$ chance of egg with Y allele

Chance of Y and Y uniting = $\frac{1}{2} \times \frac{1}{2} = \frac{1}{4}$

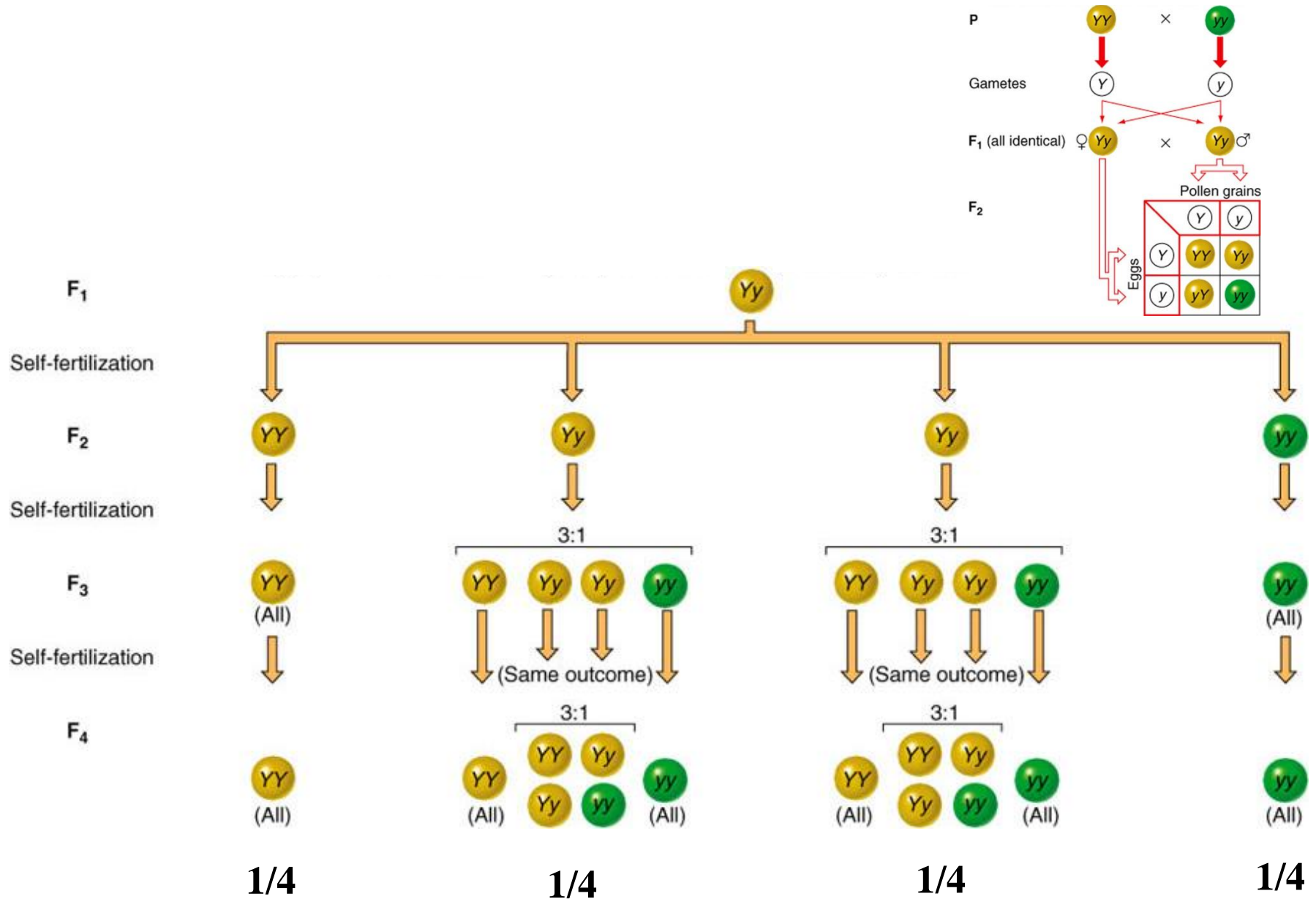
Chance of Yy offspring

$\frac{1}{2}$ chance of sperm with y allele and egg with Y allele

$\frac{1}{2}$ chance of sperm with Y allele and egg with y allele

Chance of Yy = $(\frac{1}{2} \times \frac{1}{2}) + (\frac{1}{2} \times \frac{1}{2}) = \frac{2}{4}$, or $\frac{1}{2}$

Further crosses confirm predicted ratios



Genotype and Phenotype

Phenotype (表现型, 表型)

— observable characteristic of an organism

Genotype (基因型)

— pair of alleles present in an individual

Homozygous (纯合)

— two alleles of trait are the same (YY or yy)

Heterozygous (杂合)

— two alleles of trait are different (Yy)

Homozygote (纯合子, 纯合体)

— a homozygous individual

Heterozygote (杂合子, 杂合体)

— a heterozygous individual

Genotype versus Phenotype

Genotype for the Seed Color Gene

YY

Homozygous dominant

Dominant allele — Recessive allele

Yy

Heterozygous

yy

Homozygous recessive

Phenotype



Yellow



Yellow



Green

Yy × **Yy**



1 : 2 : 1

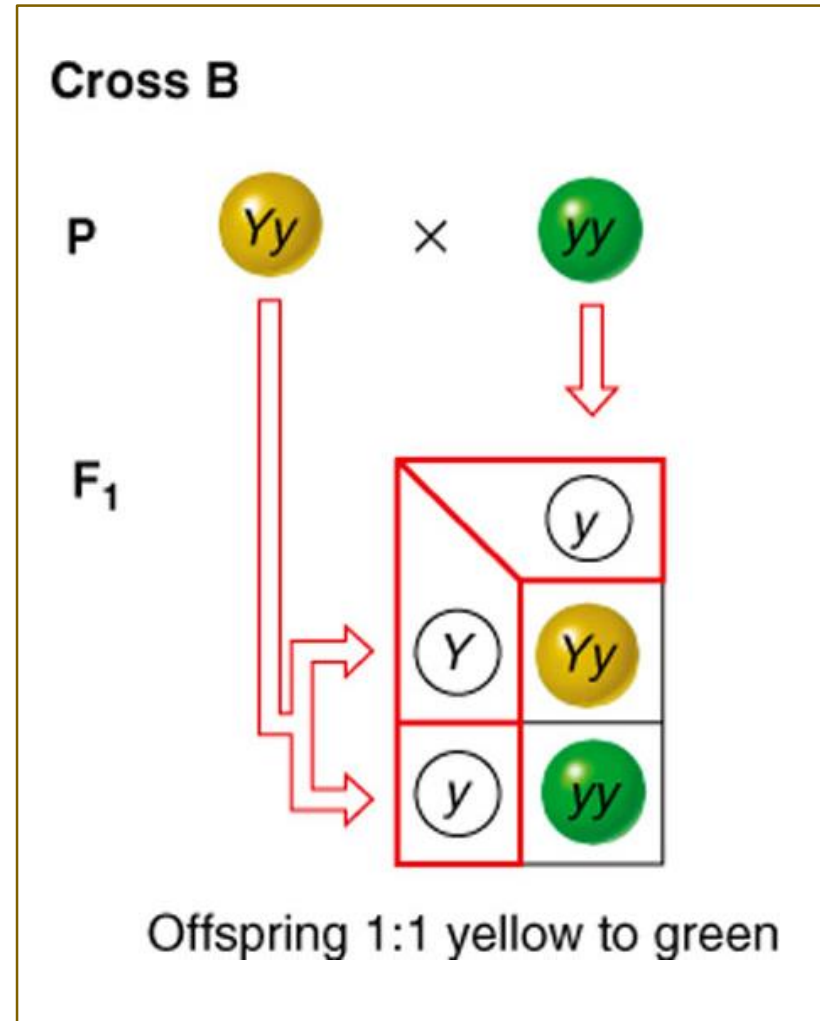
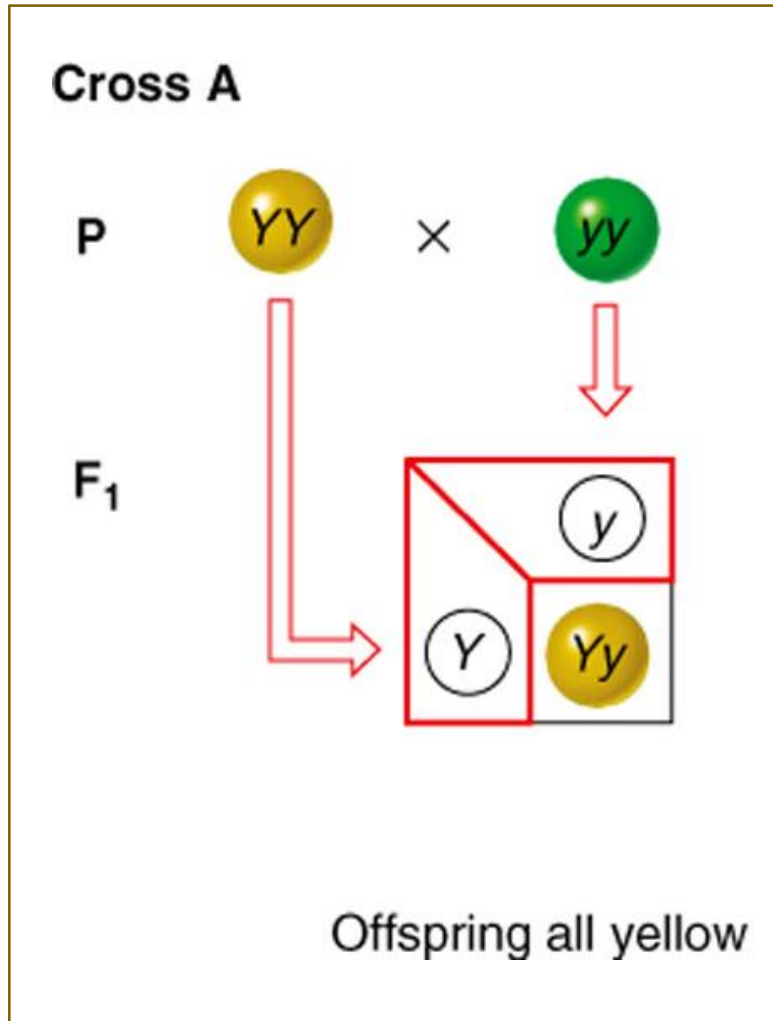
YY : Yy : yy

3 : 1

Yellow : green

How to distinguish homozygotes from heterozygotes?

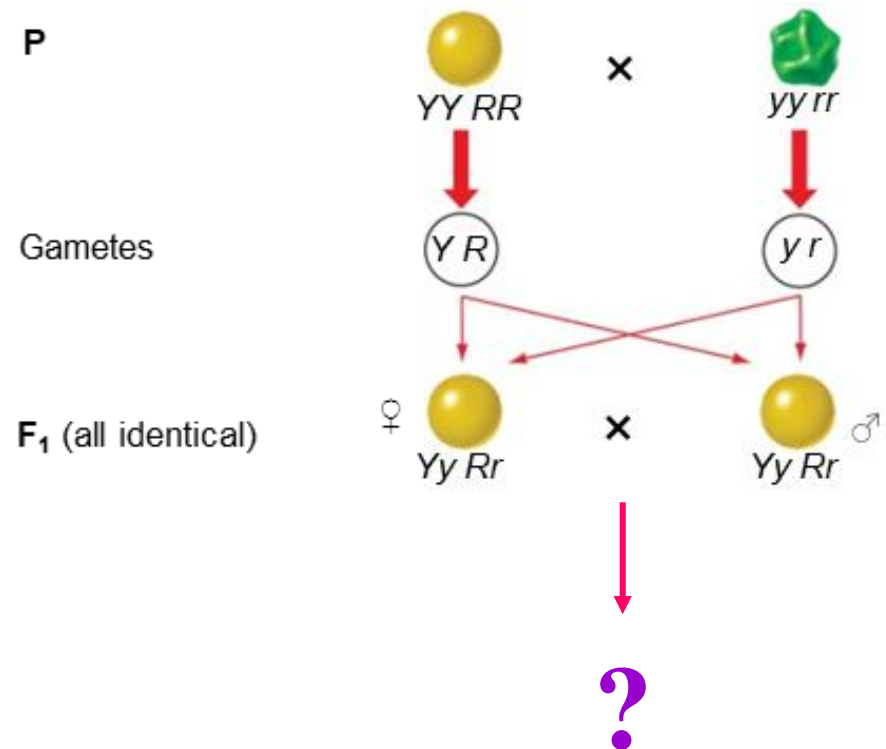
Testcross reveals unknown genotype







Testcross: to cross with a homozygous recessive

Dihybrid crosses reveal the law of independent assortment

- A dihybrid is an individual that is heterozygous at **two genes**
- Mendel designed experiments to determine if two genes segregate **independently** of one another in dihybrids
- First constructed true breeding lines for both traits, crossed them to produce dihybrid offspring, and examined the F_2 for **parental** or **recombinant** types (new combinations not present in the parents)



Dihybrid cross produces a predictable ratio of phenotypes

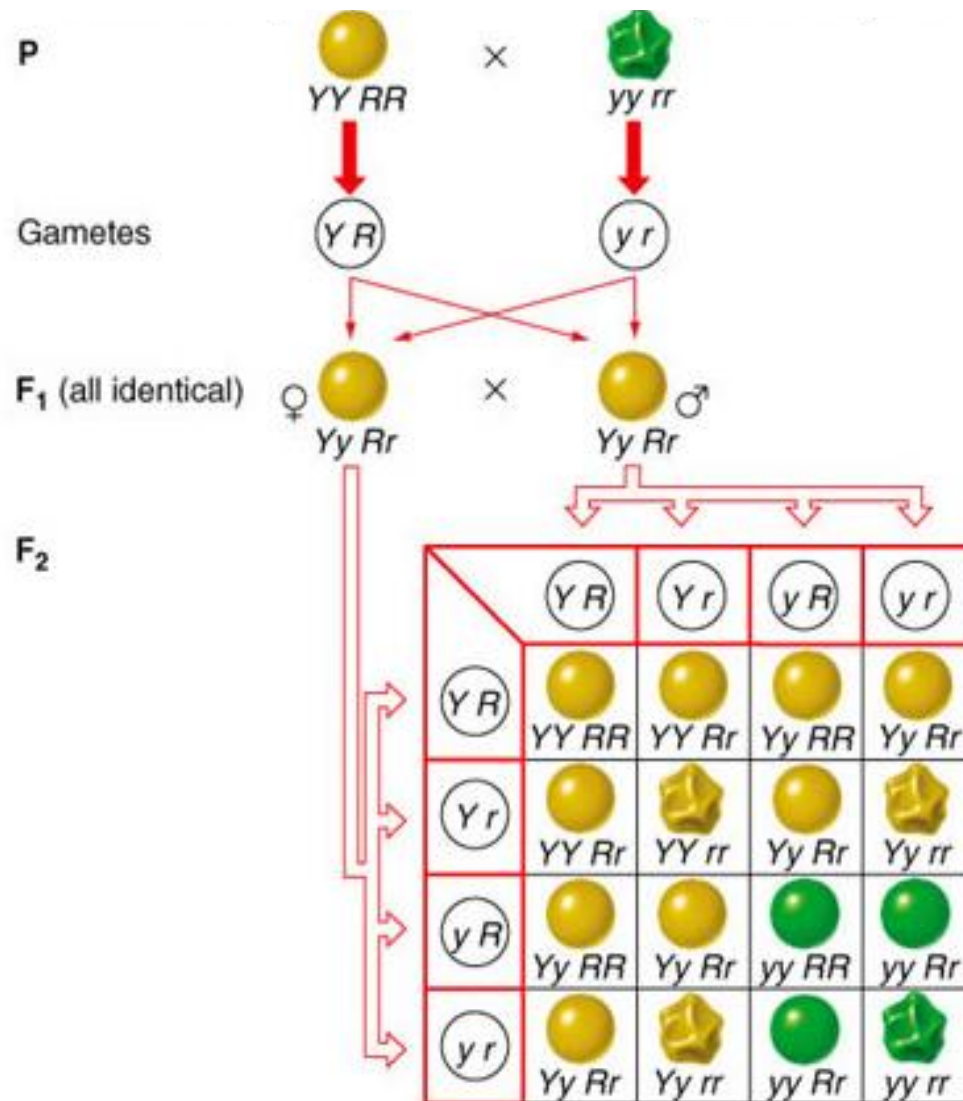
Type	Genotype	Phenotype	Number	Phenotypic Ratio
Parental	$Y- R-$	 yellow round	315	9/16
Recombinant	$yy R-$	 green round	108	3/16
Recombinant	$Y- rr$	 yellow wrinkled	101	3/16
Parental	$yy rr$	 green wrinkled	32	1/16

Ratio of yellow (dominant) to green (recessive) = 12:4 or 3:1

Ratio of round (dominant) to wrinkled (recessive) = 12:4 or 3:1

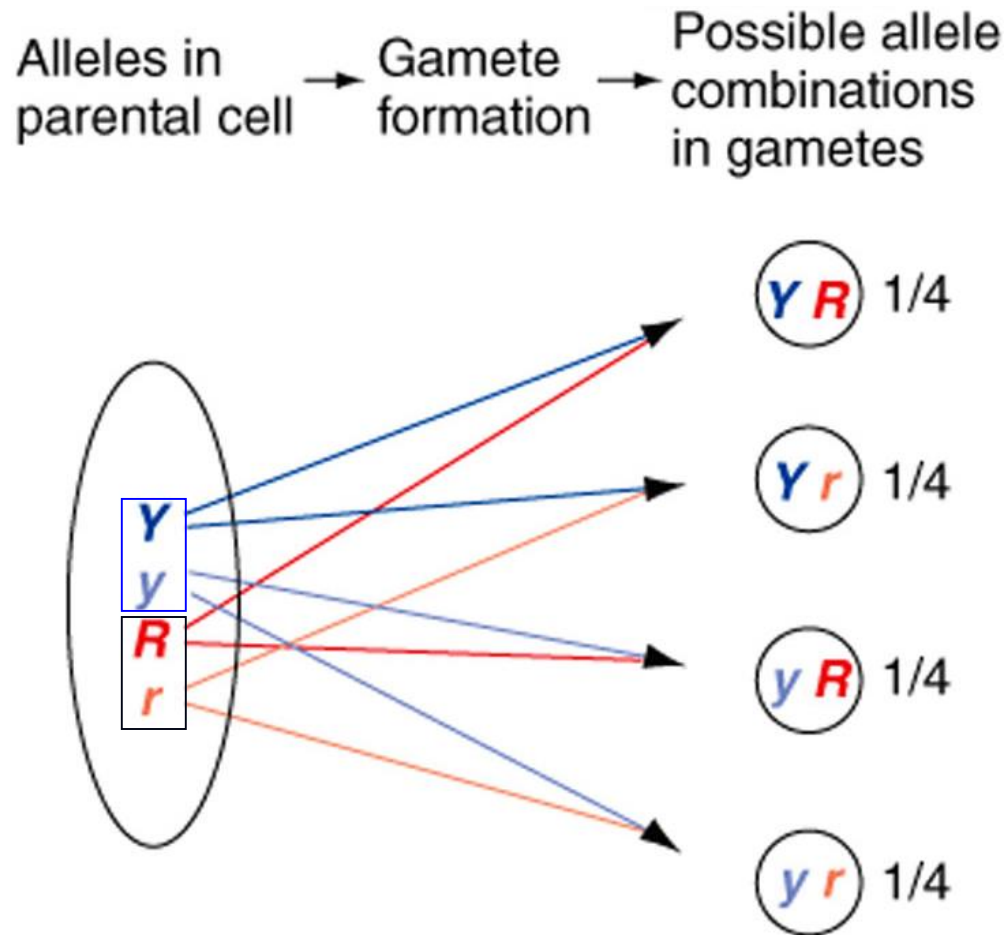
- F_2 generation contained both parental types and recombinant types
- Alleles of genes assort independently, and can thus appear in any combination in the offspring

Dihybrid cross shows parental and recombinant types

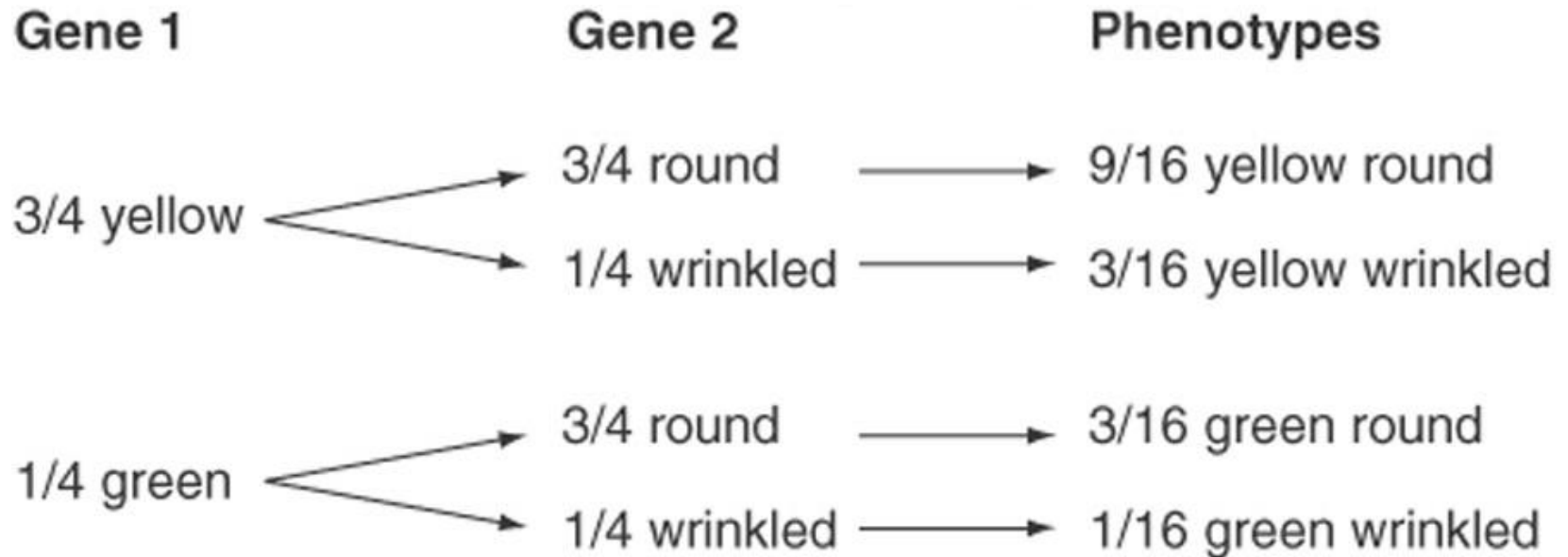


The law of independent assortment

During gamete formation different pairs of alleles segregate independently of each other



The law of independent assortment



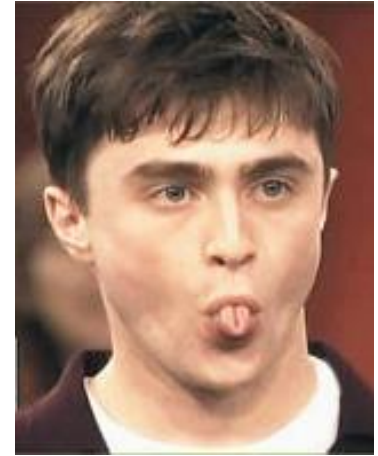
Branched-line diagram (分支图)

Summary of Mendel's work

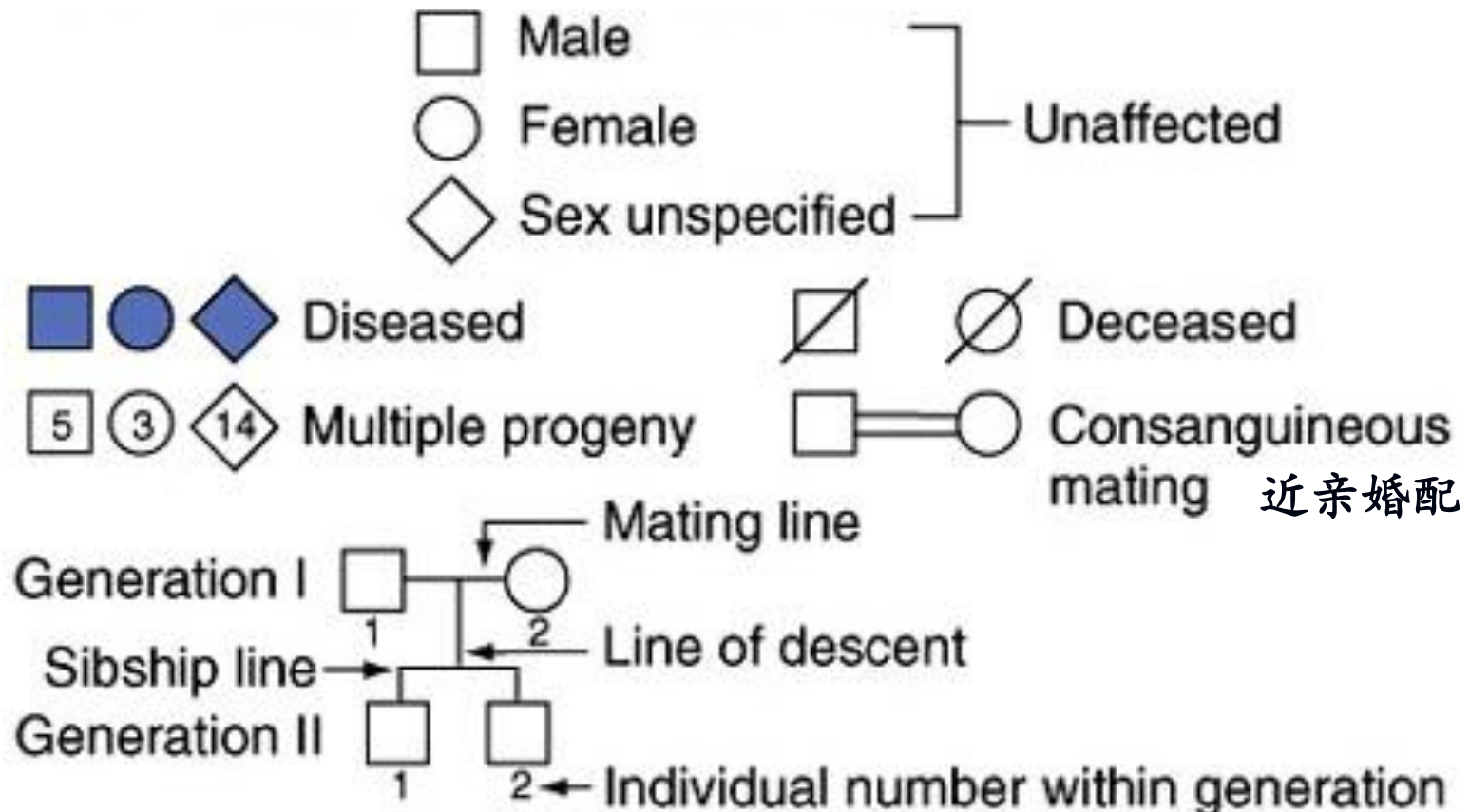
- Inheritance is **particulate**, not blending
- There are two copies of each trait in a germ cell
- Gametes contain one copy of the trait
- Alleles (different forms of the trait) **segregate randomly**
- Alleles are **dominant or recessive** - thus the difference between genotype and phenotype
- Different traits **assort independently**

Mendelian inheritance in humans

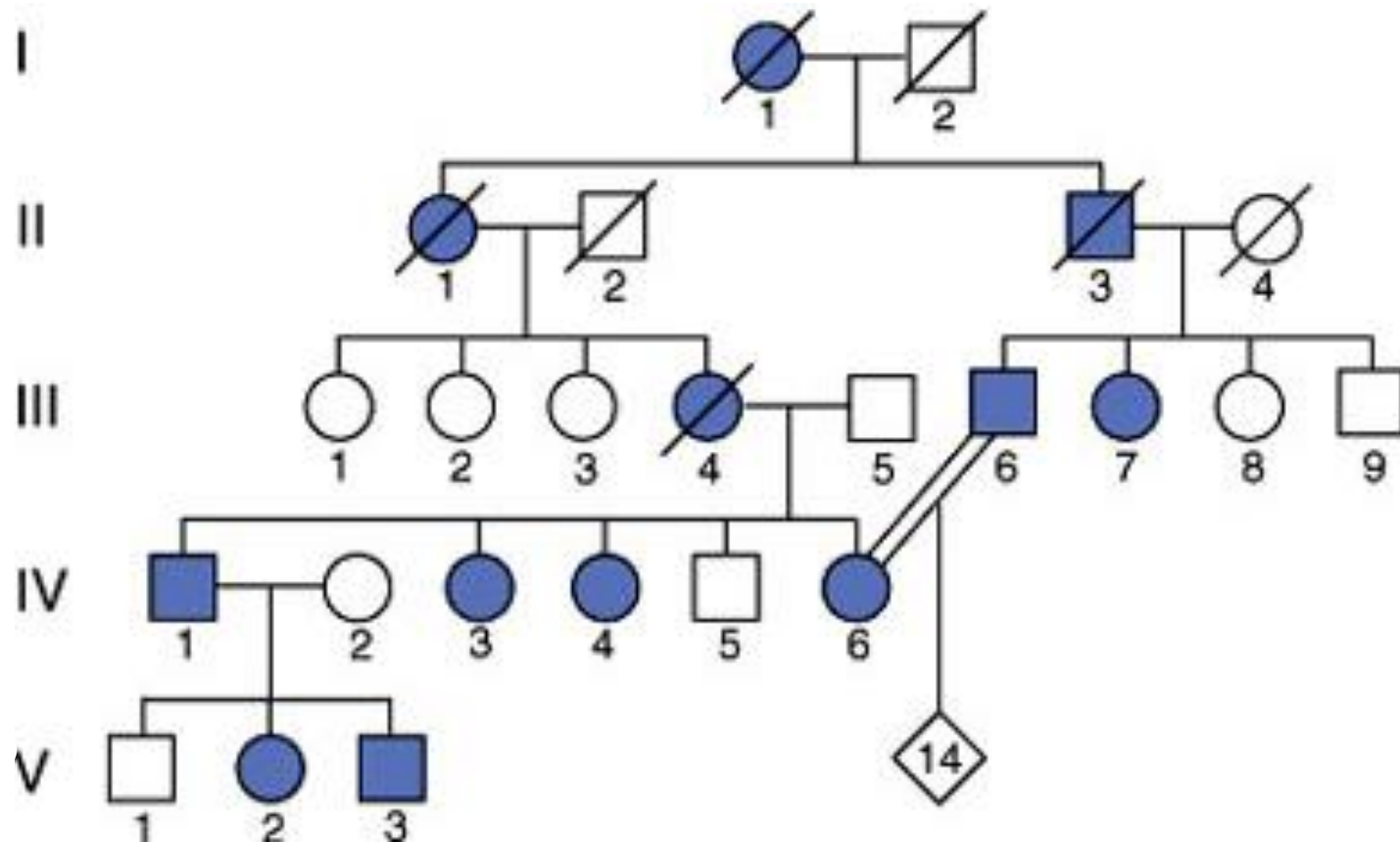
- Most traits in humans are due to the **interaction of multiple genes** and do not show a simple Mendelian pattern of inheritance.
- A few traits represent **single** genes. Examples include sickle-cell anemia, cystic fibrosis, and Huntington's disease
- In humans we use pedigrees to study inheritance
- **Pedigree (家谱)** is an orderly diagram of a family's relevant genetic features extending through multiple generations
- Pedigrees help us infer if a trait is **from a single gene** and if the trait is **dominant or recessive**



Symbols used in pedigree analysis



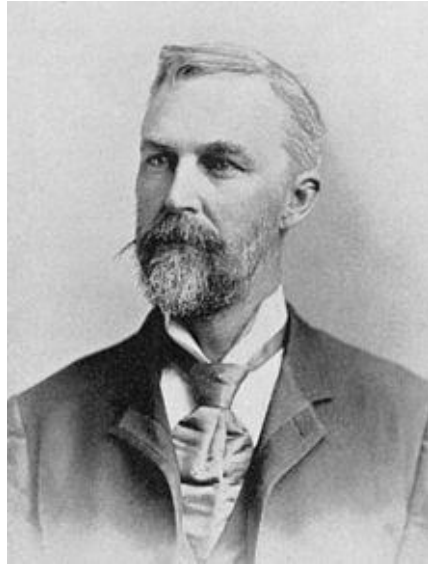
A **vertical** pattern of inheritance indicates a rare dominant trait



Huntington disease (HD): A rare dominant trait

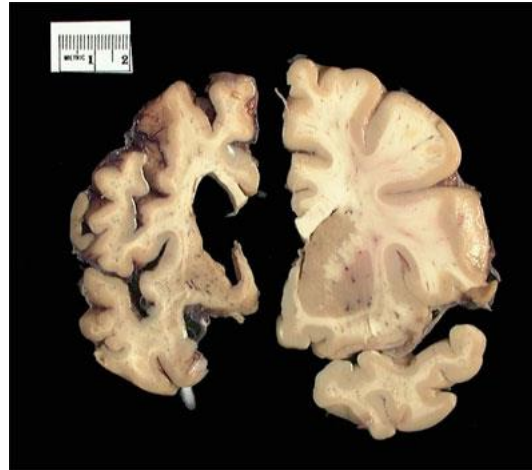
Huntington's disease: a rare dominant trait

亨廷顿舞蹈病



George Huntington

A descent into Hell



HD: A **late-onset** neurodegenerative genetic disorder that causes uncontrolled movements, emotional problems, and loss of cognition.

Poly Q - a gain of toxic function of mHtt

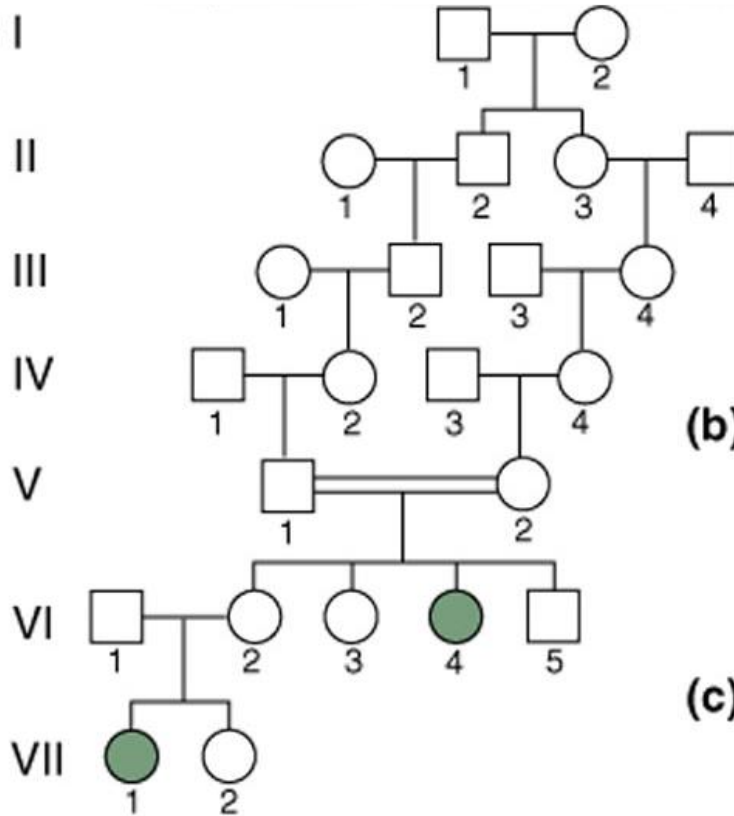


Woody Guthrie
(folk singer)

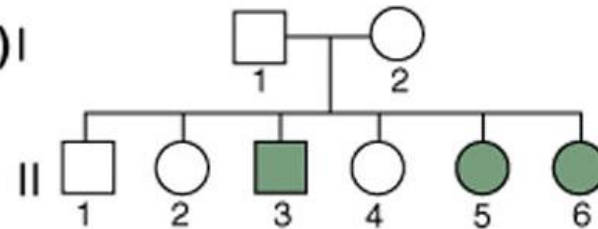
Woody inherited HD from his mother and passed it on to two of his children.

A **horizontal** pattern of inheritance indicates a rare recessive trait

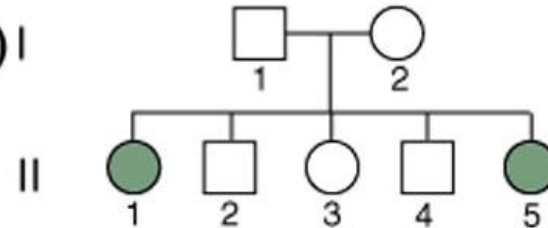
(a) I



(b) I



(c) I



Cystic fibrosis (CF): A recessive condition

囊腫性纖維化

CF, **the most commonly** inherited recessive disease among Caucasian children in the US. **One in every 2000** white Americans is born with CF

A fatal and incurable disorder in which the lungs, pancreases, intestines and other organs become clogged with a viscous mucus that interfere with breathing and digestion

粘液

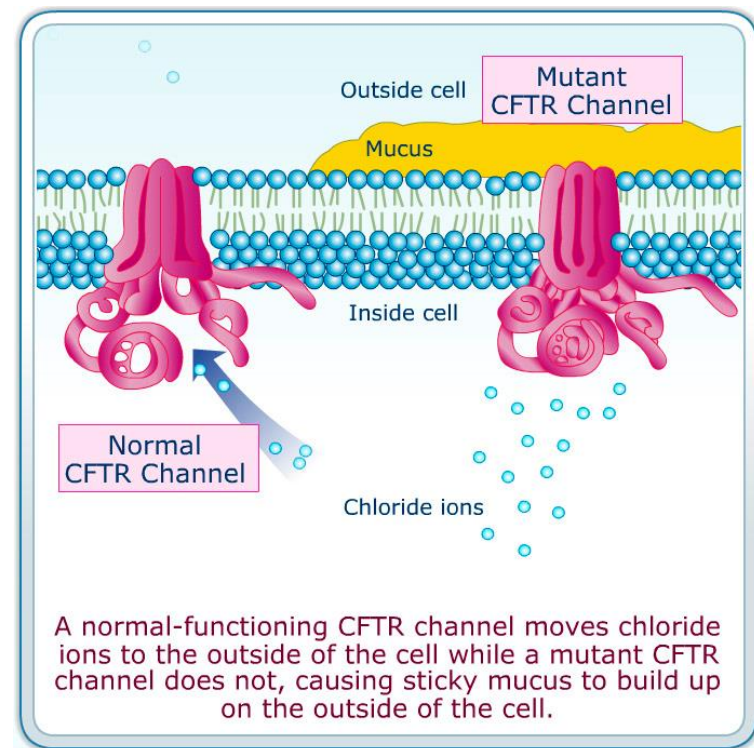


TABLE 2.1 Some of the Most Common Single-Gene Traits in Humans

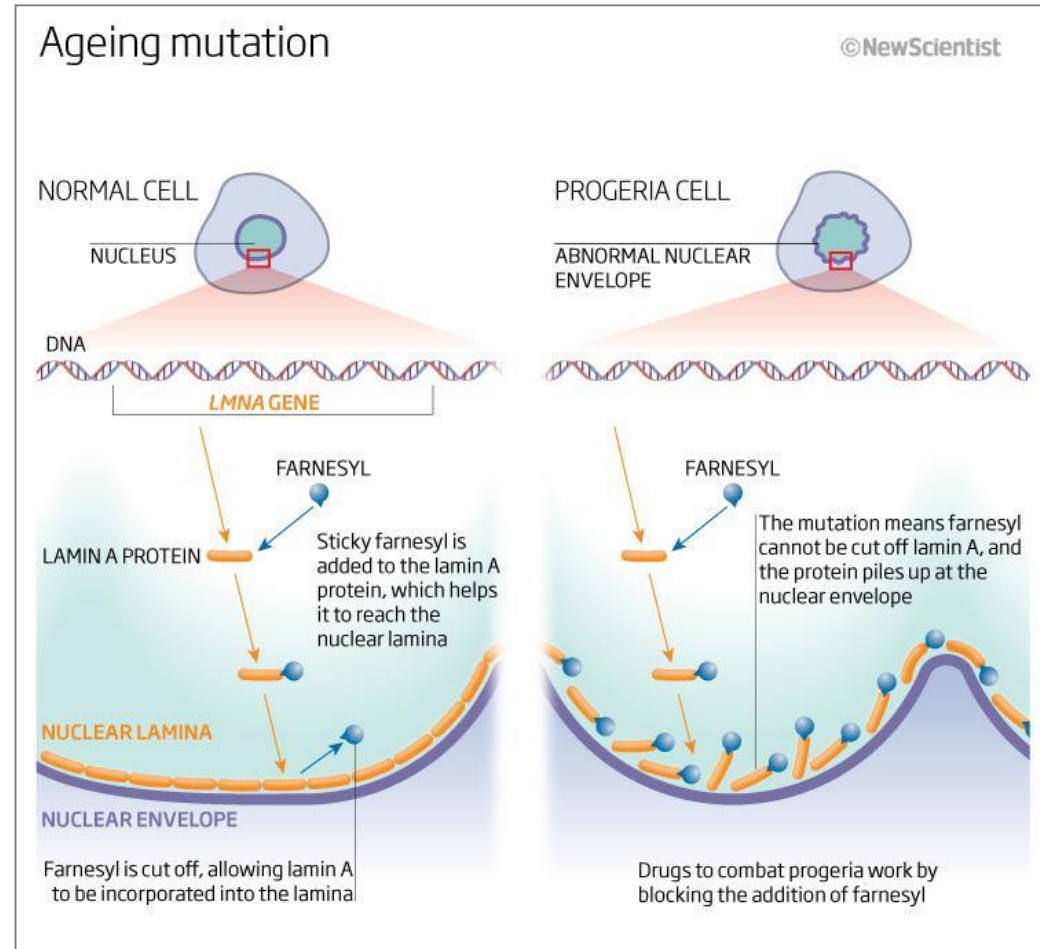
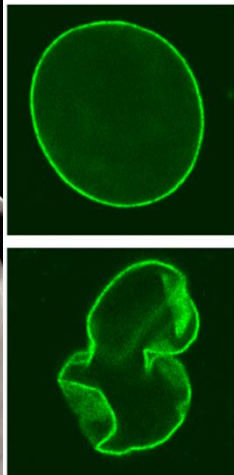
Disease	Effect	Incidence of Disease
<i>Caused by Recessive Allele</i>		
Thalassemia (chromosome 16 or 11)	Reduced amounts of hemoglobin; anemia, bone and spleen enlargement	1/10 in parts of Italy
Sickle-cell anemia (chromosome 11)	Abnormal hemoglobin; sickle-shaped red cells, anemia, blocked circulation; increased resistance to malaria	1/625 African-Americans
Cystic fibrosis (chromosome 7)	Defective cell membrane protein; excessive mucus production; digestive and respiratory failure	1/2000 Caucasians
Tay-Sachs disease (chromosome 15)	Missing enzyme; buildup of fatty deposit in brain; buildup destroys mental development	1/3000 Eastern European Jews
Phenylketonuria (PKU) (chromosome 12)	Missing enzyme; mental deficiency	1/10,000 Caucasians
Albinism (chromosome 11)	Missing enzyme; unpigmented skin, hair, and eyes	1/10,000 in Northern Ireland
<i>Caused by Dominant Allele</i>		
Hypercholesterolemia (chromosome 19)	Missing protein that removes cholesterol from the blood; heart attack by age 50	1/122 French Canadians
Huntington disease (chromosome 4)	Progressive mental and neurological damage; neurologic disorders by ages 40–70	1/25,000 Caucasians

Online Mendelian Inheritance in Man (OMIM)

人类孟德尔遗传在线

<http://www.ncbi.nlm.nih.gov/Omim>

Progeria – too young to be old

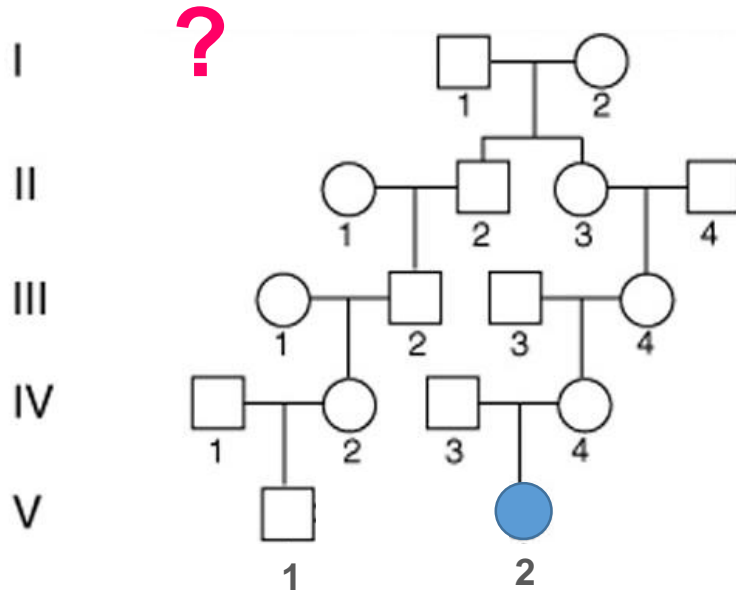


Progeria: an extremely rare genetic disorder with premature aging symptoms
there is no known cure, few people with progeria exceed 13 years of age.

Cause: mutations in the *LMNA* gene lead to failure to remove a farnesyl group and permanent affixation of the Lamin A protein to the nuclear rim.

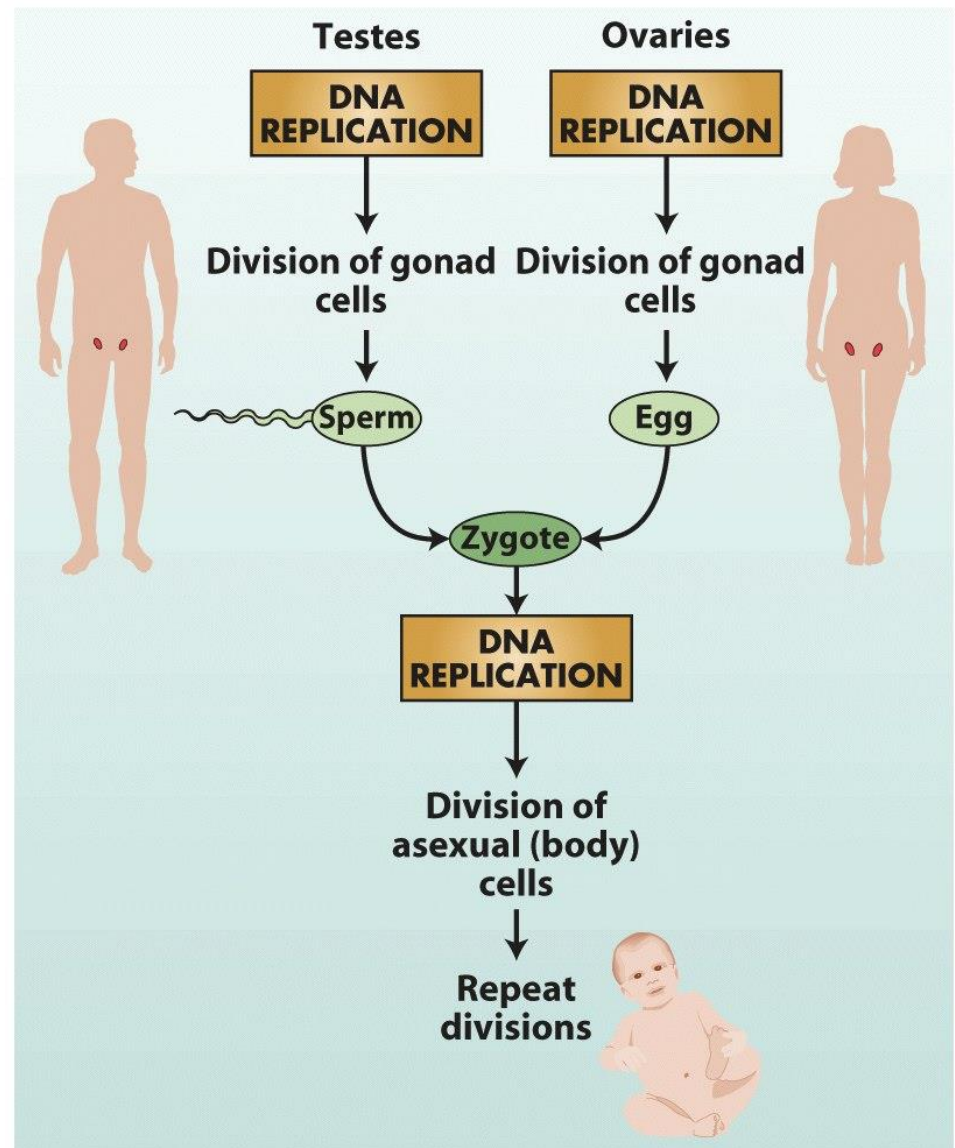
Progeria – a puzzling pedigree

dominant trait, however...



A de novo dominant trait!

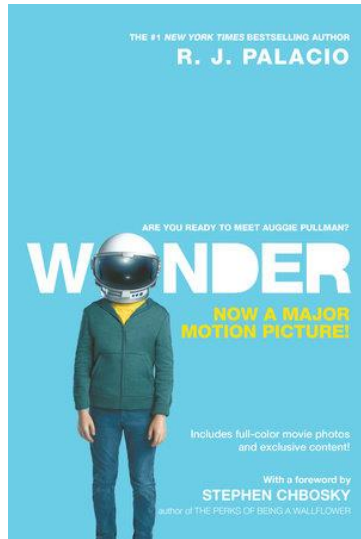
Mutation occurs during cell division in a newly conceived zygote or in the gametes of one of the parents



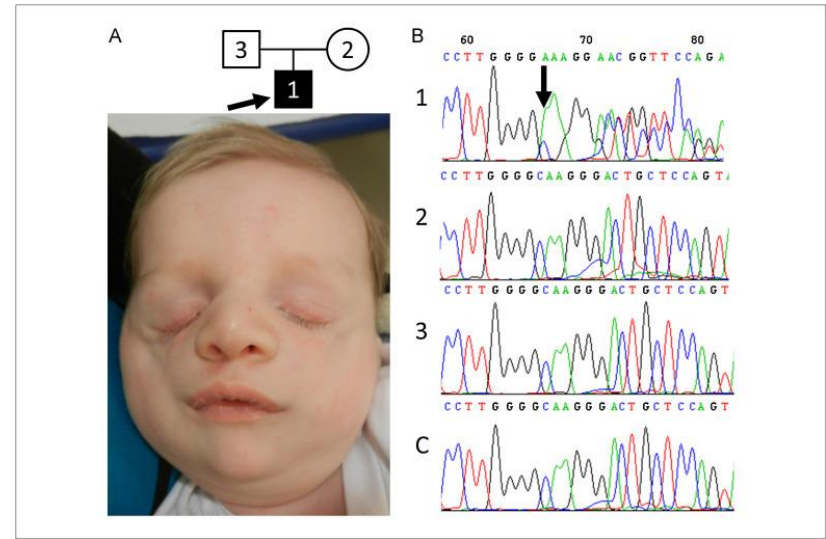
Another puzzling pedigree



2012



2017



with facial birth defects

(Marszałek-Kruk BA, et al., 2014)

Treacher Collins syndrome (TCS) – a disorder of craniofacial development. It is mostly caused by mutations in the TCOF1 gene, which is located on chromosome 5 and encodes the serine/alanine-rich protein Treacle.

A de novo dominant mutation!

Chapter I

Mendel's Law of Inheritance

I. Mendel's breakthrough

Patterns, particles, and principles of heredity

II. Extension to Mendel's laws

Complexities in relating genotype to phenotype

- 1. Single-gene inheritance**
- 2. Multifactorial inheritance**

Chapters in reference books: [H2-H3](#), [D4](#)

II. Outline of Extensions to Mendel's Analysis

1. Single-gene inheritance

- Pairs of alleles show deviations from complete dominance and recessiveness
- Different forms of the gene are not limited to two alleles
- One gene may determine more than one trait

2. Multifactorial inheritance

The phenotype arises from the interaction of one or more genes with the environment, chance, and each other

II.1. Extensions to Mendel for Single-gene inheritance

Incomplete dominance

不完全显性

Codominance

共显性

Multiple alleles

复等位基因

Pleiotropy

基因多效性

Key Words

incomplete dominance (不完全显性)

codominance (共显性/并显性)

multiple alleles (复等位基因)

pleiotropy, pleiotropism (基因多效性)

allele frequency (等位基因频率)

monomorphic (单型的/单态的)

polymorphic (多型的/多态的)

wild type (野生型)

mutant (突变型/突变体)

carrier (携带者)

lethality (致死性)

recessive lethal allele (隐性致死基因)

Dominance is not always complete

Crosses between true-breeding strains can produce hybrids with phenotypes different from both parents













Incomplete dominance

- F_1 hybrids that differ from both parents express an **intermediate** phenotype. Neither allele is dominant or recessive to the other.
- Phenotypic ratios are same as genotypic ratios.

Codominance

- F_1 hybrids express phenotype of **both** parents **equally**.
- Phenotypic ratios are same as genotypic ratios.

Summary of dominance relationships

Type of dominance	A^1/A^1	A^2/A^2	A^1/A^2 hybrids	
Complete				A^1 is dominant to A^2 A^2 is recessive to A^1
Complete				A^2 is dominant to A^1 A^1 is recessive to A^2
Incomplete				A^1 and A^2 are incompletely dominant relative to each other
Codominant				A^1 and A^2 are codominant relative to each other

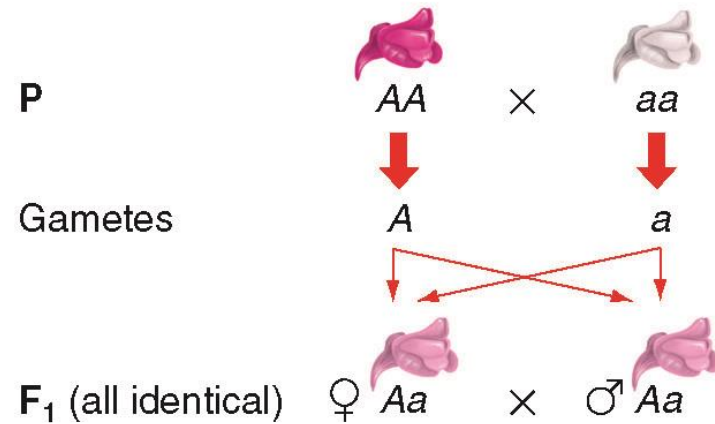
Incomplete dominance in snapdragons

金鱼草

(a) *Antirrhinum majus* (snapdragons)



(b) A Punnett square for incomplete dominance



Blending theory?

Incomplete
dominance
(不完全显性)

Incomplete dominance in horses

Cremello horse

C^{cr}/C^{cr}



Palomino horse

C/C^{cr}



Light chestnut horse

C/C



**Incomplete
dominance**
(不完全显性)

II.1. Extensions to Mendel for Single-gene inheritance

Incomplete dominance

不完全显性

Codominance

共显性

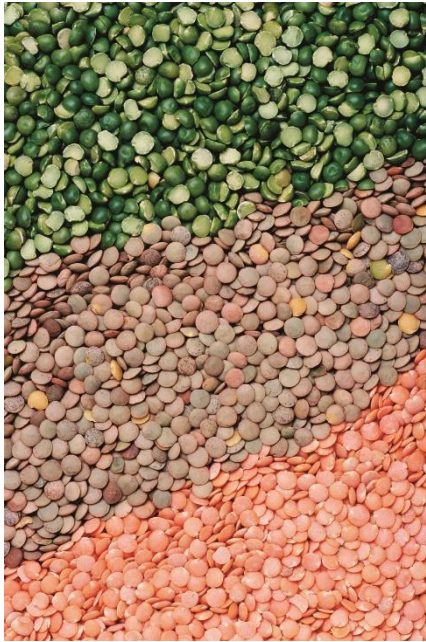
Multiple alleles

复等位基因

Pleiotropy

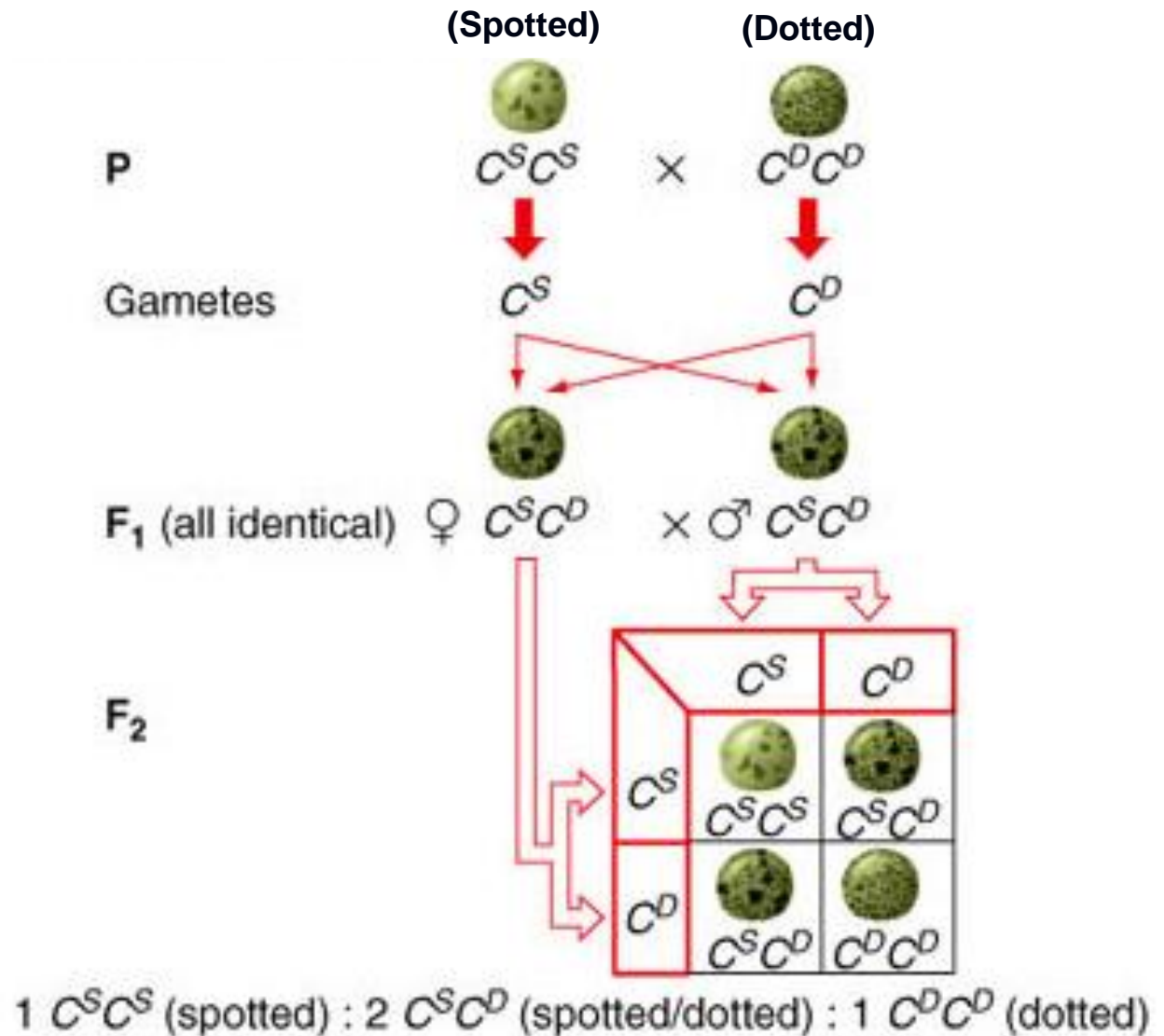
基因多效性

Codominant lentil coat patterns

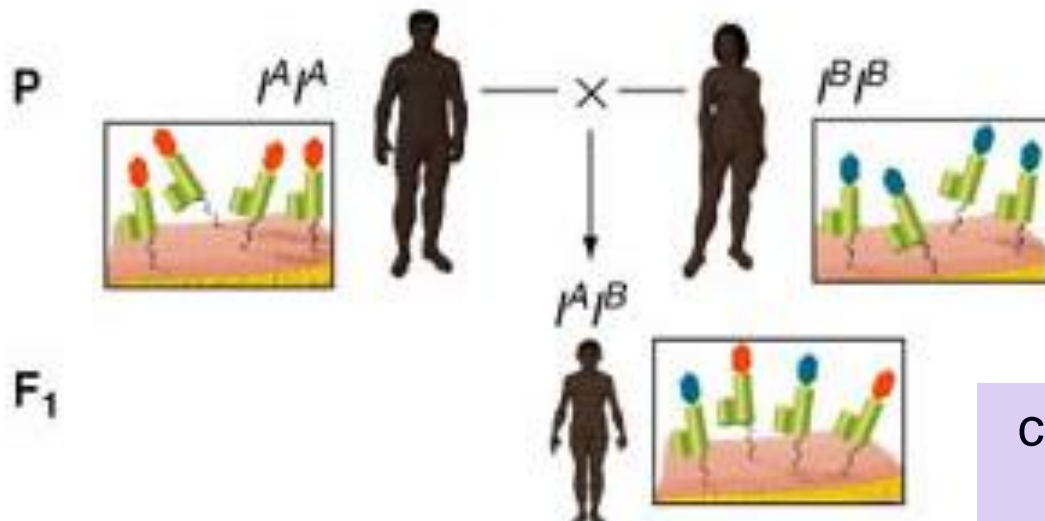
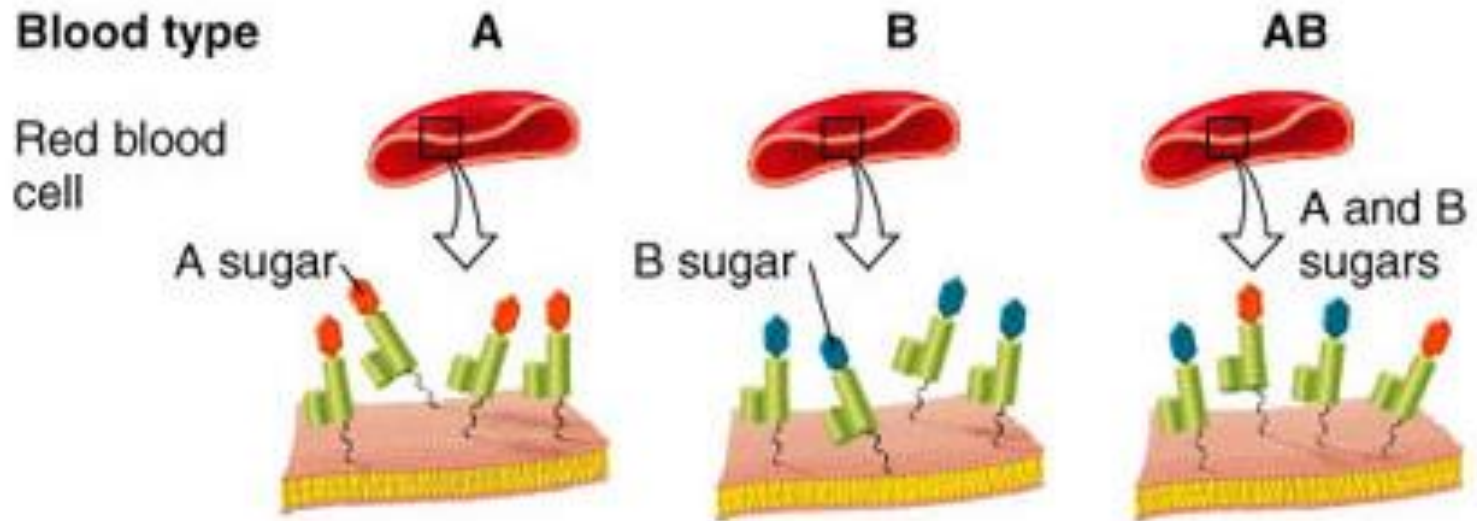


lentil (小扁豆)

Codominance
(共显性)



Codominant blood group alleles



codominance
(共显性)

Do variations on dominance relations negate Mendel's law of segregation?

- Dominance relations affect phenotype and **have no bearing on the segregation of alleles.**
- Alleles still segregate randomly.
- Gene products control expression of phenotypes differently.
- Mendel's law of segregation still applies.
- **Interpretation** of phenotype/genotype relation is **more complex.**

II.1. Extensions to Mendel for Single-gene inheritance

Incomplete dominance

不完全显性

Codominance

共显性

Multiple alleles

复等位基因

Pleiotropy

基因多效性

A gene can have more than two alleles

1. Genes may have **multiple alleles** that segregate in populations.
2. Although there may be many alleles in a **population**, **each individual carries only 2 of the alternatives.**
 - ABO blood group
 - 3 alleles
 - 6 possible ABO genotypes: $I^A I^A$, $I^B I^B$, $I^A I^B$, $I^A i$, $I^B i$, or ii
3. Dominance relations are **unique to a pair of alleles.**
 - Dominance or recessiveness is always **relative** to a second allele.
 - ABO blood group
 - I^A is completely dominant to i but codominant to I^B .
 - 6 genotypes generate 4 phenotypes.

multiple alleles
(复等位基因)

Human ABO Blood Group

(a)

Genotypes	Corresponding Phenotypes: Type(s) of Molecule on Cell
$I^A I^A$ $I^A i$	A
$I^B I^B$ $I^B i$	B
$I^A I^B$	AB
ii	O

(b)

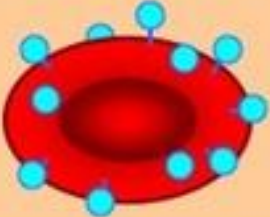






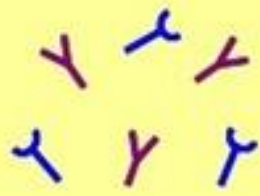
Blood Type	Antibodies in Serum
A	Antibodies against B
B	Antibodies against A
AB	No antibodies against A or B
O	Antibodies against A and B

(c)

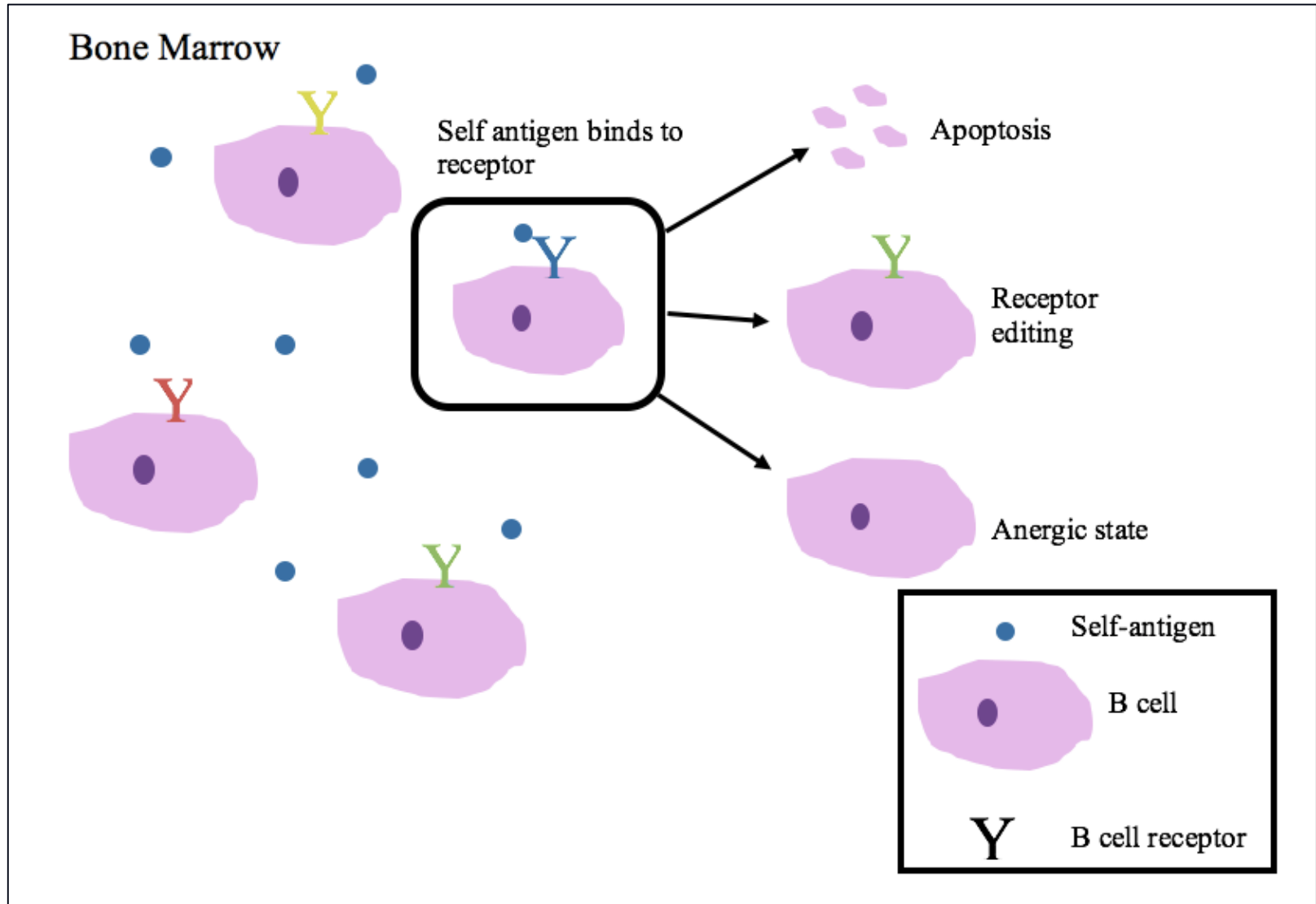
Blood Type of Recipient	Donor Blood Type (Red Cells)			
	A	B	AB	O
A	+	—	—	+
B	—	+	—	+
AB	+	+	+	+
O	—	—	—	+

multiple alleles
(复等位基因)

Human ABO Blood Group

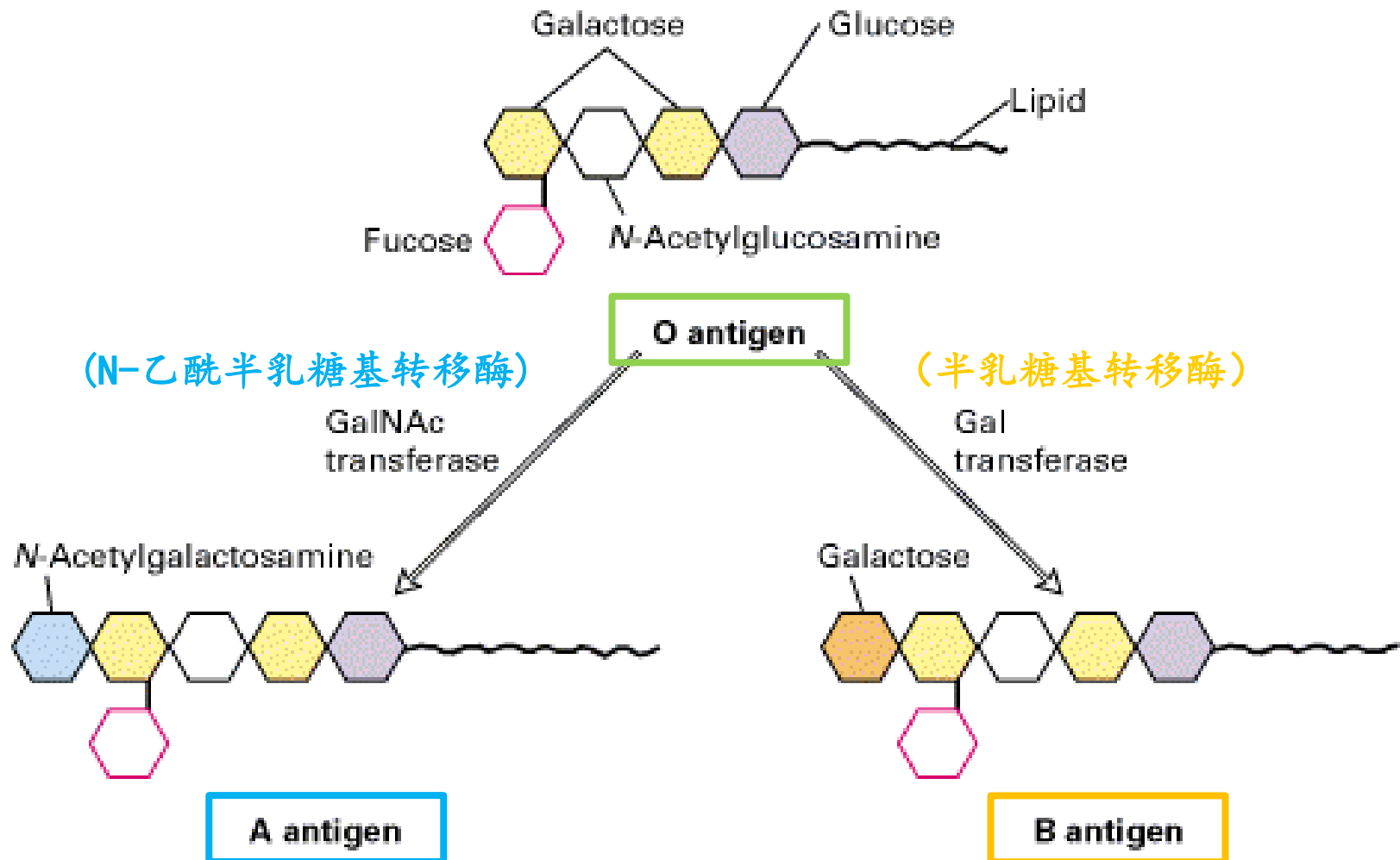
ABO Blood Groups				
Antigen (on RBC)	Antigen A 	Antigen B 	Antigens A + B 	Neither A or B 
Antibody (in plasma)	Anti-B Antibody 	Anti-A Antibody 	Neither Antibody 	Both Antibodies 
Blood Type	Type A Cannot have B or AB blood Can have A or O blood	Type B Cannot have A or AB blood Can have B or O blood	Type AB Can have any type of blood Is the universal recipient	Type O Can only have O blood Is the universal donor

B cell tolerance

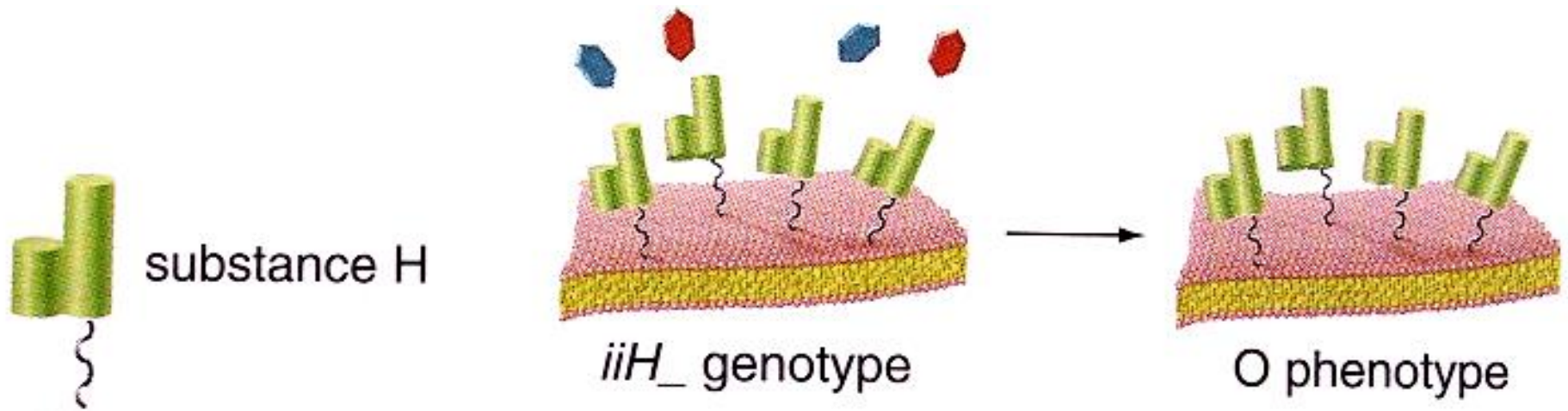


ABO blood type at the molecular level

Enzymes add sugar A or sugar B to a base consisting of a sugar polymer known as **substance H**, resulting in antigen A or antigen B respectively



ABO blood type



Blood type

A

B

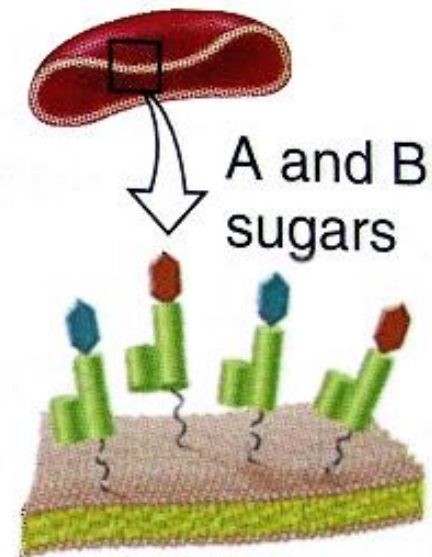
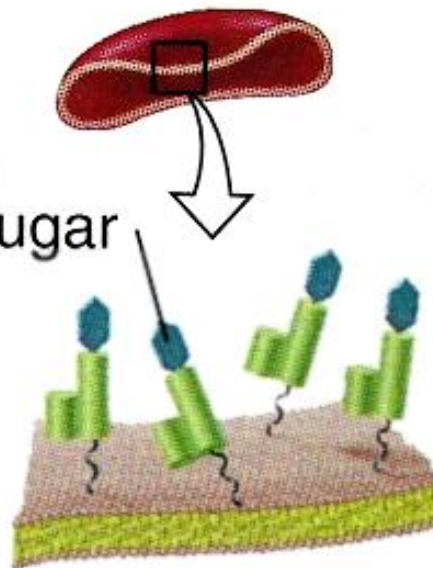
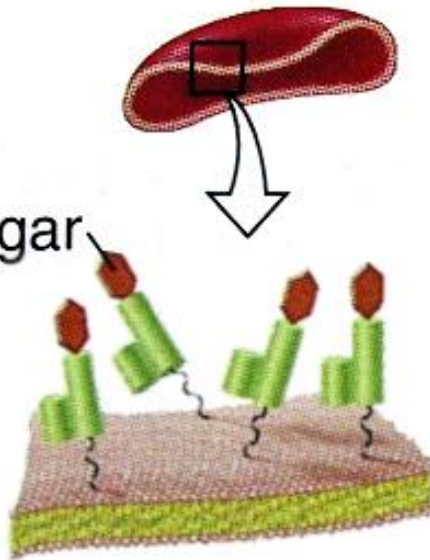
AB

Red blood cell

A sugar

B sugar

A and B sugars






















































Genetic inheritance of ABO blood type

Parental blood types	Parental genotypes	Child's possible blood type
A × A	$I^A I^A$ or $I^A i$	A, O
A × O	$I^A I^A$ or $I^A i \times ii$	A, O
? A × B		
A × AB	$I^A I^A$ or $I^A i \times I^A I^B$	A, B, AB
B × B	$I^B I^B$ or $I^B i$	B, O
B × O	$I^B I^B$ or $I^B i \times ii$	B, O
B × AB	$I^B I^B$ or $I^B i \times I^A I^B$	A, B, AB
AB × O	$I^A I^B \times ii$	A, B
AB × AB	$I^A I^B$	A, B, AB
O × O	ii	O

How do we establish dominance relations between multiple alleles?

Perform reciprocal crosses between pure breeding lines of all phenotypes.

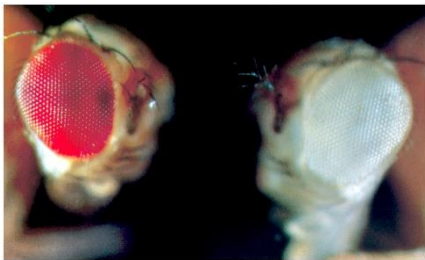
Parental Generation Parental seed coat pattern in cross Parent 1 × Parent 2	F ₁ Generation F ₁ phenotype	F ₂ Generation Total F ₂ frequencies and phenotypes	Apparent pheno- typic ratio
 × 		 798  296	3 : 1
 × 		 123  46	3 : 1
 × 		 283  107	3 : 1
 × 		 1,706  522	3 : 1
 × 		 272  72	3 : 1
 × 		 499  147	3 : 1
 × 		 1,597  549	3 : 1
 × 		 182  70	3 : 1
 × 		 168  339  157	1 : 2 : 1
    			
Dominance series: marbled-1 > marbled-2 > spotted = dotted > clear			

multiple alleles
(复等位基因)

The eye color of *Drosophila*

1910, Thomas H. Morgan identified a white male fly.

The *white* gene contains more than 100 alleles.



white⁺



white^{eosin}



white^{cherry}



white^{apricot}



*white*¹

multiple alleles
(复等位基因)

Some were named after fruits

Mutations are the source of new alleles

- Multiple alleles arise spontaneously in nature due to chance alterations in genetic material — **mutations**.
- Mutation rate varies from 1 in 10,000 to 1 in 1,000,000 per gamete per generation.
- **Allele frequency** is the percentage of the total number of gene copies represented by one allele.
- **Wild-type allele** — the most common allele in a population
- **Mutant allele** — a rare allele in the same population
- **Monomorphic** — gene with only one common, wild-type allele
- **Polymorphic** — gene with more than one common allele

II.1. Extensions to Mendel for Single-gene inheritance

Incomplete dominance

不完全显性

Codominance

共显性

Multiple alleles

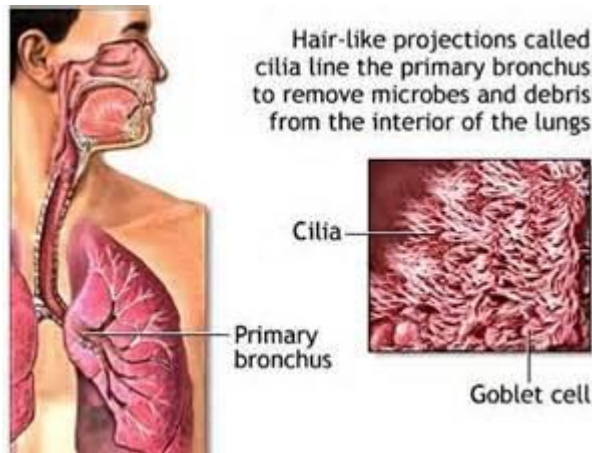
复等位基因

Pleiotropy

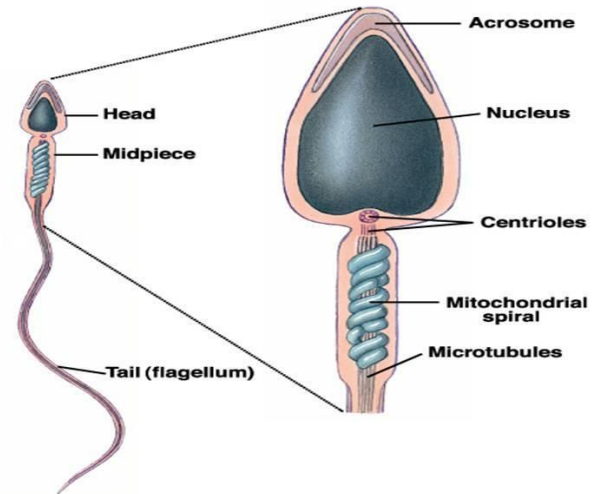
基因多效性

One gene may contribute to several visible characteristics

- **Pleiotropy** - A single gene determines more than one distinct and seemingly unrelated characteristic
- Each protein can have a **cascade of effects** on an organism

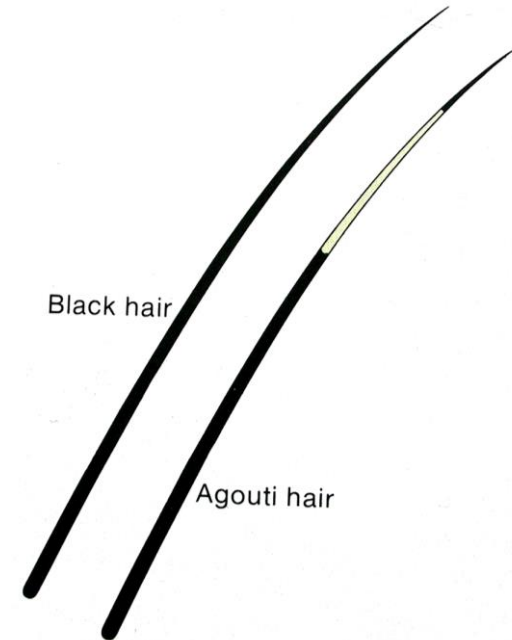


Respiratory problems



Sterile

Coat color in mice



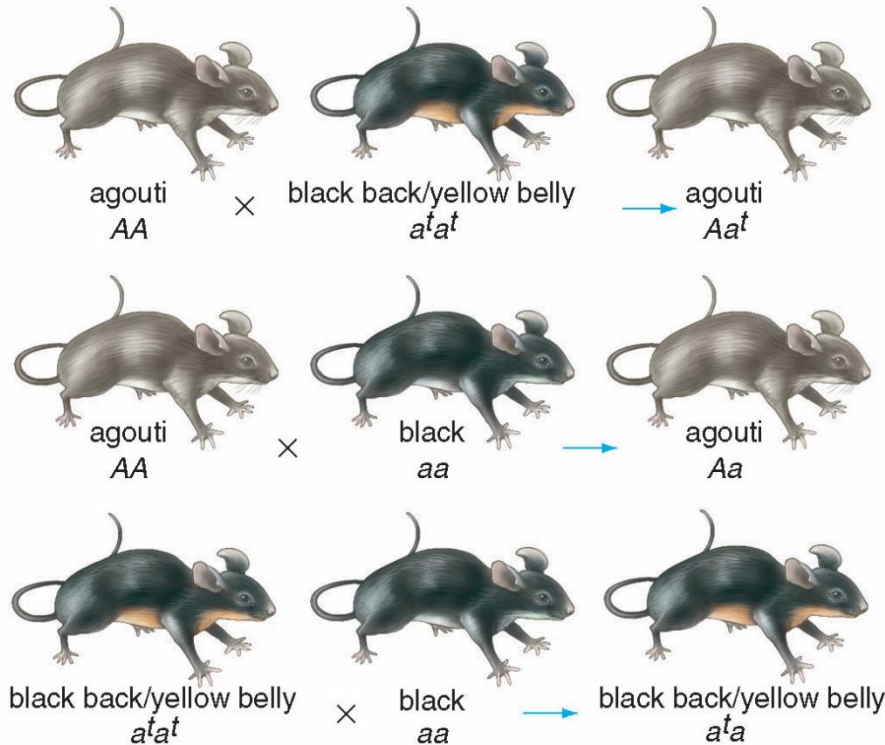
Inheritance of coat color in mice

(b) Alleles of the *agouti* gene

Genotype Phenotype

$A-$	agouti
$a^t a^t$	black/yellow
aa	black
$a^t a$	black/yellow

(c) Evidence for a dominance series



Dominance series: $A > a^t > a$

Dominance series:

$A > a^t > a$

A puzzling result

Cross A

agouti \times agouti \rightarrow all agouti

$AA \times AA \rightarrow AA$

Cross B

yellow \times yellow \rightarrow $\frac{2}{3}$ yellow : $\frac{1}{3}$ agouti

$A^Y A \times A^Y A \rightarrow A^Y A^Y : A^Y A : AA = 1:2:1$

Cross C

agouti \times yellow \rightarrow $\frac{1}{2}$ yellow : $\frac{1}{2}$ agouti

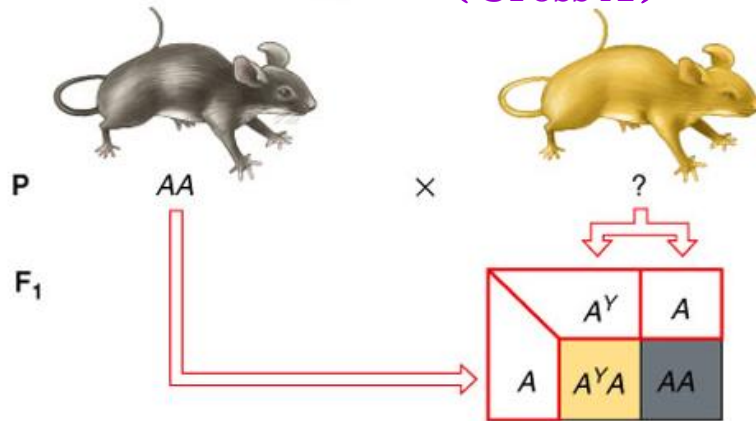
$AA \times A^Y A \rightarrow A^Y A : AA = 1:1$



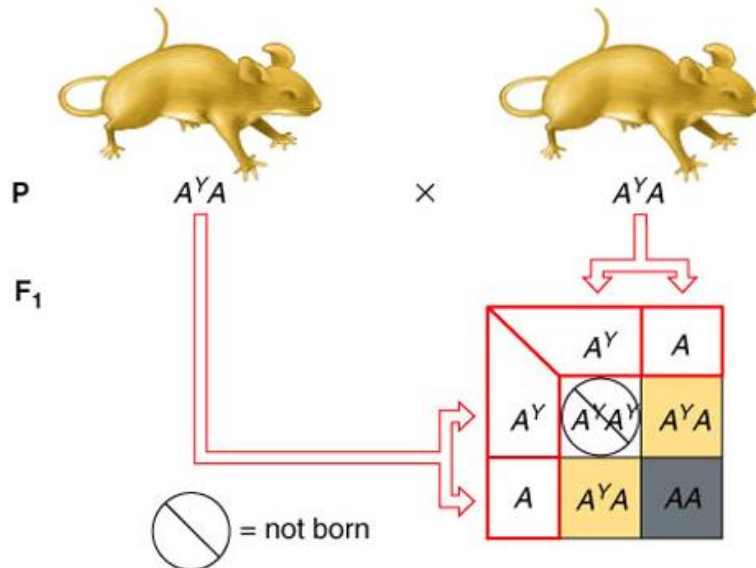
?

Pleiotropy - inheritance of coat color in mice

(a) All yellow mice are heterozygotes. (Cross A)



(b) Two copies of A^Y cause lethality. (Cross B)



A. Inbred agouti and yellow yields 1 agouti : 1 yellow

- Yellow must be $A^Y A$, and A^Y is **dominant** to A

B. yellow × yellow mice do not breed true.

- A^Y is **recessive lethal**!
 $A^Y A^Y$ die *in utero* and do not show up as progeny.

Dominance and recessiveness are defined in the context of each pair of alleles

One gene may contribute to several visible characteristics

- **Pleiotropy** - A single gene determines more than one distinct and seemingly unrelated characteristic
- Each protein can have a **cascade of effects** on an organism
- Some alleles may cause **lethality**
 - Type of pleiotropy where alleles produce a visible phenotype and affect viability
 - Alleles that affect viability often produce **deviations from a 1:2:1 genotypic and 3:1 phenotypic ratio** predicted by Mendel's Laws.

Summary on extensions to Mendel for single-gene inheritance

TABLE 3.1 For Traits Determined by One Gene: Extensions to Mendel's Analysis Explain Alterations of the 3:1 Monohybrid Ratio

What Mendel Described	Extension	Extension's Effect on Heterozygous Phenotype	Extension's Effect on Ratios Resulting from an $F_1 \times F_1$ Cross
Complete dominance	Incomplete dominance Codominance	Unlike either homozygote	Phenotypes coincide with genotypes in a ratio of 1:2:1
Two alleles	Multiple alleles	Multiplicity of phenotypes	A series of 3:1 ratios
All alleles are equally viable	Recessive lethal alleles	No effect	2:1 instead of 3:1
One gene determines one trait	Pleiotropy: one gene influences several traits	Several traits affected in different ways, depending on dominance relations	Different ratios, depending on dominance relations for each affected trait

Sickle-Cell Anemia

镰形细胞贫血症

Multiple alleles (*b* *globin*)

- Normal wild-type is *Hbb^A*
- More than 400 mutant alleles identified so far
- *Hbb^S* allele specifies abnormal peptide causing sickling among red blood cells.

Pleiotropy

- *Hbb^S* affects more than one trait.
 - Sickling
 - Resistance to malaria
 - Recessive lethality

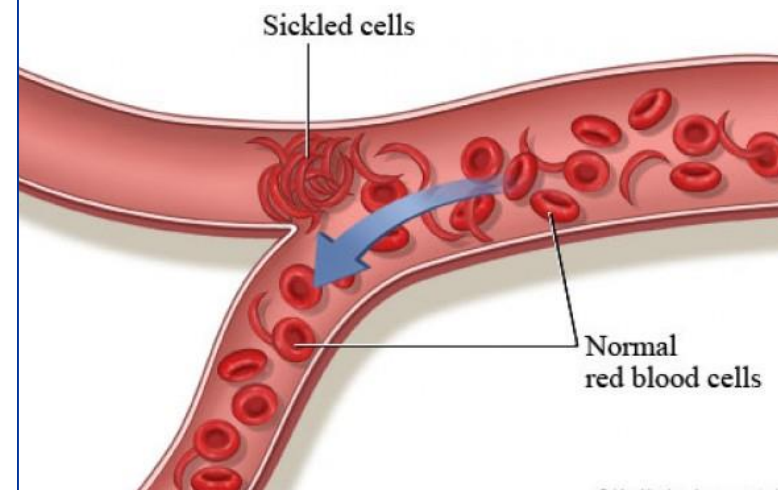
Different dominance relations

1. Clog the small blood vessels

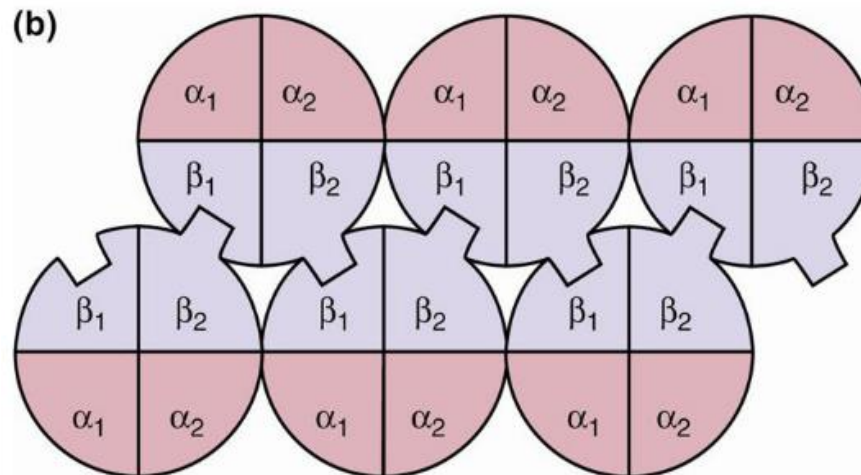
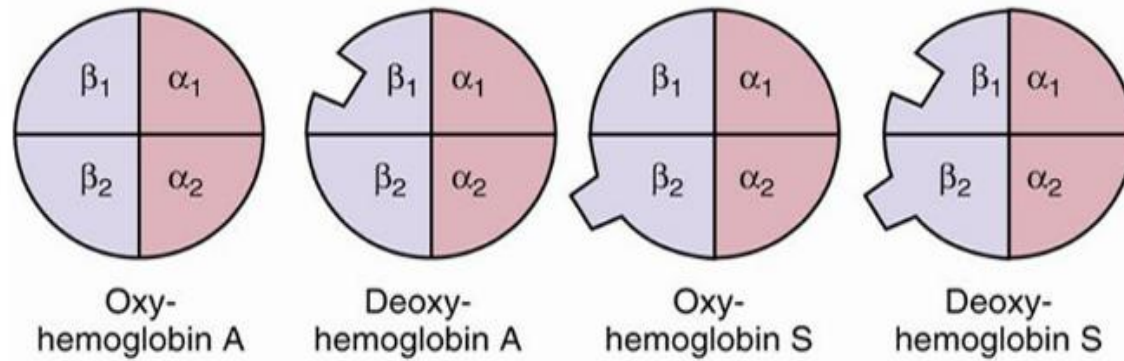
→ Shortness of breath, muscle cramps, fatigue

2. Very fragile, easily broken

→ Anemia



Oxygen and hemoglobin S polymerization



Mechanism of Sickle Cell Disease

Polymerization of Deoxygenated Sickle Hemoglobin (HbS)



Sickling of Red Blood Cell



Normal Red Blood Cells


















Sickle Cells





















The polymerization of deoxygenated sickle hemoglobin (HbS) is the primary event in the molecular pathogenesis of sickle cell disease, resulting in a deformity of the red blood cell and a marked decrease in its ability to pass through the microvasculature.

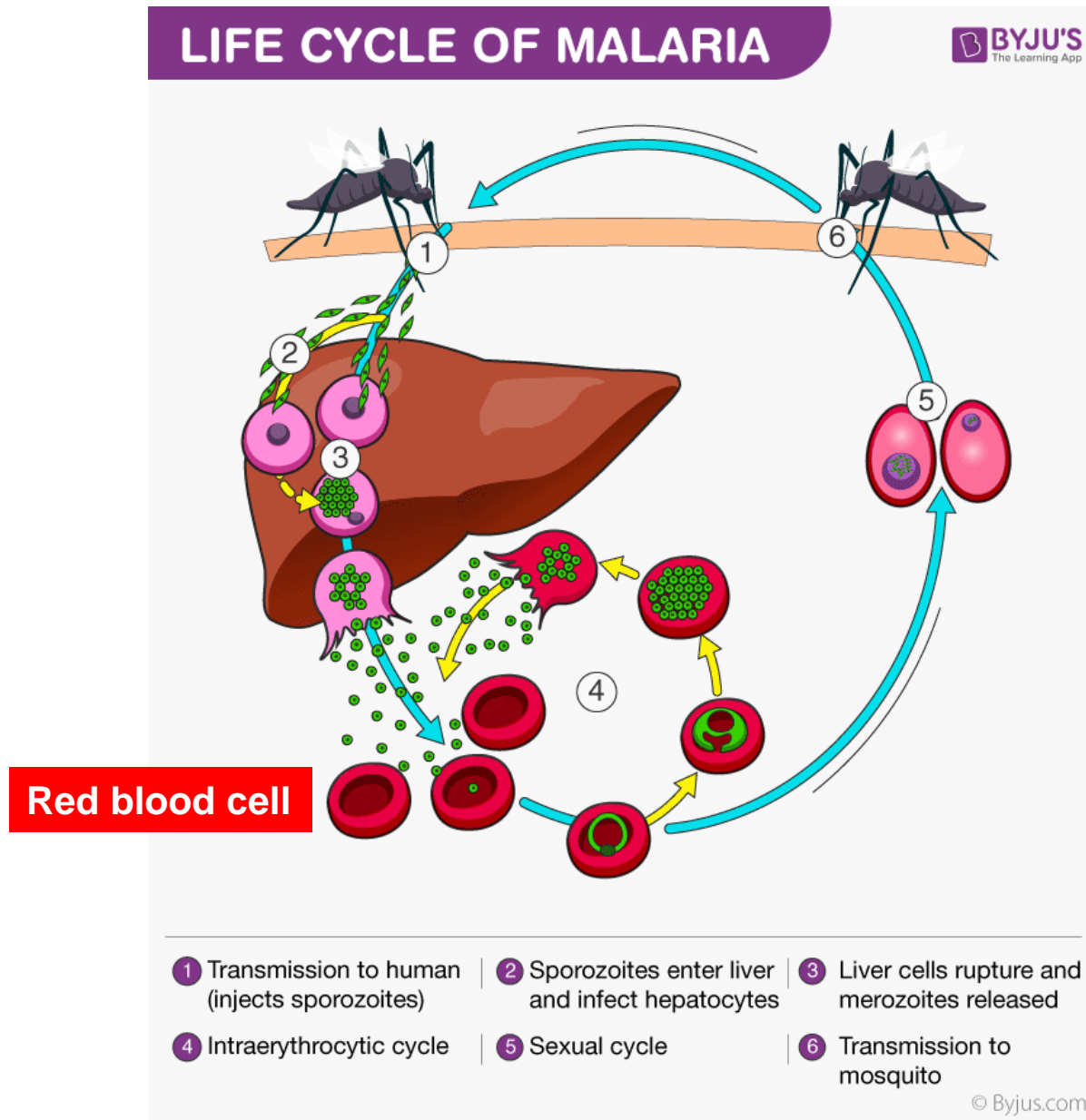
Pleiotropy of Sickle-cell syndrome

Phenotypes at Different Levels of Analysis	Normal AA	Carrier AS	Diseased SS	Dominance Relations at Each Level of Analysis
β -globin polypeptide production 珠蛋白				A and S are codominant
Malaria parasite cause sickle-shaped blood cells to break down before the malaria organism has a chance to multiply				
Red blood cell concentration at sea level	Normal 	Normal 	Lower 	S is recessive
Red blood cell shape at high altitudes	Normal 	Sickled cells present 	Severe sickling 	A and S show incomplete dominance
Red blood cell concentration at high altitudes	Normal 	Lower 	Very low, anemia 	
Susceptibility to malaria	Normal susceptibility 	Resistant 	Resistant 	S is dominant A is recessive

Pleiotropy of Sickle-cell syndrome

Phenotypes at Different Levels of Analysis	Normal AA	Carrier AS	Diseased SS	Dominance Relations at Each Level of Analysis
β -globin polypeptide production β 珠蛋白				A and S are codominant
Red blood cell shape at sea level	Normal 	Normal 	Sickled cells present 	A is dominant S is recessive
Red blood cell concentration at sea level	Normal 	Normal 	Lower 	
Red blood cell shape at high altitudes	Normal 	Sickled cells present 	Severe sickling 	A and S show incomplete dominance
Red blood cell concentration at high altitudes	Normal 	Lower 	Very low, anemia 	
Susceptibility to malaria	Normal susceptibility 	Resistant 	Resistant 	S is dominant A is recessive

Life cycle of malaria parasites



Chapter I

Mendel's Law of Inheritance

I. Mendel's breakthrough

Patterns, particles, and principles of heredity

II. Extension to Mendel's laws

Complexities in relating genotype to phenotype

- 1. Single-gene inheritance**
- 2. Multifactorial inheritance**

Chapters in reference books: [H2-H3](#), [D3](#)

Cross A

P₁

$AA \times AA$
agouti × agouti



F₁

AA
agouti



all agouti
(All survive)

Cross B

$AA^Y \times AA^Y$
yellow × yellow



AA agouti	AA^Y yellow
$A^Y A$ yellow	$A^Y A^Y$ lethal



2/3 yellow
1/3 agouti
(Survivors)

Cross C

$AA \times AA^Y$
agouti × yellow



AA AA^Y
agouti yellow



1/2 agouti
1/2 yellow
(All survive)

Syllable

Chapter	Title	Related chapters	Teaching faculty
Introduction	Genetics: the study of biology information	H1, H6, H8, D1-D2	宋 艳
Chapter 1	Mendel's laws of inheritance	H2-H3, D3	宋 艳
Chapter 2	The chromosome theory of inheritance and linkage analysis	H4-H5, D2, D4, D7	宋 艳
Chapter 3	The concepts of gene and mutation	H6-H8, H19, D2, D11, D13, D16	宋 艳
Chapter 4	Chromosome aberration	H11-H12, D12	宋 艳
Lecture	Comprehensive application of genetics	H17	宋 艳
Chapter 5	Genome analysis	H9-H10, D10	陆 剑
Chapter 6	Genetic analysis in prokaryotes	H14, H15, D7, D9, D14	陆 剑
Chapter 7	Genetic analysis in eukaryotes	H16, H18, D5, D16	陆 剑
Chapter 8	Epigenetic analysis	H16, D15	陆 剑
Chapter 9	Human disease and genetics	D9	陆 剑
Chapter 10	The genetic analysis of population and evolution	H20-H21, D19	陆 剑