Bio393: Genetic Analysis

Dr. Erik Andersen
Stefan Zdraljevic (TA)

Lectures: Tues. and Thurs. 9:30-10:50 AM Tech LG68

Discussion: Fri. 9-10:50 AM Tech M120

Please take the introductory survey on the course website

bio393.andersenlab.org/

bio393.andersenlab.org

Date	Topic
April 5	Mendelian Inheritance, Basic probability, PS#1 out
April 7	Chromosome theory, mitosis, and meiosis
April 8	Recombination and mapping
April 12	Screens, selections, mutants, and dosage
April 14	Complementation
April 15	**QUIZ #1**, Genetic interactions: epistasis
April 19	Genetic interactions: enhancement and suppression
April 21	**NO CLASS**
April 22	**PROBLEM SET #1 Due**
April 26	Principles and methods of genetic analysis I
April 28	Principles and methods of genetic analysis II
April 29	**MIDTERM EXAMINATION**

Date	Topic
May 3	Developmental genetics I, PS#2 out
May 5	Developmental genetics II
May 6	**QUIZ #2**
May 10	Behavioral genetics
May 12	Human variation and allele frequency spectrum
May 13	**PROBLEM SET #2 Due**
May 17	Pedigrees and phase, PS#3 out
May 19	Linkage mapping and LOD scores
May 20	**QUIZ #3**
May 24	Linkage disequilibrium and population structure
May 26	Complex traits and GWAS
May 27	Human genetics and the future, class discussion
May 31	**PROBLEM SET #3 Due, Quiz make-up**

FINAL, 12-2 PM Thurs, June 9

Lecture 1

Point Distribution

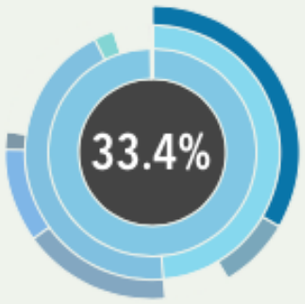
Problem sets	15%	60 points (20 points each)
Quizzes	18.75%	75 points (25 points each)
Participation	6.25%	25 points
Midterm	30%	120 points
Final	30%	120 points

Genetics is…

- not just a series of techniques.
- rapidly moving.
- transformed by cheap and quick genome sequencing.
- a necessary skill set in medicine.

Your Ancestry Composition

Here's the breakdown of your ancestry deriving from all ancestors on both sides of your family.



ITALIAN

Your Father's Line

Along your father's line, you have ancestry in Europe/the Near East in the past few hundred years, that traces back to eastern Africa around 50,000 years ago.

Famous Relative!

Warren Buffett is distantly related to you on your father's side.

Your Extended DNA Family

Guess what? If you have a large piece of identical DNA in common with someone, then you're related. You have 846 DNA relatives in 23andMe. Explore their info to learn more about your own ancestry.

Close Family	2nd & 3rd Cousins	4th Cousins	Distant Cousins
2	7	353	484

Your Mother's Line

Along your mother's line, you have ancestry in Europe/the Near East in the past few hundred years, that traces back to eastern Africa around 50,000 years ago.

Top Relative Surnames

Surname	Count	Enrichment
Tompkins	6	58

From Your Ancestry Expert

It's remarkable what you can discover from a little saliva. On this page are the highlights of what we've learned about your ancestry, based just on your DNA. Enjoy!

Dr. Joanna Mountain, PhD

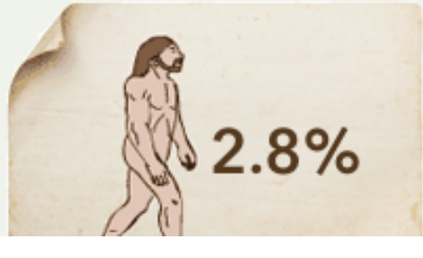
Joanna Mountain is 23andMe's Senior Director of Research. A former Stanford professor, she has traveled the world studying genetics and human history.

AS SEEN ON

Ancestry Help

Neanderthal Ancestry

You have an estimated 2.8% Neanderthal DNA, which puts you in the 68th percentile among European 23andMe members.



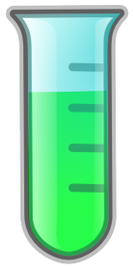
Precision Medicine Initiative (PMI)

Biological Function

Genetics

Study organisms with components removed

Biochemistry



Study components removed from the organism

Genes — **Proteins**

Molecular Biology

The father of genetics: Gregor Mendel

Mendel the genius: Choice of model organism

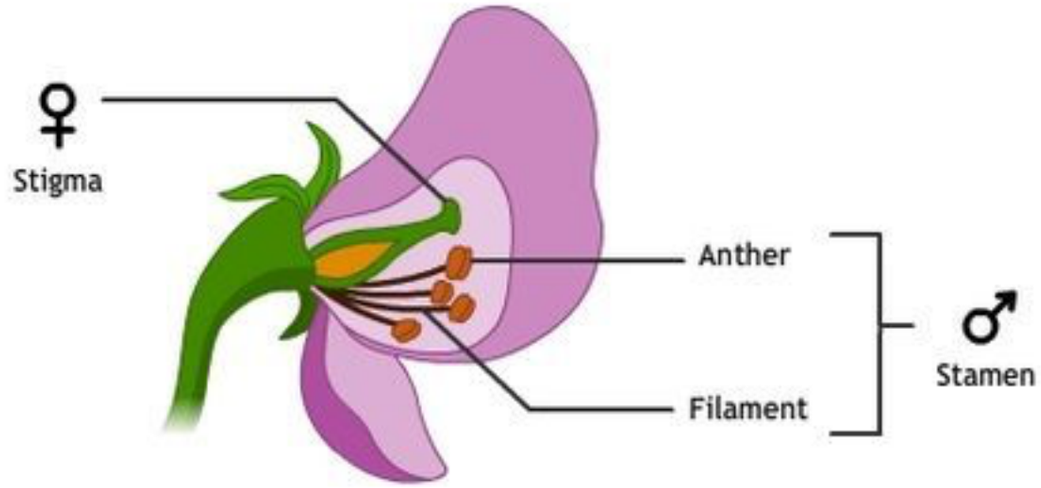
Hawkweed

Honey bees

Mice

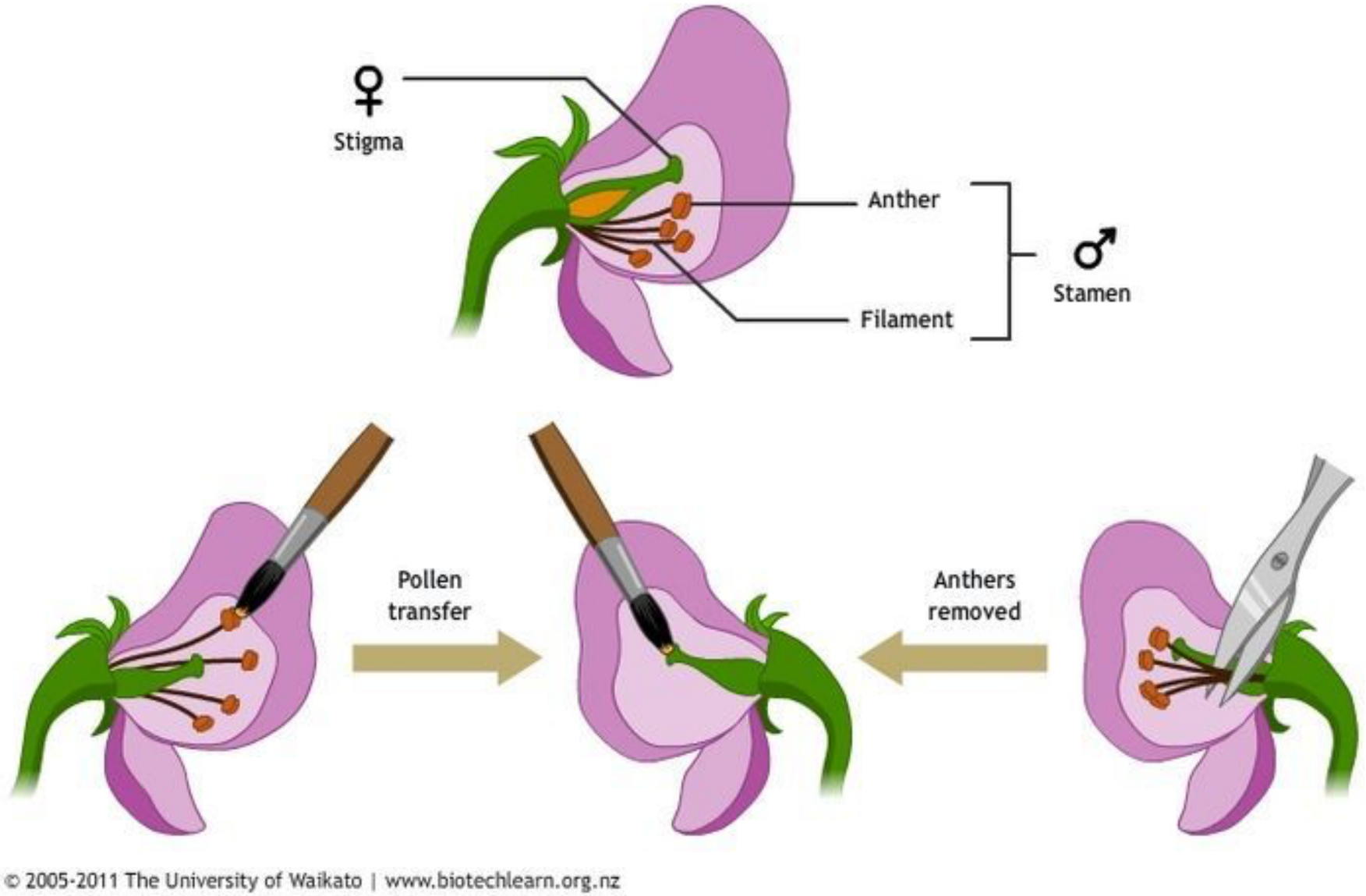
Mendel the genius: Choice of model organism

1. Control of genetic crosses



Mendel the genius: Choice of model organism

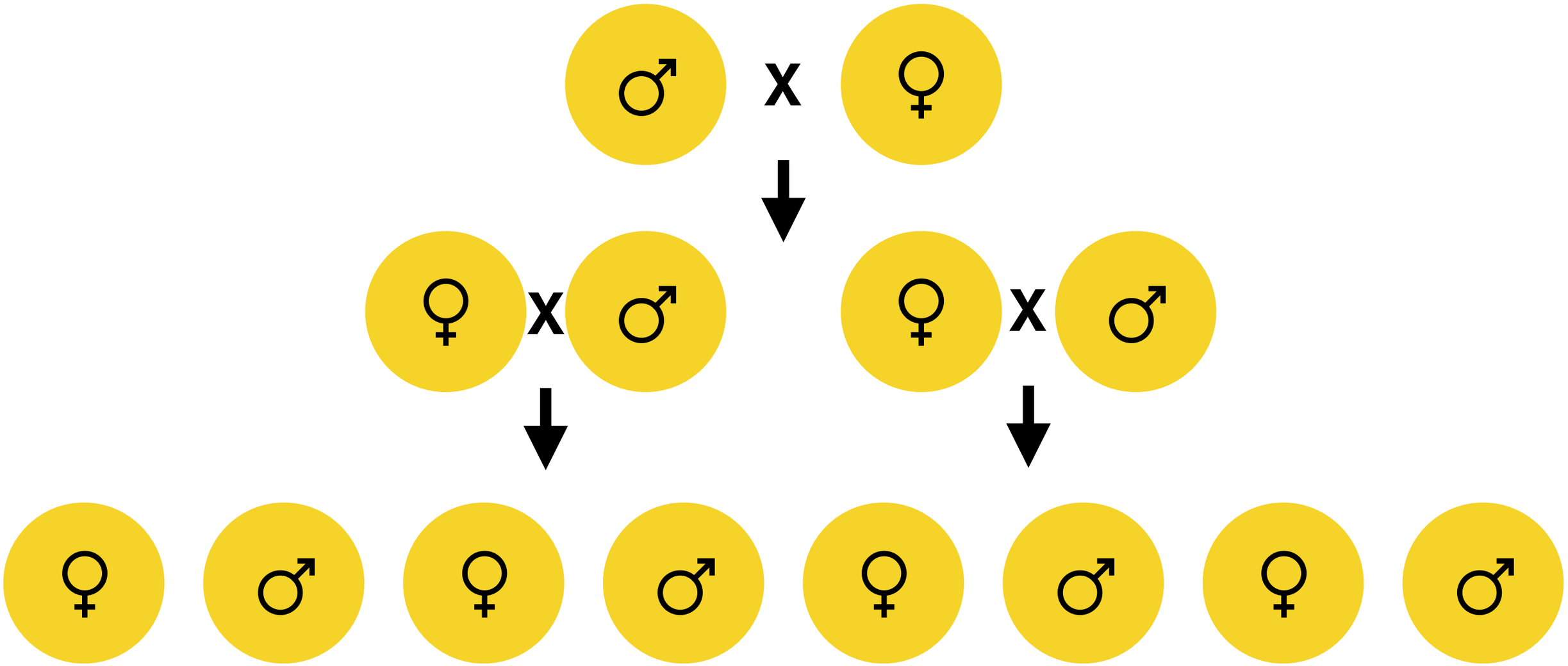
1. Control of genetic crosses



Mendel the genius: Choice of model organism

1. Control of genetic crosses

2. Reproducible true-breeding strains

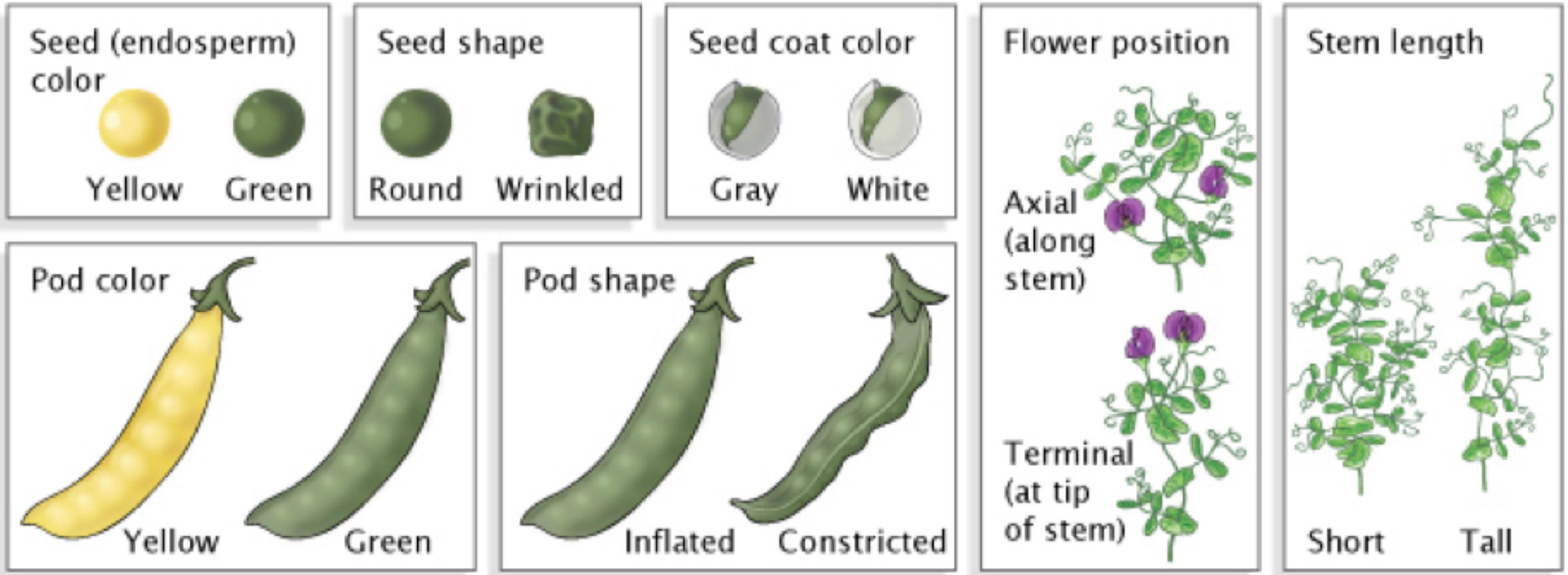


Mendel the genius: Choice of model organism

1. Control of genetic crosses

2. Reproducible true-breeding strains

3. Focus on specific traits or characters



Source of true-breeding strains

Thomas Knight

Mendel the genius: Choice of model organism

1. Control of genetic crosses

2. Reproducible true-breeding strains

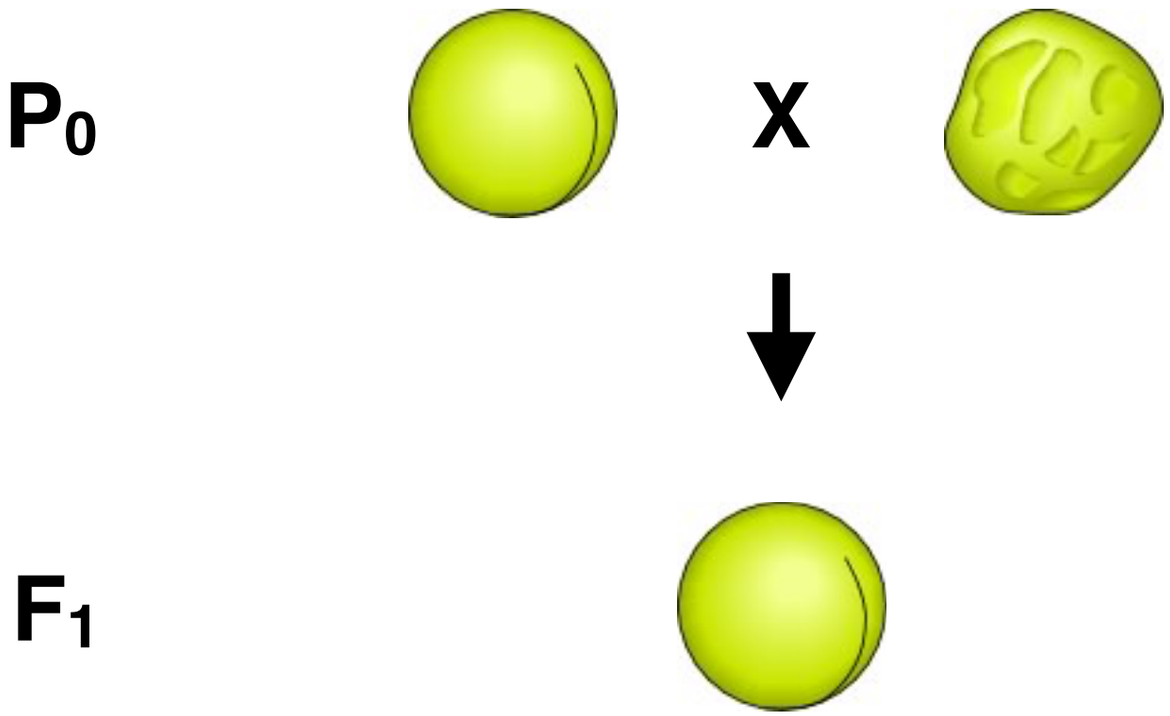
3. Focus on specific traits or characters

4. Quantification and record keeping

“Opportunity is missed by most people because it is dressed in overalls and looks like work.”

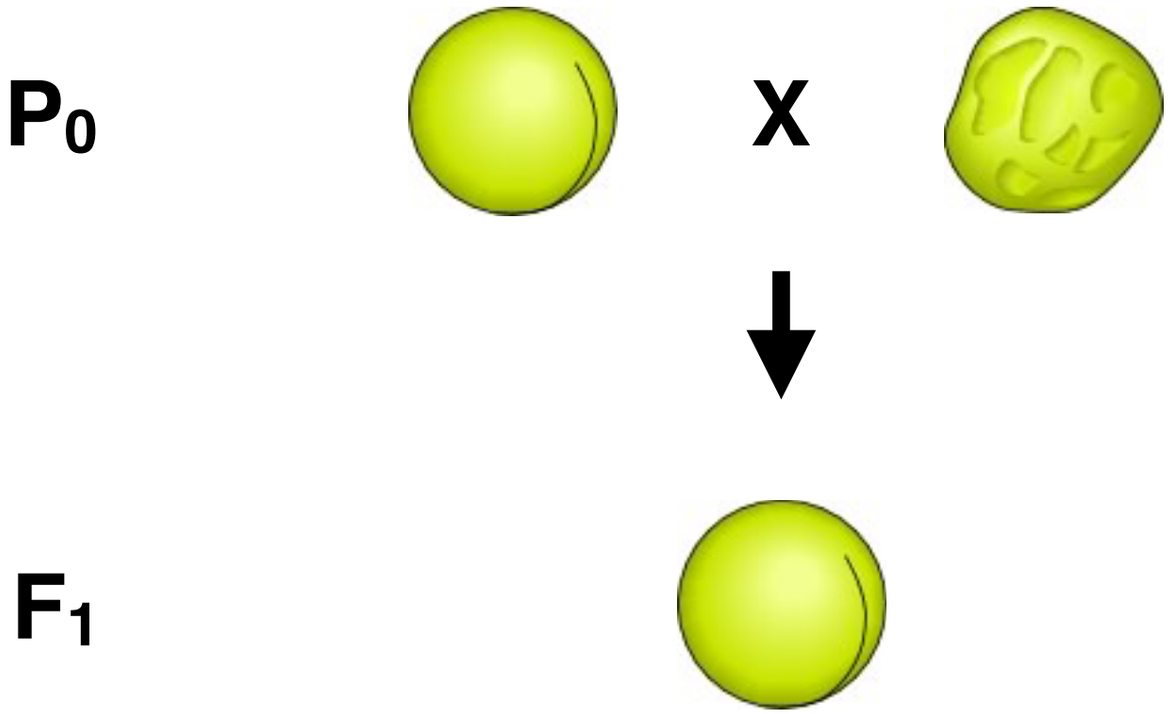
Thomas A. Edison

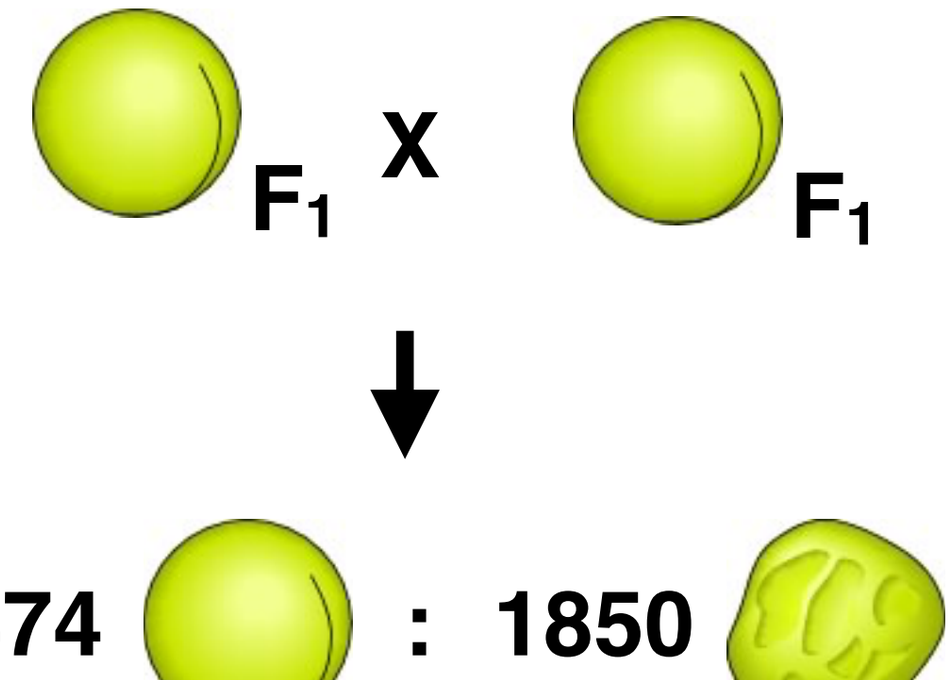
Lecture 1

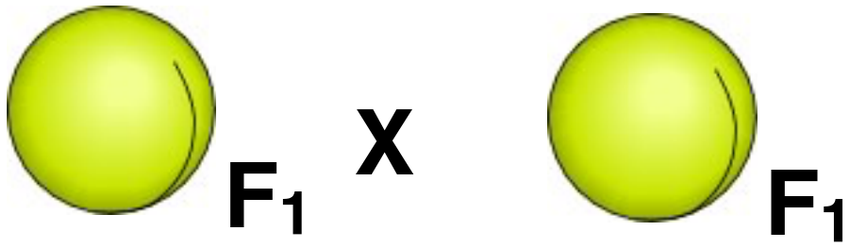


Trait (character)
Phenotype
Dominant
Recessive
Genotype
Gene (factor)

Law of dominance

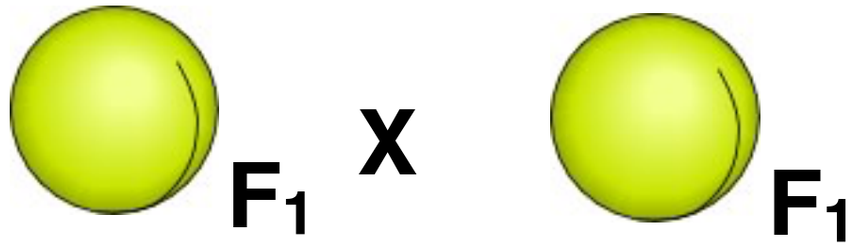

P0
X
F1


F1
X
F1
Hybrid cross
5474
:
1850



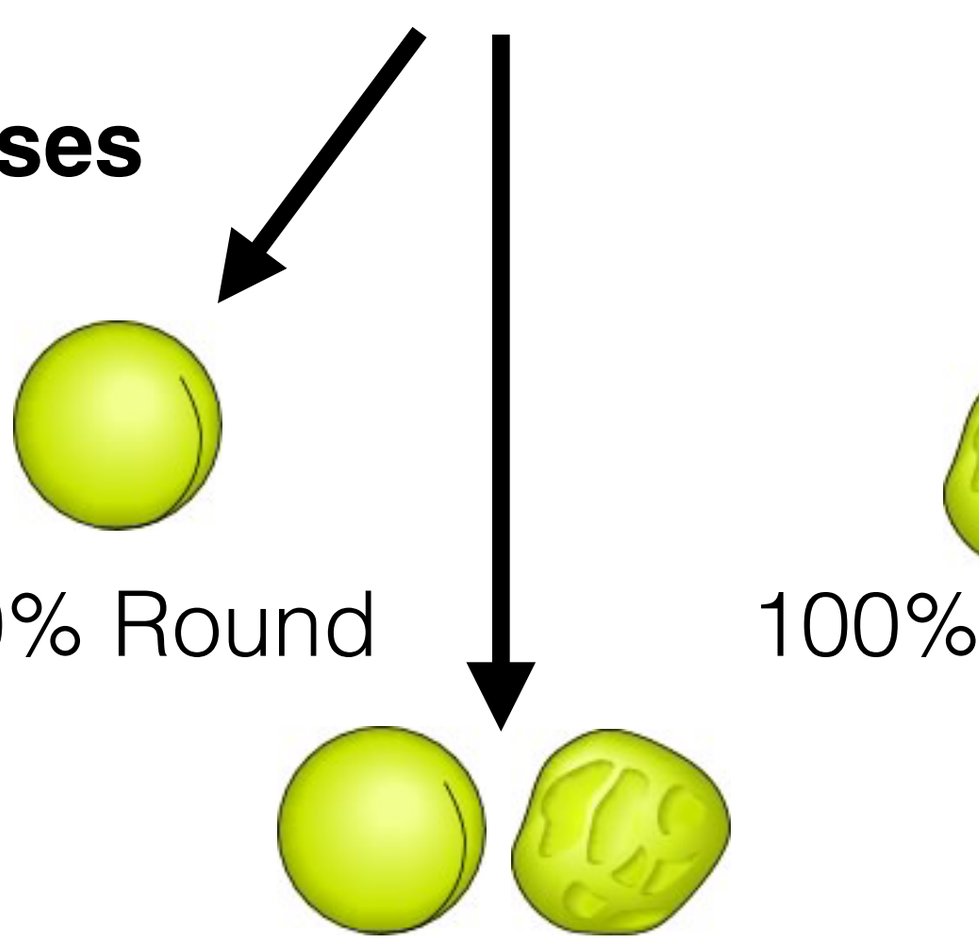
Hybrid cross

3:1 Phenotypic ratio



Hybrid cross

Self crosses

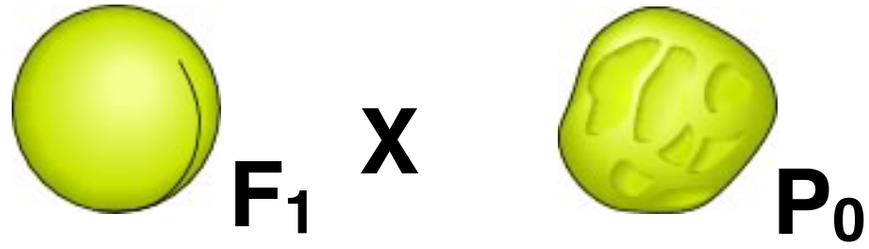


100% Round

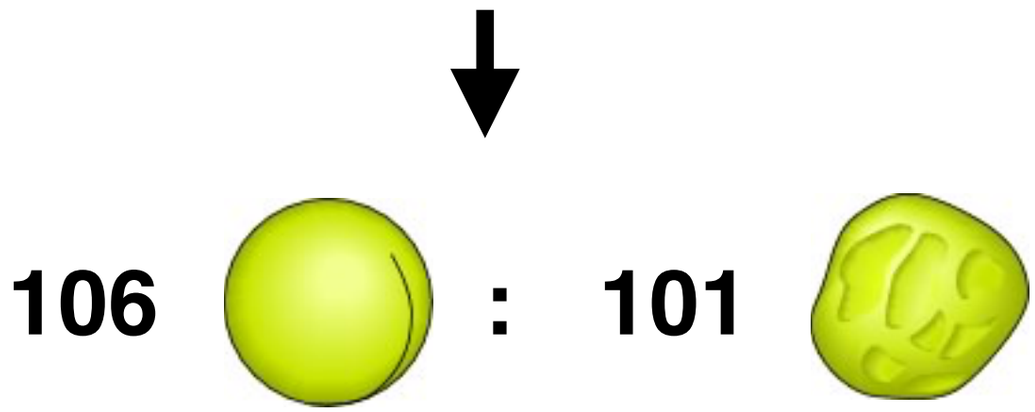
100% Wrinkled

3:1 Round:Wrinkled

Allele
Heterozygous
Homozygous

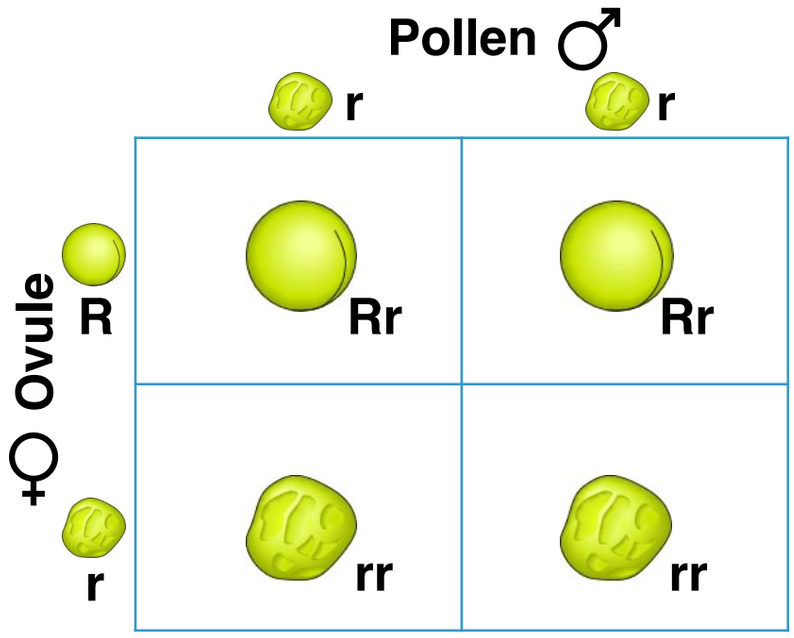


Test cross



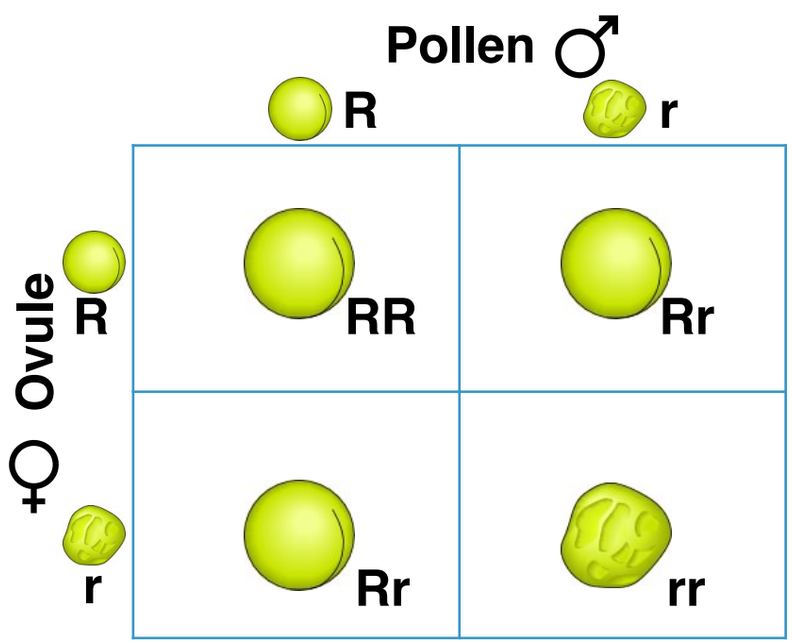
1:1 Phenotypic ratio

Test cross



1:1 Phenotypic ratio

Hybrid cross



3:1 Phenotypic ratio

Gametes only carry one allele of gene.

Every individual carries a pair of alleles.

Law of segregation

Law of dominance

Alleles that confer the recessive phenotype
will be masked by alleles that confer the dominant phenotype

OR

What you see in the F1 is the dominant phenotype

Law of segregation

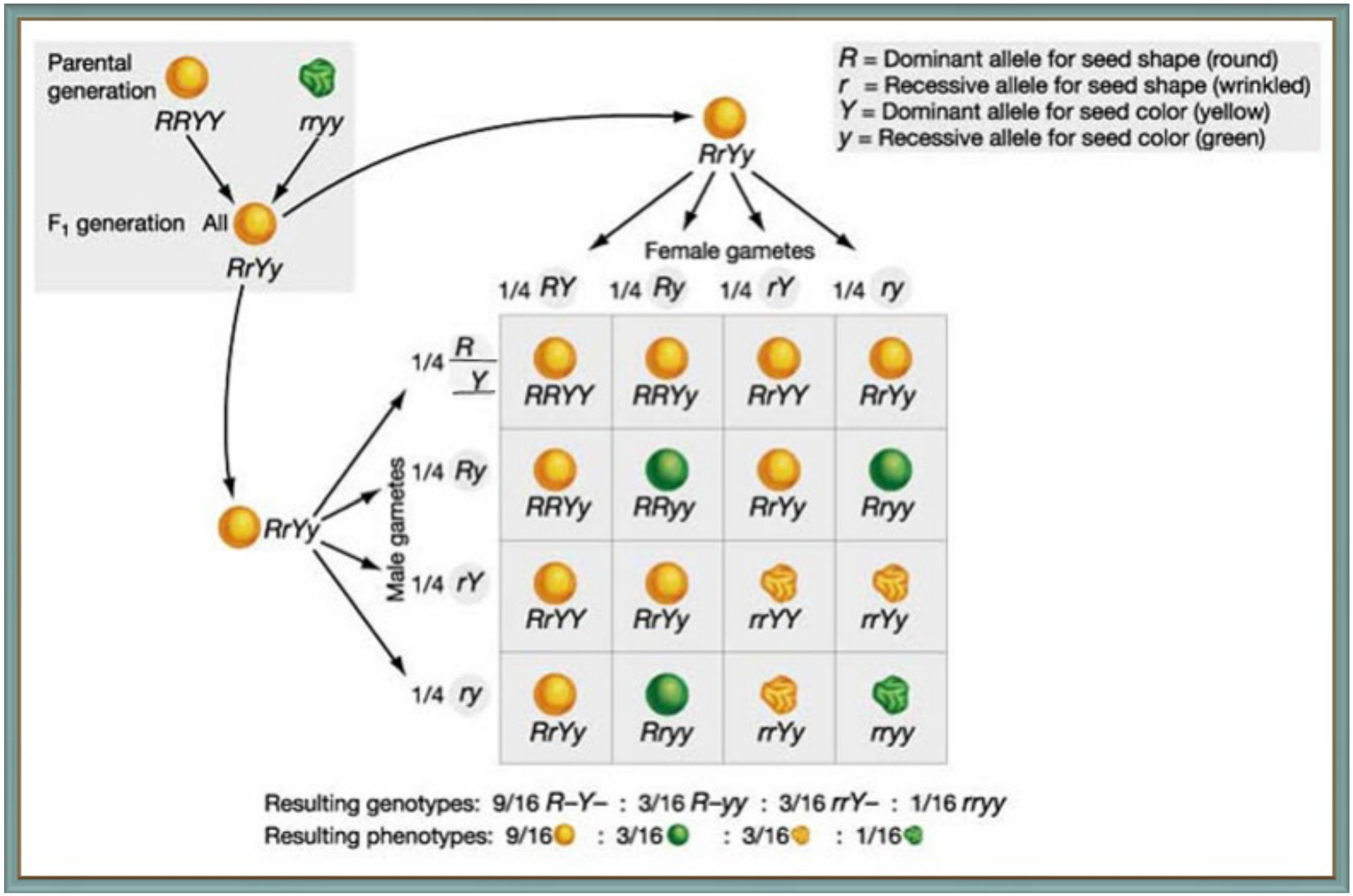
Every individual contains a pair of alleles.

Gametes (egg or sperm) carry only one allele of each gene.

The union of egg and sperm is random.

Character	Dominant Trait	×	Recessive Trait	F_2 Generation Dominant:Recessive	Ratio
Flower color	Purple 	×	White 	705:224	3.15:1
Flower position	Axial 	×	Terminal 	651:207	3.14:1
Seed color	Yellow 	×	Green 	6022:2001	3.01:1
Seed shape	Round 	×	Wrinkled 	5474:1850	2.96:1
Pod shape	Inflated 	×	Constricted 	882:299	2.95:1
Pod color	Green 	×	Yellow 	428:152	2.82:1
Stem length	Tall 	×	Dwarf 	787:277	2.84:1

What about the inheritance of two traits at the same time?



Law of independent assortment

When two or more characteristics are inherited,
the alleles assort independently of each other
during gamete production,

making an equal probability of alleles occurring together.

Punnett squares are tedious…basic probability

Take a diploid parent with genotype AA.

Probability of gamete A is p(A) = 1
Probability of gamete a is p(a) = 0

Take a diploid parent with genotype Aa.

Probability of gamete A is p(A) = 0.5
Probability of gamete a is p(a) = 0.5

Punnett squares are tedious…basic probability

Product rule: the prob. of two independent events occurring together is the product of the probabilities of each independent event occurring alone.

In cross Aa x Aa, probability of aa is p(a) x p(a) = 0.5 x 0.5 = 0.25

Sum rule: the prob. of an event is the sum of the probabilities of each individual possible event.

In cross Aa x Aa, probability of offspring A- is

p(AA) + p(Aa) + p(aA) = (0.5x0.5) + (0.5x0.5) + (0.5x0.5) = 0.75

p(AA) + p(Aa) + p(aA) = 1 - p(aa) = 1 - 0.25 = 0.75

Gregor Mendel's work was "lost" for 34 years!

Carl Correns

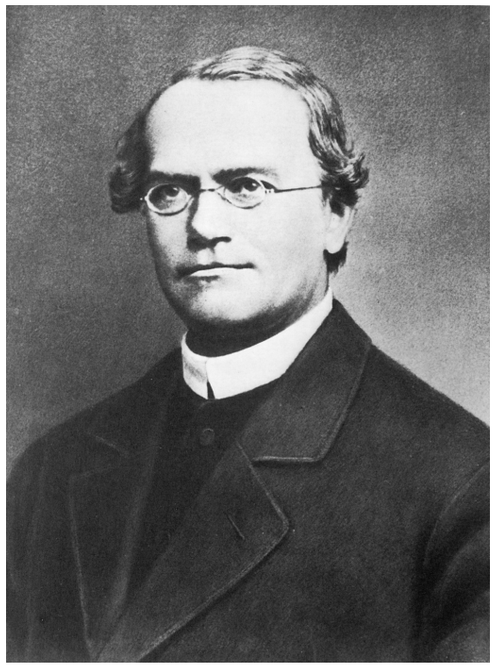
Erich von Tschermak

William Spillman

Hugo de Vries

Why did Mendel's work stand the test of time?

Gregor Mendel was lucky!



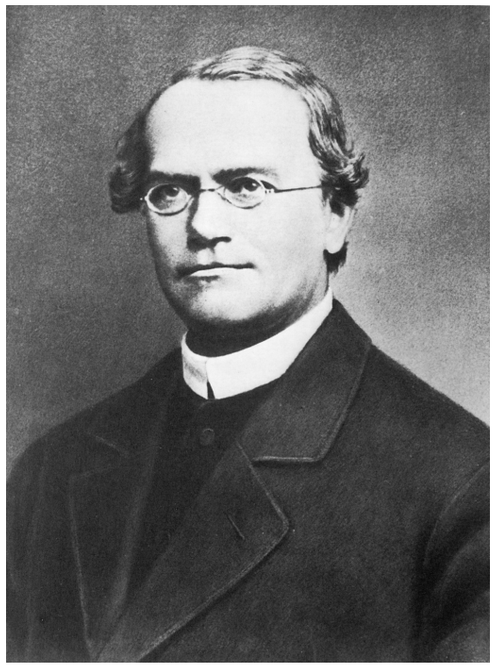
1. Peas are diploid (two copies of every chromosome).

Polyploidy

Examples of Polyploid Plants	
Name	**Number**
Common wheat	**6N** = 42
Tobacco	**4N** = 48
Potato	**4N** = 48
Banana	**3N** = 27
Boysenberry	**7N** = 49
Strawberry	**8N** = 56

Many **ferns** are polyploid with chromosome number up to 400N

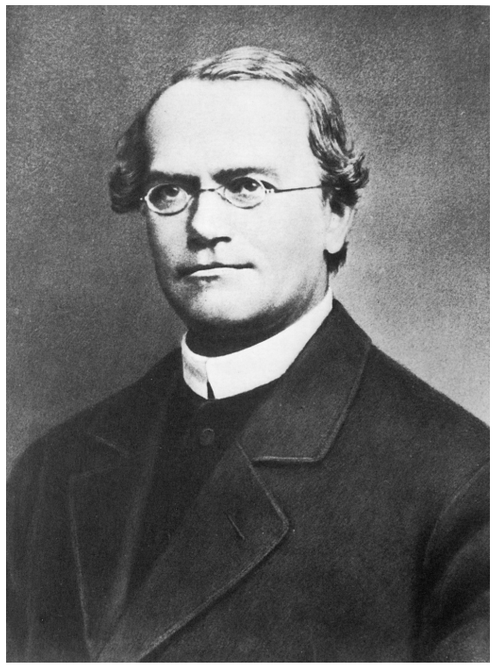
Gregor Mendel was lucky!



1. Peas are diploid (two copies of every chromosome).

2. Traits could have been multigenic (controlled by many genes).

Gregor Mendel was lucky!

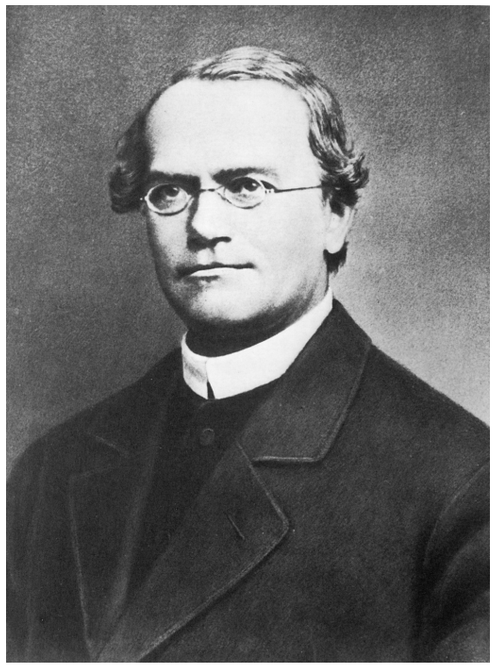


1. Peas are diploid (two copies of every chromosome).

2. Traits could have been multigenic (controlled by many genes).

3. Genes could have been linked (violate Law of Ind. Assortment).

Gregor Mendel was lucky!



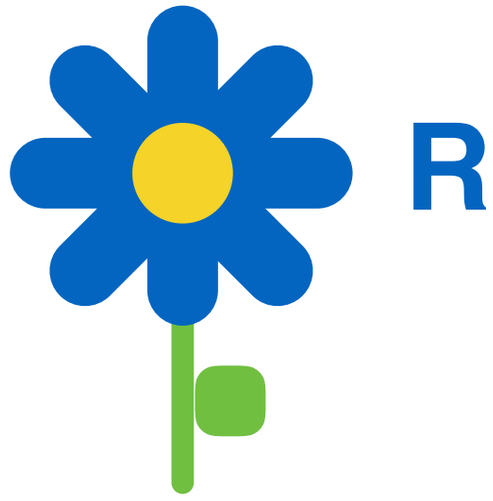
1. Peas are diploid (two copies of every chromosome).

2. Traits could have been multigenic (controlled by many genes).

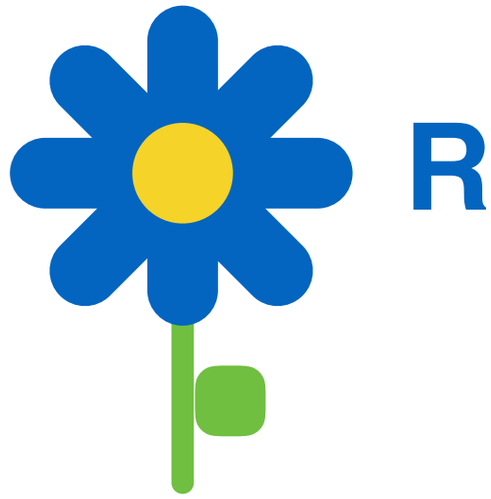
3. Genes could have been linked (violate Law of Ind. Assortment).

4. Traits could have been co-dominant or incomplete dominant.

Three different types of dominance



Three different types of dominance

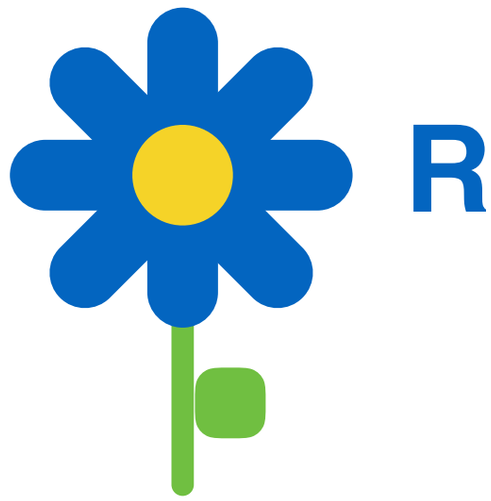


Complete

Incomplete

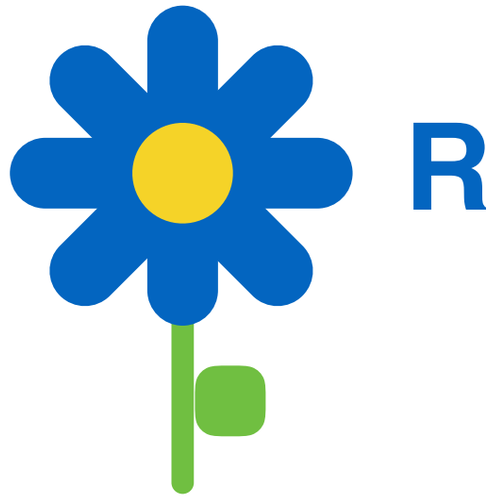
Co-dominant

Three different types of dominance



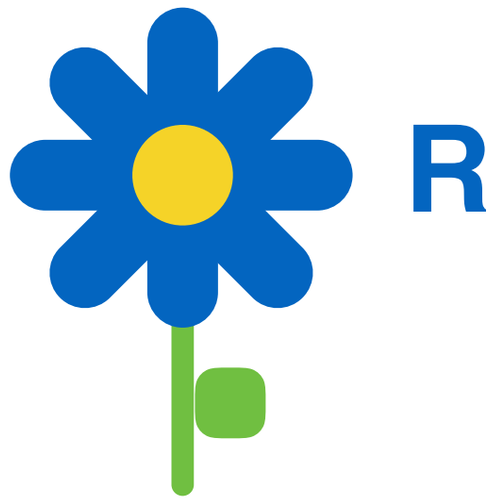
Complete	Incomplete	Co-dominant
RR	Red	Red	Red

Three different types of dominance



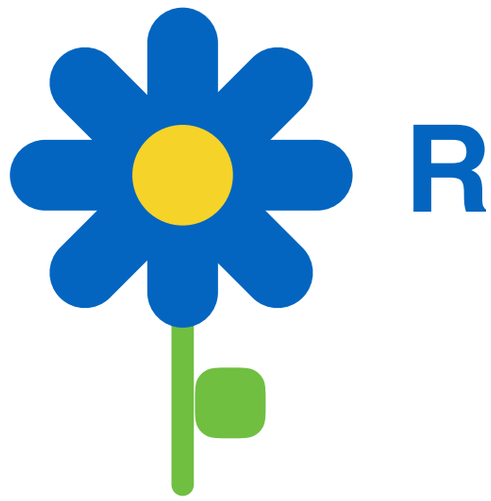
Complete	Incomplete	Co-dominant
RR	Red	Red	Red
RR	Blue	Blue	Blue

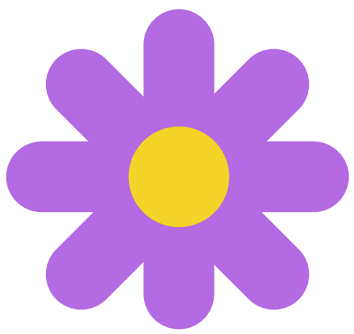
Three different types of dominance



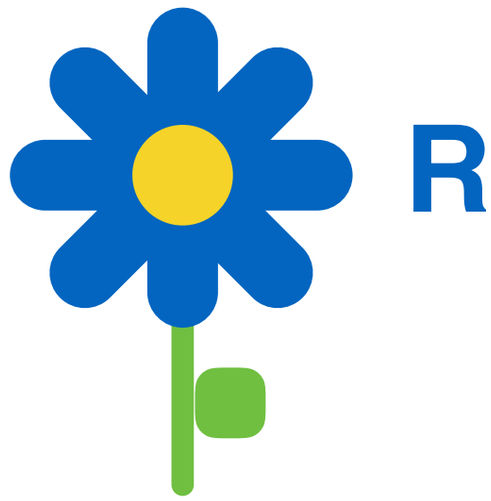
Complete	Incomplete	Co-dominant
RR	Red	Red	Red
RR	Blue	Blue	Blue
RR			

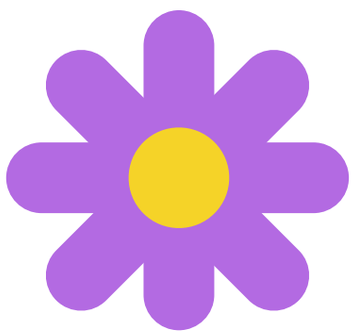
Three different types of dominance



Complete	Incomplete	Co-dominant
RR	Red	Red	Red
RR	Blue	Blue	Blue
RR			

Three different types of dominance



	<u>Complete</u>	<u>Incomplete</u>	<u>Co-dominant</u>
RR	Red	Red	Red
RR	Blue	Blue	Blue
RR			

Incomplete dominance:
Different alleles confer a mixed phenotype

Co-dominance:
Phenotypes caused by different alleles are visible at the same time

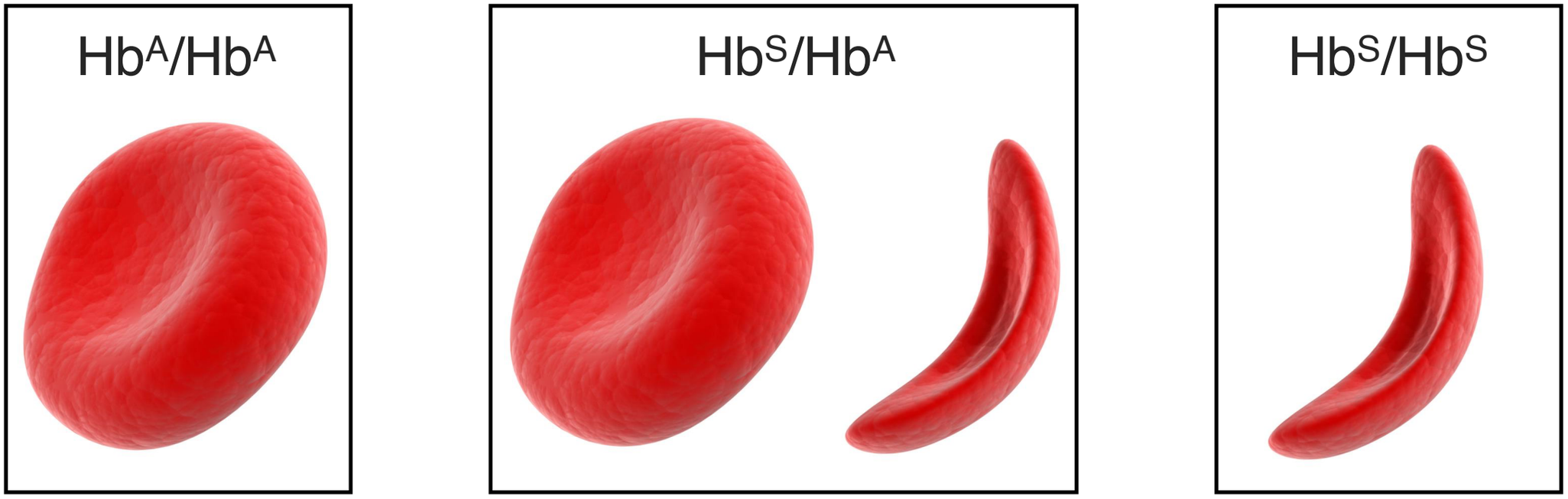
Hb^A/Hb^A

Normal
RBCs

Hb^S/Hb^S

Sickle
RBCs

Co-dominance:
Phenotypes caused by different alleles are visible at the same time

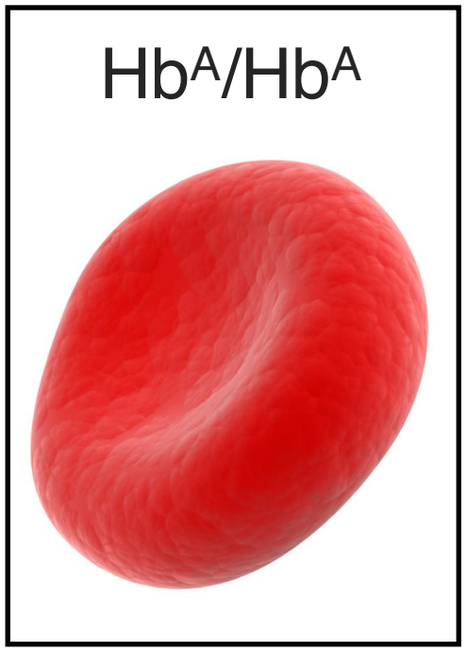


Normal RBCs

Both normal and sickle RBCs

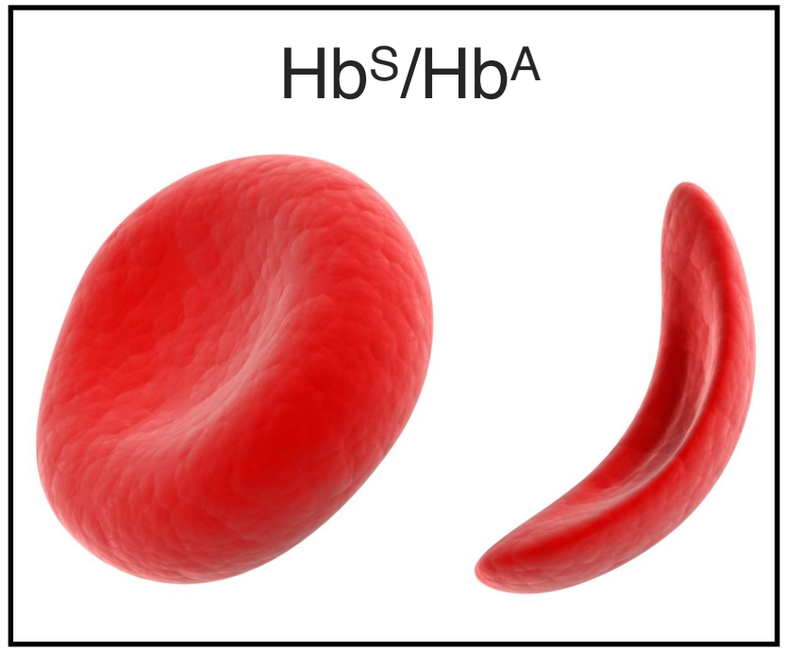
Sickle RBCs

Co-dominance:
Phenotypes caused by different alleles are visible at the same time



Normal RBCs

Malaria-sensitive



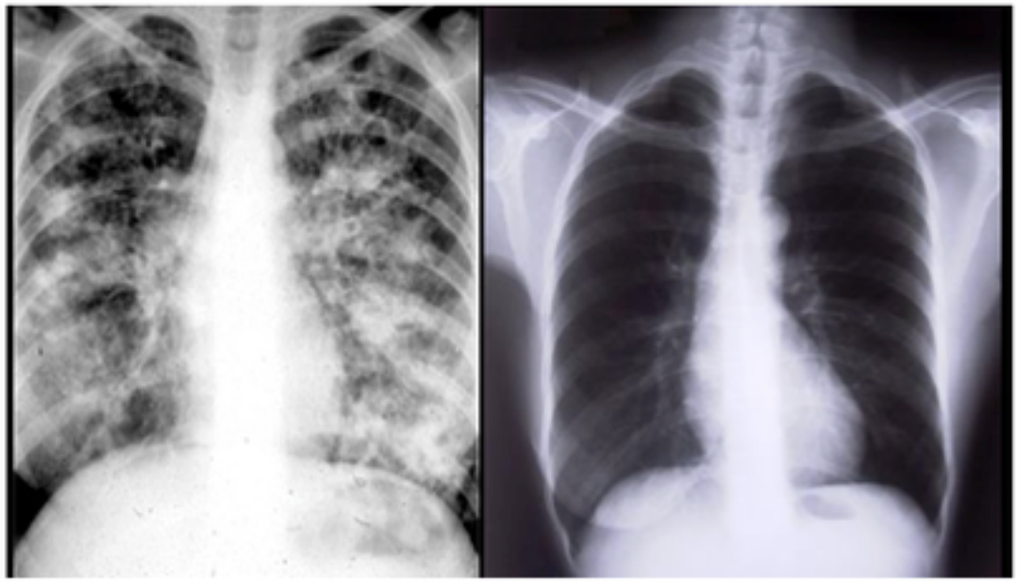
Both normal and sickle RBCs

Malaria-resistant

Sickle RBCs

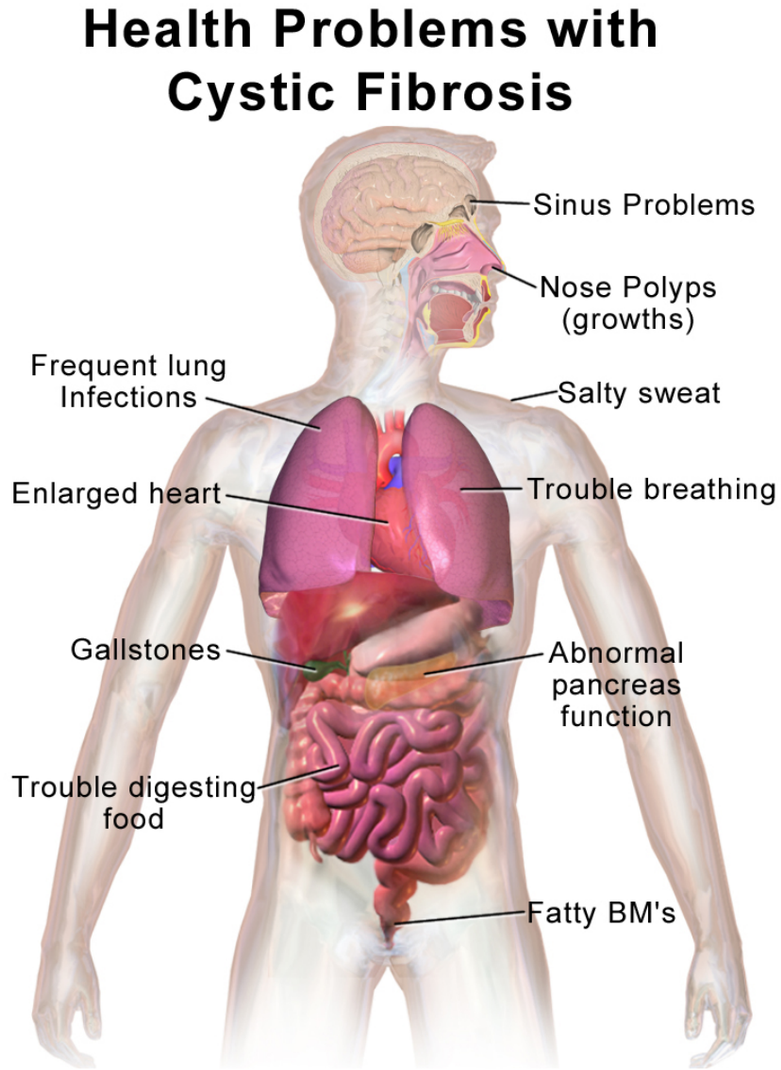
Malaria-resistant

Cystic fibrosis is a debilitating disorder



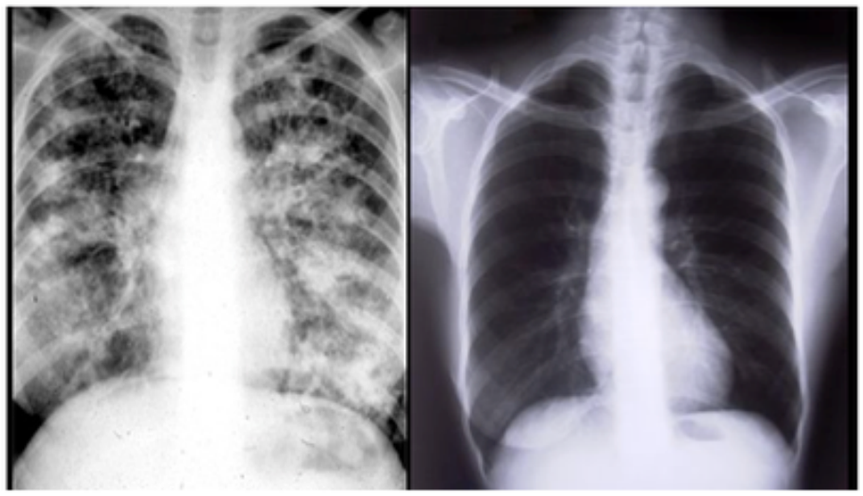
Cystic Fibrosis Lung

Healthy Lung



- Rare disease affects 1/10,000 live births
- Breathing difficulties caused by thick mucus
- Pancreas, liver, kidneys, and intestine are also deficient

Cystic fibrosis is inherited in families



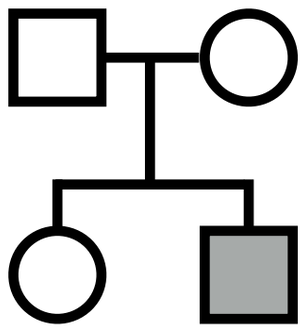
Cystic Fibrosis Lung Healthy Lung

Unaffected male

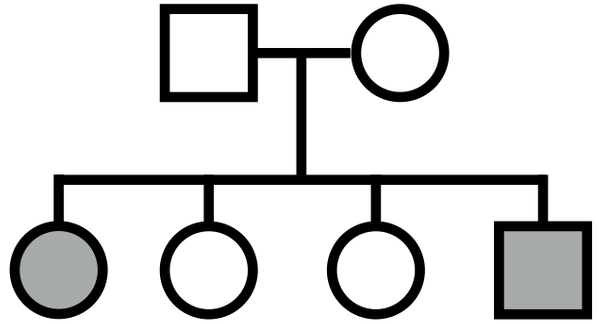
Unaffected female

CF male

CF female



Family #1



Family #2

What is the trait?

Dominance?

Genetics is a powerful discovery and analytical tool