Bio393: Genetic Analysis

Dr. Erik Andersen

Shannon Brady (TA)

Tues. and Thurs. 9:30-10:50 AM Tech L170

Office hours and problem solving: Fridays 1-3 PM Cook 3118

Point Distribution

Problem sets	30%	100 points (20 pts each)
Participation	10%	33 points
Midterm	30%	100 points
Final	30%	100 points

bio393.andersenlab.org

Date	Topic
March 28	Mendelian Inheritance, Basic probability, PS#1 out
March 30	Chromosome theory, recombination, and mapping
April 4	Screens, selections, mutants, and dosage
April 6	Complementation
April 11	Enhancement and suppression, PS#2 out
April 13	Genetic interactions: epistasis
April 18	Principles and methods of genetic analysis I
April 20	Principles and methods of genetic analysis II
April 25	**MIDTERM EXAMINATION**

Date	Topic
April 27	Developmental genetics I, PS#3 out
May 2	Developmental genetics II
May 4	Behavioral genetics
May 9	Variation and allele frequency spectrum, PS#4 out
May 11	Pedigrees and phase
May 16	Linkage mapping and LOD scores
May 18	Linkage disequilibrium and population structure
May 23	Complex traits and GWAS, PS#5 out
May 25	Human genetics and the future, class discussion
May 30	NO CLASS Reading week
June 1	NO CLASS Reading week

FINAL: Tuesday, June 6, 12-2 PM

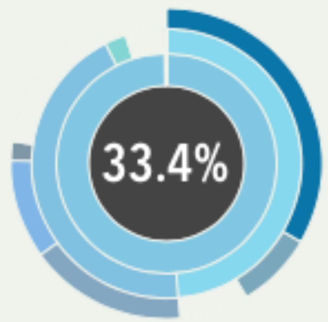
Genetics is…

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

23andMe

Your Ancestry Composition

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



ITALIAN

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.

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

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.

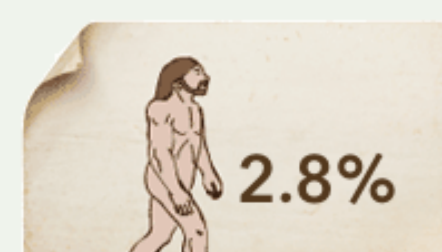
Your Mother's Line

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.

Ancestry Help

Neanderthal Ancestry

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



Famous Relative!

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

Top Relative Surnames

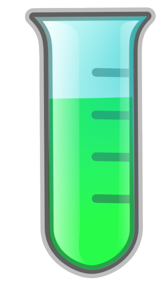
Surname	Count	Enrichment
Tompkins	6	58

Precision Medicine Initiative (PMI)

Biological Function

Genetics

Biochemistry



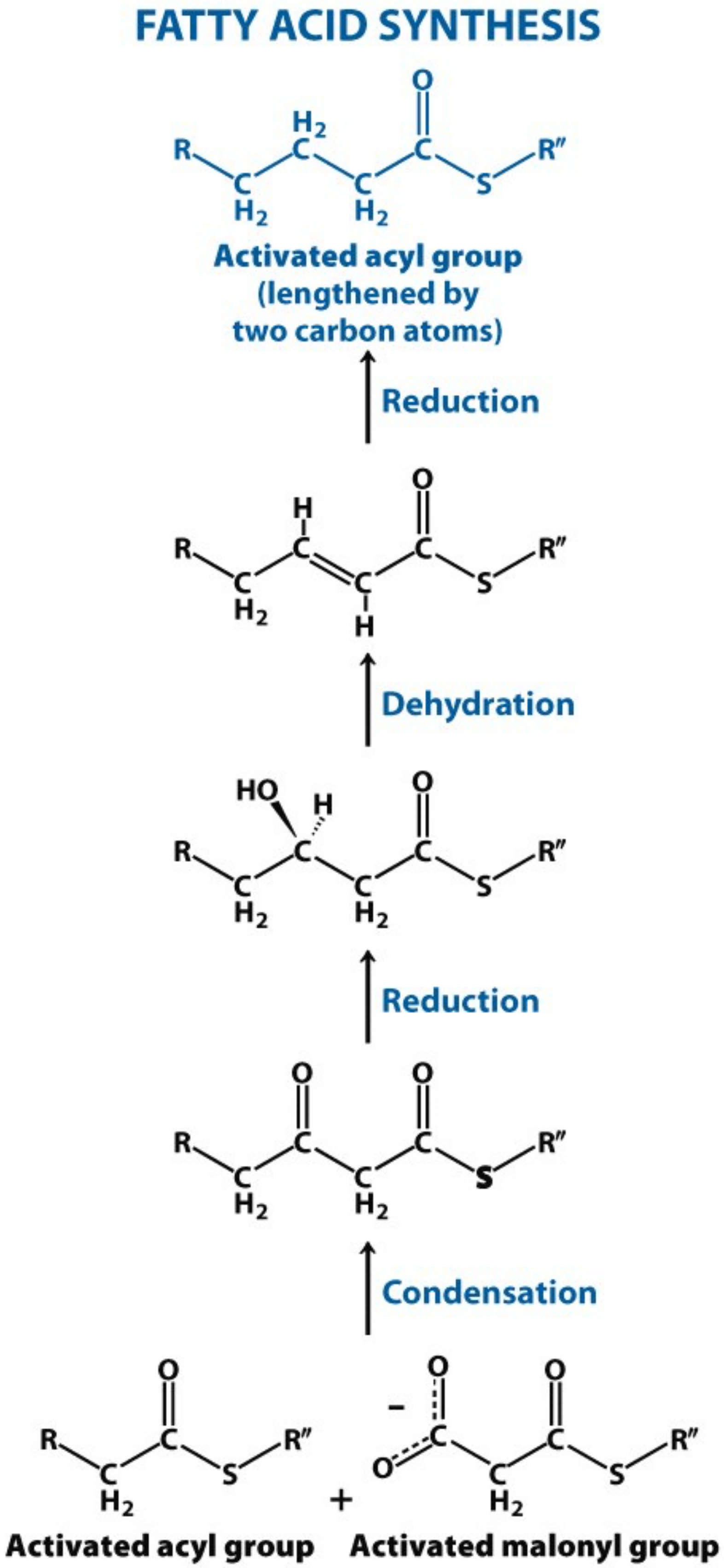
Study organisms
with components
removed

Genes — **Proteins**

Study components
removed
from the organism

Molecular
Biology

No single discipline provides the data to define the system



Discussion:

How do we find the factors involved in fatty acid synthesis?

Figure 22.2
Biochemistry, Seventh Edition

The father of genetics: Gregor Mendel

Mendel the genius: Choice of model organism

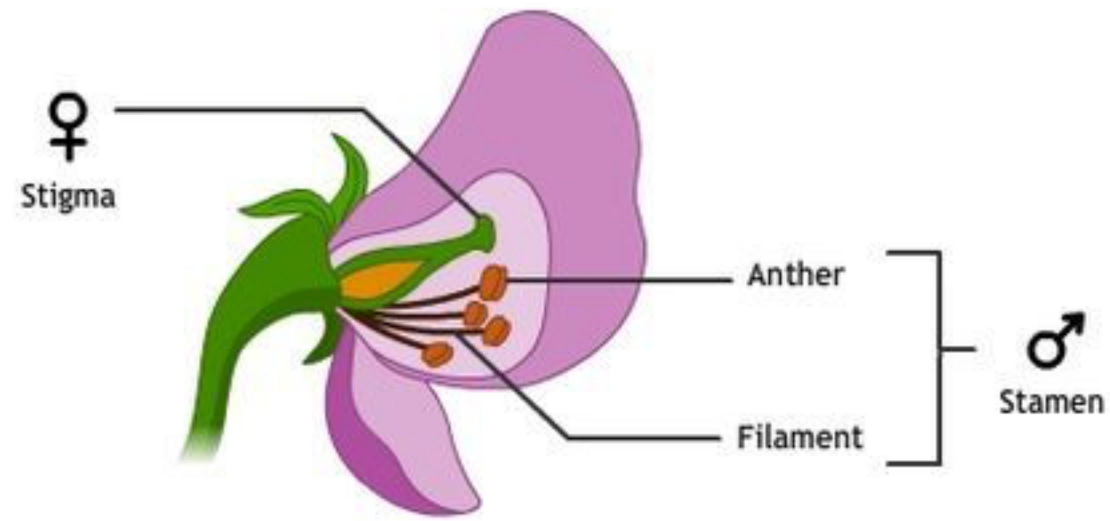
Hawkweed

Honey bees

Mice

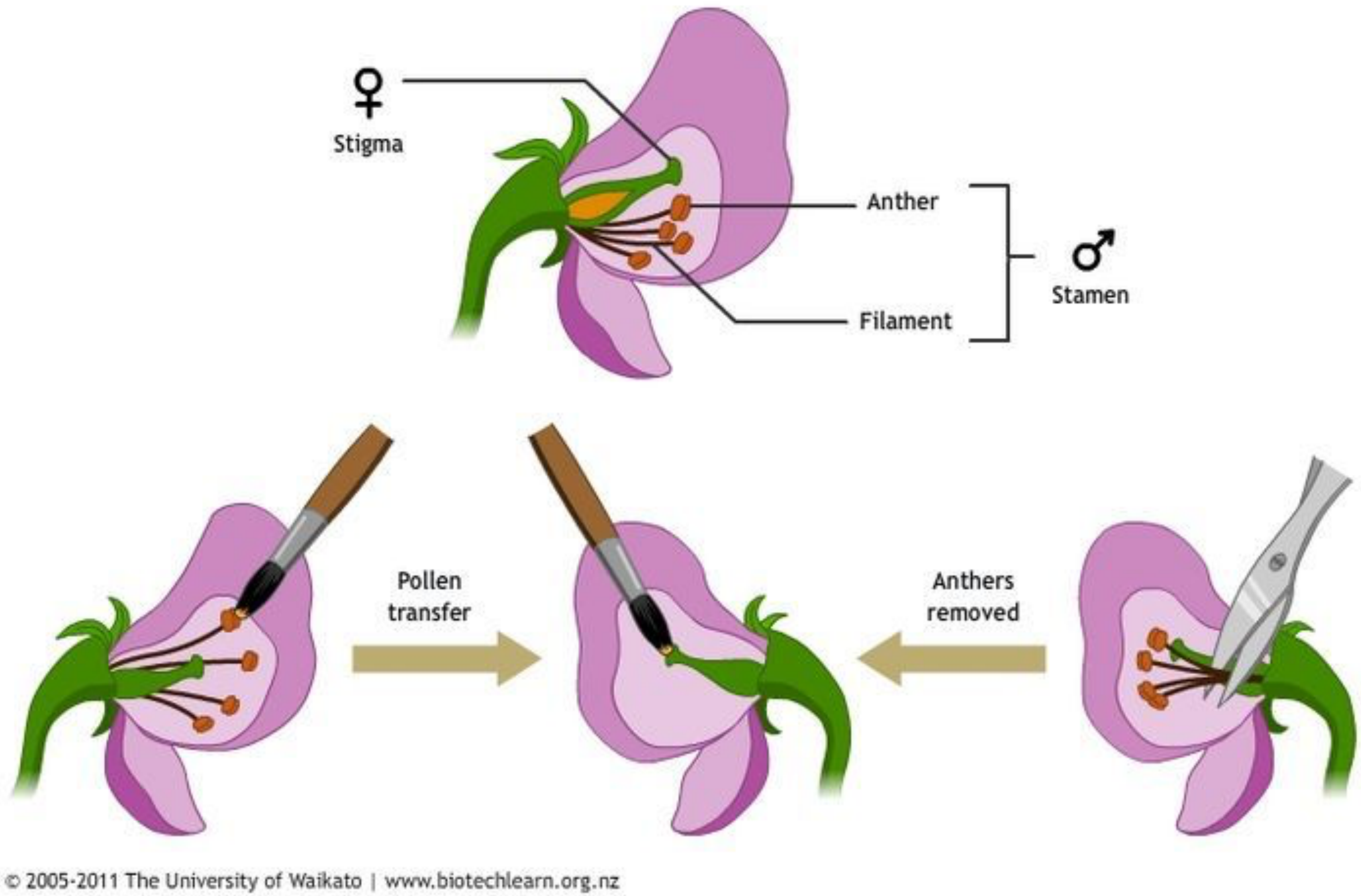
Mendel the genius: Choice of model organism

1. Control of genetic crosses



Mendel the genius: Choice of model organism

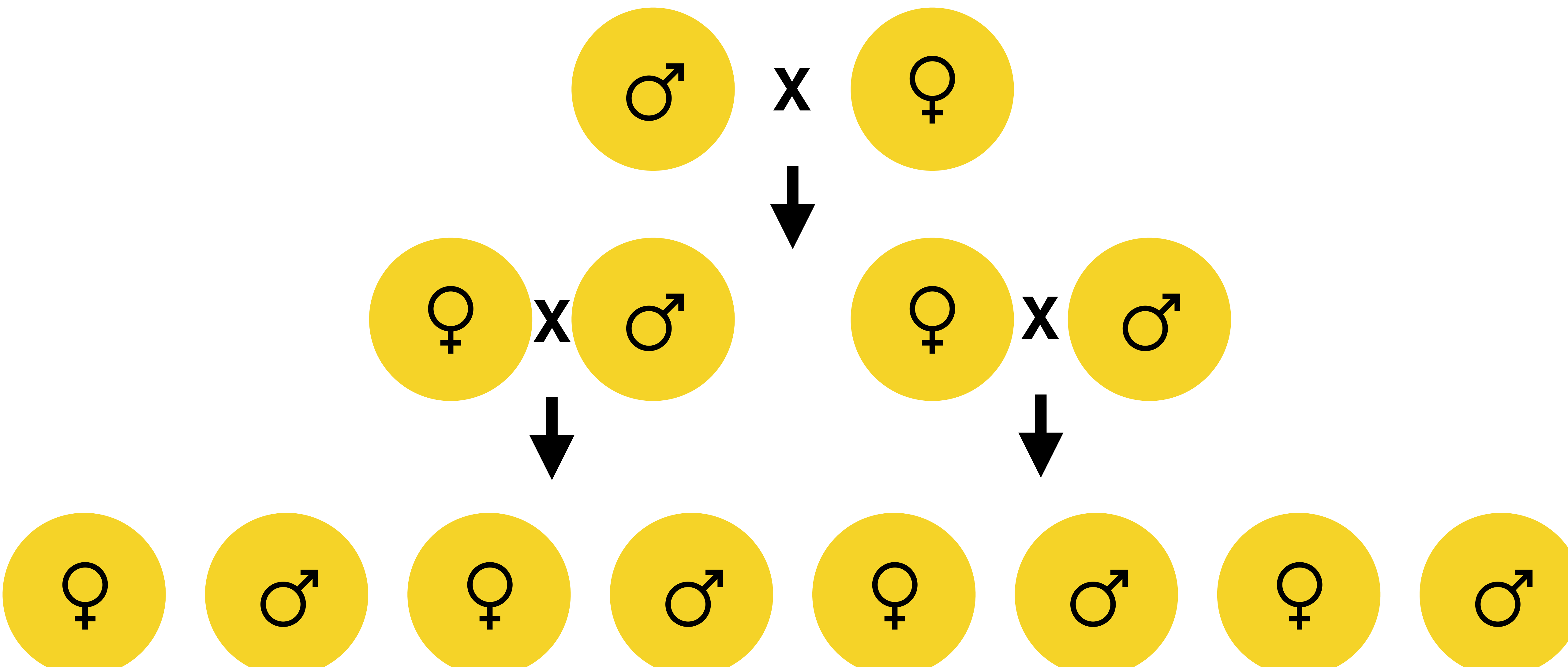
1. <u>Control</u> of genetic crosses



Mendel the genius: Choice of model organism

1. Control of genetic crosses

2. Reproducible true-breeding strains

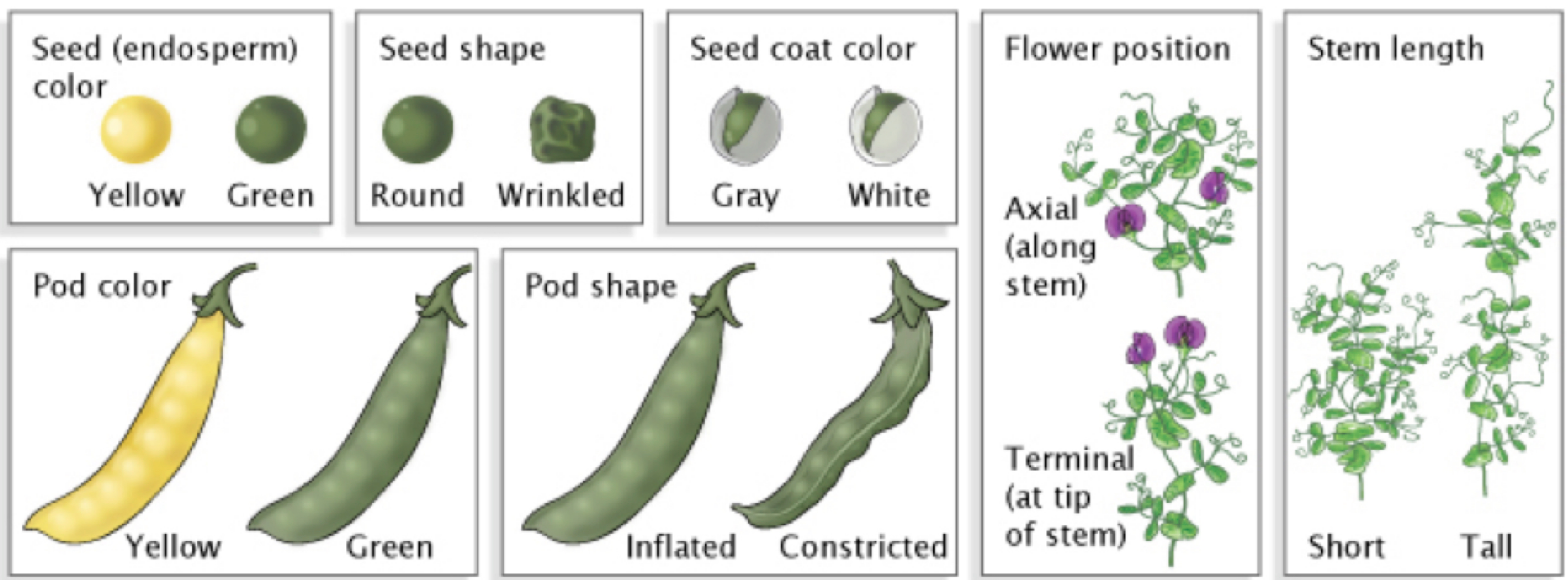


Mendel the genius: Choice of model organism

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. <u>Control</u> of genetic crosses

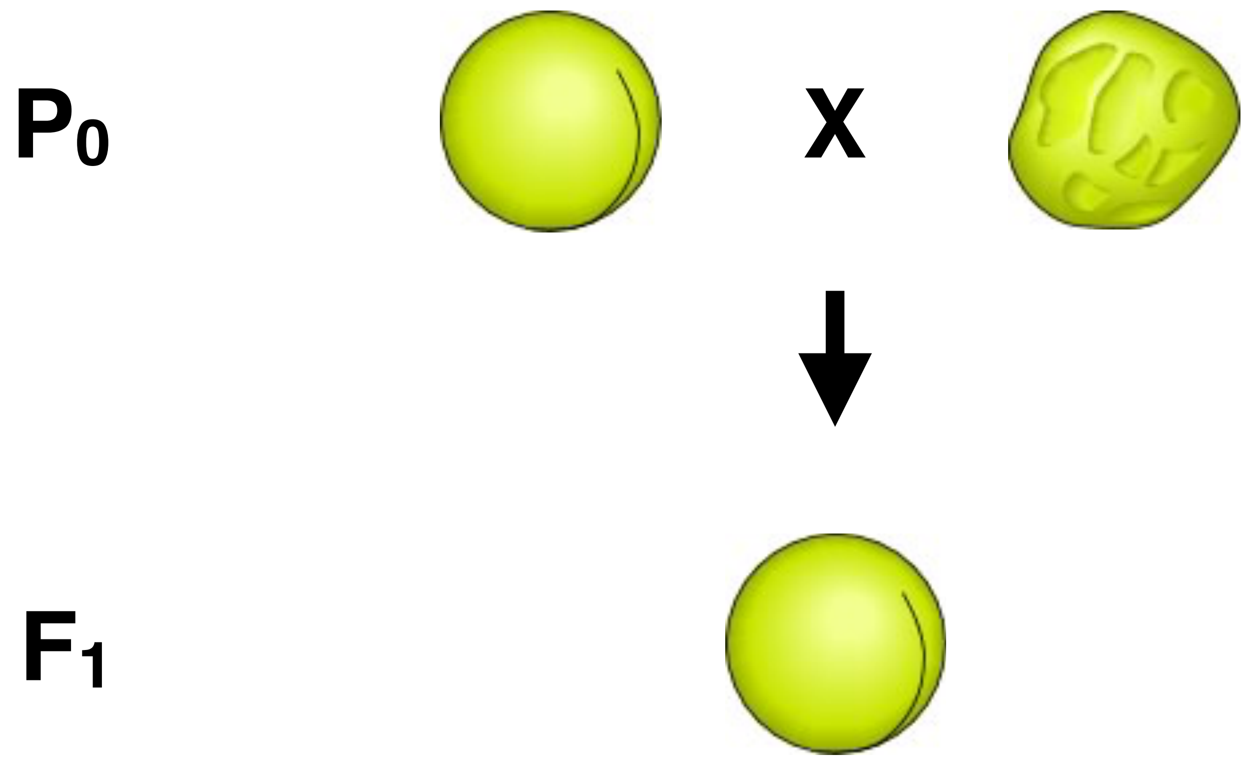
2. <u>Reproducible</u> true-breeding strains

3. <u>Focus</u> on specific traits or characters

4. <u>Quantification</u> and record keeping

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

Thomas A. Edison

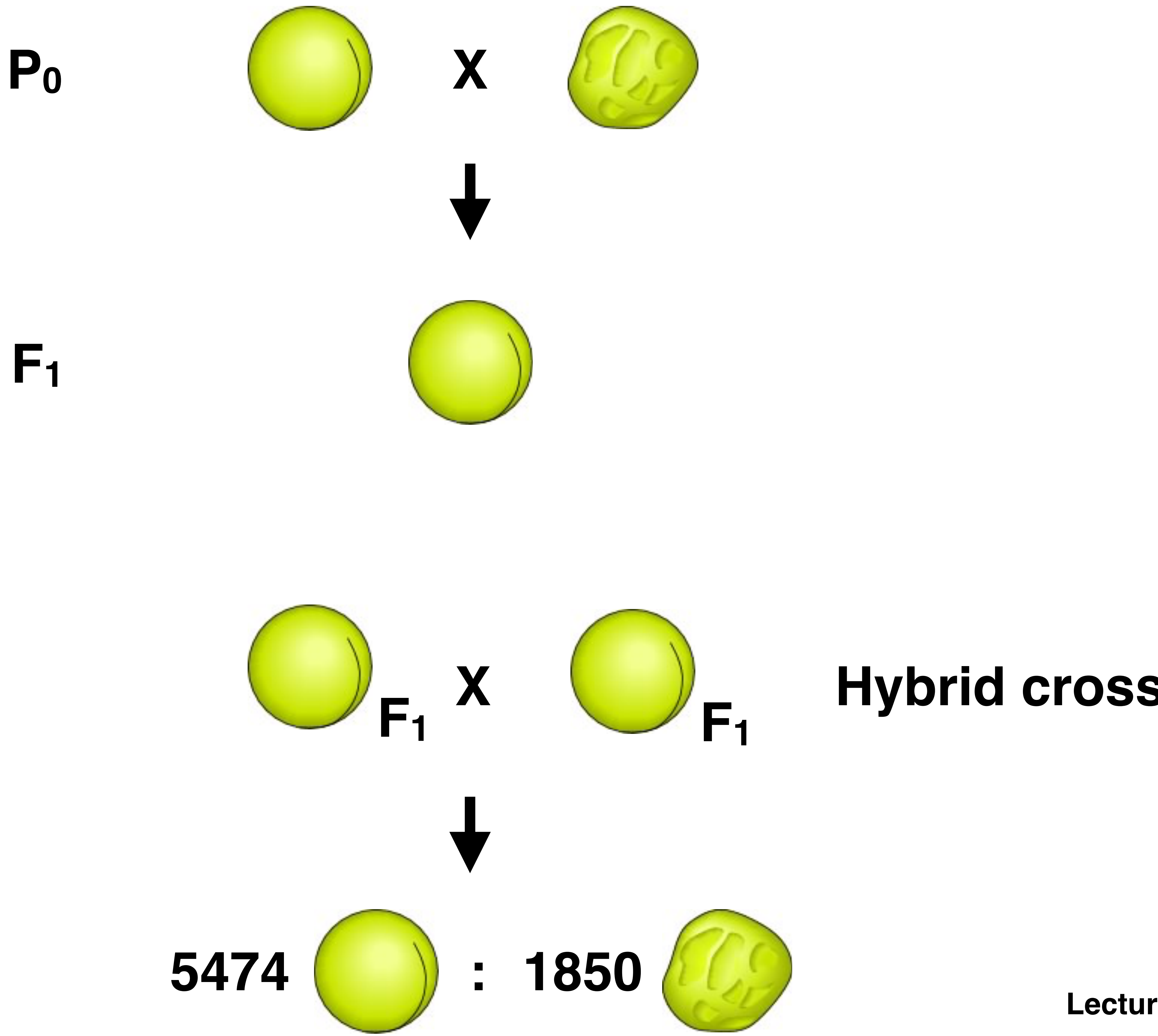


Trait (character)
Phenotype
Dominant
Recessive

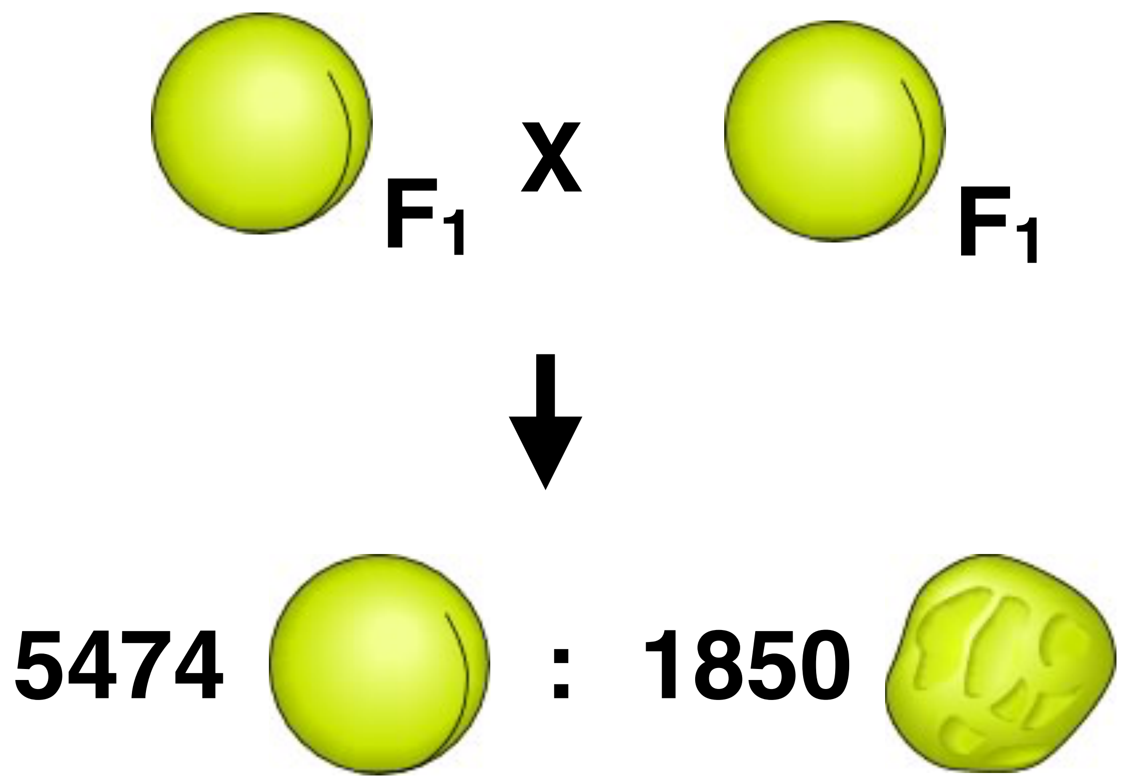
Law of dominance

What is a gene?

Genotype
Gene (factor)

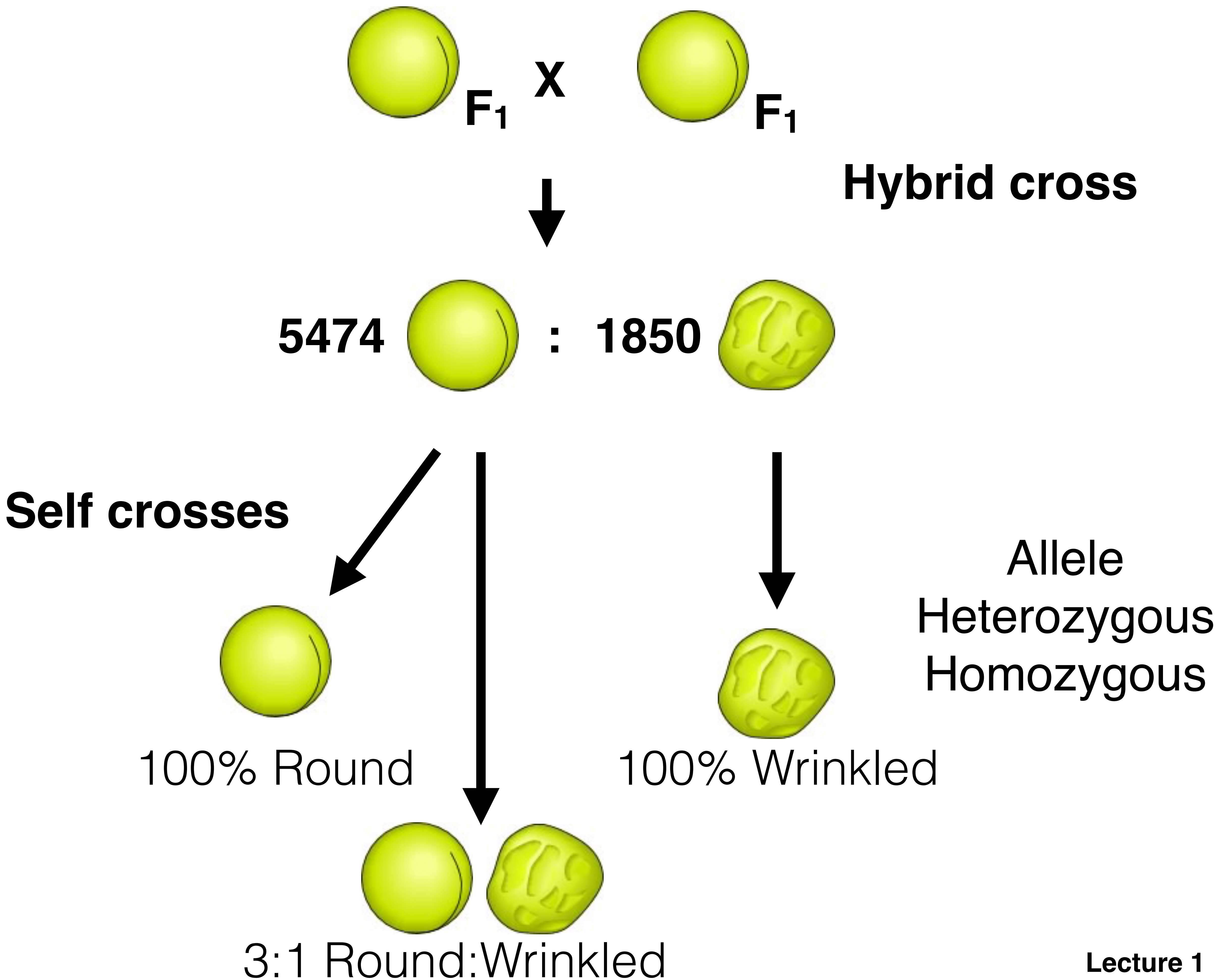


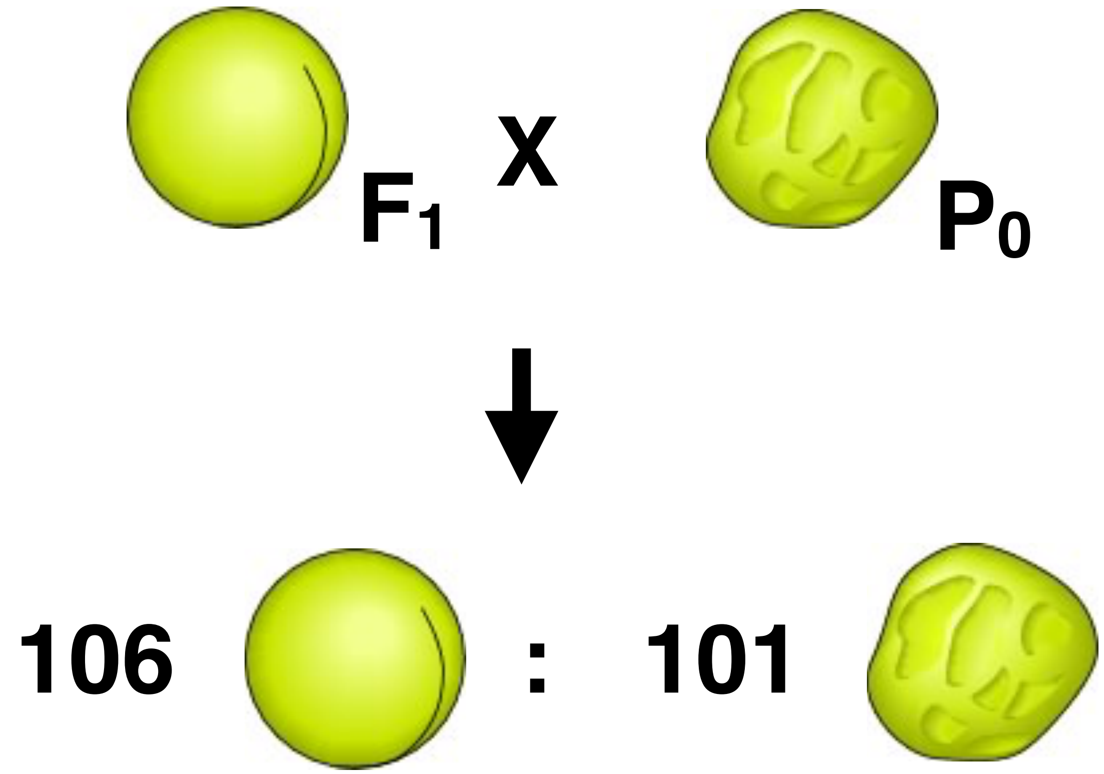
P0
X
F1
F1
X
F1
Hybrid cross
5474
:
1850



Hybrid cross

3:1 Phenotypic ratio

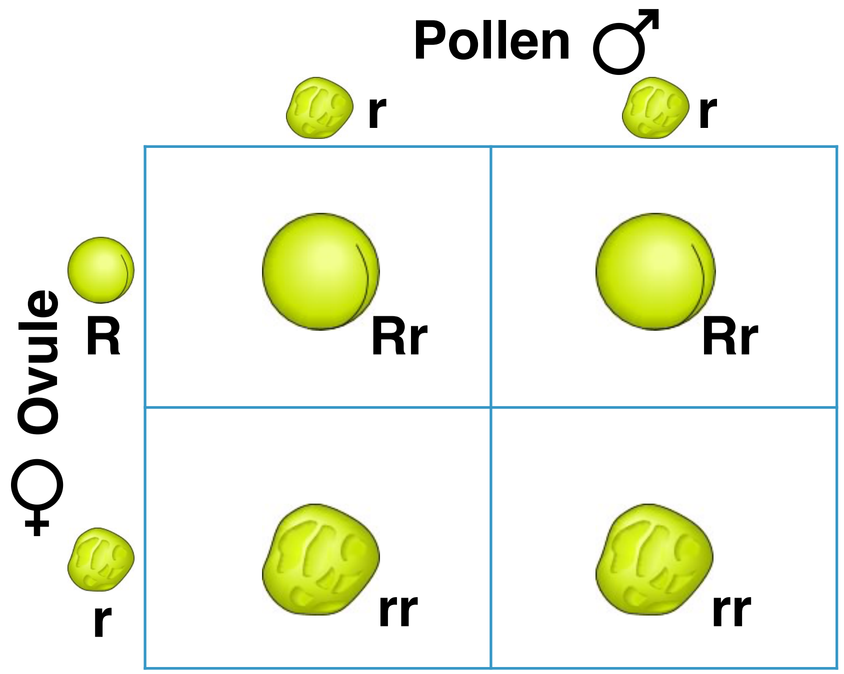

F1
X
F1
Hybrid cross
5474
:
1850
Self crosses
Allele
Heterozygous
Homozygous
100% Round
100% Wrinkled
3:1 Round:Wrinkled



Test cross

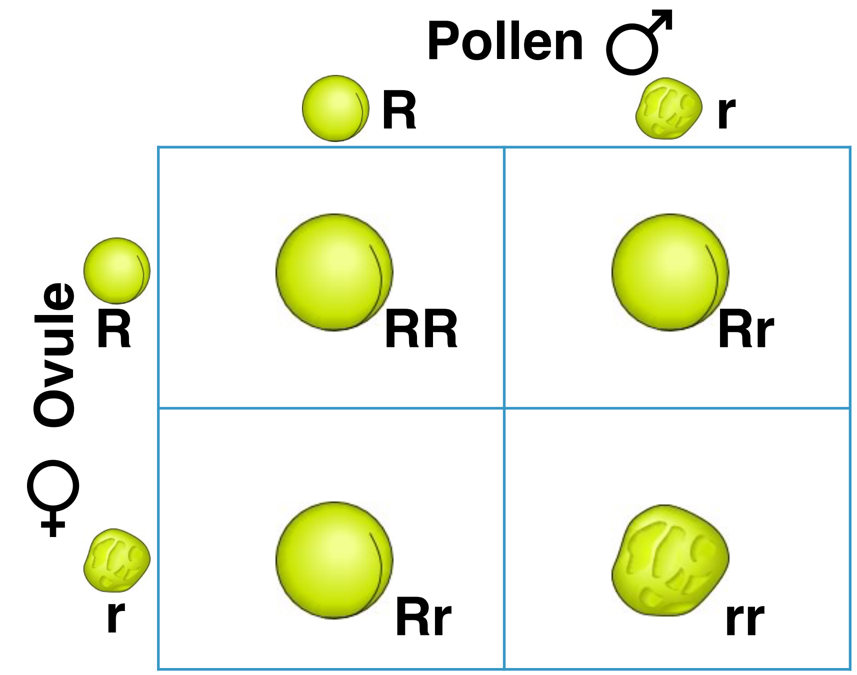
1:1 Phenotypic ratio

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

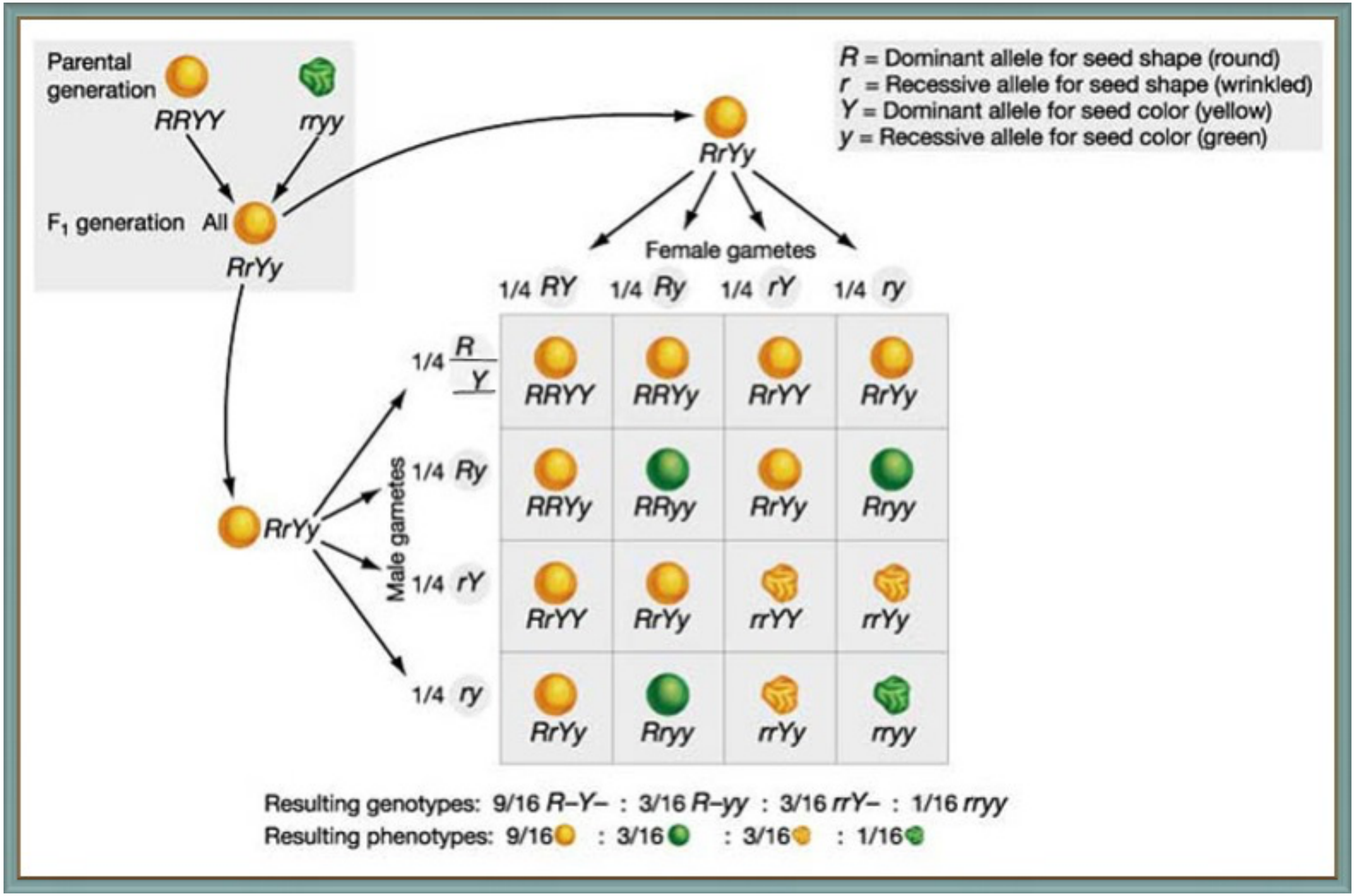
Every individual contains a pair of alleles.

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

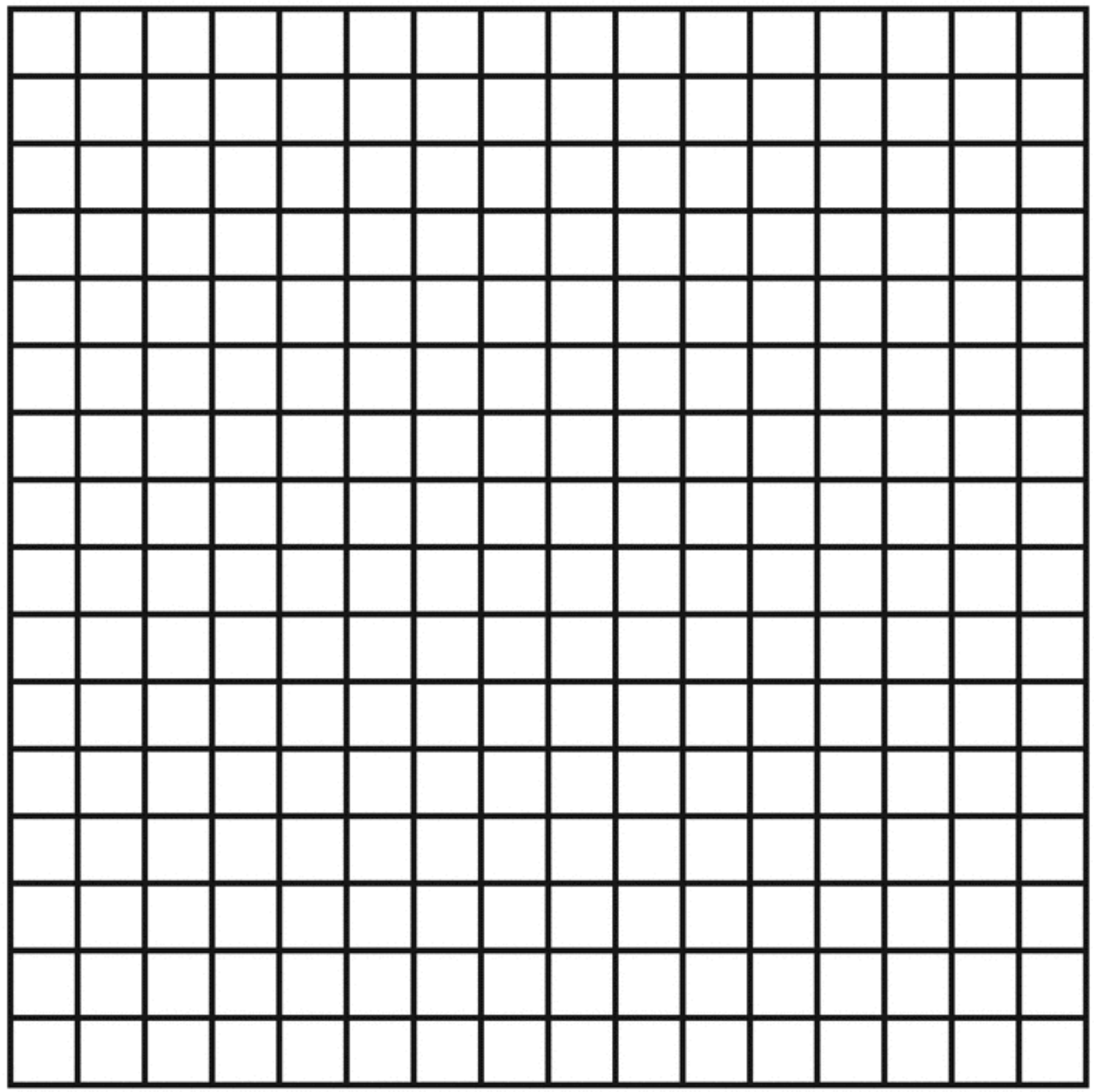
p(AA) + p(Aa) + p(aA) = (0.5x0.5) + (0.5x0.5) + (0.5x0.5) = 0.75

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

Punnett squares are tedious…basic probability

AaBbCcDd x AaBbCcDd

Probability of offspring that is AAB-Ccdd?



Punnett squares are tedious…basic probability

AaBbCcDd x AaBbCcDd

Probability of offspring that is AAB-Ccdd?

p(AA) x (p(BB)+p(Bb)+p(bB)) x (p(Cc)+p(cC)) x p(dd)

1/4 x 3/4 x 1/2 x 1/4

3/128

What if you don't see that phenotypic fraction?

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!

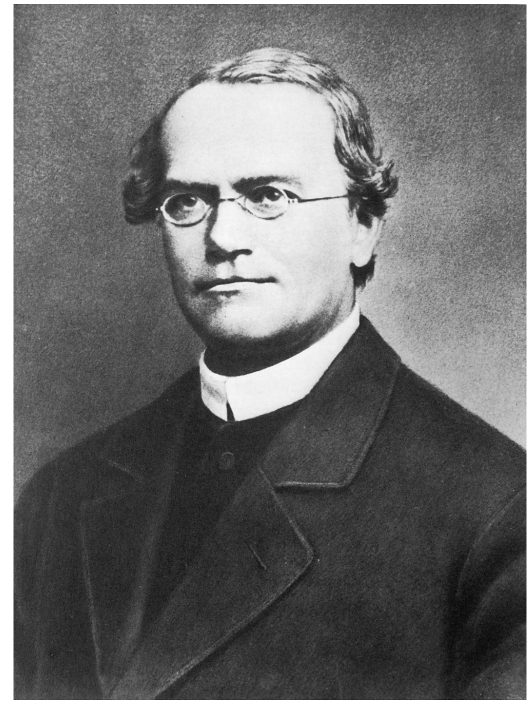
1. Peas are diploid (two copies of every chromosome).

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).

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

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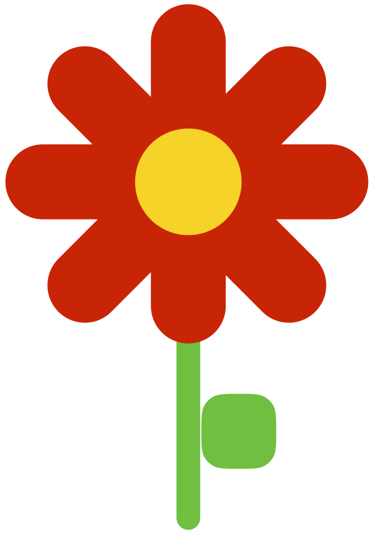
1. Peas are diploid (two copies of every chromosome).

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

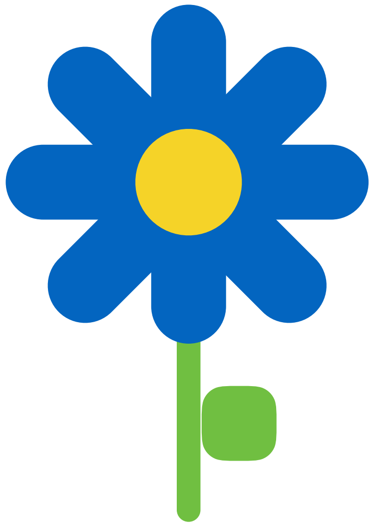
3. Genes could have been linked (violate Law of Ind. Assortment).

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

Three different types of dominance

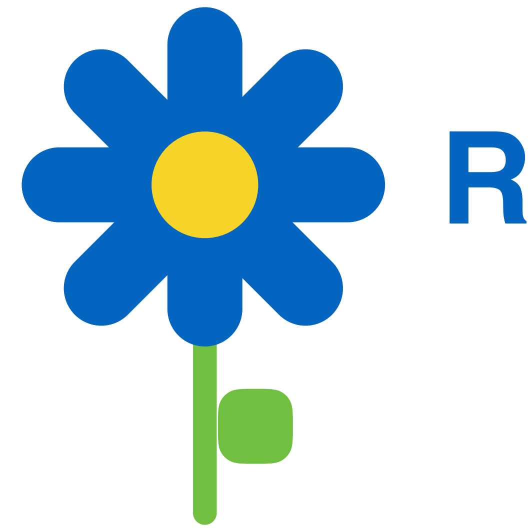


R



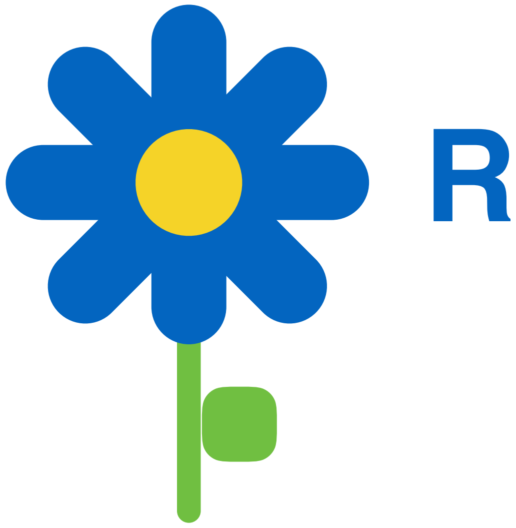
R

Three different types of dominance



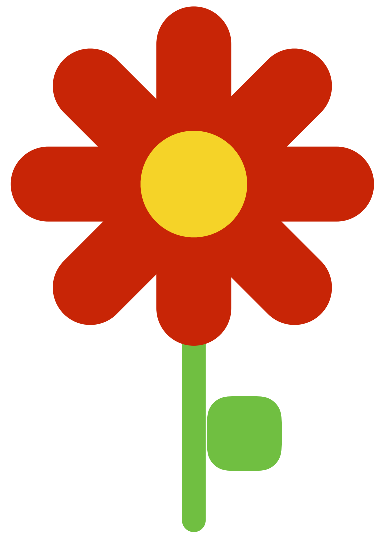
<u>**Complete**</u> <u>**Incomplete**</u> <u>**Co-dominant**</u>

Three different types of dominance

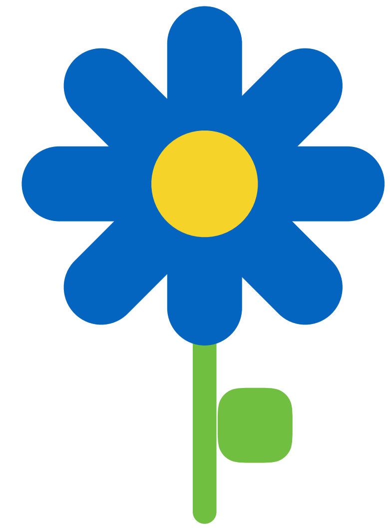


	Complete	**Incomplete**	**Co-dominant**
RR	Red	Red	Red

Three different types of dominance



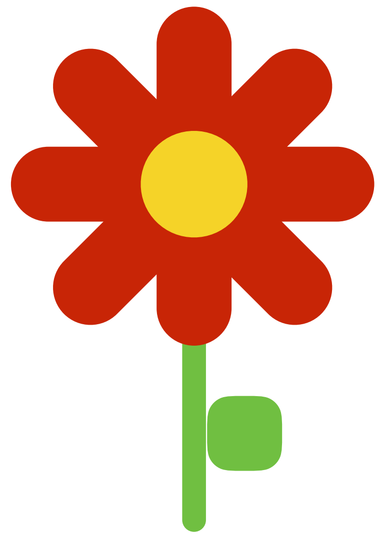
R



R

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

Three different types of dominance



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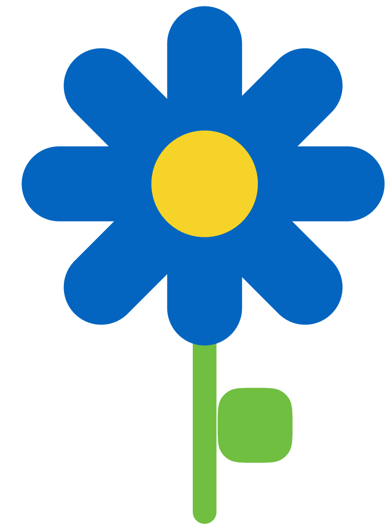
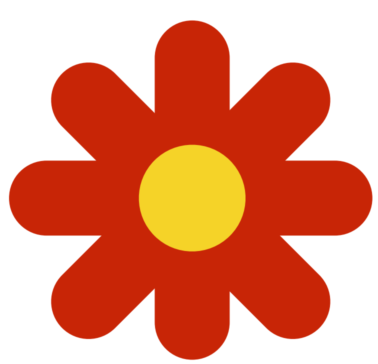
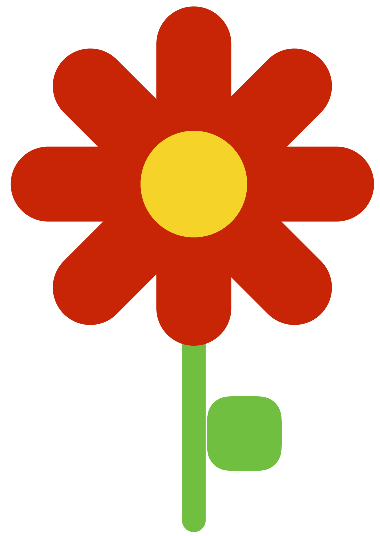


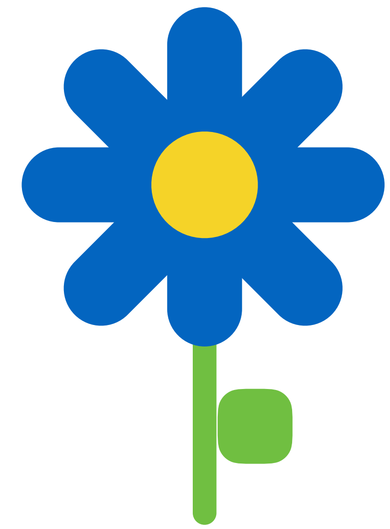
R

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

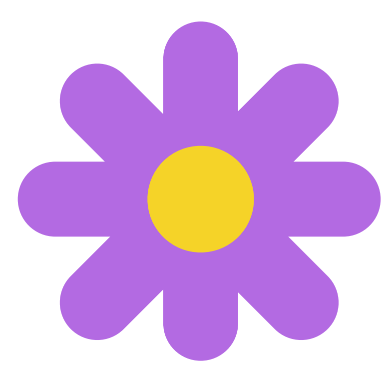
Three different types of dominance



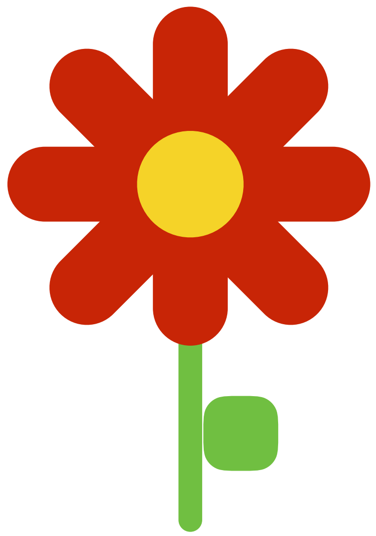
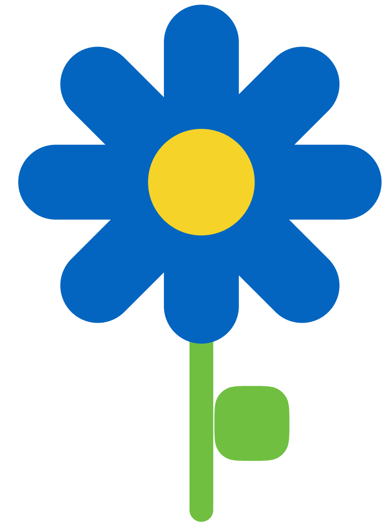
R

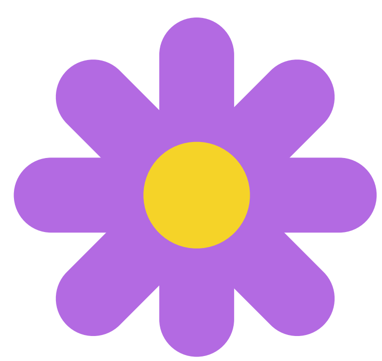


R

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

Three different types of dominance

 R  R

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

Incomplete dominance:
Different alleles confer a mixed phenotype

Hemoglobin sickle-cell allele

Hb^A/Hb^A

Normal
RBCs

Hb^S/Hb^S

Mostly sickle
RBCs

Hemoglobin sickle-cell allele

Hb^A/Hb^A

Normal RBCs

Hb^A/Hb^S

Both normal and sickle RBCs

Hb^S/Hb^S

Mostly sickle RBCs

Co-dominant

Hemoglobin sickle-cell allele

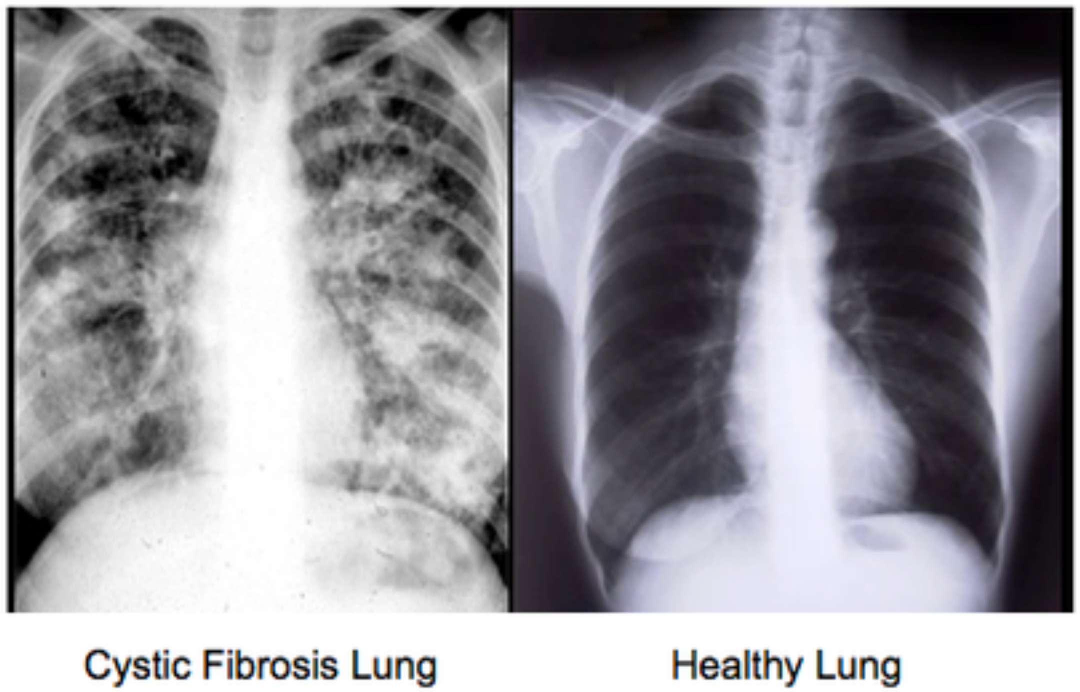
	Hb^A/Hb^A	Hb^A/Hb^S	Hb^S/Hb^S
			
Co-dominant	Normal RBCs	Both normal and sickle RBCs	Mostly sickle RBCs
Dominant	Malaria-sensitive	Malaria-resistant	Malaria-resistant

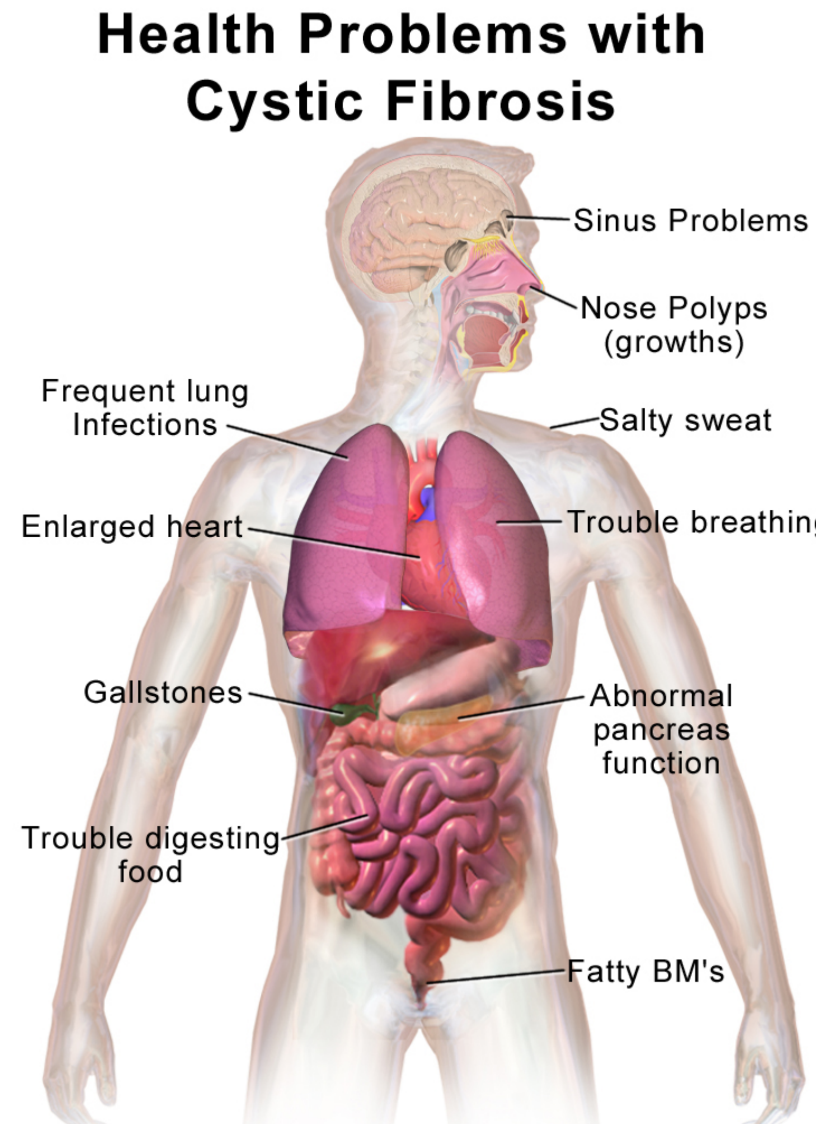
Hemoglobin sickle-cell allele

	Hb^A/Hb^A	Hb^A/Hb^S	Hb^S/Hb^S
			
Co-dominant	Normal RBCs	Both normal and sickle RBCs	Mostly sickle RBCs
Dominant	Malaria-sensitive	Malaria-resistant	Malaria-resistant
Recessive	No sickling disease	No sickling disease	Severe sickling disease

Is Hb^S a dominant or recessive allele?

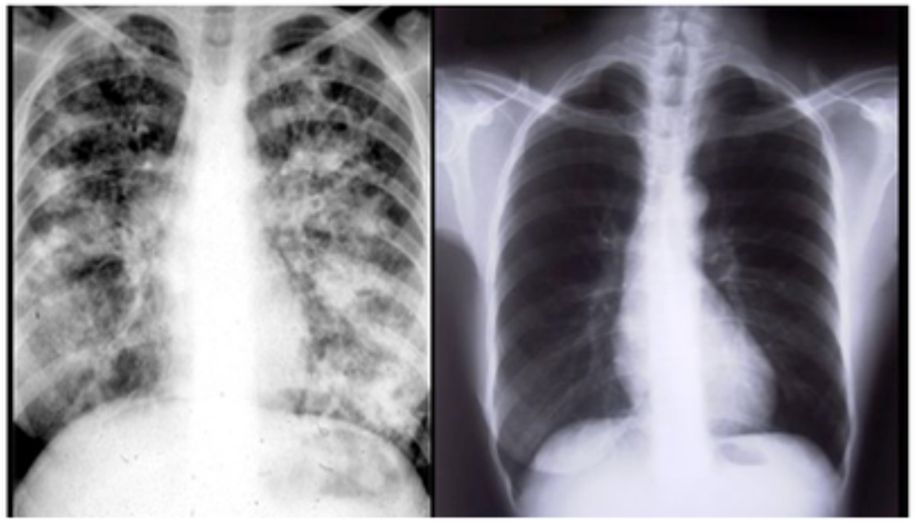
Cystic fibrosis is a debilitating disorder





- 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



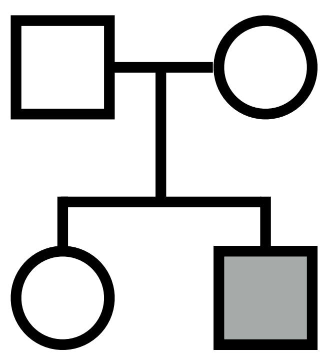
Cystic Fibrosis Lung Healthy Lung

Unaffected male

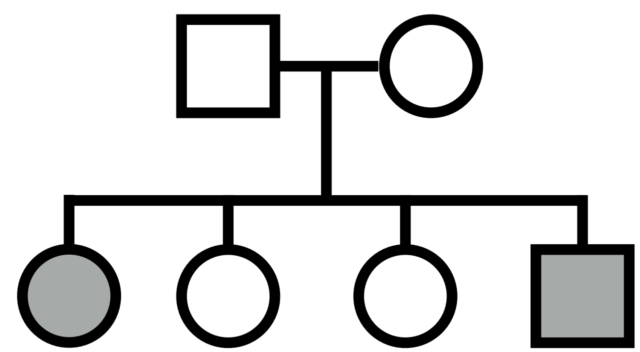
Unaffected female

CF male

CF female



Family #1

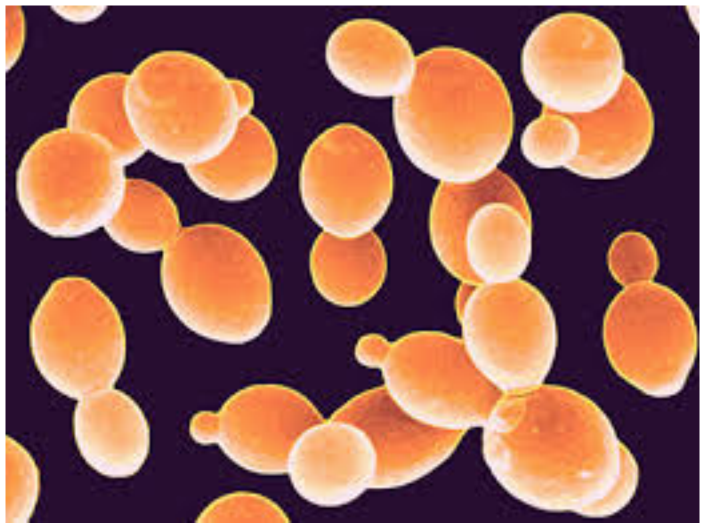


Family #2

What is the trait?

Dominance?

Genetics is a powerful discovery and analytical tool



Lecture 1