Bio393: Biomedical Genetics

Dr. Erik Andersen

Monday, Wednesday, and Friday 10:00 - 10:50 AM

Office hours and problem solving: Fridays 3-5 PM Silverman 3510

bio393.andersenlab.org

Lecture 1

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Point distribution		
Problem sets	22%	56 points (8 pts each)
Participation	3%	8 points
Midterms	50%	128 points (64 pts each)
Final	25%	64 points

Problem sets…

- should be completed and turned in at 5 PM on Fridays
- are scored as completed (not correct answers)
- comprise old exam and quiz questions
- should be completed independently
- will be reviewed from 3 - 5 PM on Fridays

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Date	Lecture topic
Mon. Apr. 1	Mendelian Inheritance, Basic probability
Wed. Apr. 3	Chromosome theory, recombination, and mapping I
Fri. Apr. 5	Chromosome theory, recombination, and mapping II, Problem set #1 due
Mon. Apr. 8	Screens, selections, mutants, and dosage
Wed. Apr. 10	Complementation
Fri. Apr. 12	Enhancement and suppression I, Problem set #2 due
Mon. Apr. 15	Enhancement and suppression II
Wed. Apr. 17	MIDTERM #1 (covers first third of class)

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Date	Lecture topic
Fri. Apr. 19	Genetic interactions: epistasis I, No problem set after midterm
Mon. Apr. 22	Genetic interactions: epistasis II
Wed. Apr. 24	Principles and methods of genetic analysis I
Fri. Apr. 26	Principles and methods of genetic analysis II, Problem set #3 due
Mon. Apr. 29	Principles and methods of genetic analysis III
Wed. May 1	Developmental genetics
Fri. May 3	Behavioral genetics, Problem set #4 due, Office hours in Silverman 4150
Mon. May 6	MIDTERM #2 (covers second third of class)

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Date	Lecture topic
Wed. May 8	Variation and allele frequency spectrum I
Fri. May 10	Variation and allele frequency spectrum II, Problem set #5 due
Mon. May 13	Pedigrees and phase I
Wed. May 15	Pedigrees and phase II
Fri. May 17	Linkage mapping and LOD scores, Problem set #6 due
Mon. May 20	Linkage disequilibrium and pop. structure
Wed. May 22	Complex traits, GWAS
Fri. May 24	NO CLASS, Memorial Day break
Mon. May 27	NO CLASS, Memorial Day
Wed. May 29	Human genetics and the future
Fri. May 31	Make-up, Genetics Escape Room Pre-test, Review, Problem set #7 due
Mon. Jun. 3	NO CLASS Reading week, Genetics Escape Room (optional)
Wed. Jun. 5	NO CLASS Reading week
Fri. Jun. 7	10 AM - 12 PM, FINAL EXAMINATION (covers last third of class)

Please fill out the pre-course survey

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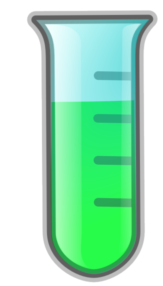
Biological Function

Genetics

Study organisms with components removed (mutants)

Biochemistry

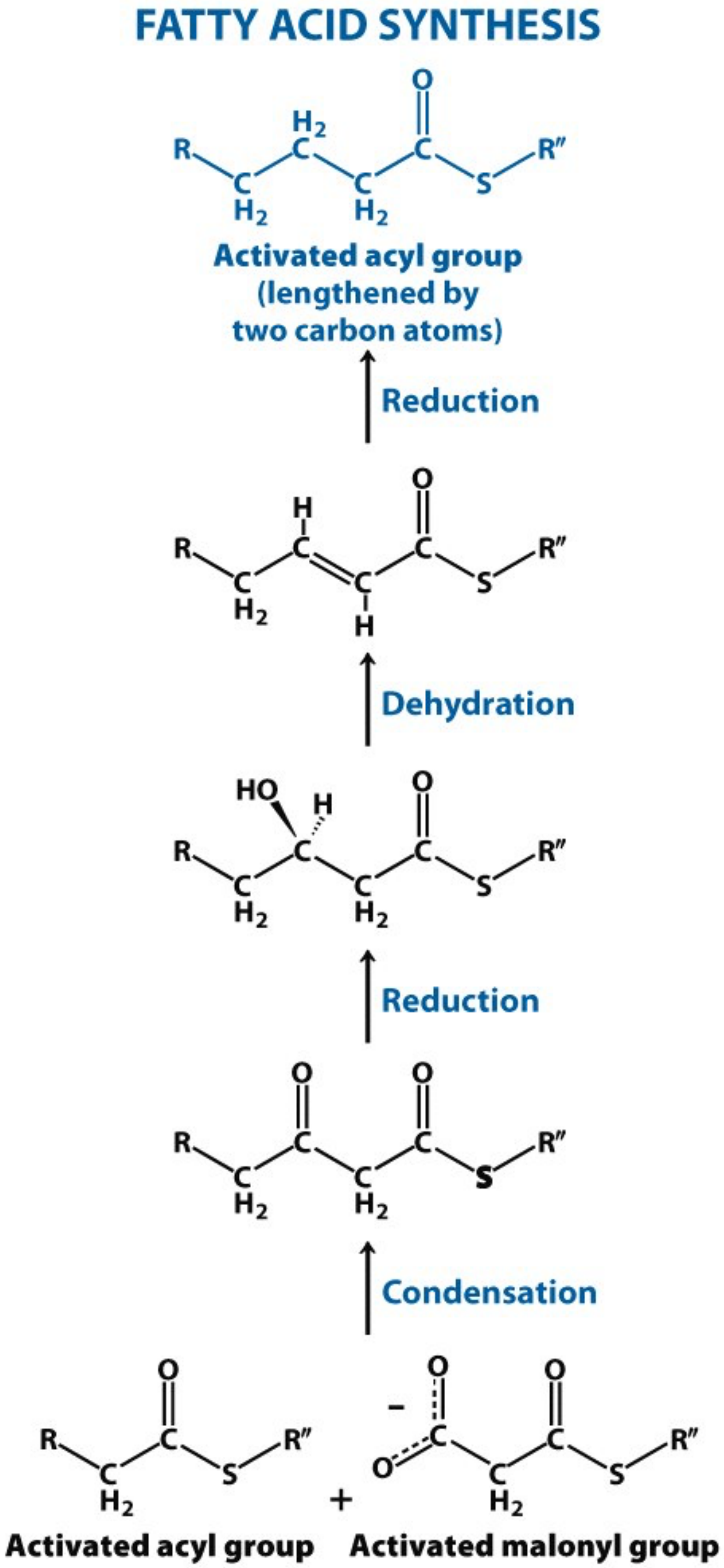


Study components removed from the organism

Genes — **Proteins**

Molecular Biology

No single discipline provides the data to define the system



Discussion:

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

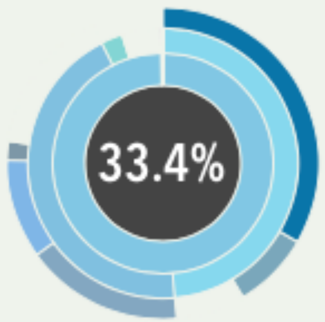
Figure 22.2
Biochemistry, Seventh Edition

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.

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.

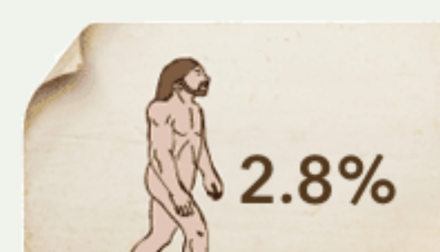
Your Mother's Line

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.



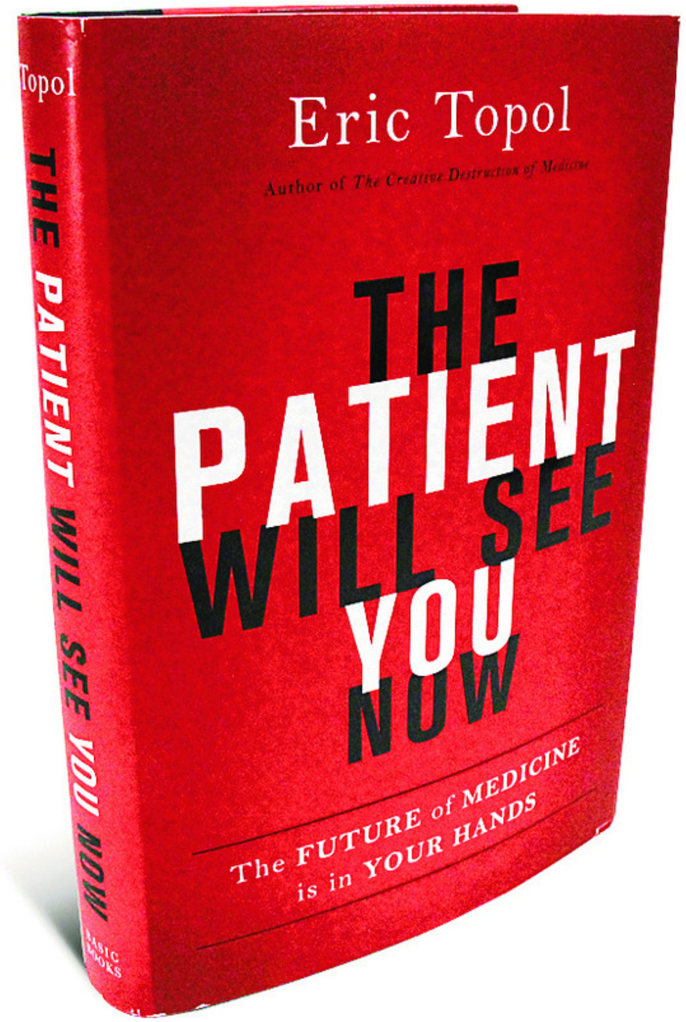
Famous Relative!

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

Top Relative Surnames

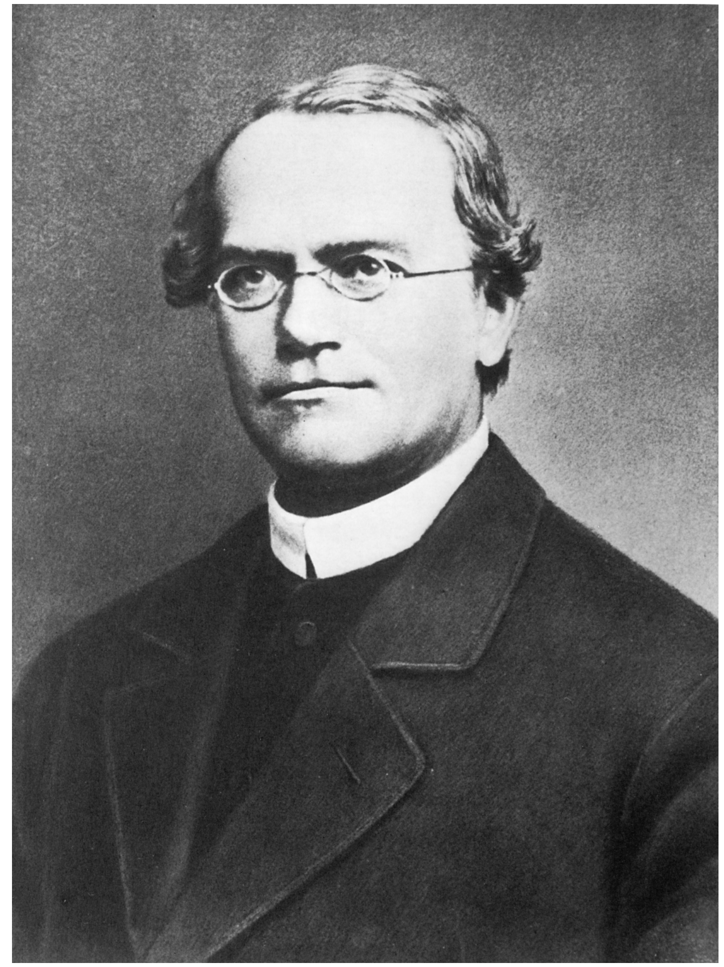
Surname	Count	Enrichment
Tompkins	6	58

Precision Medicine Initiative (PMI); All of Us



With sequencing, do we still need genetics?

The father of genetics: Gregor Mendel



Mendel the genius: Choice of model organism

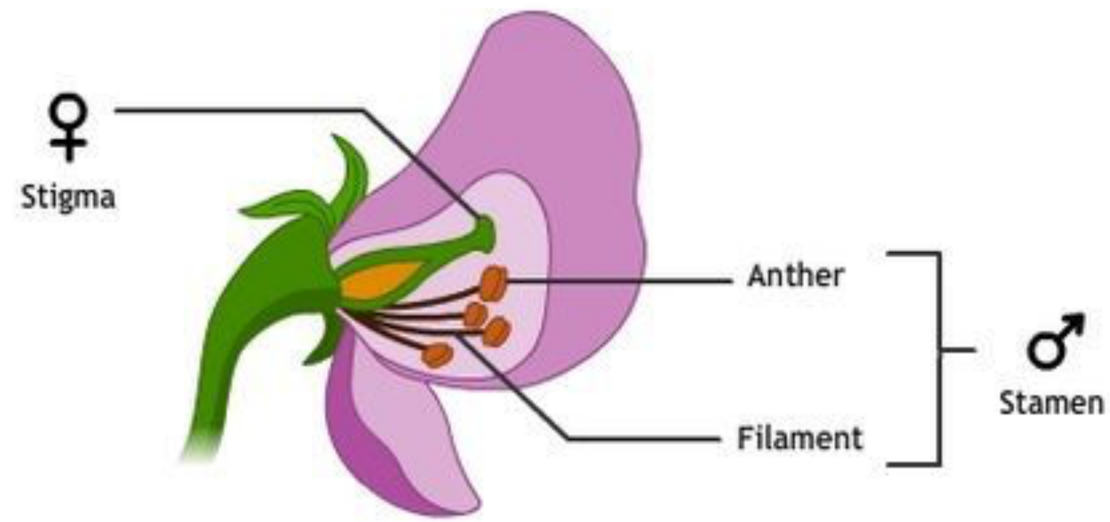
Hawkweed

Honey bees

Mice

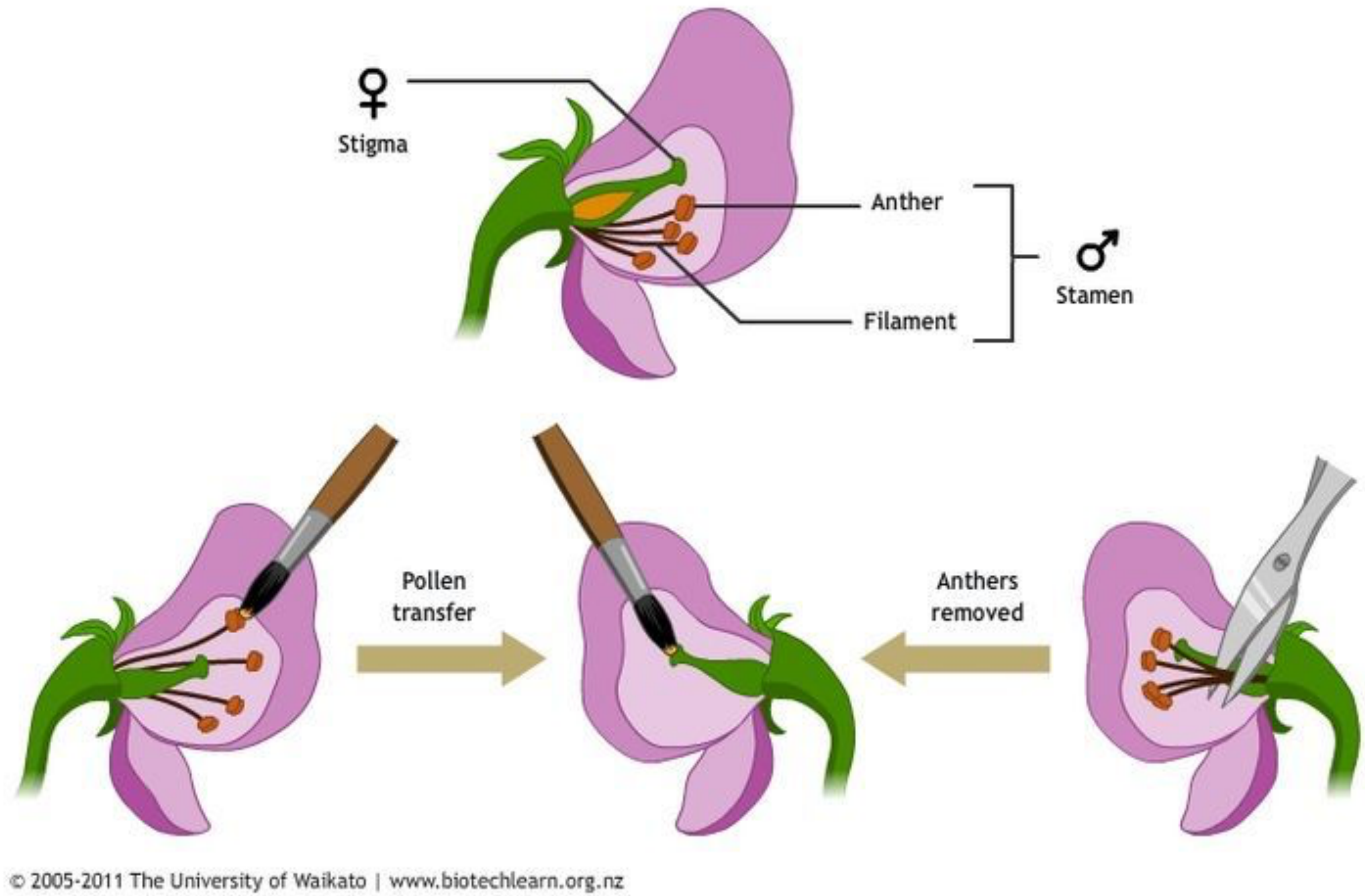
Mendel the genius: Choice of model organism

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



Mendel the genius: Choice of model organism

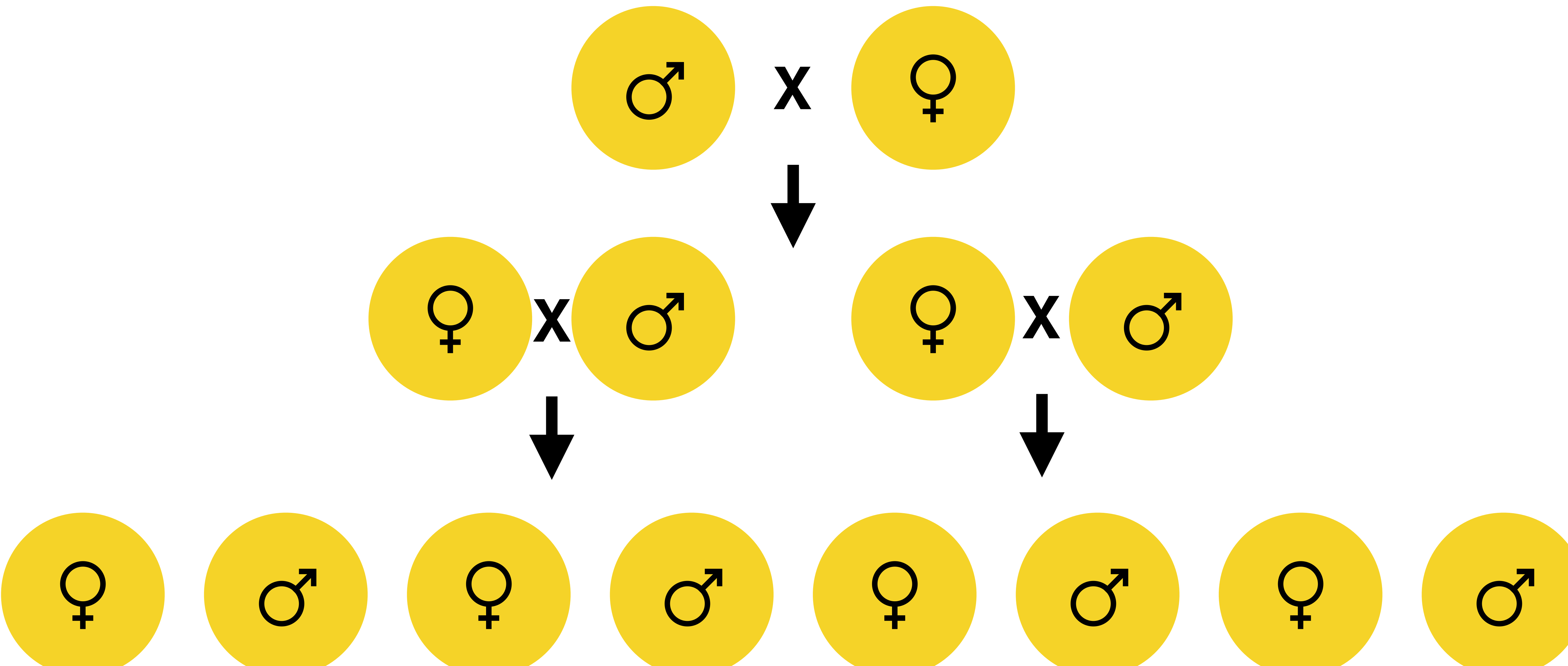
1. <u>Control</u> of genetic crosses



Mendel the genius: Choice of model organism

1. Control of genetic crosses

2. Reproducible true-breeding strains

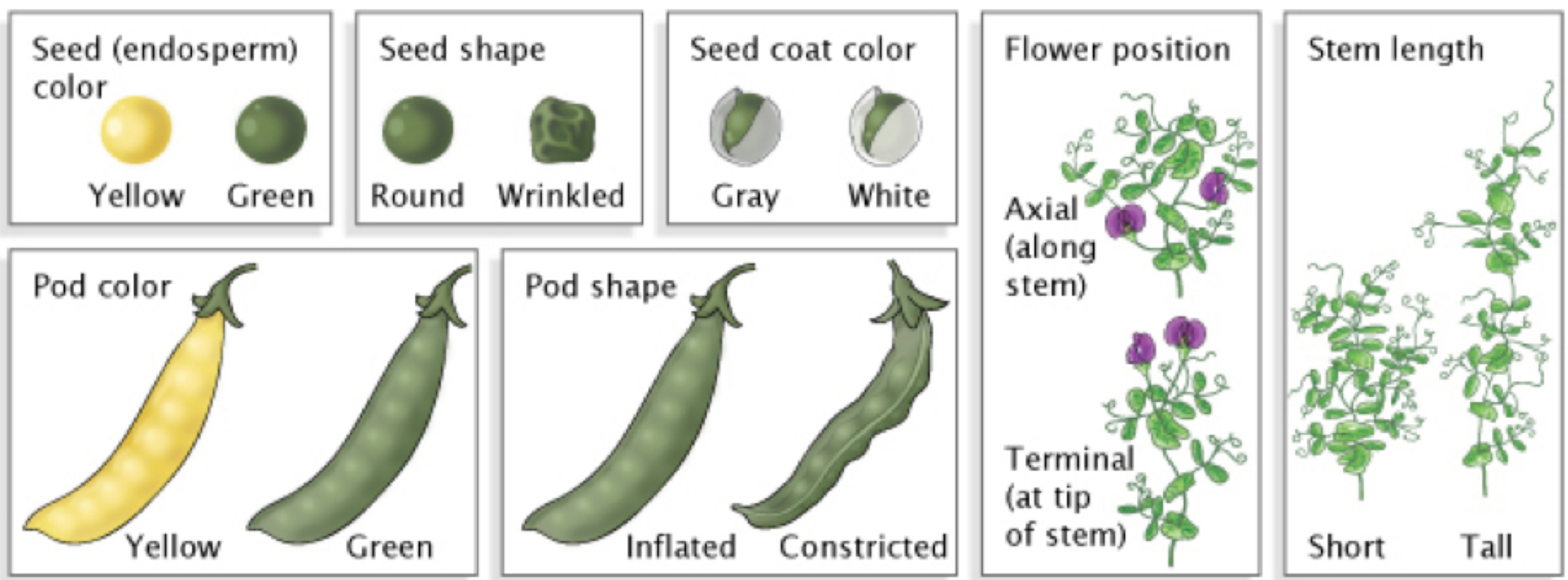


Mendel the genius: Choice of model organism

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

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

3. <u>Focus</u> 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

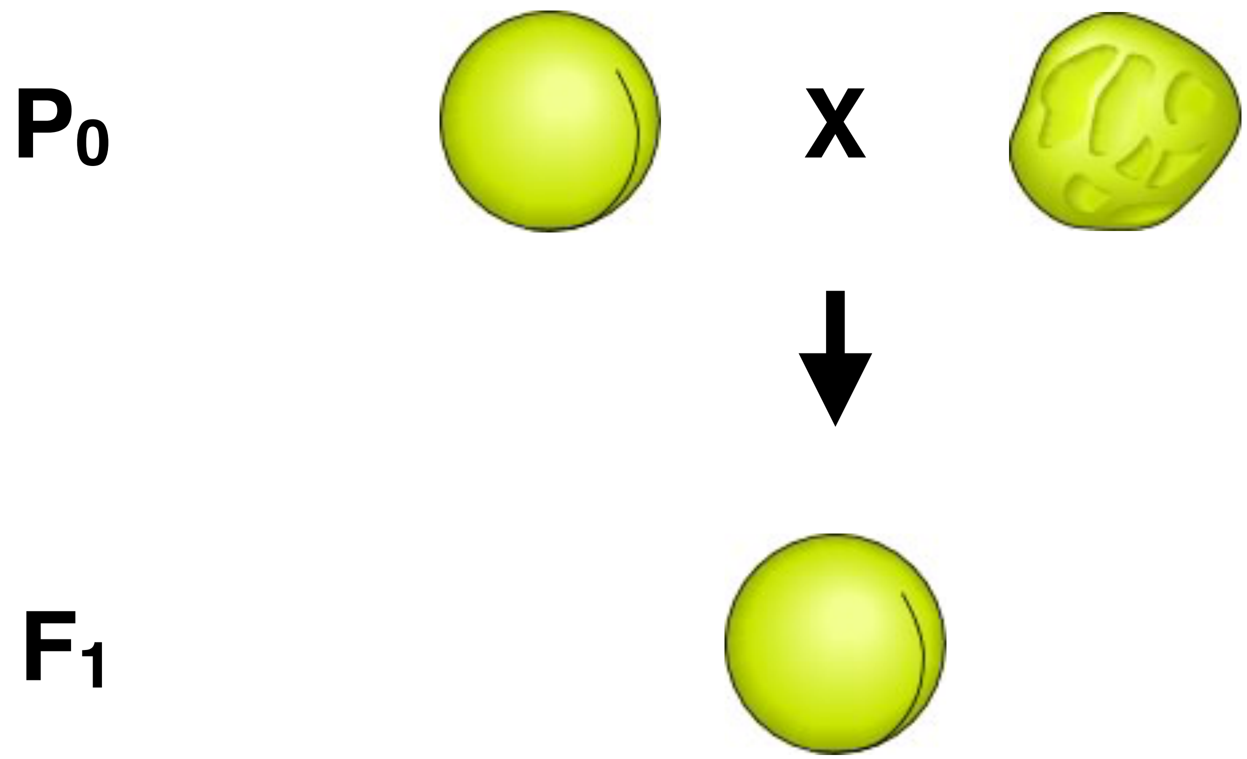
2. <u>Reproducible</u> true-breeding strains

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

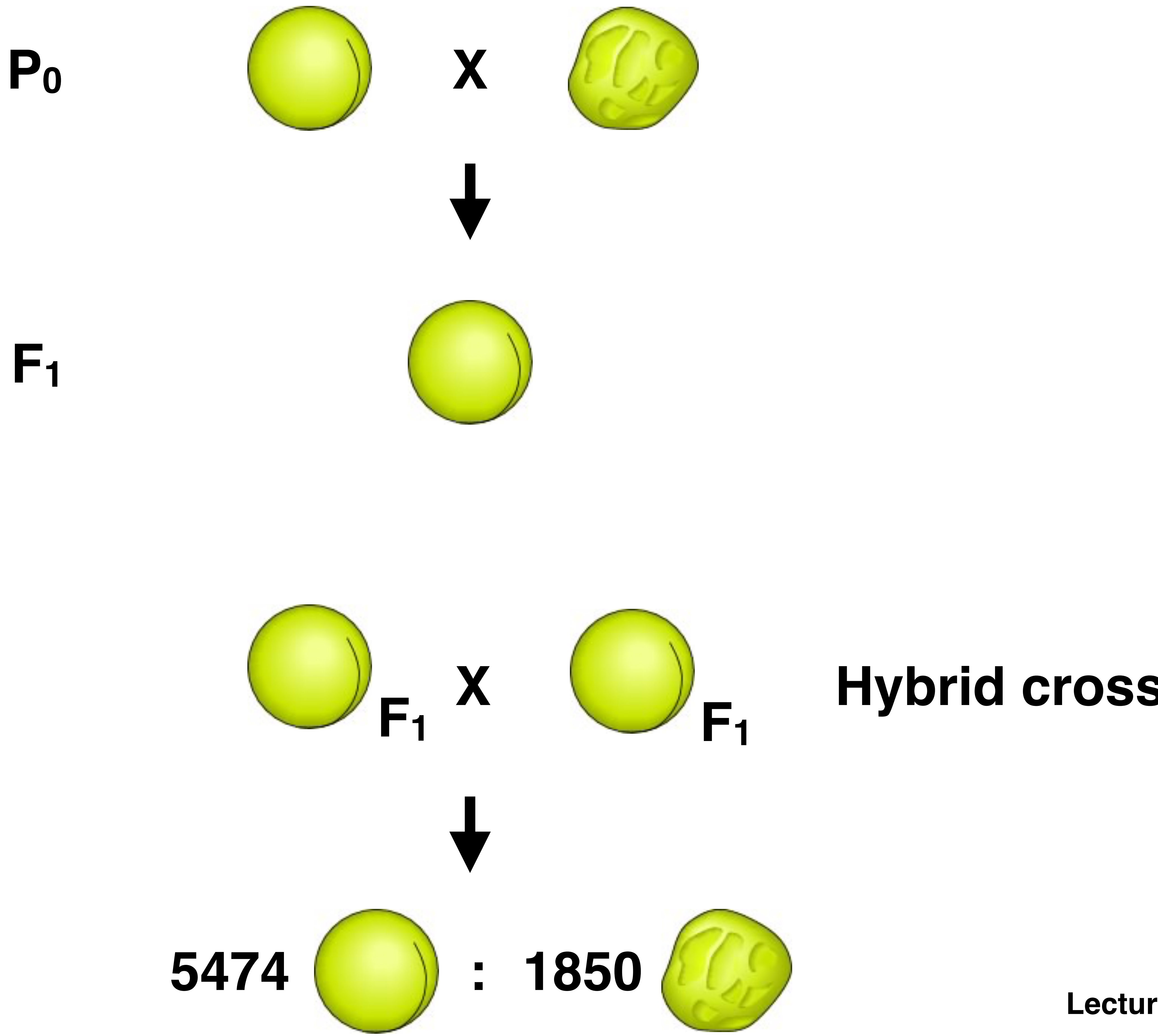


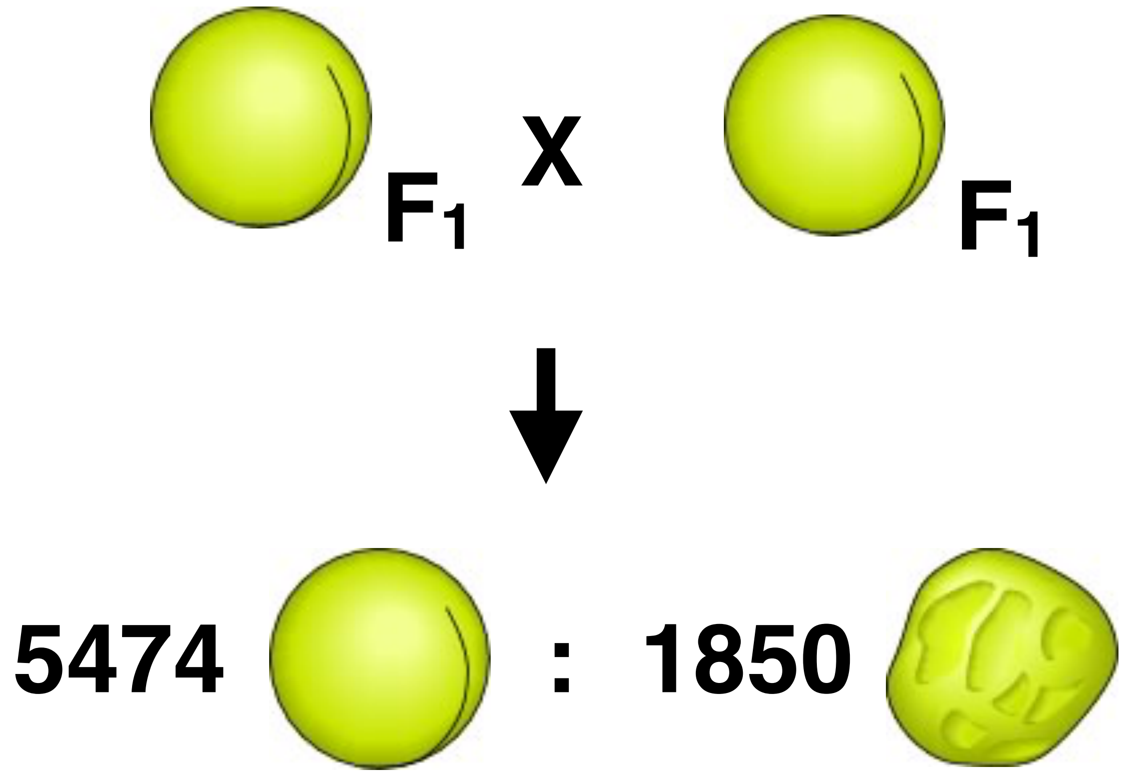
Trait (character)
Phenotype
Dominant
Recessive

Law of dominance

What is a gene?

Genotype
Gene (factor)

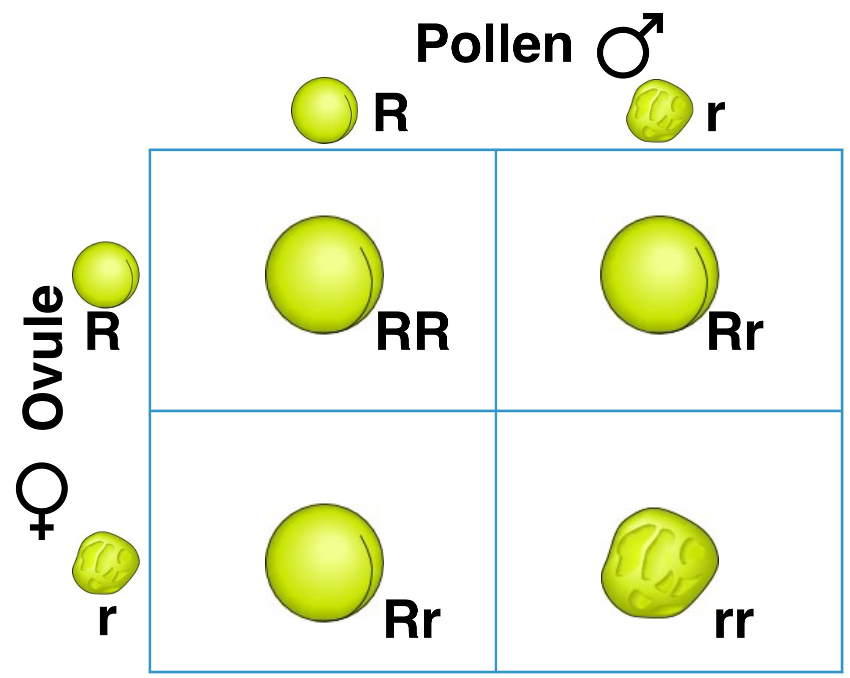

P0
X
F1
F1
X
F1
Hybrid cross
5474
:
1850



Hybrid cross

3:1 Phenotypic ratio

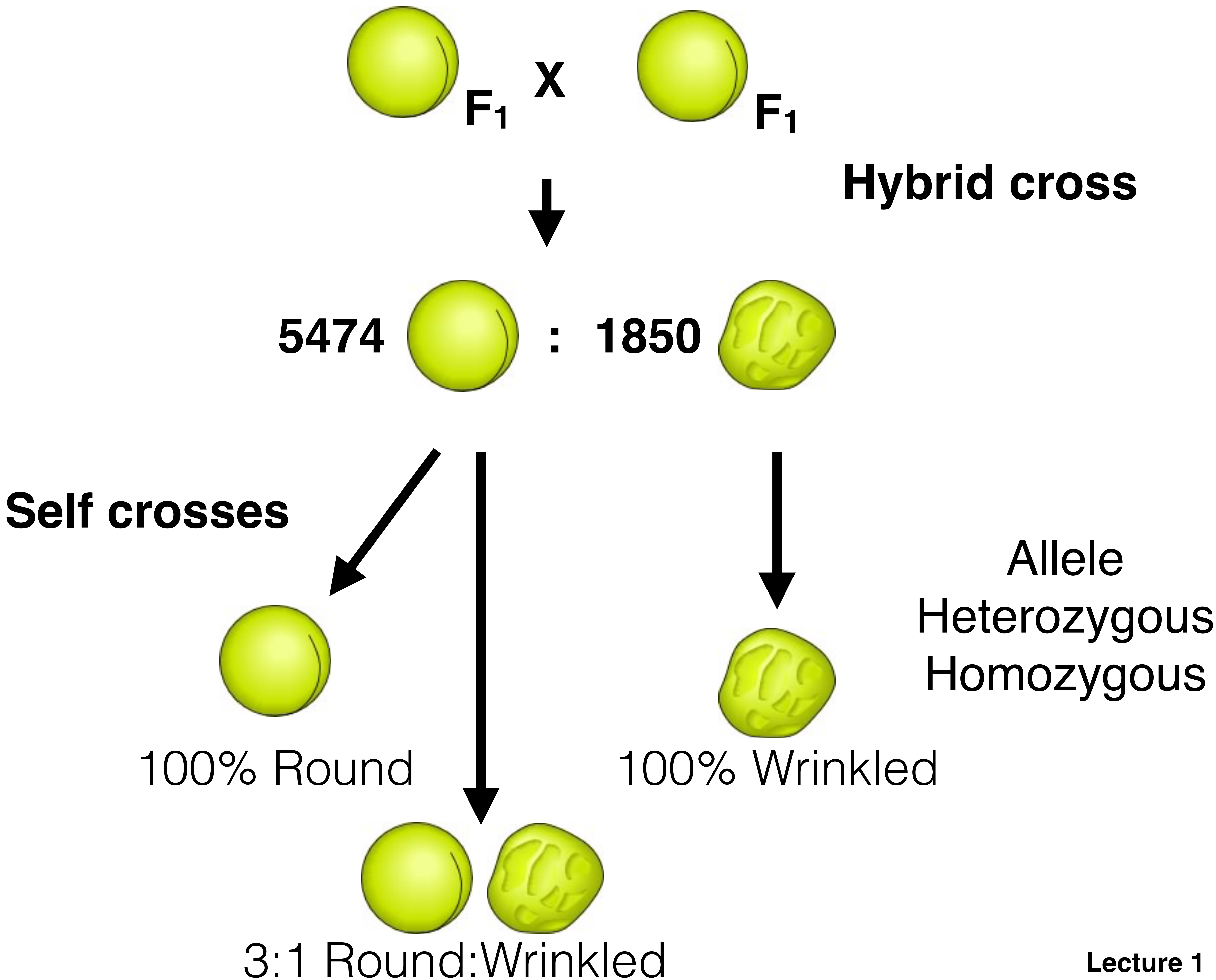
Hybrid cross



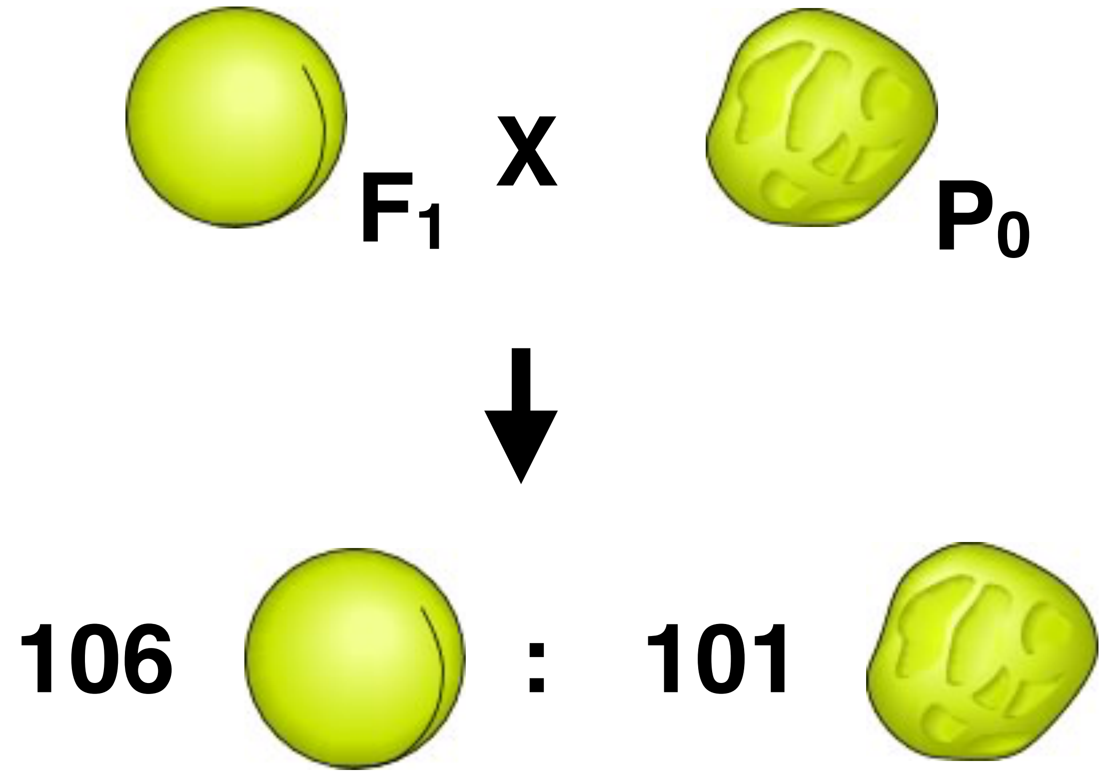
3:1 Phenotypic ratio

Gametes only carry one allele of gene.

Every individual carries a pair of alleles.



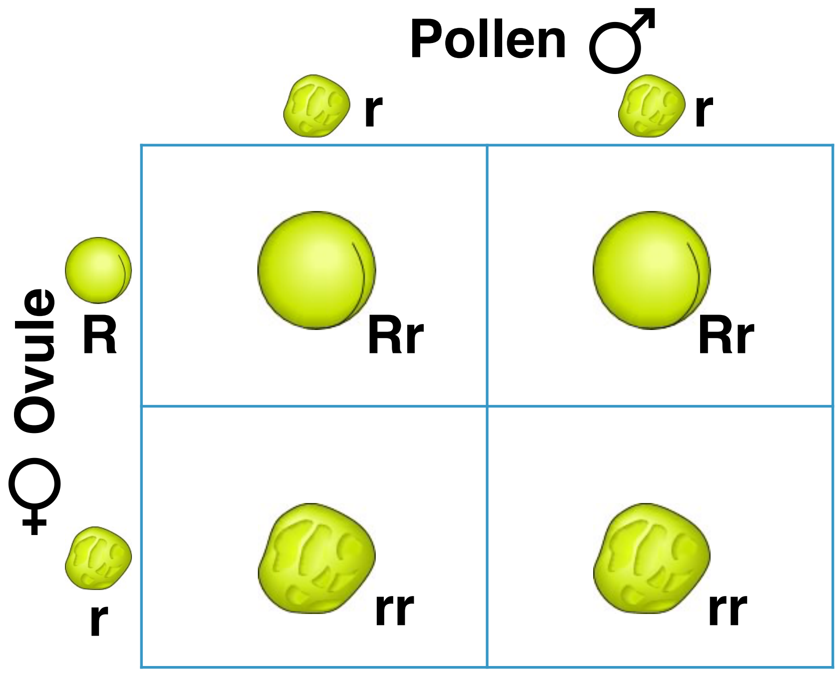
F_1 X F_1
Hybrid cross
5474 : 1850
Self crosses
Allele
Heterozygous
Homozygous
100% Round
100% Wrinkled
3:1 Round:Wrinkled



Test cross

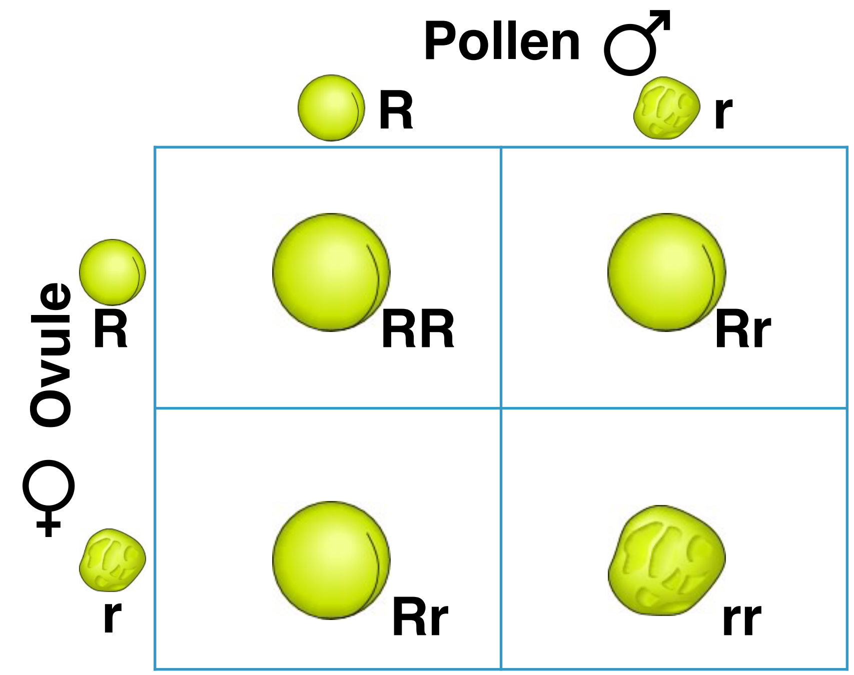
1:1 Phenotypic ratio

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

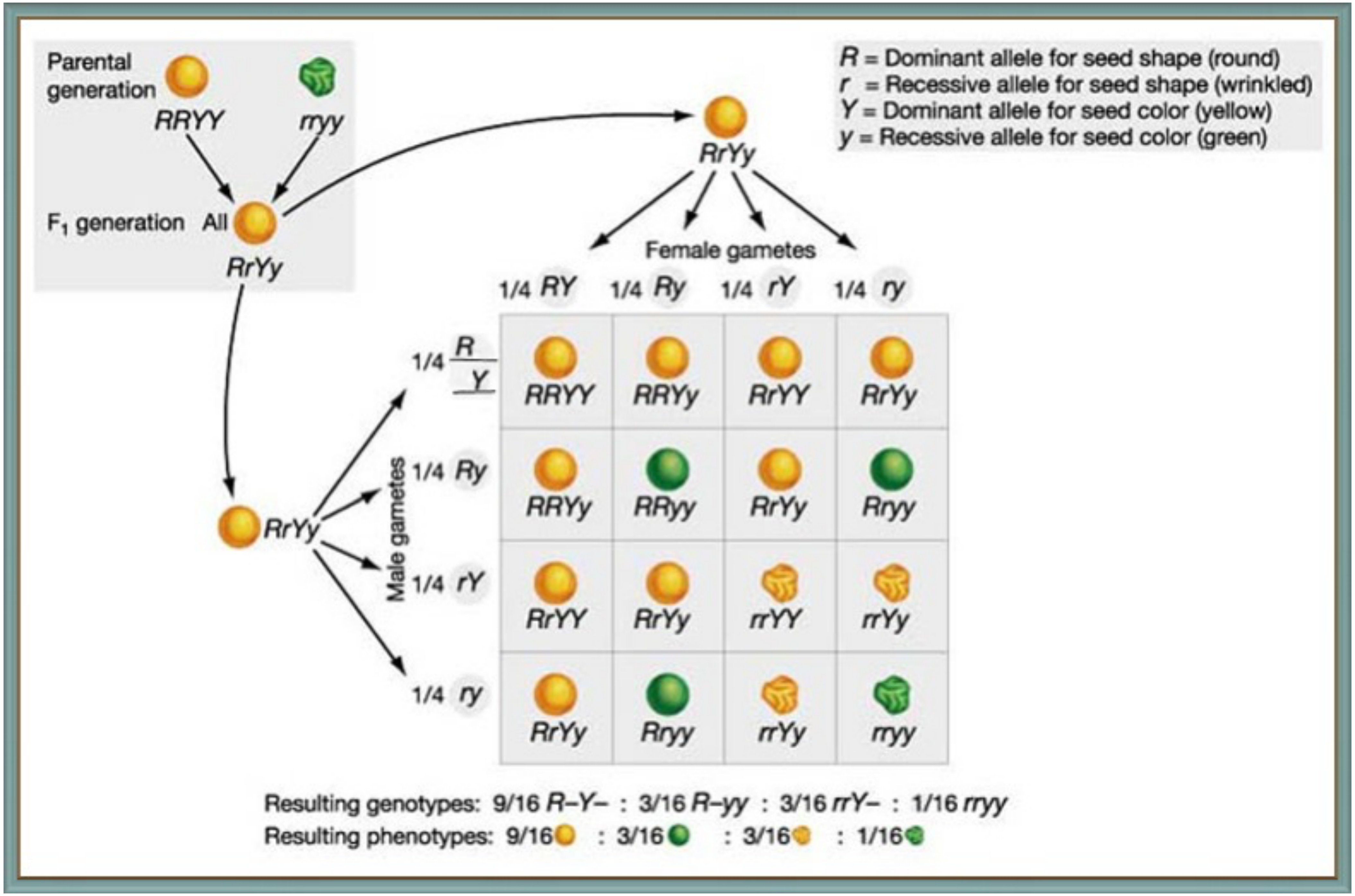
Every individual contains a pair of alleles.

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.

Character	Dominant Trait	×	Recessive Trait	F_2 Generation Dominant:Recessive	Ratio
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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

We're talking about gamete probabilities

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 $p(a) \times p(a) = 0.5 \times 0.5 = 0.25$

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

$$p(AA) + p(Aa) + p(aA) = (0.5 \times 0.5) + (0.5 \times 0.5) + (0.5 \times 0.5) = 0.75$$

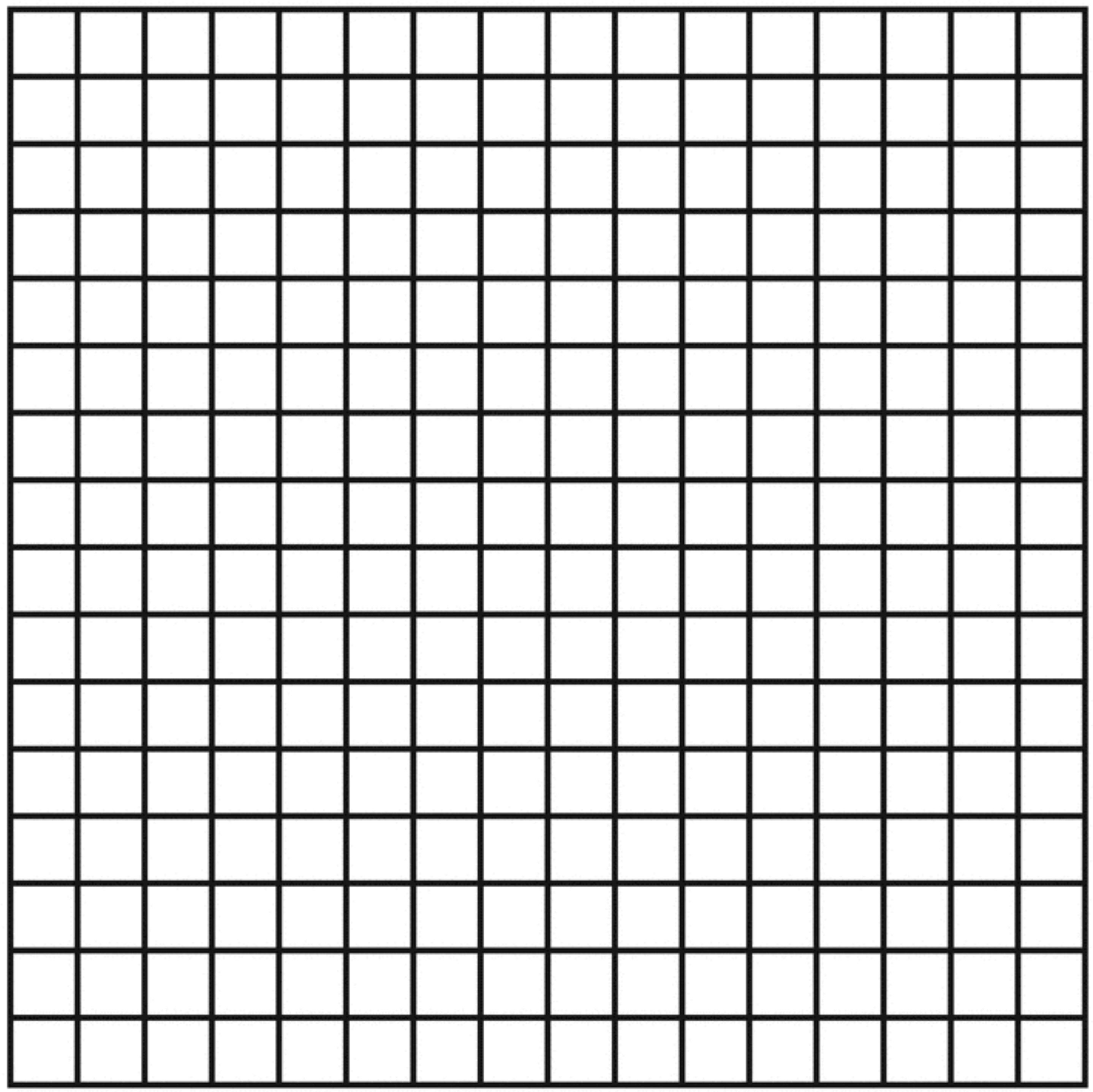
$$p(AA) + p(Aa) + p(aA) = 1 - p(aa) = 1 - 0.25 = 0.75$$

We're talking about gamete probabilities

Punnett squares are tedious…basic probability

AaBbCcDd x AaBbCcDd

Probability of offspring that is genotype of 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?

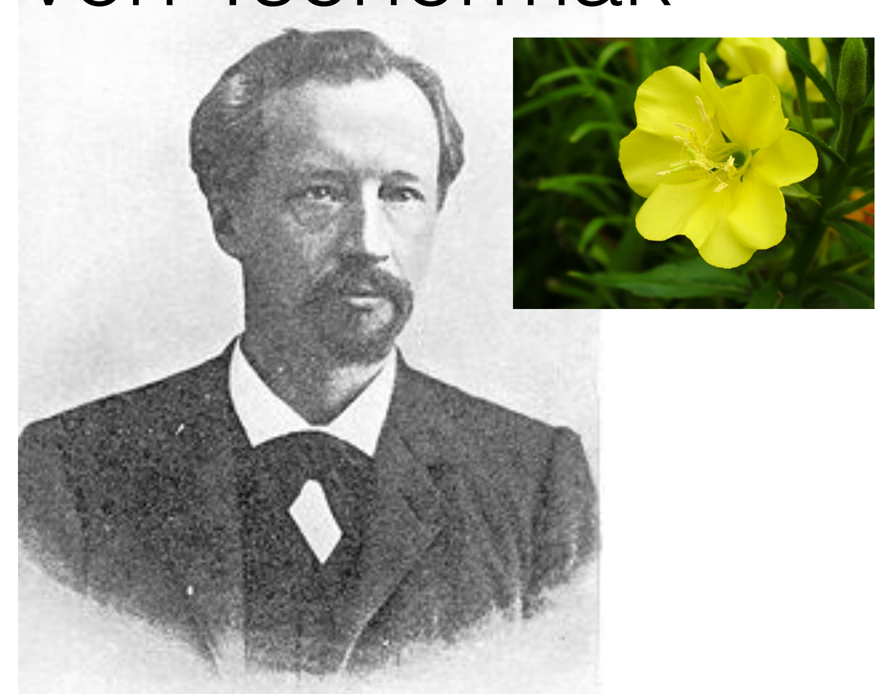
Lethality of combinations, didn't count enough, or epistasis

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?

1. Peas are great model system with controlled crosses and defined traits

2. He worked hard, counted, made and tested his models

3. He was lucky!

Gregor Mendel was lucky!

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

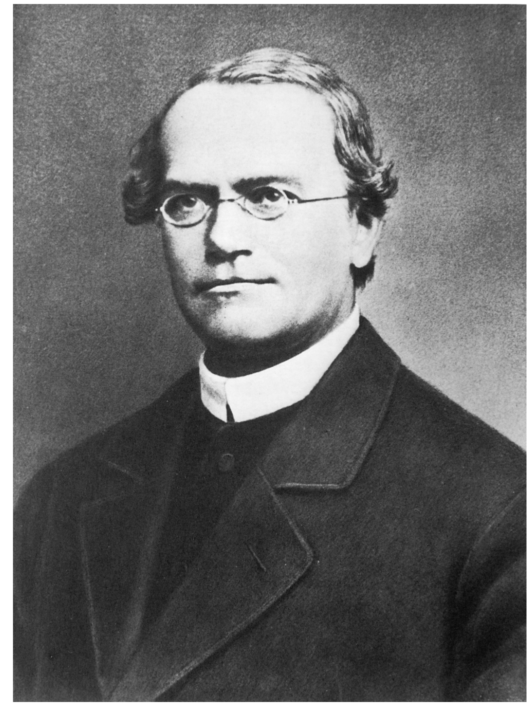
Polyploidy

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

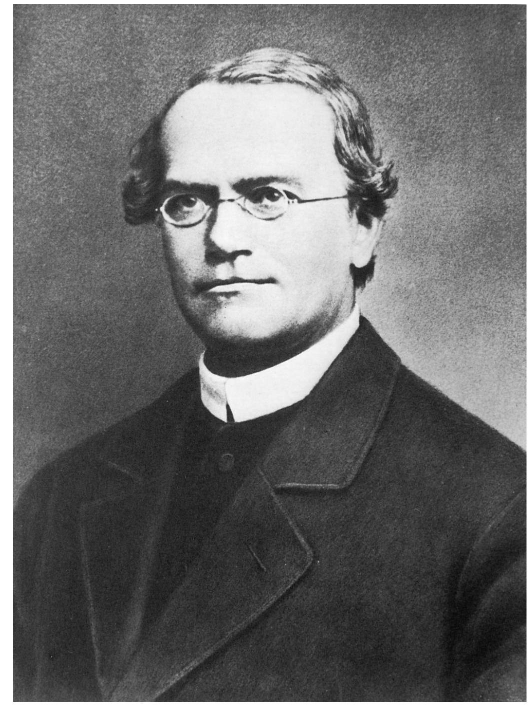
Gregor Mendel was lucky!



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

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

Gregor Mendel was lucky!



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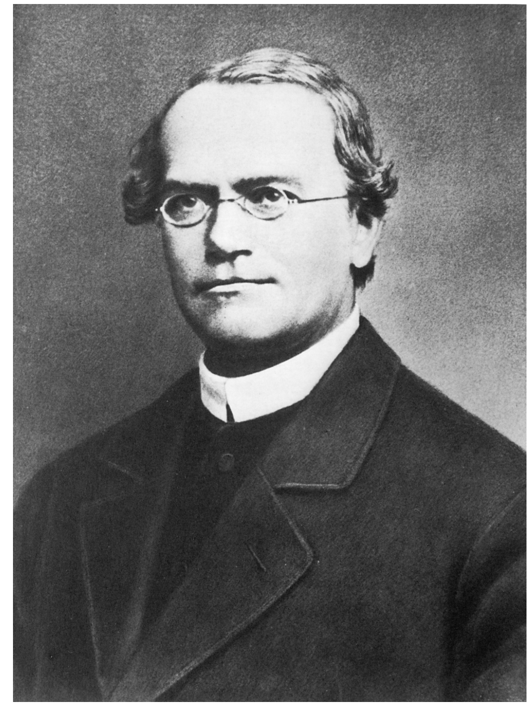
Gregor Mendel was lucky!



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.