Independent Inheritance
Sex-linked Inheritance

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What is inheritance?

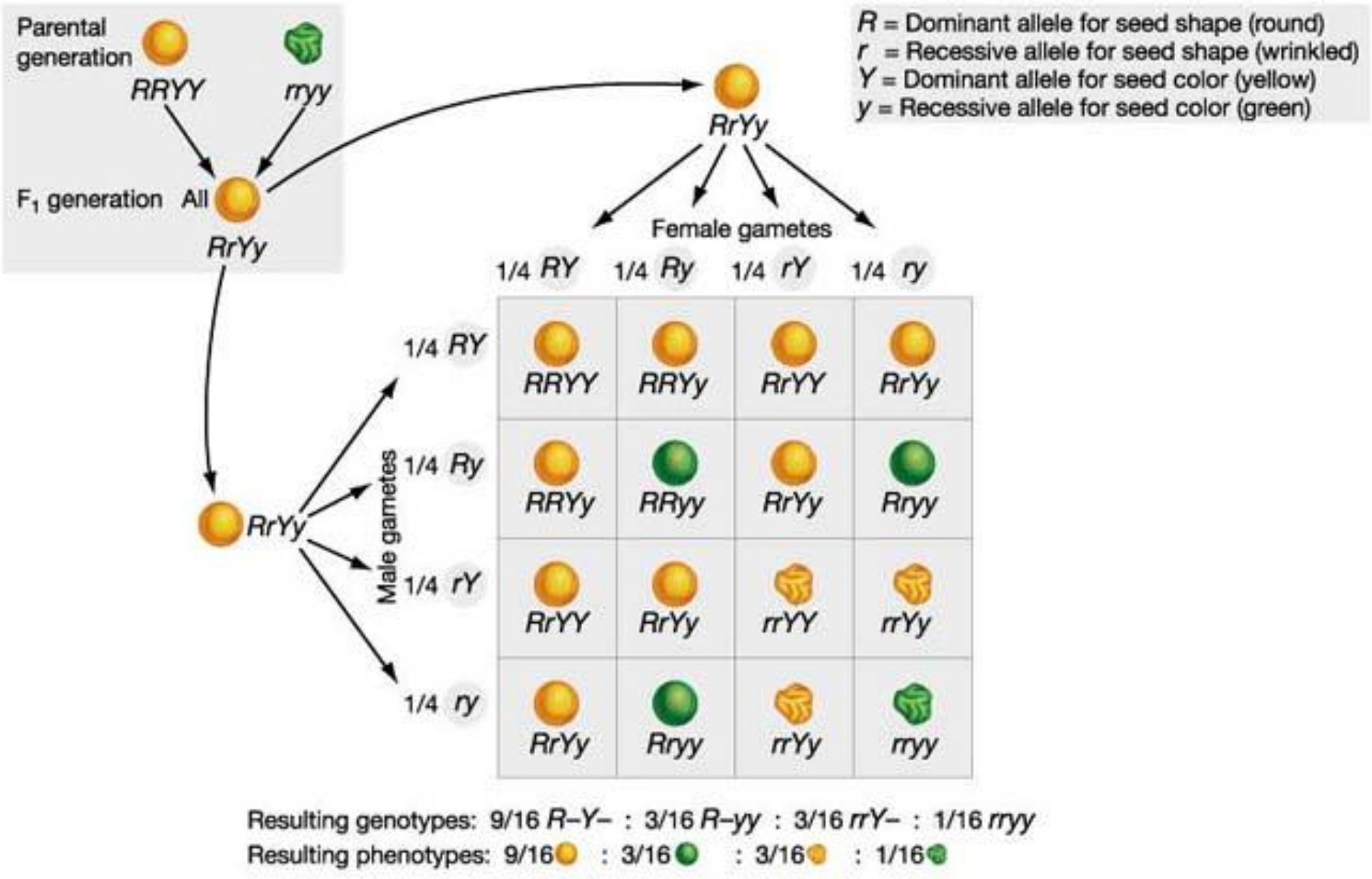
- **Inheritance** - is the process by which genetic information is passed on from parent to child. This is why members of the same family tend to have similar characteristics.

Mendelian inheritance

- The simplest form of inheritance was uncovered from the work of an Austrian monk called **Gregor Mendel in 1865.**
- From years of experiments using the common pea plant, Mendel was able to describe the way in which genetic characteristics are passed down from generation to generation.
- Gregor used peas in his experiments primarily because he could easily control their fertilisation, by transferring pollen from plant to plant with a tiny paintbrush.
- Sometimes he transferred pollen to and from flowers on the same plant (self-fertilisation) or from another plant's flowers (cross fertilisation).

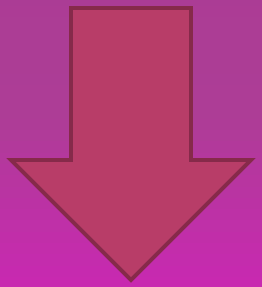
Mendel studies seven characteristics in the garden pea

	Flower color	Flower position	Seed color	Seed shape	Pod shape	Pod color	Stem length
P	Purple × White	Axial × Terminal	Yellow × Green	Round × Wrinkled	Inflated × Constricted	Green × Yellow	Tall × Dwarf
F_1	Purple	Axial	Yellow	Round	Inflated	Green	Tall


Parental generation
RRYY
rryy
F1 generation All
RrYy
RrYy
R = Dominant allele for seed shape (round)
r = Recessive allele for seed shape (wrinkled)
Y = Dominant allele for seed color (yellow)
y = Recessive allele for seed color (green)
Female gametes
1/4 RY
1/4 Ry
1/4 rY
1/4 ry
Male gametes
1/4 RY
1/4 Ry
1/4 rY
1/4 ry
RrYy
RRYY RRYy RrYY RrYy
RRYy RRyy RrYy Rryy
RrYY RrYy rrYY rrYy
RrYy Rryy rrYy rryy
Resulting genotypes: 9/16 R–Y– : 3/16 R–yy : 3/16 rrY– : 1/16 rryy
Resulting phenotypes: 9/16 : 3/16 : 3/16 : 1/16

The results from this and further experiments led Gregor Mendel to come up with 3 key principles of inheritance:

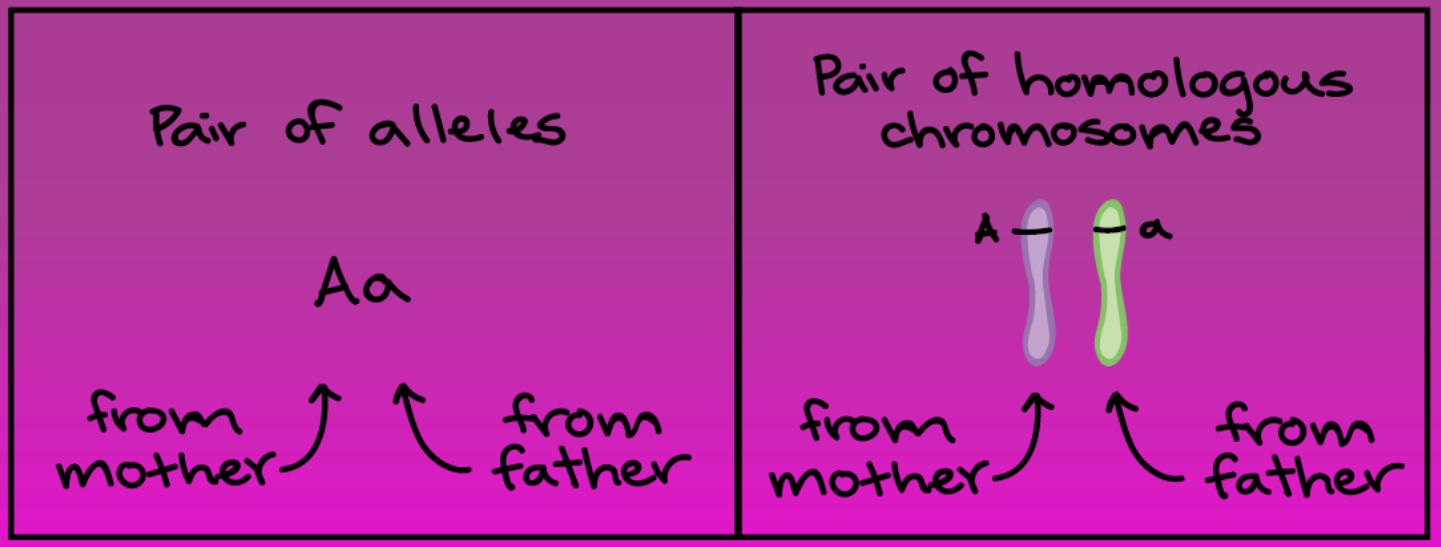
1. The inheritance of each trait is determined by ‘factors’ (now known as genes) that are passed onto descendants.
2. Individuals inherit one ‘factor’ from each parent for each trait.
3. A trait may not show up in an individual but can still be passed onto the next generation.



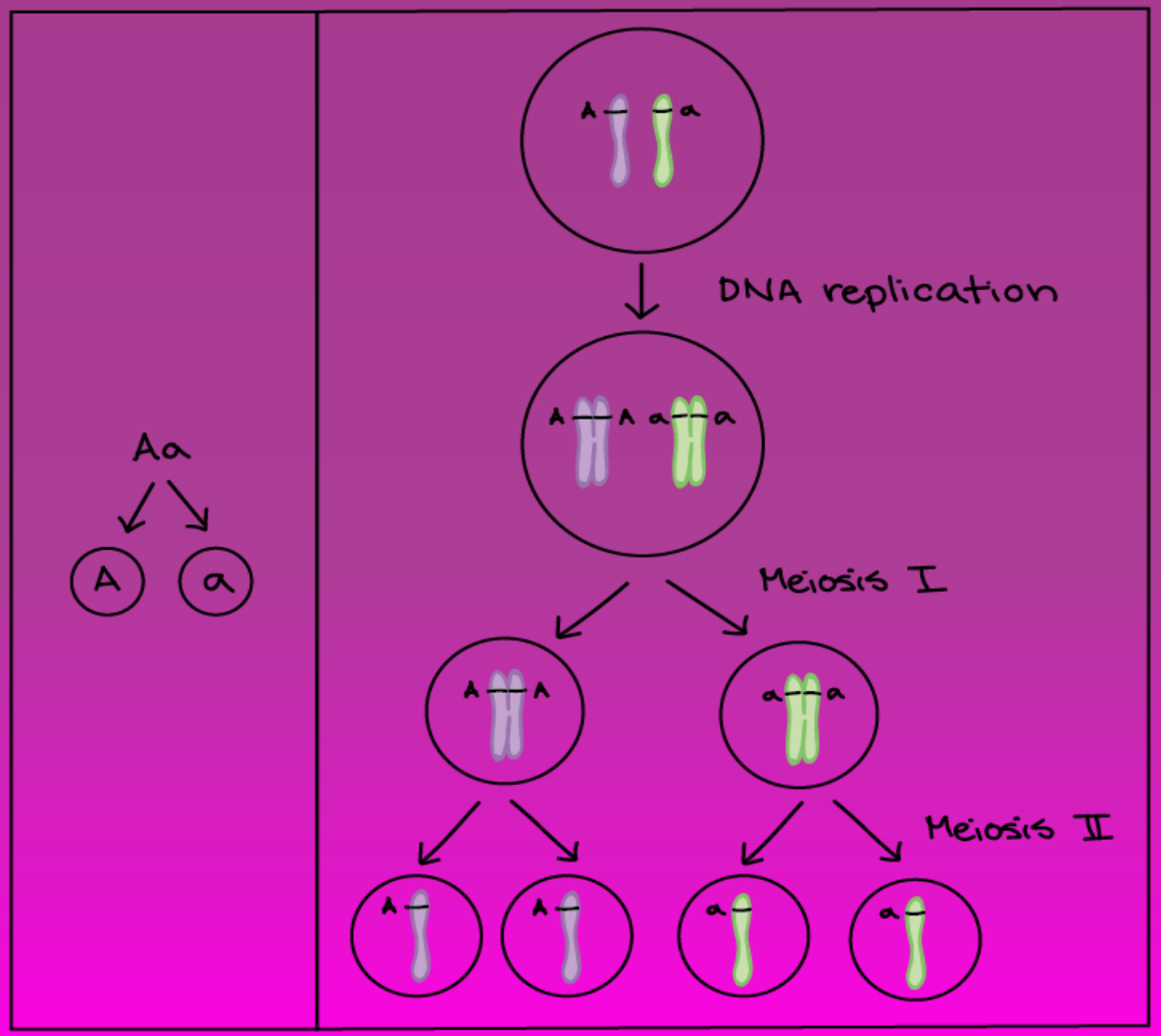
Genetic traits that follow these principles of inheritance are called Mendelian.

Thomas Morgan's school

Chromosomes, like Mendel's genes, come in matched (homologous) pairs in an organism. For both genes and chromosomes, one member of the pair comes from the mother and one from the father.

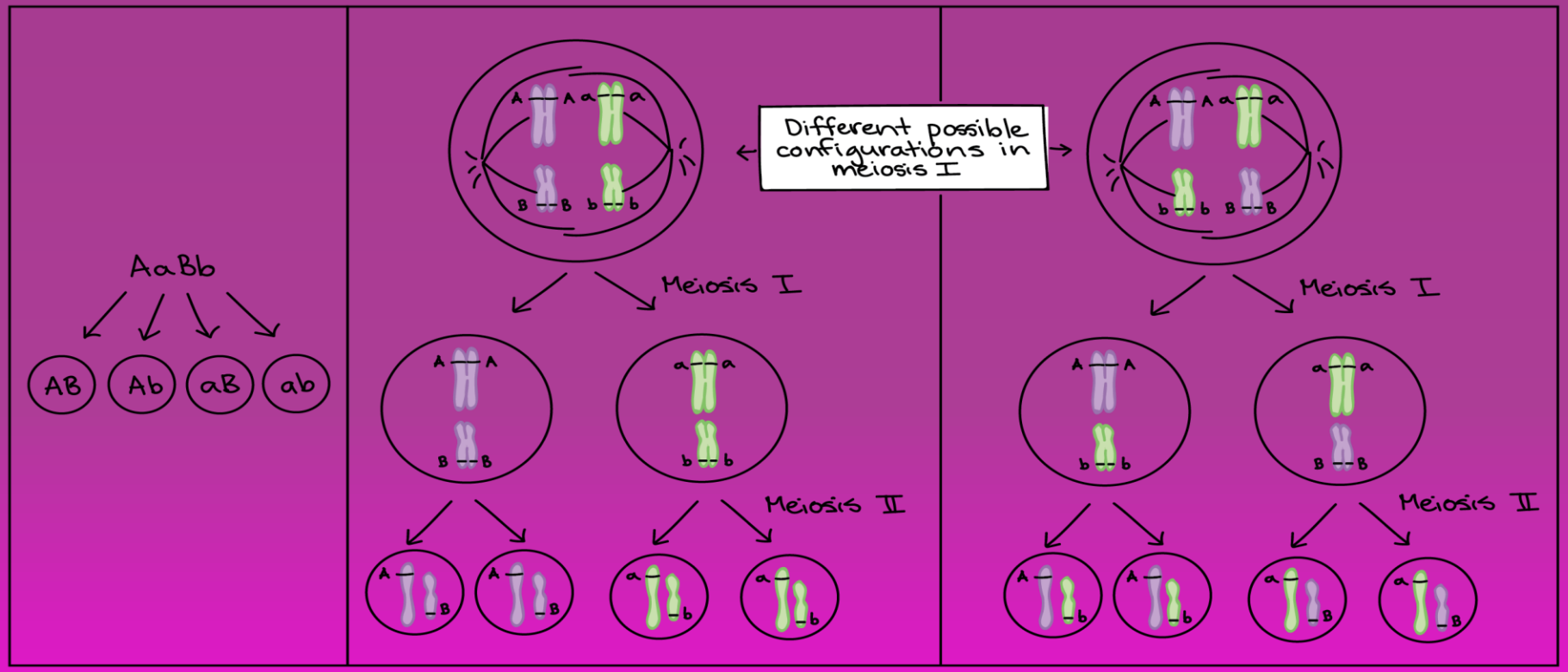


- The members of a homologous pair separate in meiosis, so each sperm or egg receives just one member. This process mirrors segregation of alleles into gametes in Mendel's law of segregation.



Gametogenesis (meiosis)

- The members of different chromosome pairs are sorted into gametes independently of one another in meiosis, just like the alleles of different genes in Mendel's law of independent assortment.



Columbia University Fly Room.

T. H. Morgan: Fun with fruit flies

- Morgan chose the fruit fly, *Drosophila melanogaster*, for his genetic studies. What fruit flies may lack in charisma (depending on your taste in insects), they make up for in practicality: they're cheap, easy, and fast to grow.

It is necessary to create genetic collections for genetic analysis. The collection of mouse varieties collected in the Jackson Laboratory in the United States, the Institute of Cytology and Genetics of the Siberian Branch of the Academy of Sciences of the USSR now SB RAS.

These COLLECTIONS containing ordinary morphological and other mutants have dies with vaious tissue compatibility genes. They are used in experimental oncology.

THE LARGEST COLLECTION IS THE GENETIC LINES OF DROSOPHIL. THESE COLLECTIONS are based in the universities of Europe and the USA.

The Bloomington Drosophila Stock Center (BDSC) supports a large, worldwide community of scientists using the insect Drosophila melanogaster as a model organism for biomedical experimentation. The goals of the BDSC are to provide a collection of documented living stocks of broad value to current research, to preserve documented strains with clear future value, and to provide information and support services that promote maximal exploitation of these materials. These goals facilitate research by providing universal and rapid access to the most generally useful stocks, by preserving specialty genotypes with exceptional characteristics, and by providing information that helps researchers identify stocks appropriate to their needs.

Drosophila is used extensively in studies of biological processes relevant to human health and investigations of molecular mechanisms underlying disease, because genetic technologies available to Drosophila researchers are among the most sophisticated in any multicellular organism.

As the most comprehensive source of stocks for genetic experimentation with Drosophila, the BDSC is central to the success of many research projects including a large number of NIH grants. The first specific aim of this proposal is to continue acquiring, maintaining and distributing Drosophila strains and to continue developing associated information resources to meet the research needs of Drosophila scientists while maintaining and promoting excellent user support.

Key to this aim is the administration and advancement of the highly successful cost recovery program that finances operational expenses from user fees. Consequently, the proposal focuses on support and development of the core management team as the most effective way to leverage the investment of NIH resources.

The second specific aim is to undertake research to increase the utility of a subset of BDSC stocks which have been preserved for their distinctive mutant phenotypes. The work will experimentally map mutations in these stocks to specific transcription units in the genome sequence and will substantially increase the usefulness and relevance of the stocks to researchers investigating the functional significance of molecularly defined genes.

Genetically labeled strains (auxotrophic mutants, mutants defective in repair systems, recombination, etc.) are retained in collections of fungi and bacteria.

In the collections contain forms that differ or are similar phenotypically according to the most diverse characteristics, having a different origin. These can be gene, chromosomal, or genomic mutations. To solve special problems on the basis of the collection material, special test forms, line-analyzers with various recessive or dominant markers, with chromosome rearrangements - deletions, inversions, translocations, moving genetic elements that prevent the passage of crossing-over, or changing the localization and activity of that or another gene; series of mono-, tri-, and nullisomics over different chromosomes, and so on.

Genetic collections are usually created on the basis of selection and genetic centers and institutes, as well as universities.

The world's largest center for preserving the hereditary diversity of many crop plants is the All-Union Institute of Plant Industry named after N.I. Vavilov. It has strong points and experimental stations, where studies are conducted to determine the reaction rate of thousands of samples for each culture.

The oldest collection among plants should be called the corn collection in the United States. It contains a variety of patterns with mutations that control the mutability and expressiveness of genes, the behavior of chromosomes in meiosis and mitosis; enzyme systems; structure of endosperm; formation and distribution of chlorophyll; the structure of various elements of the generative system; nuclear and non-nuclear mutants, and the like. In this collection collected more than 3 thousand samples, identified by scientists in America and other countries.

In the USA universities, there are also collections of barley, aneuploidy wheat and other plants. In Germany, the central seed bank of Arabidopsis, containing 149 natural races and more than 500 mutants, was created. Similar banks are organized in other countries - the USA, England, Spain, the Netherlands, etc.

The Leningrad State University (nowadays, Saint Petersburg State University) has created a unique collection of winter and spring rye, which is unique in terms of volume and possibilities of using it for studying genetics. It contains more than 100 auto-sterile forms that differ from the standard type by one or more features, as well as over 300 auto-sterile lines, many of which also have genetic markers. In addition, LSU has collections of strawberries, radish, and barley. In Moldova there are the largest collections of tomatoes, corn and other crops. In Leningrad, the All-Union Institute of Plant Protection collected a collection of mycological herbarium necessary for studying the nature of immunity in plants. The importance of this collection cannot be overestimated, since more than 1500 diseases, the causative agents of which are 50 thousand species of fungi, now affect the leading agricultural crops. In this case, some pathogens are capable of affecting several plant species. The collection contains herbarium specimens of affected plants with their pathogen and pure parasite cultures. It collected about 150 thousand samples of mushrooms; more than 600 thousand samples of pathogens are in the relevant national collections of the United States.

Banks of human and animal cell cultures are now acquiring great importance in connection with the possibility of retaining a hybridoma in them, resulting from the fusion of normal lymphocyte cells with myeloma cells, giving hybridomas myeloma properties - the capacity for unlimited growth. Hybridomas are used to produce monoclonal antibodies, i.e. antibodies produced by descendants of a single cell. They have high specificity and are directed against one antigenic determinant. Cell cultures are used to produce biologically active substances of high purity, for the determination of histone-compatibility antigens during transplantation, etc. among the banks of cell cultures preserved by preservation in liquid nitrogen, one can name the American collection of type cultures; human cell cultures obtained from normal and sick people with hereditary pathologies, the cell lines of mouse tumors

- Morgan's crucial, chromosome theory-verifying experiments began when he found a mutation in a gene affecting fly eye color. This mutation made a fly's eyes white, rather than their normal red.
- Unexpectedly, Morgan found that the eye color gene was inherited in different patterns by male and female flies. Male flies have an X and a Y chromosome (XY), while female flies have two X chromosomes (XX). It didn't take Morgan long to realize that the eye color gene was being inherited in the same pattern as the X chromosome.

Based on these results, Morgan arrived at three important conclusions:

- The appearance of white eyes in females shows that this trait is not lethal in females.
- All possible combinations of white eyes and sex are possible.
- The white-eye trait can be carried over to females when F_1 females are crossed with white-eyed males.

Table 1: Expected Mendelian Ratios versus Morgan's Actual Results

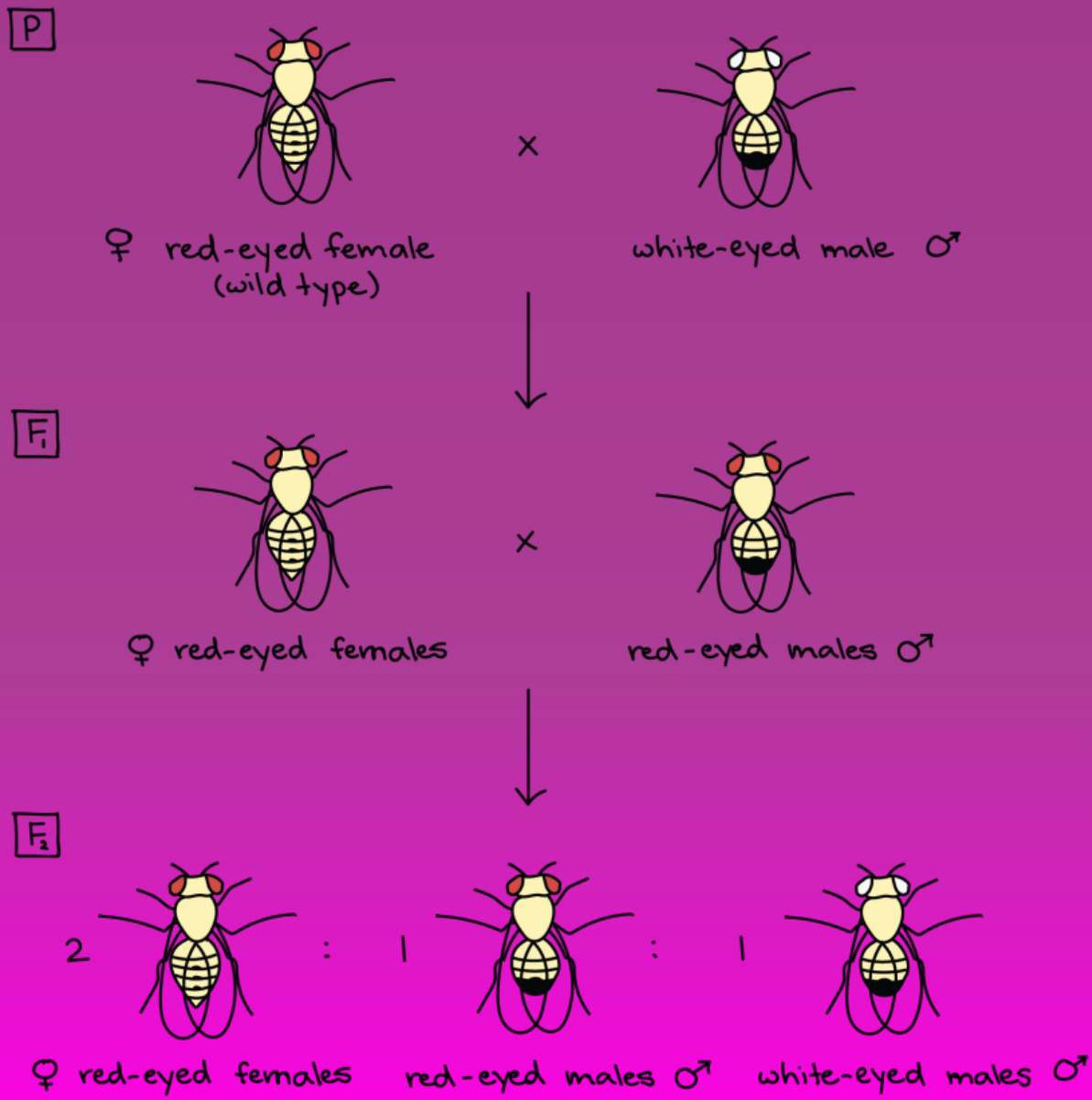
Cross	Outcome	
	Expected Phenotypes	Observed Phenotypes
P_1 Red ♀ × P_1 White ♂	F_1 = All Red	F_1 = All Red*
F_1 Red ♀ × F_1 Red ♂	75% Red ♀ and ♂ 25% White ♀ and ♂	50% Red ♀ 25% Red ♂ 25% White ♂

- He further recognized that the inheritance of the sex determination chromosomes in ***Drosophila*** seemed to follow closely with the inheritance of the white-eye phenotype. But what was the exact relationship between eye color and sex?

Table 2: Sex Chromosome Inheritance in Fruit Flies

		Male Gametes	
		X	*Y*
Female Gametes	*X*	*XX*	*XY*
	X	*XX*	*XY*

What made Morgan think that the eye color gene was on the X chromosome?

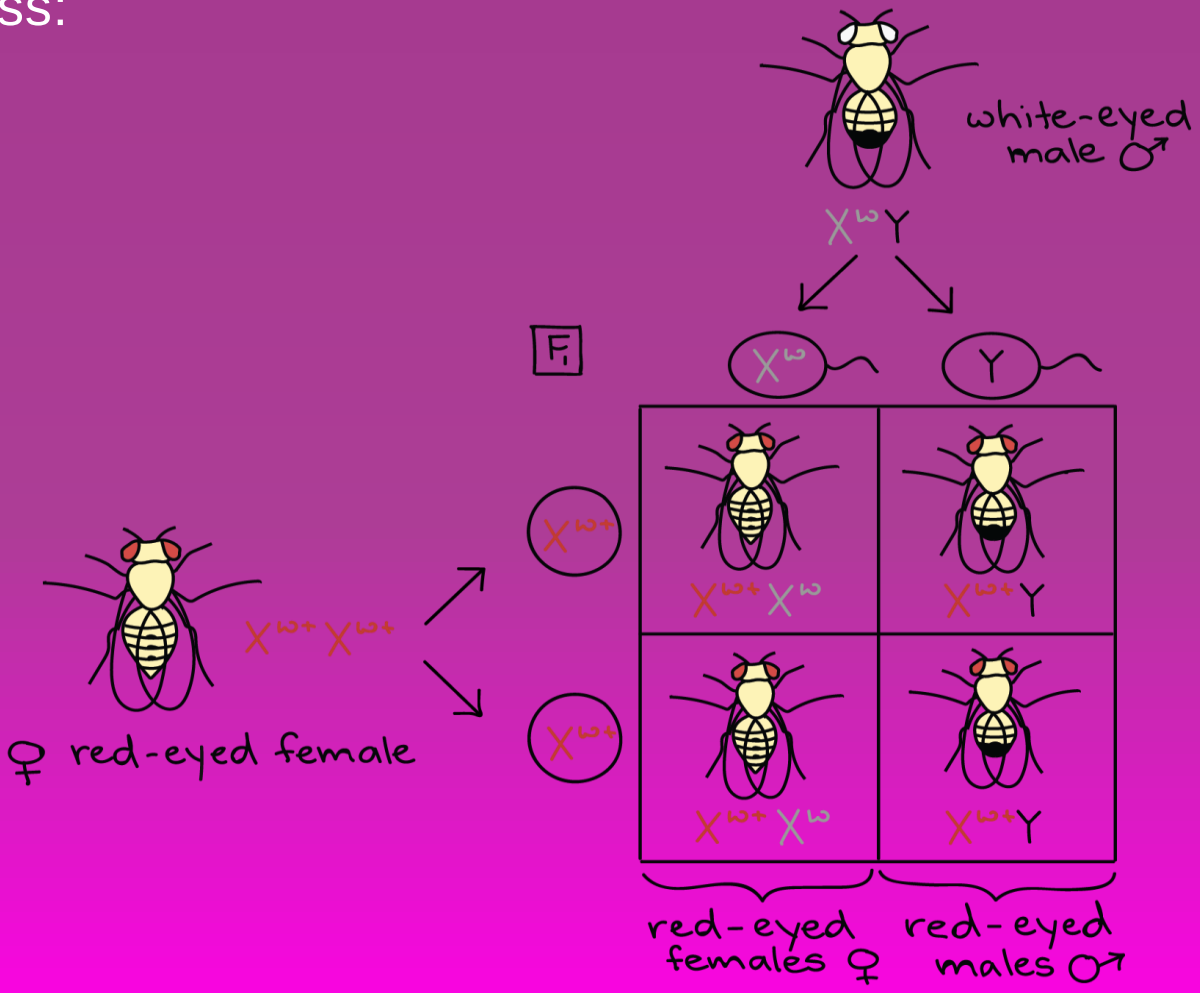


Sex-linked inheritance

If eye color is inherited along with the X chromosome, then it can be denoted as a linked trait by tagging the X chromosome with a symbol, as follows:

- X^{+} = Red-eye trait (wild type)
- X^{w} = White-eye trait

- Let's see how inheritance of the X chromosome can explain what Morgan saw. Earlier, we said that female flies have an XX genotype and male flies have an XY genotype. If we stick the eye color gene on the X chromosome (writing it as a little subscript, w+*w*+w, plus for red and w*ww* for white), we can use a Punnett square to show Morgan's first cross:



Morgan's Test Crosses

- In his initial test cross aimed at exploring the precise relationship between eye color and sex, Morgan bred white-eyed males (X^wY) with wild-type red-eyed females (X^+X^+). This cross yielded only red-eyed offspring, as summarized in Table 3.

Table 3: Morgan's First Test Cross

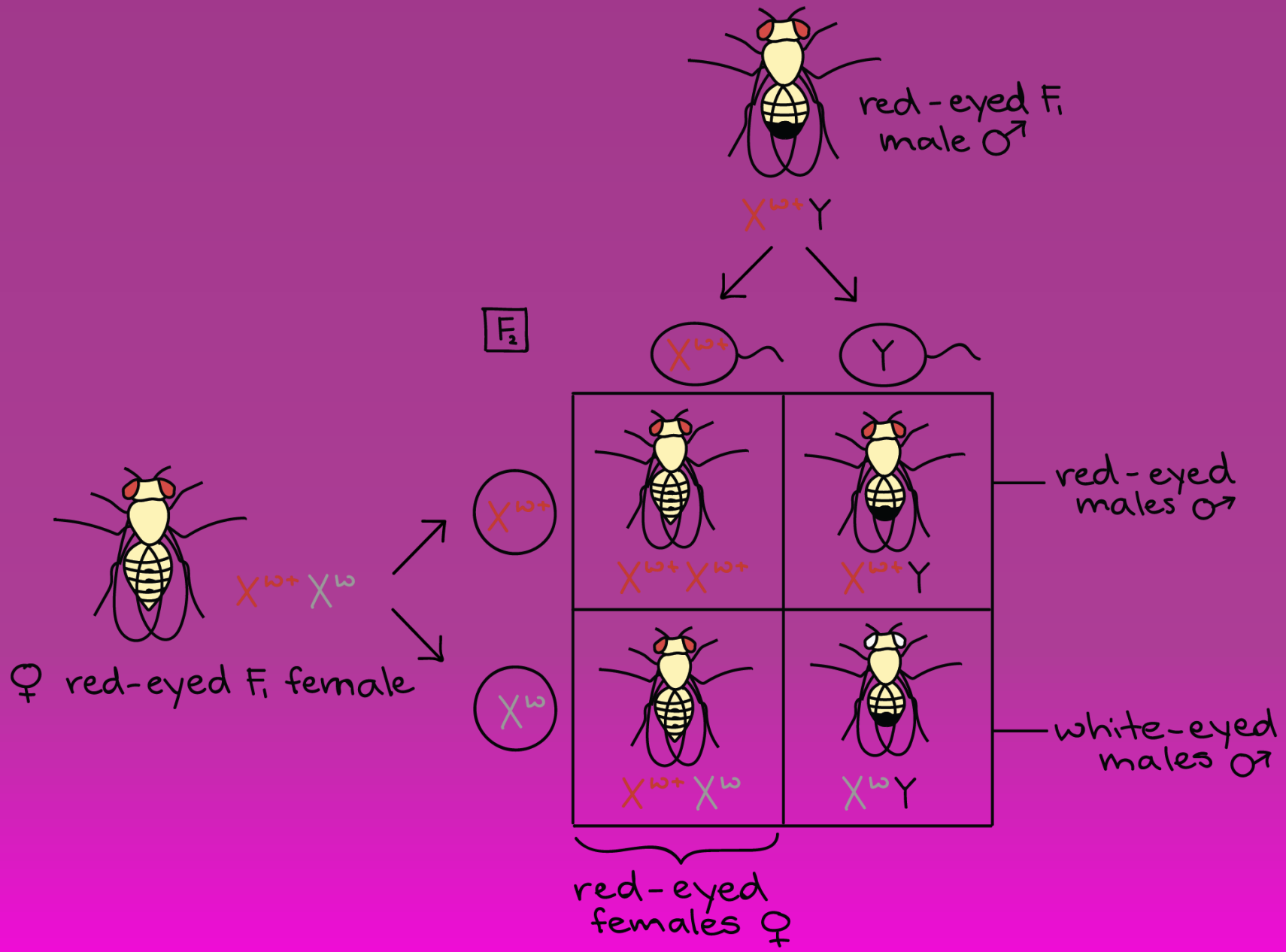
		Male Gametes	
		X^w	Y
Female Gametes	X^+	X^+X^w	X^+Y
	X^+	X^+X^w	X^+Y

Next, Morgan decided to cross two flies from the F_1 generation—specifically, a red-eyed female (X^+X^w) and a red-eyed male (X^+Y)—to test for a recessive pattern of inheritance. This cross is depicted in Table 4.

Table 4: Morgan's Second Test Cross

		Male Gametes	
		X^+	Y
Female Gametes	X^+	X^+X^+	X^+Y
	X^w	X^+X^w	X^wY

As shown in the table, the offspring of this cross exhibited a 3:1 ratio of red eyes to white eyes, which indicated that white eyes were recessive. Moreover, all of the white-eyed F_2 offspring were male.


red-eyed F1 male ♂
$X^{w+}Y$
F2
X^{w+}
Y
X^{w+}
X^{w}
$X^{w+}X^{w+}$
$X^{w+}Y$
$X^{w+}X^{w}$
$X^{w}Y$
red-eyed males ♂
white-eyed males ♂
red-eyed females ♀
$X^{w+}X^{w}$
♀ red-eyed F1 female

Next, as previously discussed, Morgan conducted a third cross to determine whether white eyes were lethal in female flies. Here, he bred red-eyed females ($X^{+}X^{w}$) with white-eyed males ($X^{w}Y$), as summarized in Table 5

Table 5: Morgan's Third Test Cross

		Male Gametes	
		X^{w}	**Y**
Female Gametes	X^{+}	$X^{+}X^{w}$	$X^{+}Y$
	X^{w}	$X^{w}X^{w}$	$X^{w}Y$

“Play in the dark”

Finally, Morgan opted to conduct a fourth cross to determine whether the white-eye trait followed the inheritance of the X chromosome from maternal gametes to male offspring. This reciprocal F_1 cross was the most crucial part of this series of experiments, because Morgan could make some very concrete predictions if the trait was indeed sex-linked. Specifically, because the white-eyed trait appeared to be recessive, Morgan could predict that a white-eyed female would probably be homozygous recessive.

- To test these predictions, Morgan crossed a white-eyed female with a red-eyed male.

Table 6: Morgan's Fourth Test Cross

		Male Gametes	
		X^+	Y
Female Gametes	X^w	X^+X^w	X^wY
	X^w	X^+X^w	X^wY

Morgan was awarded the Nobel Prize

- Because this cross yielded all white-eyed males and all red-eyed females, Morgan could indeed conclude that the white-eye trait followed a sex-linked pattern of inheritance.
- Interestingly, within a year of this public criticism of chromosome theory, Morgan set out to test the idea of inherited chromosomal factors using *Drosophila*, Morgan never looked back, and he developed a huge following of accomplished students over the next few decades.

Indeed, for his work with *Drosophila*, Morgan was awarded the Nobel Prize in 1933.

- alternation of generations in plants and there sex determination

Crossing-over (Sturtevant)

- **Santimorganid** - a measure of the distance between the polymorphic fragments of the genome (loci) on the genetic map.
- One santimorganid frequency corresponds to 1% recombination between loci in the progeny. The statement that the genetic distance between the **locus "A" locus and "B" is equal to 20 sM, means that the frequency of recombinant descendants test cross will be equal to 20%**
- **In humans on average 1 santimorganid contains approximately 1 million base pairs.**