The Chromosomal basis of inheritance.

Introduction

- It was not until 1900 that biology finally caught up with Gregor Mendel.
- Independently, Karl Correns, Erich von Tschermak, and Hugo de Vries all found that Mendel had explained the same results 35 years before.
- Still, resistance remained about Mendel's laws of segregation and independent assortment until evidence had mounted that they had a physical basis in the behavior of chromosomes.
- Mendel's hereditary factors are the genes located on chromosomes.

Mendelian inheritance has its physical basis in the behavior of chromosomes during sexual life cycles.

- Around 1900, cytologists and geneticists began to see parallels between the behavior of chromosomes and the behavior of Mendel's factors.
  - Chromosomes and genes are both present in pairs in diploid cells.
  - Homologous chromosomes separate and alleles segregate during meiosis.
  - Fertilization restores the paired condition for both chromosomes and genes.

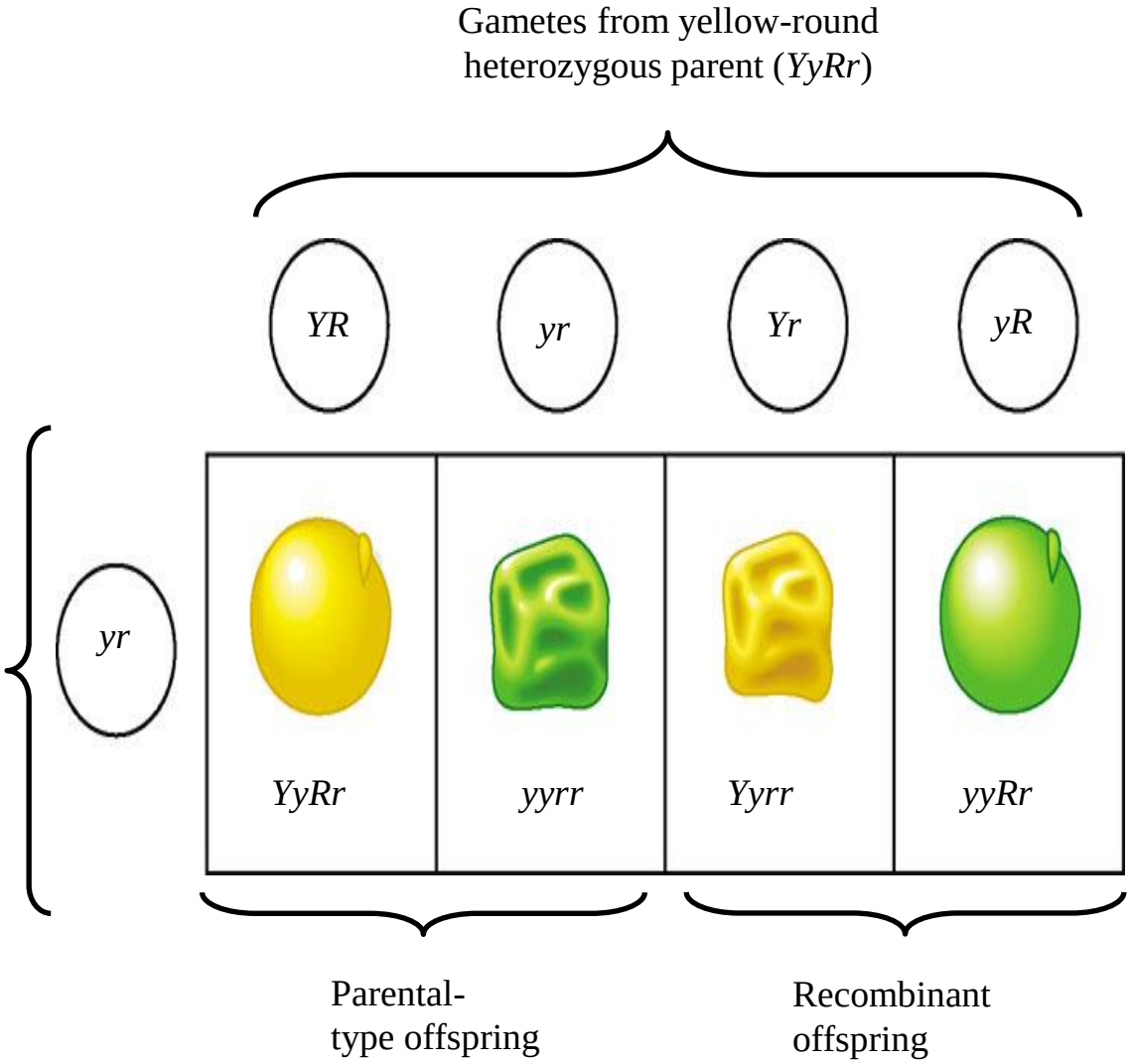
- Around 1902, Walter Sutton, Theodor Boveri, and others noted these parallels and a **chromosome theory of inheritance** began to take form.

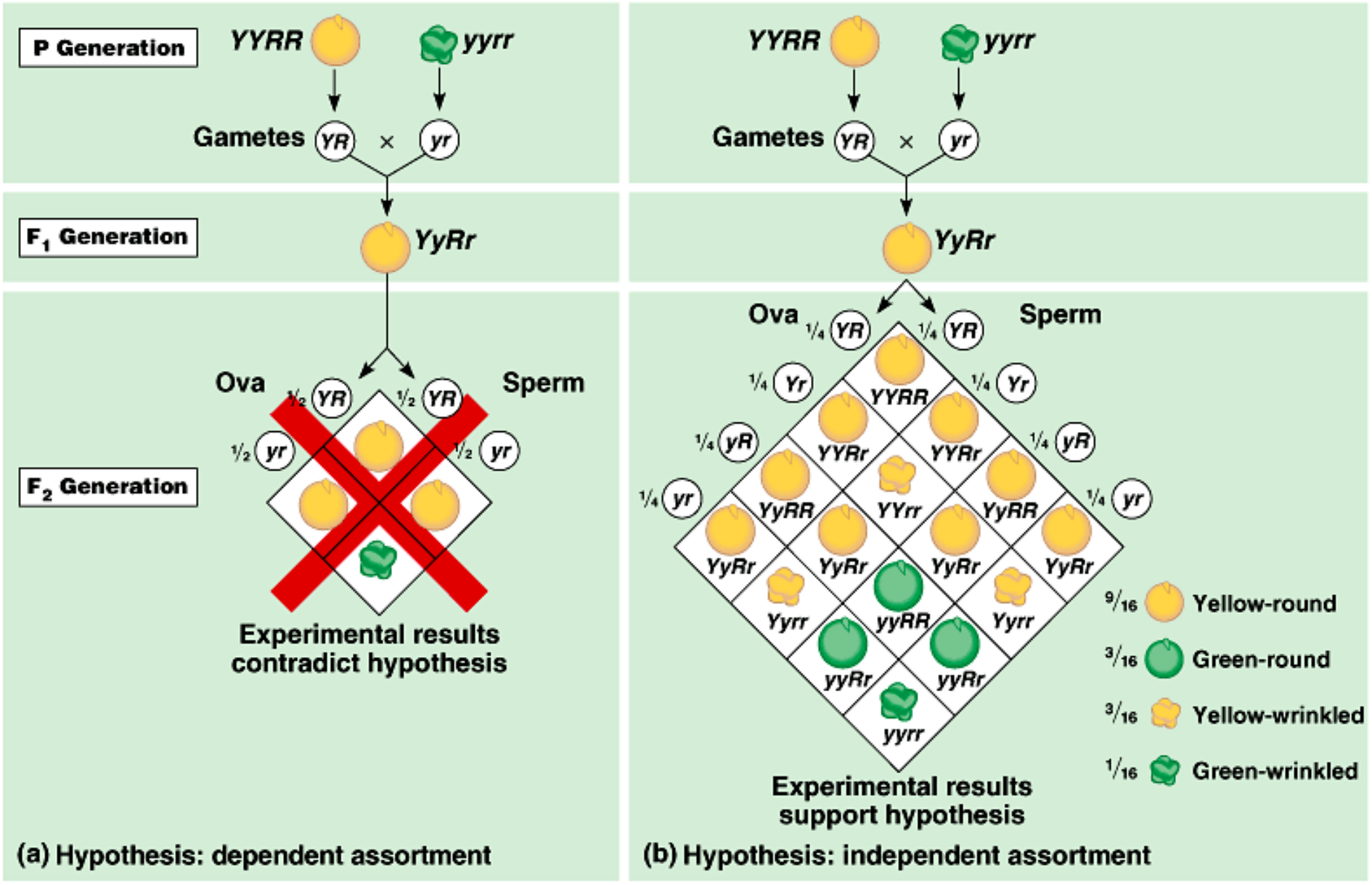
  - The chromosome theory of inheritance states that
    - Mendelian genes have specific loci on chromosomes
    - Chromosomes undergo segregation and independent assortment

Independent assortment of chromosomes and crossing over produce genetic recombinants.

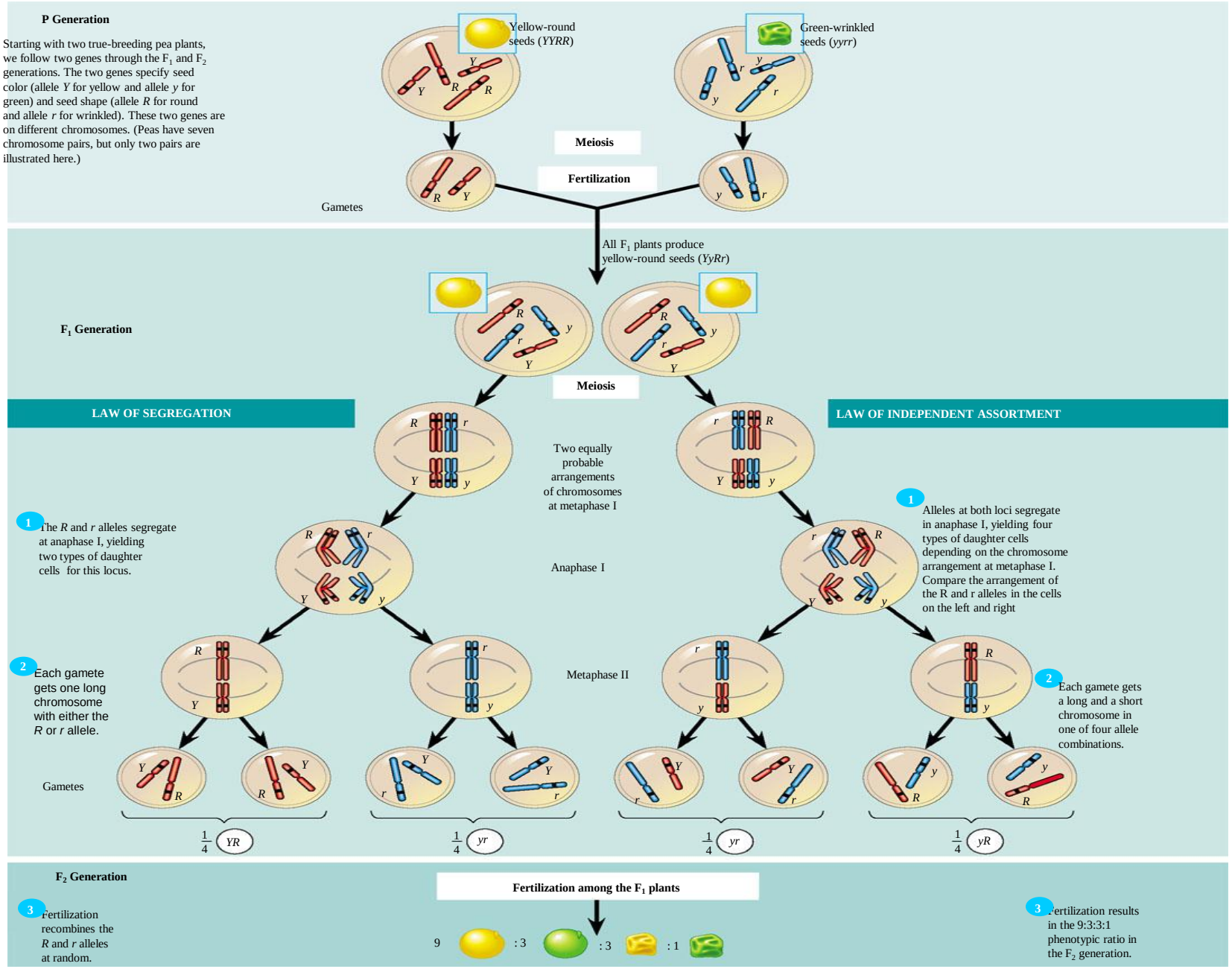
- The production of offspring with new combinations of traits inherited from two parents is **genetic recombination**.
- Genetic recombination can result from independent assortment of genes located on non-homologous chromosomes or from crossing over of genes located on homologous chromosomes.

Parental versus recombinant type





• The chromosomal basis of Mendel's laws

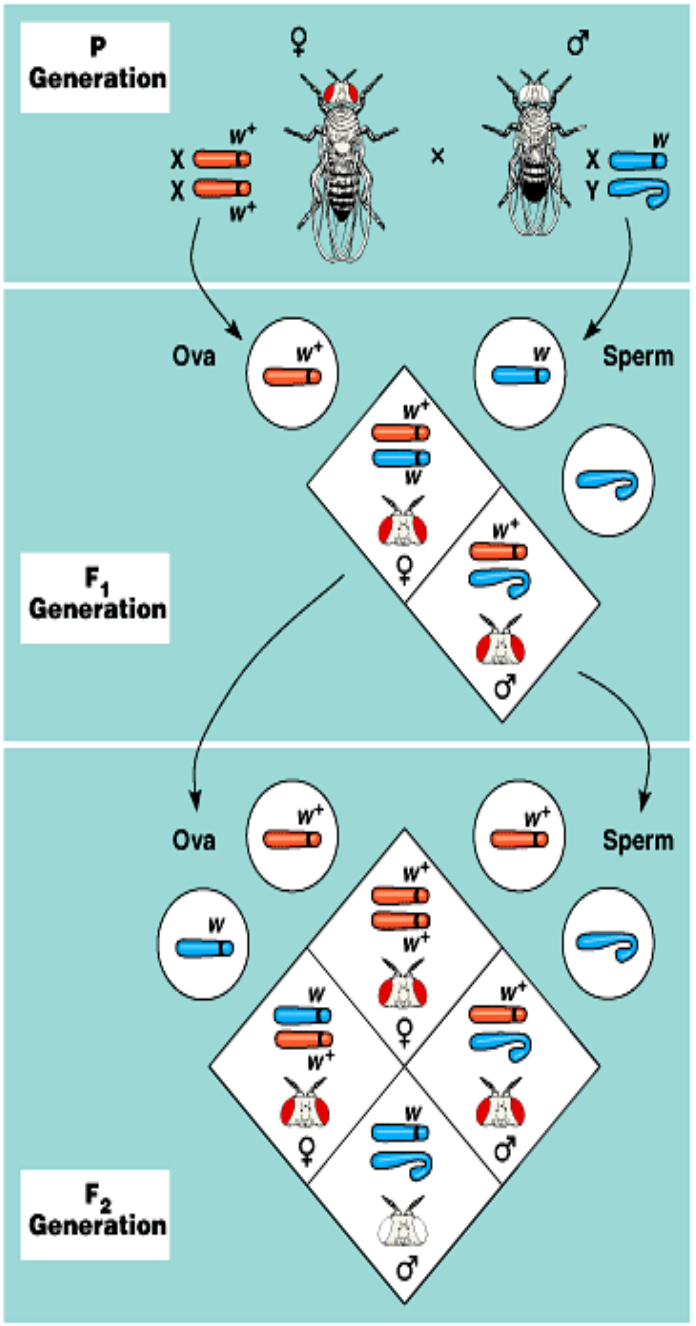


Morgan traced a gene to a specific chromosome.

- Thomas Hunt Morgan was the first to associate a specific gene with a specific chromosome in the early 20th century.
- Like Mendel, Morgan made an insightful choice as an experimental animal, *Drosophila melanogaster*, a fruit fly species that eats fungi on fruit.
  - Fruit flies are prolific breeders and have a generation time of two weeks.
  - Fruit flies have three pairs of autosomes and a pair of sex chromosomes (XX in females, XY in males).

- Morgan spent a year looking for variant individuals among the flies he was breeding.
  - He discovered a single male fly with white eyes instead of the usual red.
- The normal character phenotype is the **wild type**.
- Alternative traits are *mutant phenotypes*.

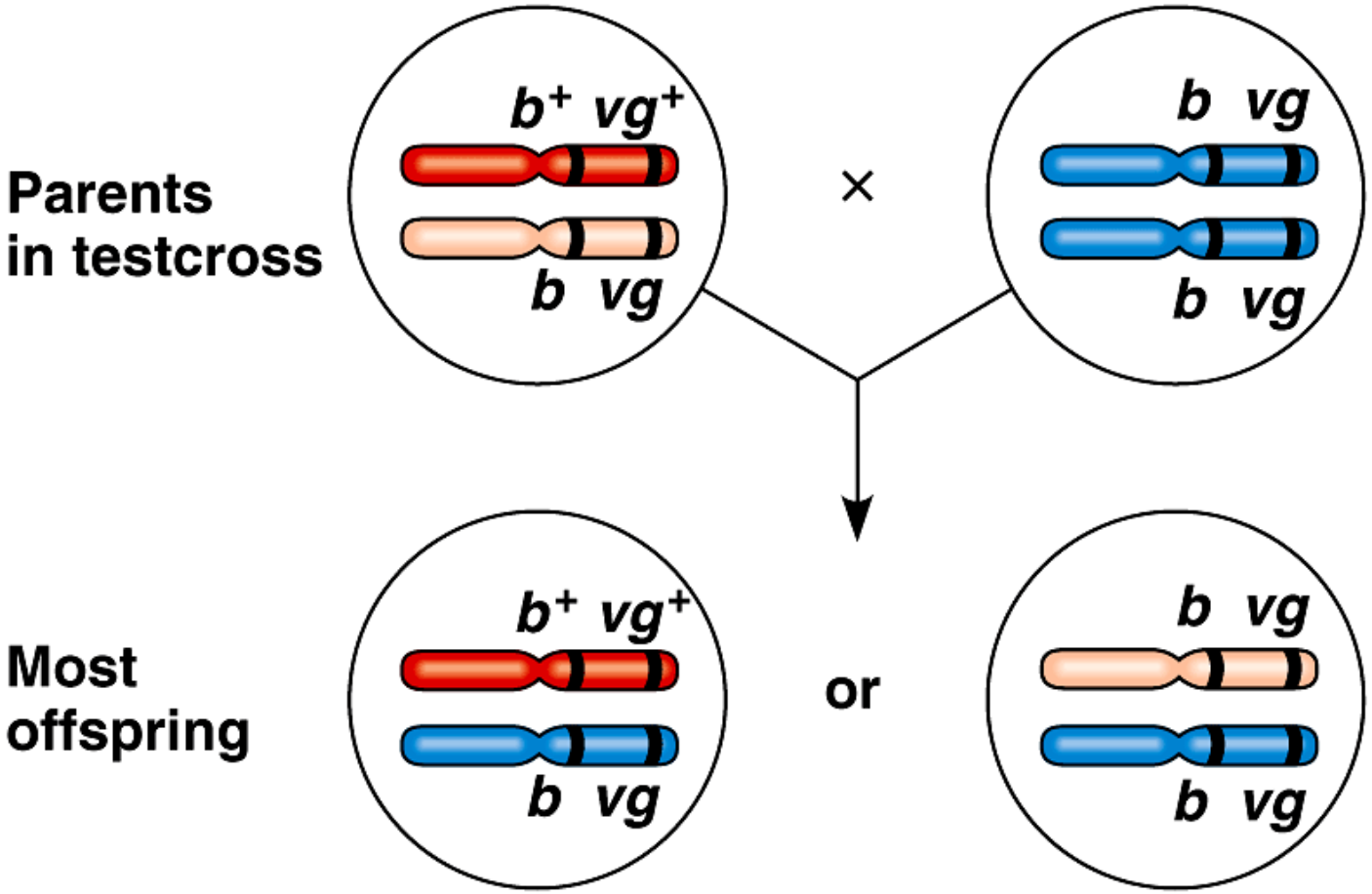
- Morgan deduced that the gene with the white-eyed mutation is on the X chromosome alone, a sex-linked gene.
  - Females (XX) may have two red-eyed alleles and have red eyes or may be heterozygous and have red eyes.
  - Males (XY) have only a single allele and will be red eyed if they have a red-eyed allele or white-eyed if they have a white-eyed allele.



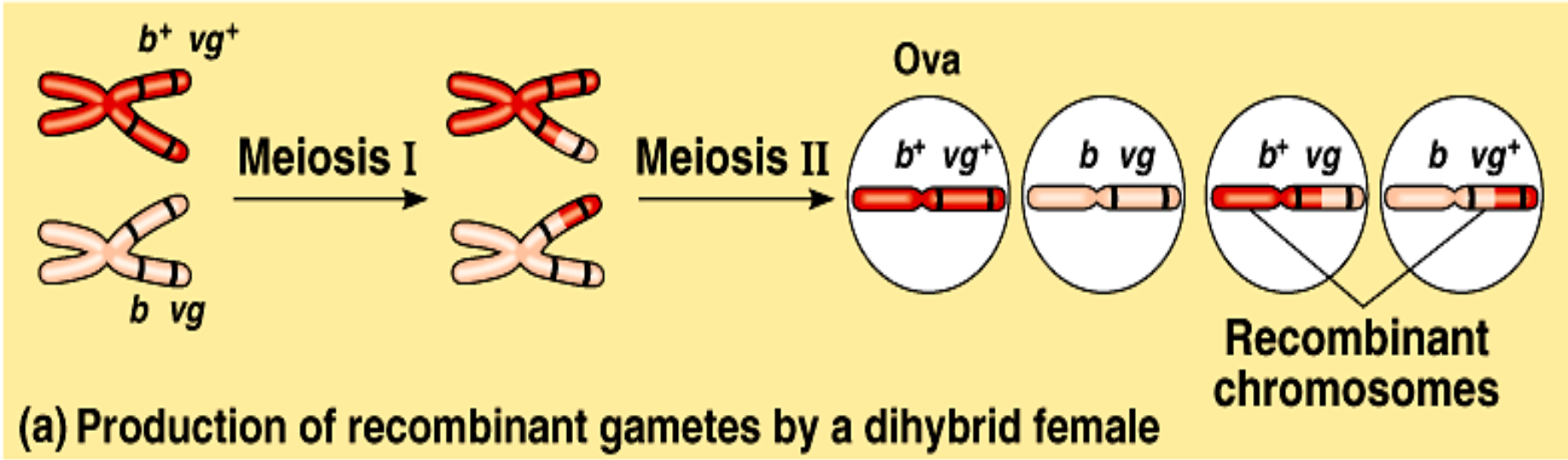
Linked genes tend to be inherited together because they are located on the same chromosome.

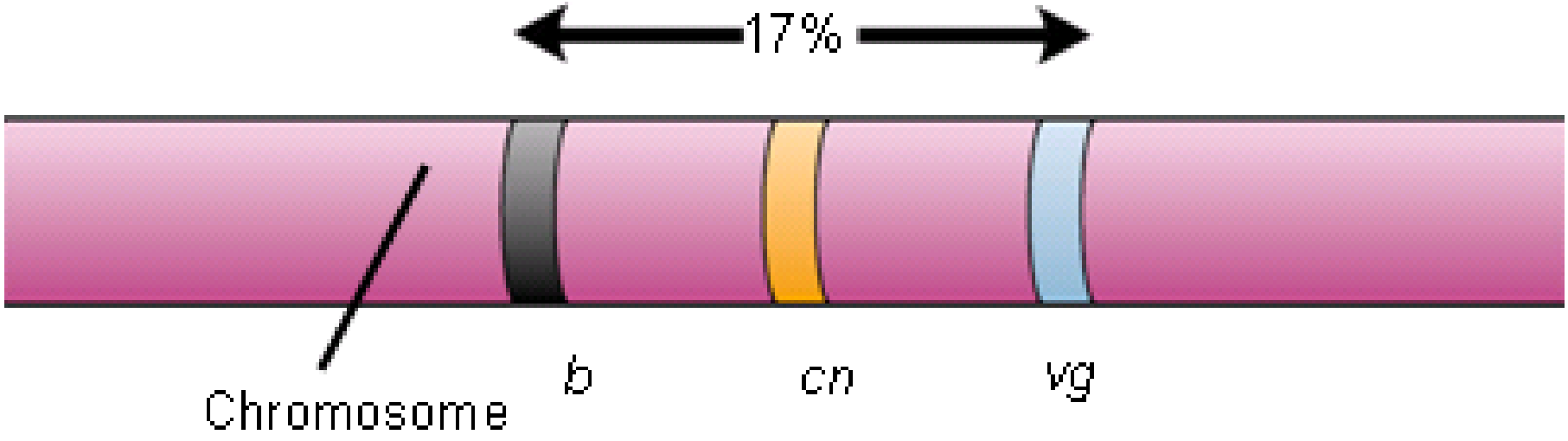
- Each chromosome has hundreds or thousands of genes.
- Genes located on the same chromosome, **linked genes**, tend to be inherited together because the chromosome is passed along as a unit.
- Results of crosses with linked genes deviate from those expected according to independent assortment.

- Morgan reasoned that body color and wing shape are usually inherited together because their genes are on the same chromosome.



- Morgan proposed that some mechanism occasionally exchanged segments between homologous chromosomes.
  - This switched alleles between homologous chromosomes.
- The actual mechanism, crossing over during prophase I, results in the production of more types of gametes than one would predict by Mendelian rules alone.

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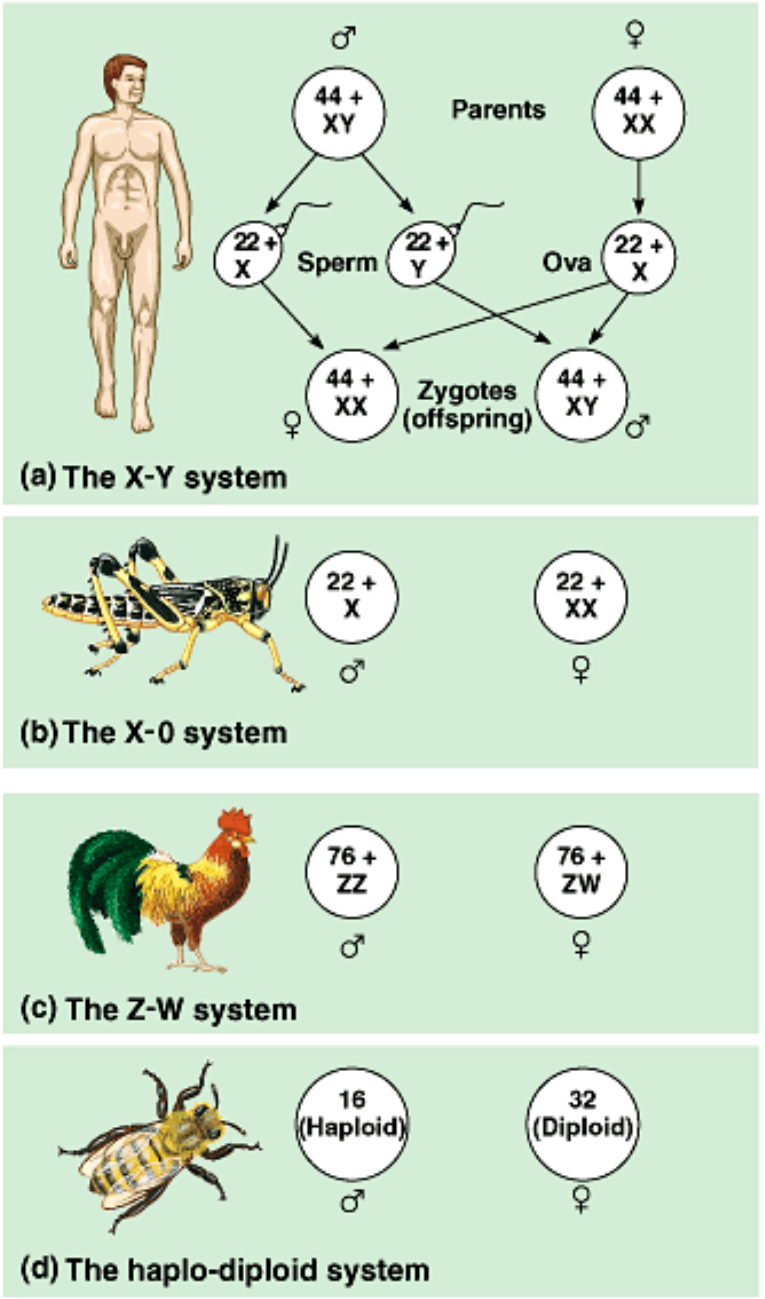
- Some genes on a chromosome are so far apart that a crossover between them is virtually certain.
- In this case, the frequency of recombination reaches is its maximum value of 50%, and the genes act as if found on separate chromosomes and are inherited independently.
  - In fact, several genes studies by Mendel are located on the same chromosome.
    - For example**, seed color** and **flower color** are far enough apart that **linkage is not observed**.
    - Plant **height** and **pod shape** should **show linkage**, but Mendel never reported results of this cross.

The chromosomal basis of sex varies with the organism.

- Although the anatomical and physiological differences between women and men are numerous, the chromosomal basis of sex is rather simple.
- In human and other mammals, there are two varieties of sex chromosomes, X and Y.
  - An individual who inherits two X chromosomes usually develops as a female.
  - An individual who inherits an X and a Y chromosome usually develops as a male.

- This X-Y system of mammals is not the only chromosomal mechanism of determining sex.
- Other options include the X-0 system, the Z-W system, and the haplo-diploid system.



Sex-linked genes have unique patterns of inheritance.

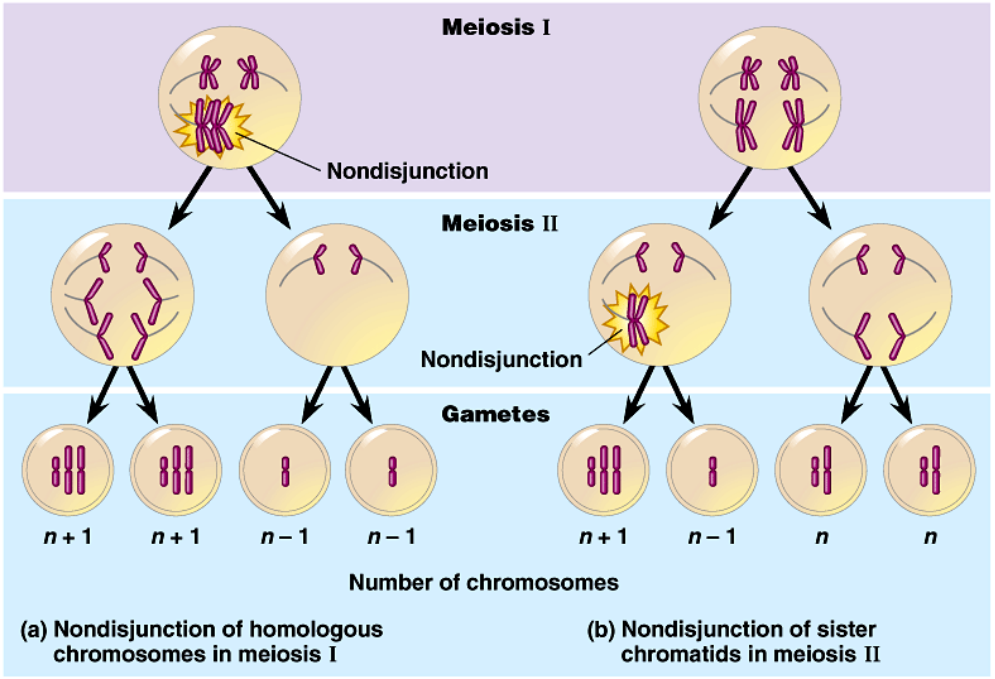
- In addition to their role in determining sex, the sex chromosomes, especially the X chromosome, have genes for many characters unrelated to sex.
- These *sex-linked* genes follow the same pattern of inheritance as the white-eye locus in *Drosophila*.

Errors and Exceptions in Chromosomal Inheritance

- Sex-linked traits are not the only notable deviation from the inheritance patterns observed by Mendel.
- Also, gene mutations are not the only kind of changes to the genome that can affect phenotype.
- Major chromosomal aberrations and their consequences produce exceptions to standard chromosome theory.

Alterations of chromosome number or structure cause some genetic disorders.

- **Nondisjunction** occurs when problems with the meiotic spindle cause errors in daughter cells.
  - This may occur if tetrad chromosomes do not separate properly during meiosis I.
  - Alternatively, sister chromatids may fail to separate during meiosis II.



- As a consequence of nondisjunction, some gametes receive two of the same type of chromosome and another gamete receives no copy.
- Offspring results from fertilization of a normal gamete with one after nondisjunction will have an abnormal chromosome number or **aneuploidy**.
  - **Trisomic** cells have three copies of a particular chromosome type and have 2n + 1 total chromosomes.
  - **Monosomic** cells have only one copy of a particular chromosome type and have 2n - 1 chromosomes.
- If the organism survives, aneuploidy typically leads to a distinct phenotype.

Down Syndrome

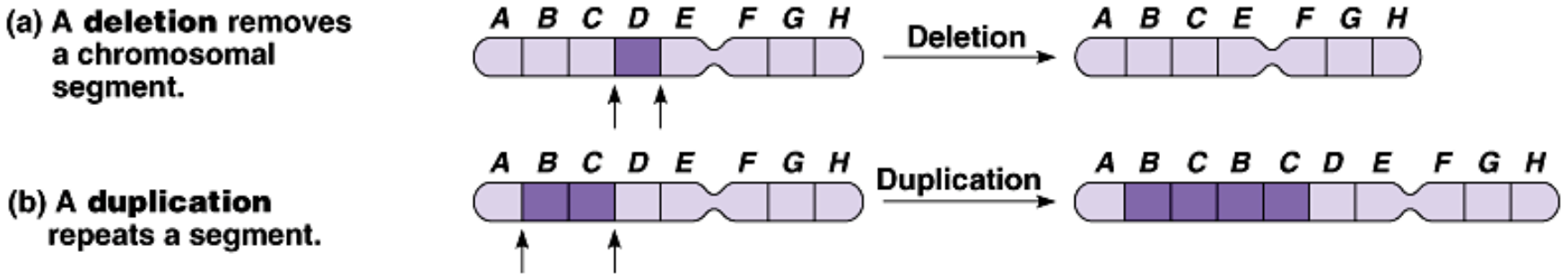
- Down syndrome
  - Is usually the result of an extra chromosome 21, trisomy 21

- Organisms with more than two complete sets of chromosomes, have undergone **polypoidy**.
- This may occur when a normal gamete fertilizes another gamete in which there has been nondisjunction of all its chromosomes.
  - The resulting zygote would be ***triploid*** (3n).
- Alternatively, if a 2n zygote failed to divide after replicating its chromosomes, a ***tetraploid*** (4n) embryo would result from subsequent successful cycles of mitosis.

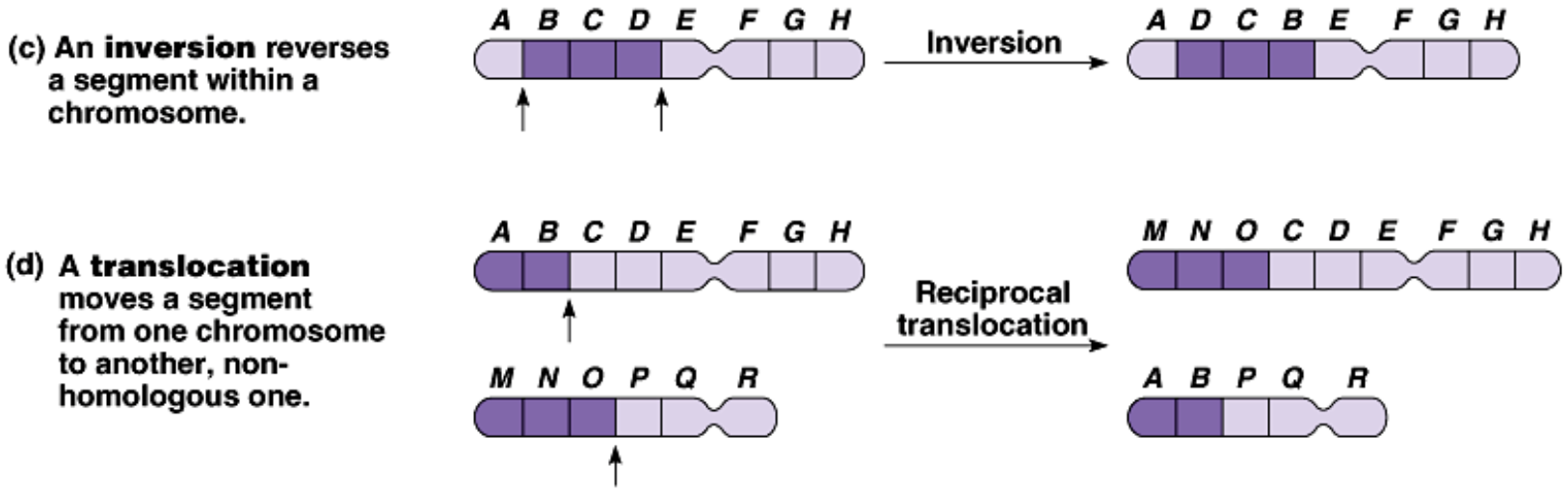
- **Polyploidy** is relatively common among plants and much less common among animals.
  - The spontaneous origin of polyploid individuals plays an important role in the evolution of plants.
  - Both fishes and amphibians have polyploid species.
  - Recently, researchers in Chile have identified a new rodent species which may be the product of polyploidy.

- Polyploids are more nearly normal in phenotype than aneuploids.
- One extra or missing chromosome apparently upsets the genetic balance during development more than does an entire extra set of chromosomes.

- Breakage of a chromosome can lead to four types of changes in chromosome structure.
- A **deletion** occurs when a chromosome fragment lacking a centromere is lost during cell division.
  - This chromosome will be missing certain genes.
- A **duplication** occurs when a fragment becomes attached as an extra segment to a sister



- An **inversion** occurs when a chromosomal fragment reattaches to the original chromosome but in the reverse orientation.
- In **translocation**, a chromosomal fragment joins a nonhomologous chromosome.
  - Some translocations are reciprocal, others are not.



The phenotypic effects of some mammalian genes depend on whether they were inherited from the mother or the father (genomic imprinting).

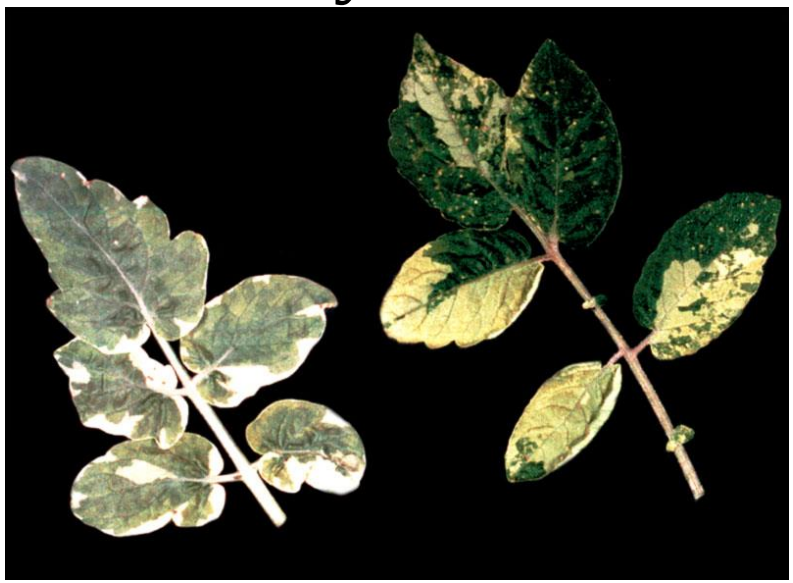
- For most genes it is a reasonable assumption that a specific allele will have the same effect regardless of whether it was inherited from the mother or father.
- However, for some traits in mammals, it does depend on which parent passed along the alleles for those traits.
  - The genes involved may or may not lie on the X chromosome.
  - Involves “essential” silencing of one allele during gamete formation

- Two disorders, ***Prader-Willi syndrome*** and ***Angelman syndrome***, with different phenotypic effects are due to the same cause, a deletion of a specific segment of chromosome 15.
  - Individuals with Prader-Willi syndrome are characterized by mental retardation, obesity, short stature, and unusually small hands and feet.
  - These individuals inherit the abnormal chromosome from their **father**.
  - Individuals with Angelman syndrome exhibit spontaneous laughter, jerky movements, and other motor and mental symptoms.
  - This is inherited from the **mother**.

Extra-nuclear genes exhibit a non-Mendelian pattern of inheritance.

- Not all of a eukaryote cell's genes are located in the nucleus.
- Extra-nuclear genes are found on small circles of DNA in mitochondria and chloroplasts.
- These organelles reproduce themselves.
- Their cytoplasmic genes do not display Mendelian inheritance.

- Karl Correns in 1909 first observed cytoplasmic genes in plants.
- He determined that the coloration of the offspring was determined only by the maternal parent.
- These coloration patterns are due to genes in the plastids which are inherited only via the ovum, not the pollen.



- Because a zygote typically inherits all its mitochondria/chloroplasts only from the ovum, all such genes in demonstrate maternal inheritance.
- Several rare human disorders are produced by mutations to mitochondrial DNA.
  - These primarily impact ATP supply by producing defects in the electron transport chain or ATP synthase.
  - Tissues that require high energy supplies (for example, the nervous system and muscles) may suffer energy deprivation from these defects.
  - Other mitochondrial mutations may contribute to diabetes, heart disease, and other diseases of aging.

X inactivation in Female Mammals

- In mammalian females
  - One of the two X chromosomes in each cell is randomly inactivated during embryonic development

Two cell populations in adult cat:

Early embryo:

X chromosomes

Cell division and X chromosome inactivation

Active X

Orange fur

Inactive X

Inactive X

Black fur

Active X

Allele for black fur