Chapter 15

The Chromosomal Basis of Inheritance

PowerPoint® Lecture Presentations for

Biology

Eighth Edition

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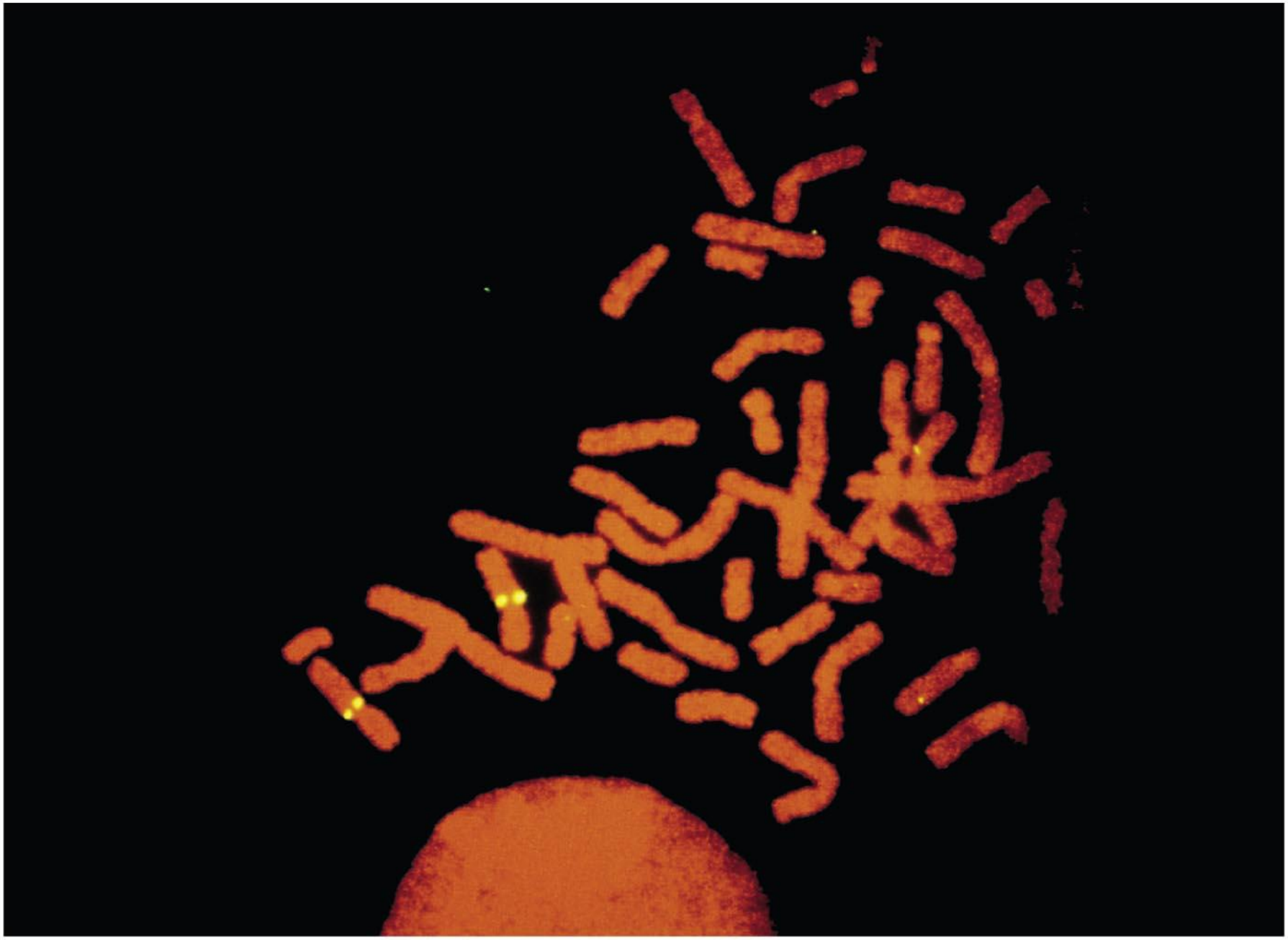
Overview: Locating Genes Along Chromosomes

- Mendel's "hereditary factors" were genes, though this wasn't known at the time
- Today we can show that genes are located on chromosomes
- The location of a particular gene can be seen by tagging isolated chromosomes with a fluorescent dye that highlights the gene

Fig. 15-1



Concept 15.1: Mendelian inheritance has its physical basis in the behavior of chromosomes

- Mitosis and meiosis were first described in the late 1800s
- The **chromosome theory of inheritance** states:
  - Mendelian genes have specific loci (positions) on chromosomes
  - Chromosomes undergo segregation and independent assortment
- The behavior of chromosomes during meiosis was said to account for Mendel's laws of segregation and independent assortment

Fig. 15-2

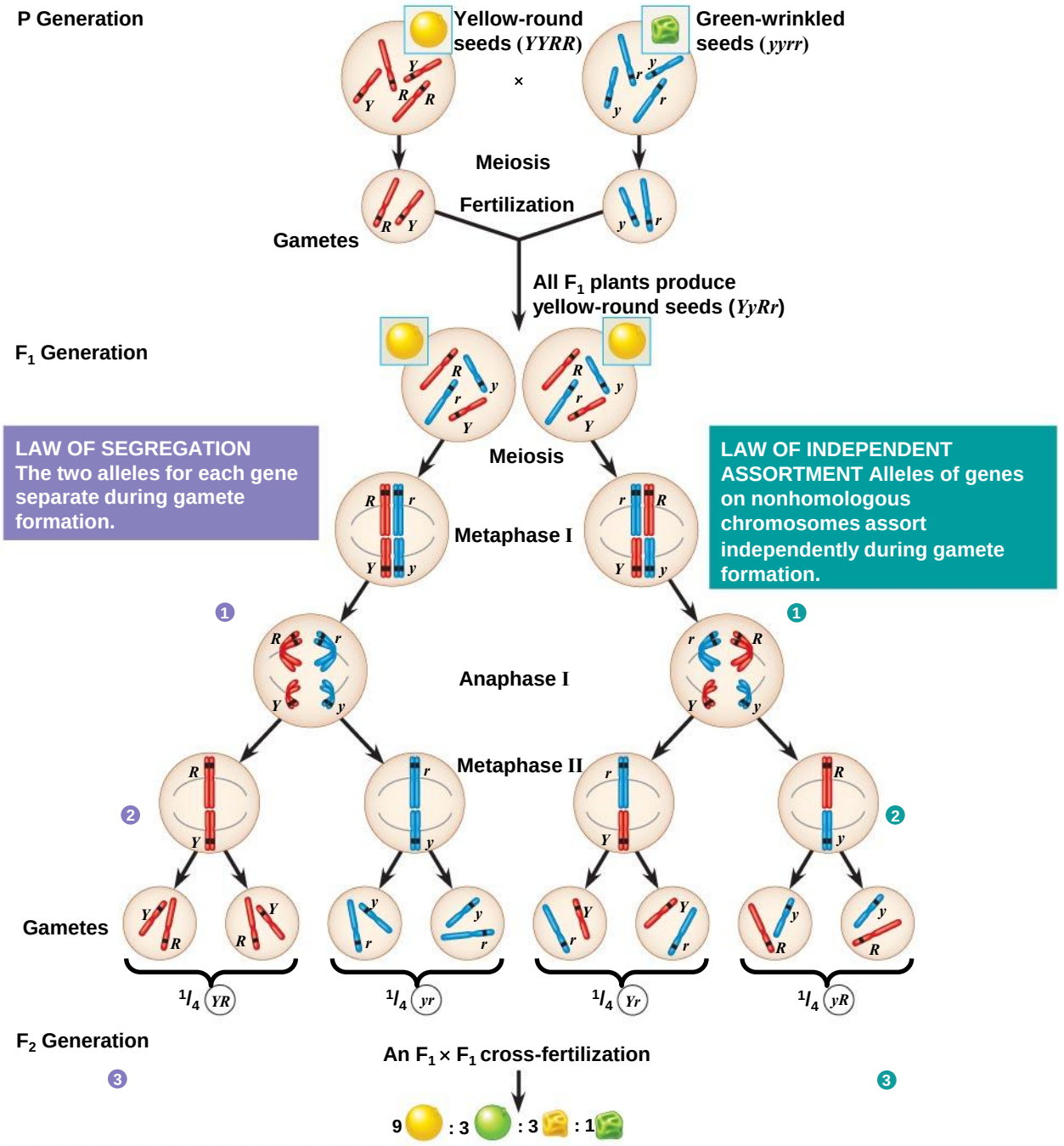


Fig. 15-2a

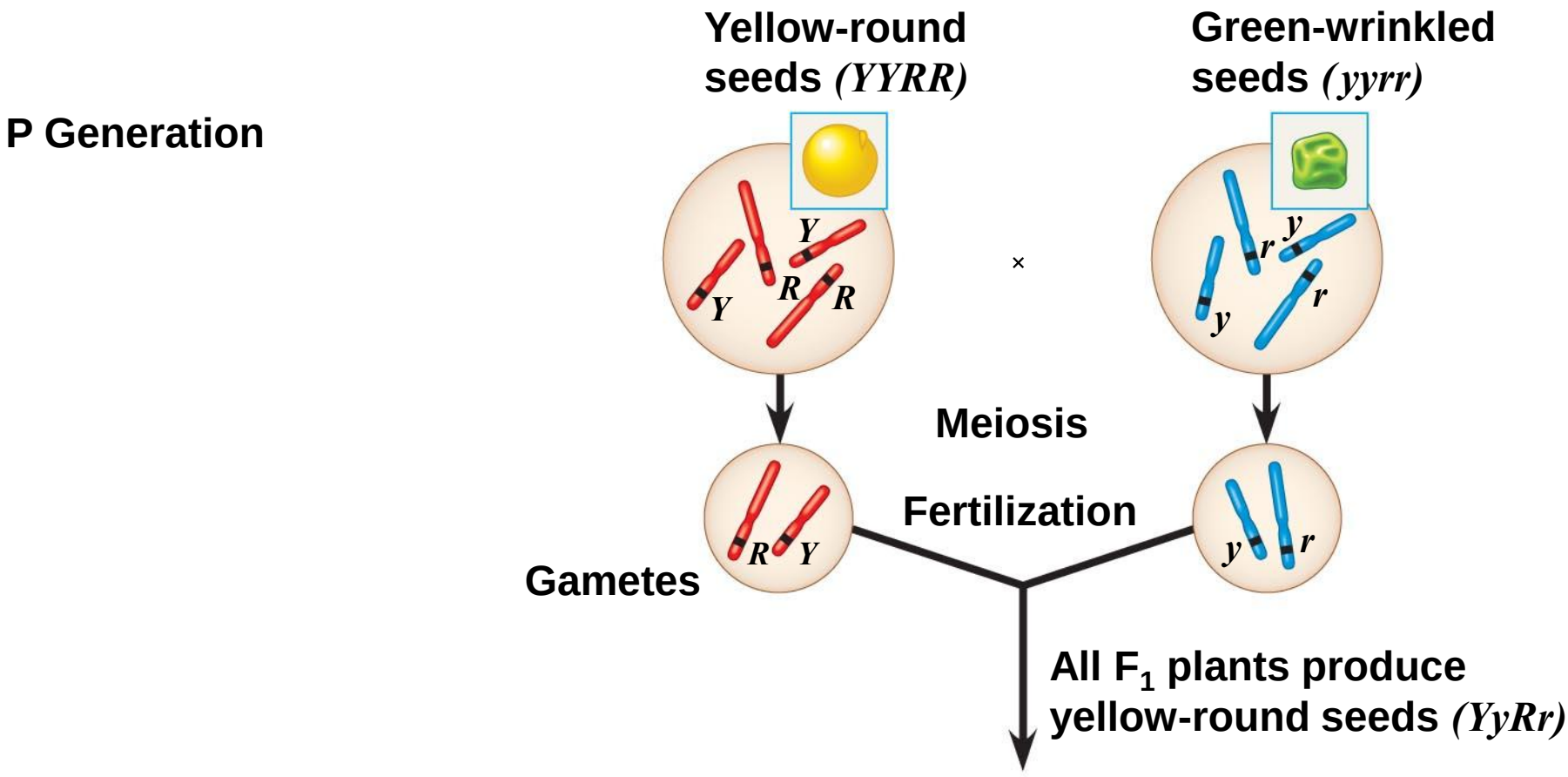


Fig. 15-2b

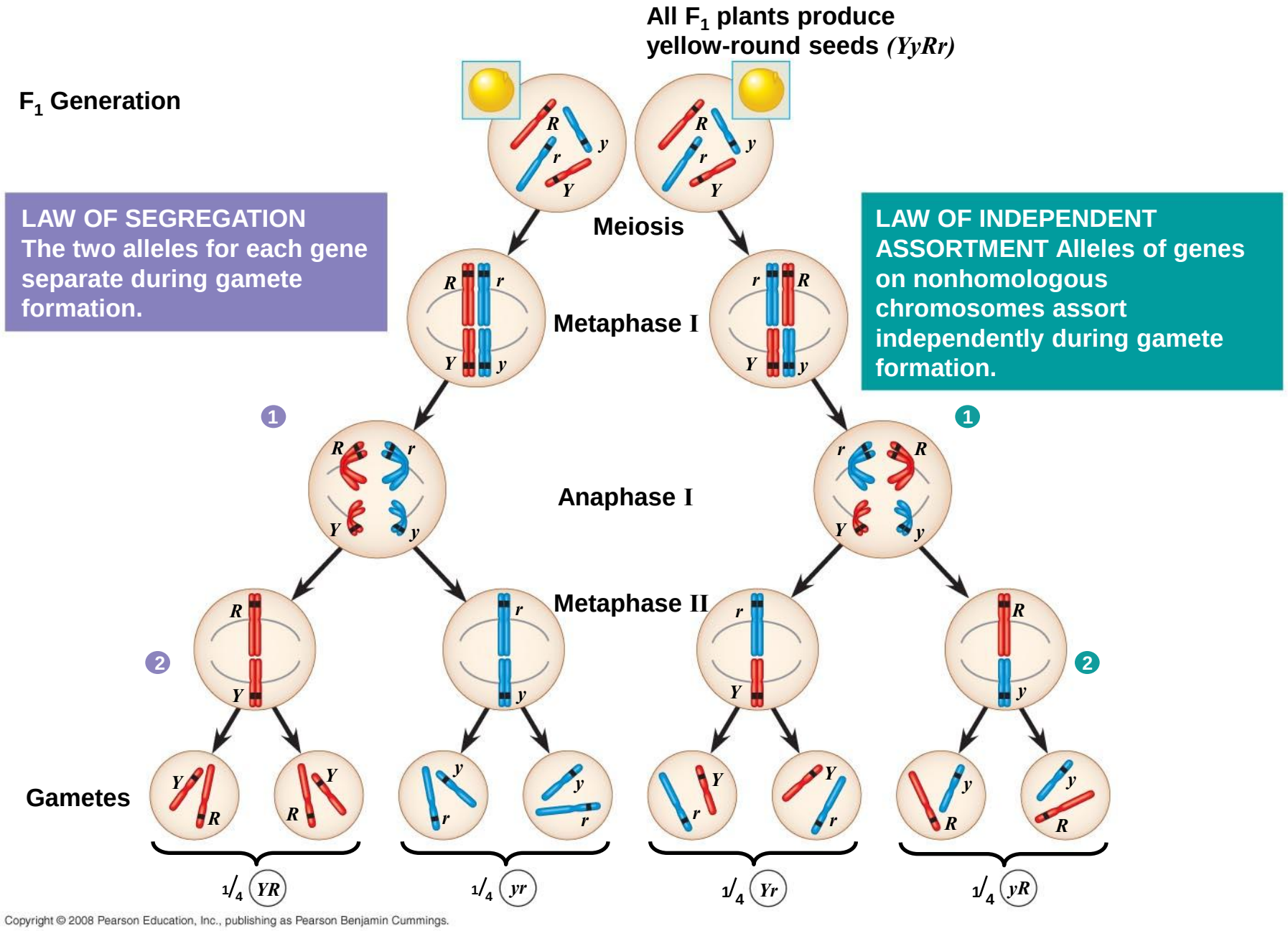
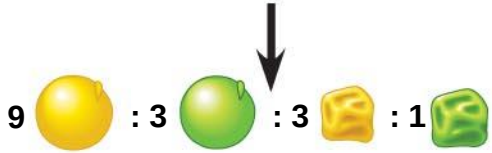


Fig. 15-2c

F_2 Generation

3

An $F_1 \times F_1$ cross-fertilization



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Morgan's Experimental Evidence: *Scientific Inquiry*

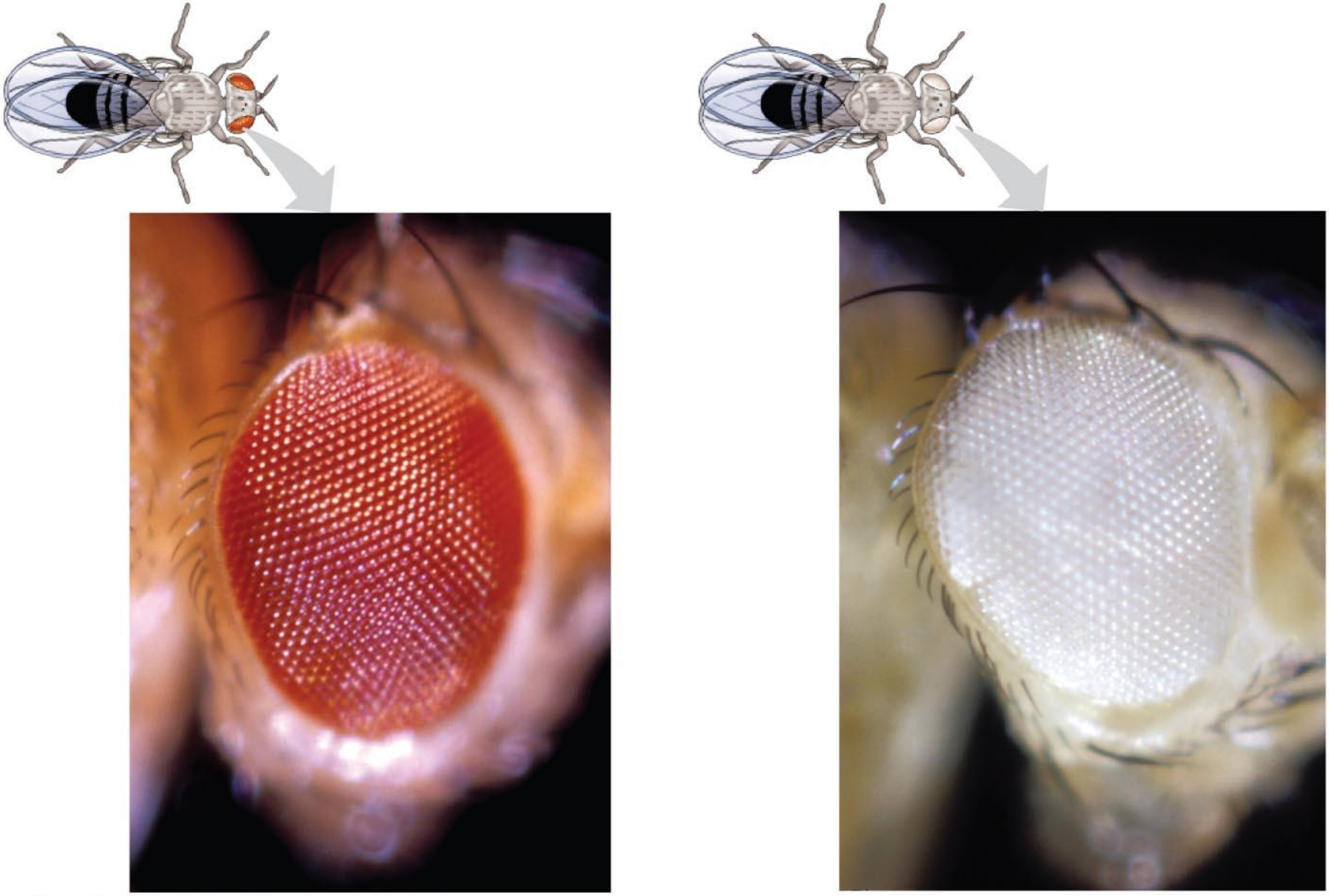
- The first solid evidence associating a specific gene with a specific chromosome came from Thomas Hunt Morgan, an embryologist
- Morgan's experiments with fruit flies provided convincing evidence that chromosomes are the location of Mendel's heritable factors

Morgan's Choice of Experimental Organism

- Several characteristics make fruit flies a convenient organism for genetic studies:
  - They breed at a high rate
  - A generation can be bred every two weeks
  - They have only four pairs of chromosomes

- Morgan noted **wild type**, or normal, phenotypes that were common in the fly populations
- Traits alternative to the wild type are called *mutant phenotypes*

Fig. 15-3



Correlating Behavior of a Gene's Alleles with Behavior of a Chromosome Pair

- In one experiment, Morgan mated male flies with white eyes (mutant) with female flies with red eyes (wild type)
  - The F_1 generation all had red eyes
  - The F_2 generation showed the 3:1 red:white eye ratio, but only males had white eyes
- Morgan determined that the white-eyed mutant allele must be located on the X chromosome
- Morgan's finding supported the chromosome theory of inheritance

Fig. 15-4

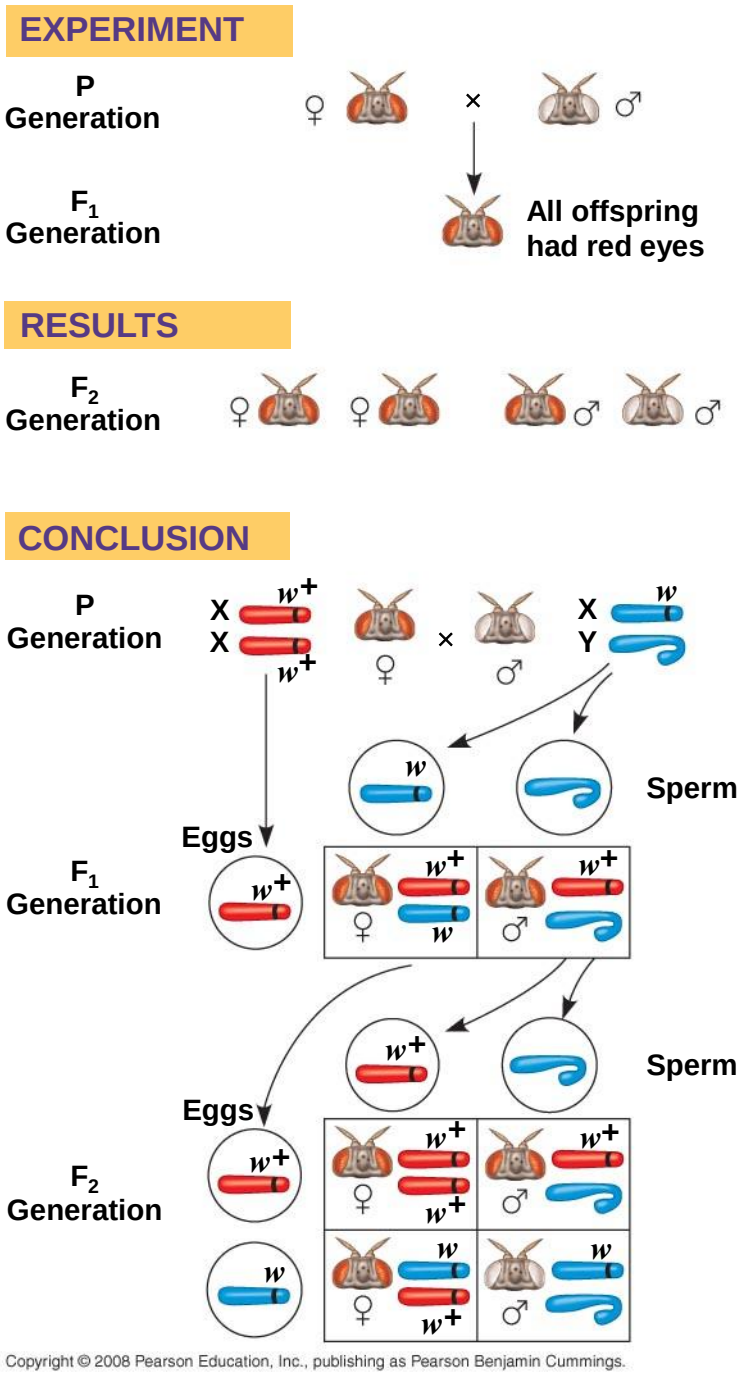


Fig. 15-4a

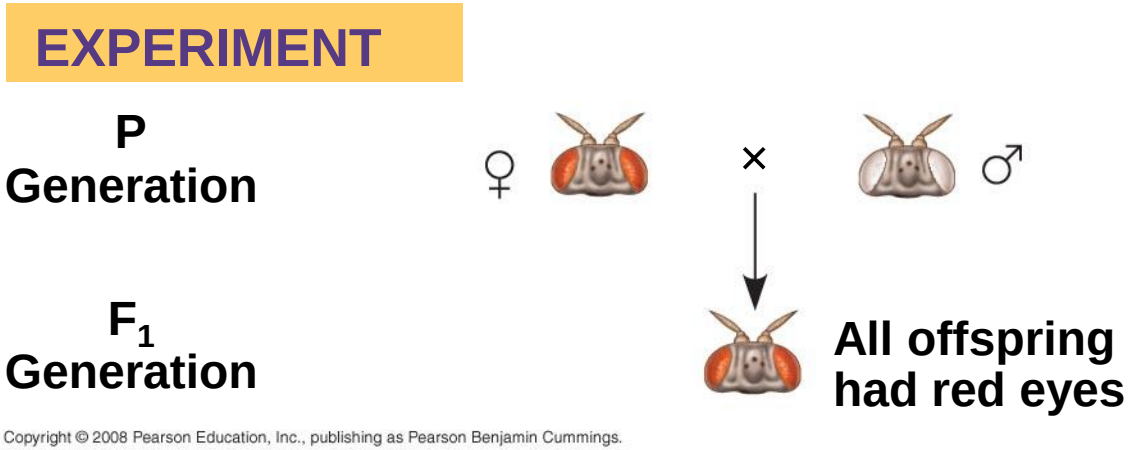


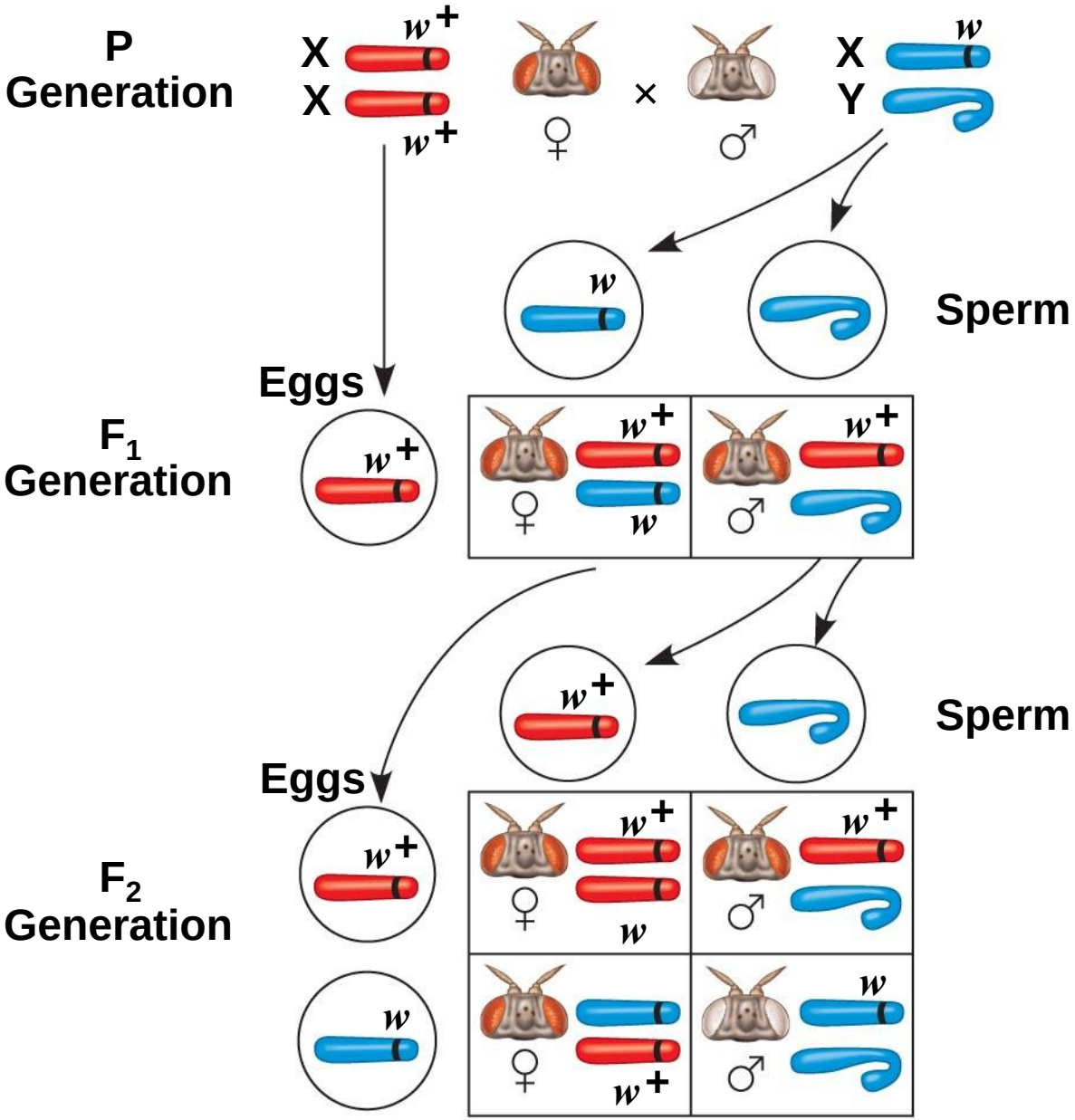
Fig. 15-4b

RESULTS

F_2 Generation

Fig. 15-4c

CONCLUSION



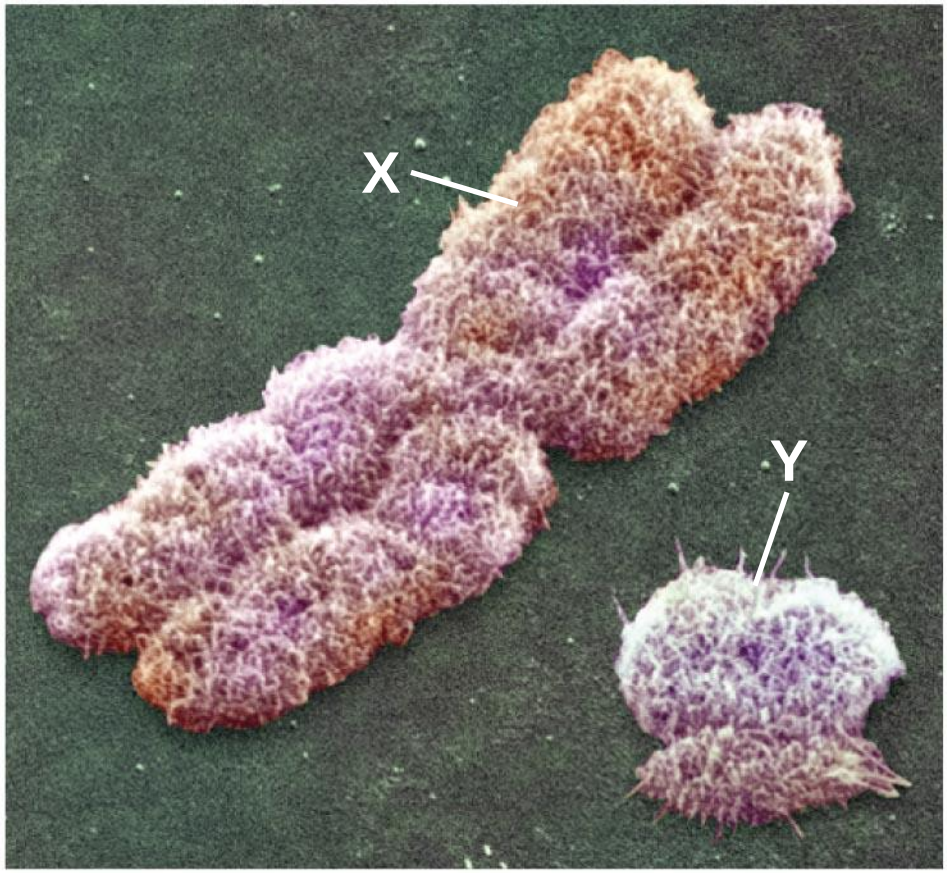
Concept 15.2: Sex-linked genes exhibit unique patterns of inheritance

- In humans and some other animals, there is a chromosomal basis of sex determination

The Chromosomal Basis of Sex

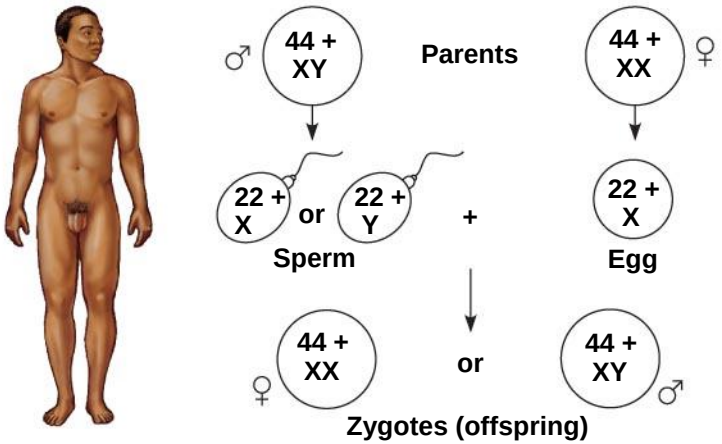
- In humans and other mammals, there are two varieties of sex chromosomes: a larger X chromosome and a smaller Y chromosome
- Only the ends of the Y chromosome have regions that are homologous with the X chromosome
- The *SRY* gene on the Y chromosome codes for the development of testes

Fig. 15-5

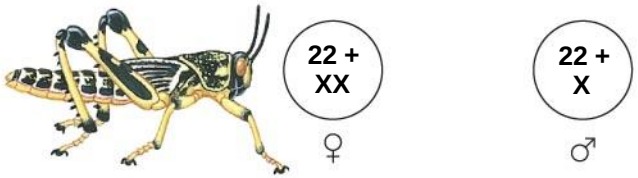


- Females are XX, and males are XY
- Each ovum contains an X chromosome, while a sperm may contain either an X or a Y chromosome
- Other animals have different methods of sex determination

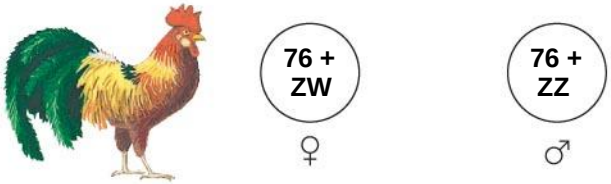
Fig. 15-6



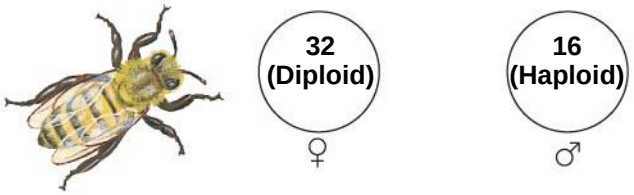
(a) The X-Y system



(b) The X-0 system

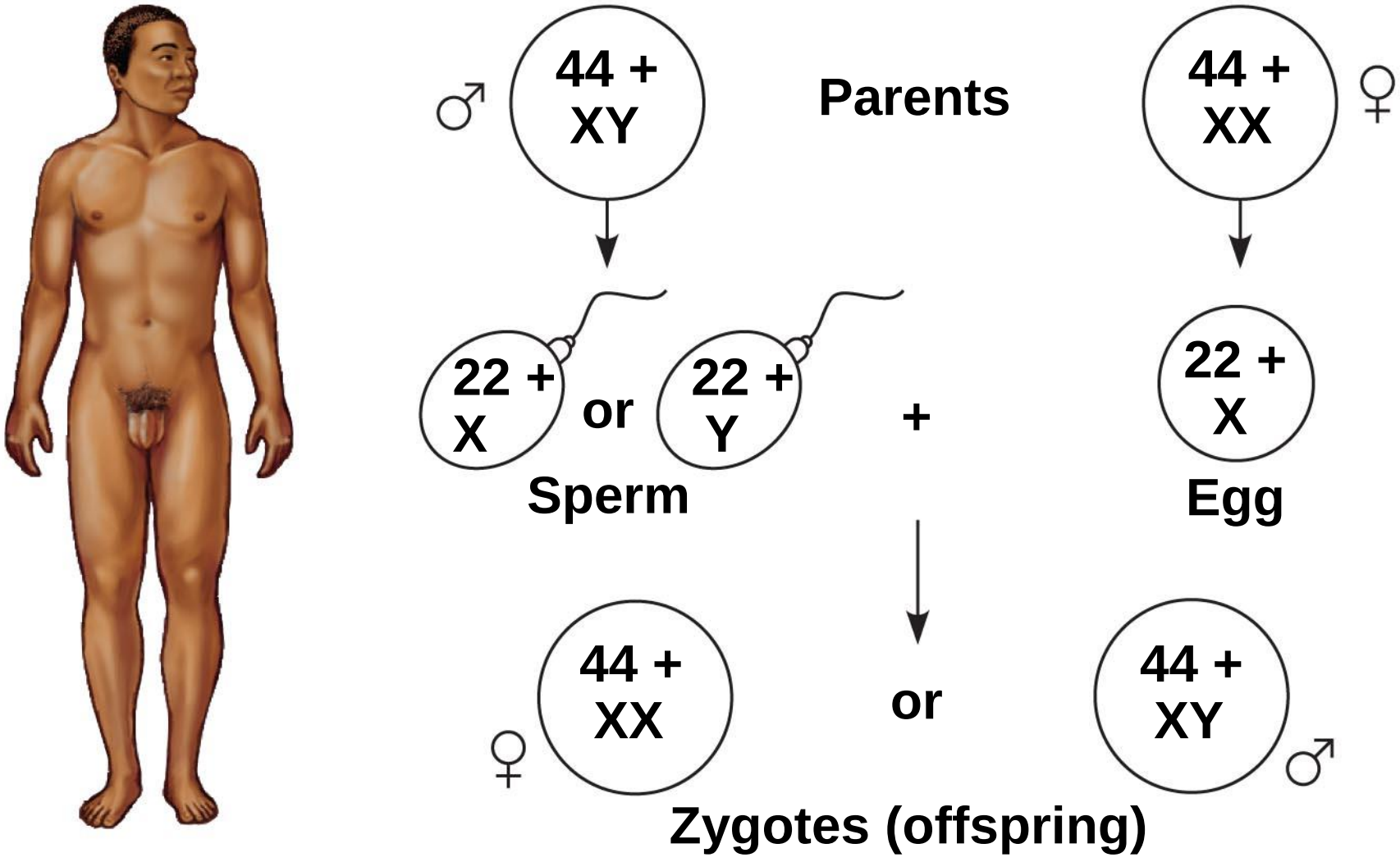


(c) The Z-W system



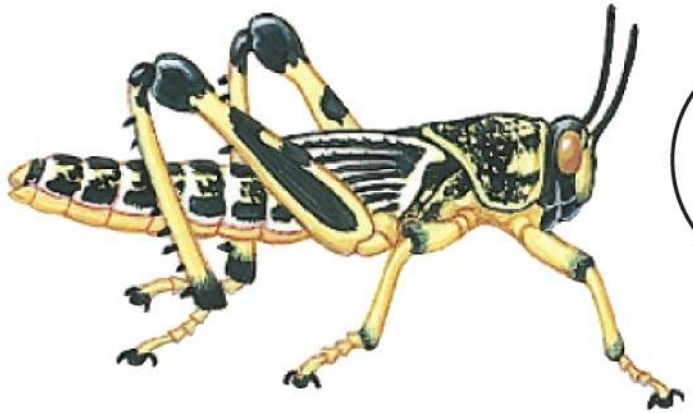
(d) The haplo-diploid system

Fig. 15-6a



(a) The X-Y system

Fig. 15-6b



22 + XX

♀

22 + X

♂

(b) The X-0 system

Fig. 15-6c

76 + ZW

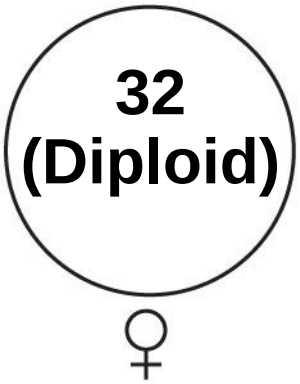
♀

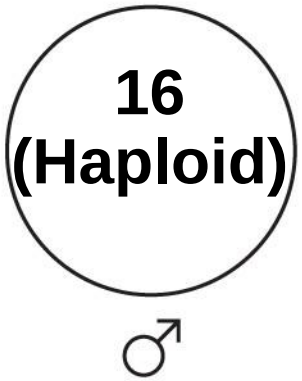
76 + ZZ

♂

(c) The Z-W system

Fig. 15-6d





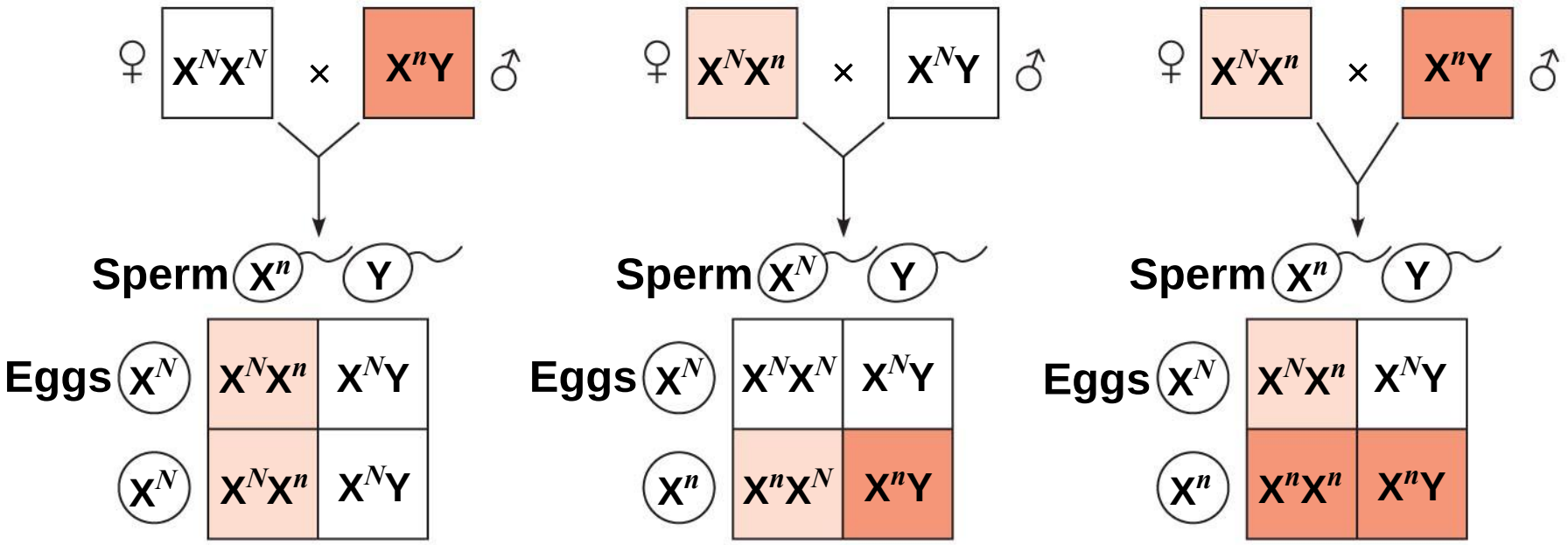
(d) The haplo-diploid system

Inheritance of Sex-Linked Genes

- The sex chromosomes have genes for many characters unrelated to sex
- A gene located on either sex chromosome is called a **sex-linked gene**
- In humans, sex-linked usually refers to a gene on the larger X chromosome

- Sex-linked genes follow specific patterns of inheritance
- For a recessive sex-linked trait to be expressed
  - A female needs two copies of the allele
  - A male needs only one copy of the allele
- Sex-linked recessive disorders are much more common in males than in females

Fig. 15-7

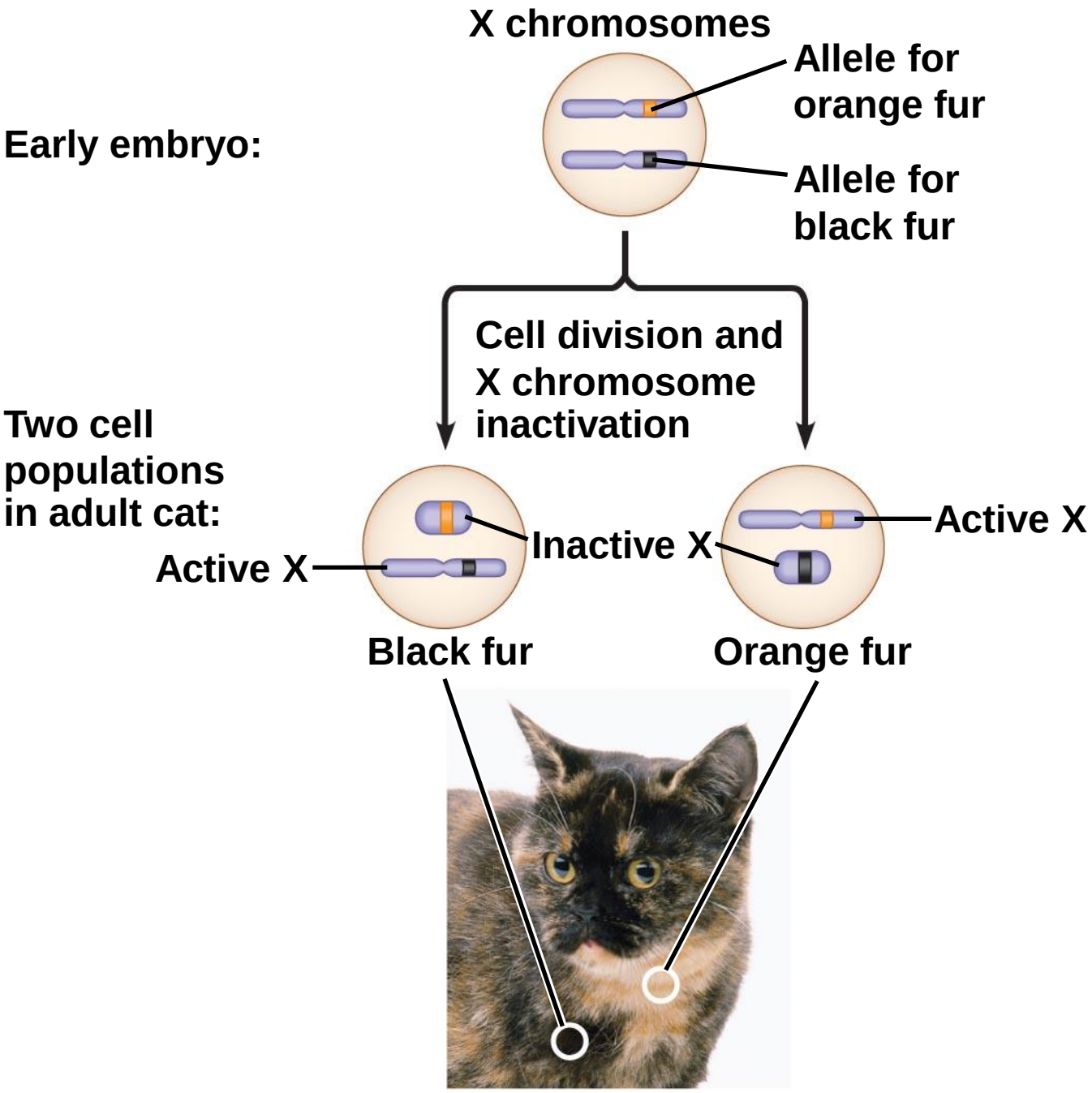


- Some disorders caused by recessive alleles on the X chromosome in humans:
  - Color blindness
  - **Duchenne muscular dystrophy**
  - **Hemophilia**

X Inactivation in Female Mammals

- In mammalian females, one of the two X chromosomes in each cell is randomly inactivated during embryonic development
- The inactive X condenses into a **Barr body**
- If a female is heterozygous for a particular gene located on the X chromosome, she will be a mosaic for that character

Fig. 15-8



Concept 15.3: Linked genes tend to be inherited together because they are located near each other on the same chromosome

- Each chromosome has hundreds or thousands of genes
- Genes located on the same chromosome that tend to be inherited together are called **linked genes**

How Linkage Affects Inheritance

- Morgan did other experiments with fruit flies to see how linkage affects inheritance of two characters
- Morgan crossed flies that differed in traits of body color and wing size

Fig. 15-UN1

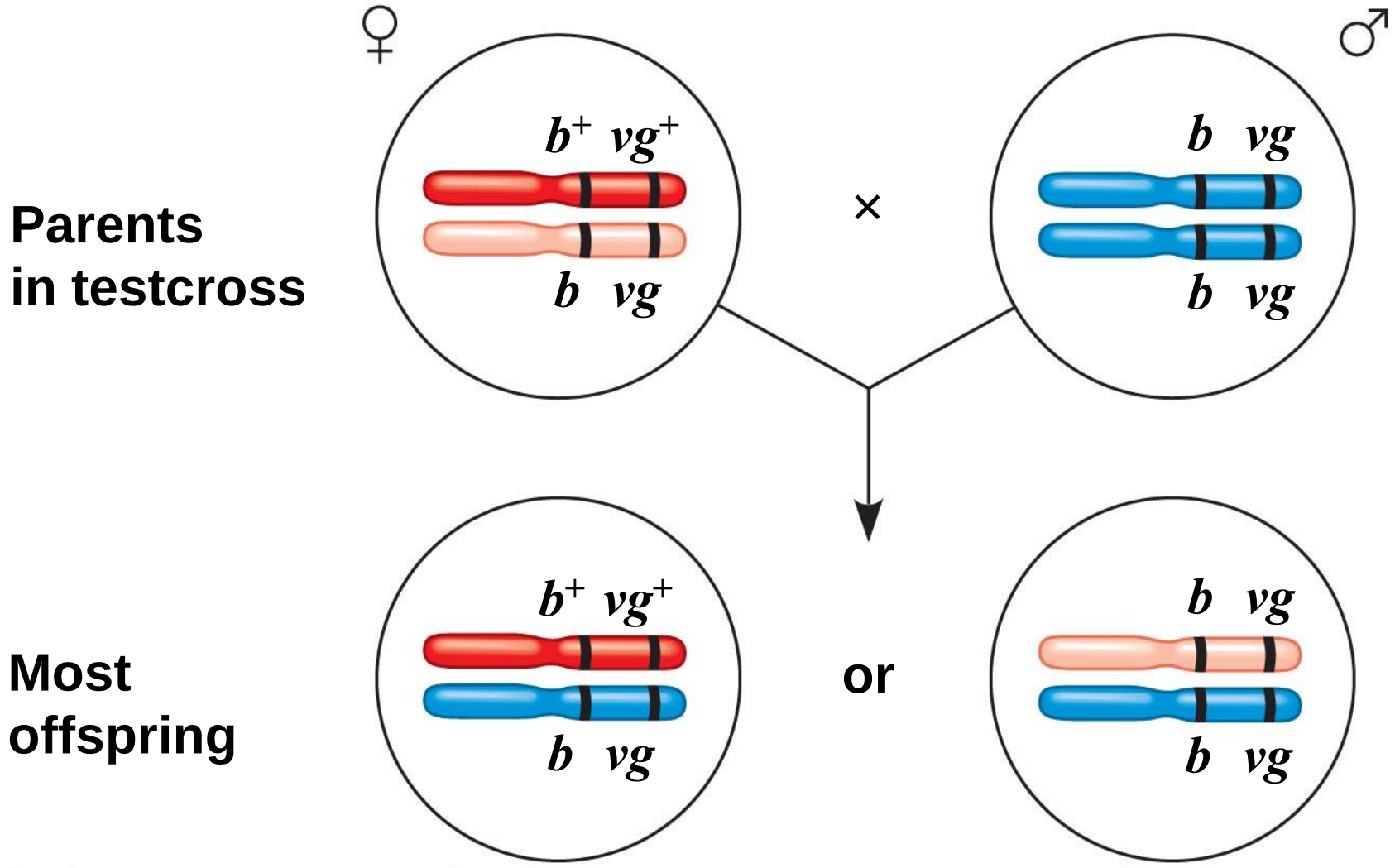


Fig. 15-9-1

EXPERIMENT

P Generation (homozygous)

Wild type (gray body, normal wings)

$b^+ \ b^+ \ vg^+ \ vg^+$

×

Double mutant (black body, vestigial wings)

$b \ b \ vg \ vg$

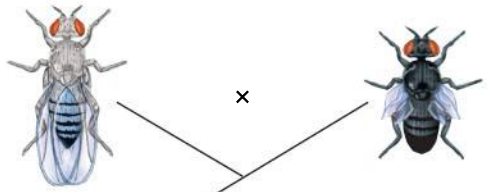
Fig. 15-9-2

EXPERIMENT

P Generation (homozygous)

Wild type (gray body, normal wings)

$b^+ \ b^+ \ vg^+ \ vg^+$



Double mutant (black body, vestigial wings)

b b vg vg

F_1 dihybrid (wild type)

$b^+ \ b \ vg^+ \ vg$

TESTCROSS

×

Double mutant

b b vg vg

Fig. 15-9-3

EXPERIMENT

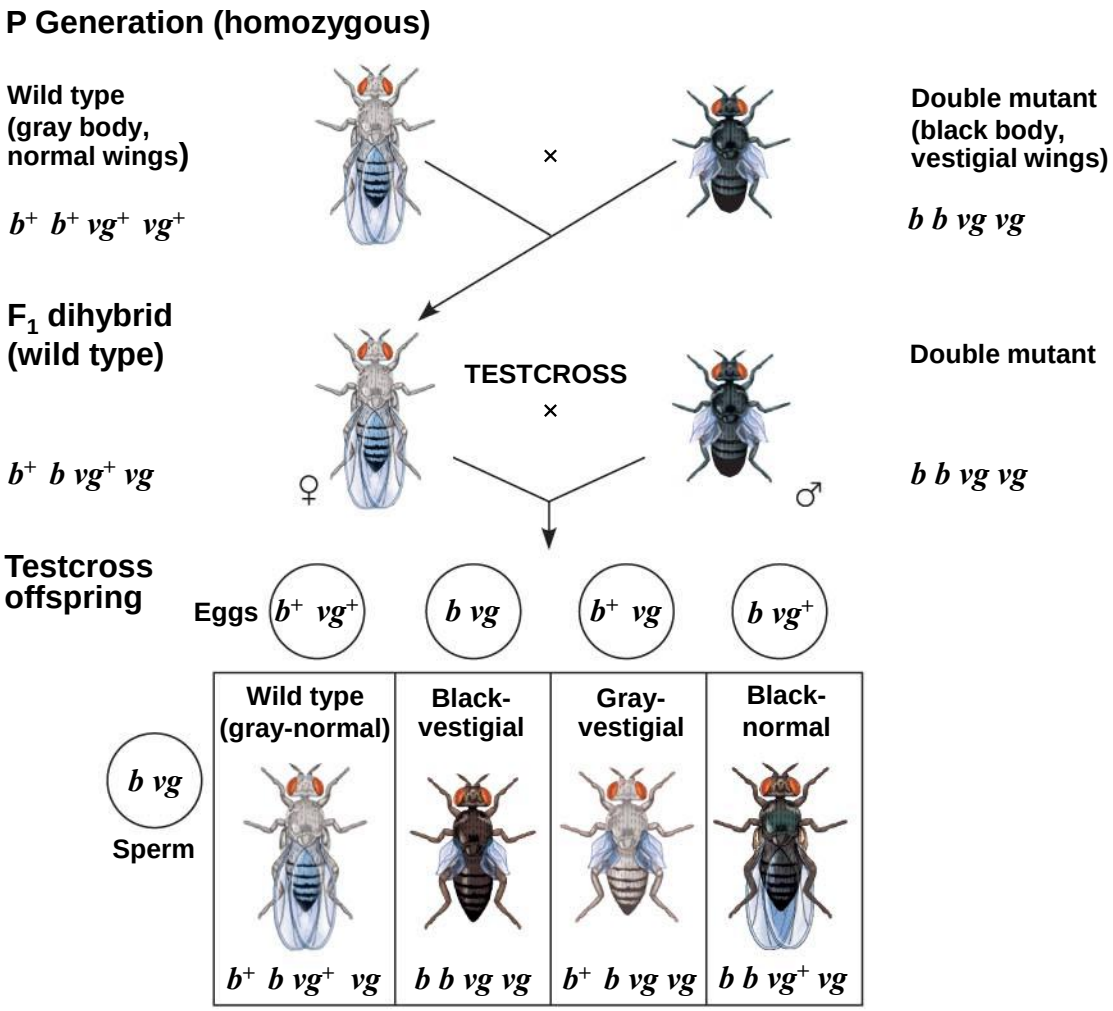


Fig. 15-9-4

EXPERIMENT

P Generation (homozygous)

Wild type (gray body, normal wings)

$b^+ \; b^+ \; vg^+ \; vg^+$

×

Double mutant (black body, vestigial wings)

$b \; b \; vg \; vg$

F_1 dihybrid (wild type)

$b^+ \; b \; vg^+ \; vg$

TESTCROSS

×

♀ ♂

Double mutant

$b \; b \; vg \; vg$

Testcross offspring

Eggs: $b^+ \; vg^+$ | $b \; vg$ | $b^+ \; vg$ | $b \; vg^+$

Sperm: $b \; vg$

Wild type (gray-normal)	Black-vestigial	Gray-vestigial	Black-normal
$b^+ \; b \; vg^+ \; vg$	$b \; b \; vg \; vg$	$b^+ \; b \; vg \; vg$	$b \; b \; vg^+ \; vg$

PREDICTED RATIOS

If genes are located on different chromosomes:	1	:	1	:	1	:	1
If genes are located on the same chromosome *and* parental alleles are always inherited together:	1	:	1	:	0	:	0

RESULTS

	965	:	944	:	206	:	185

- Morgan found that body color and wing size are usually inherited together in specific combinations (parental phenotypes)
- He noted that these genes do not assort independently, and reasoned that they were on the same chromosome

- However, nonparental phenotypes were also produced
- Understanding this result involves exploring **genetic recombination**, the production of offspring with combinations of traits differing from either parent

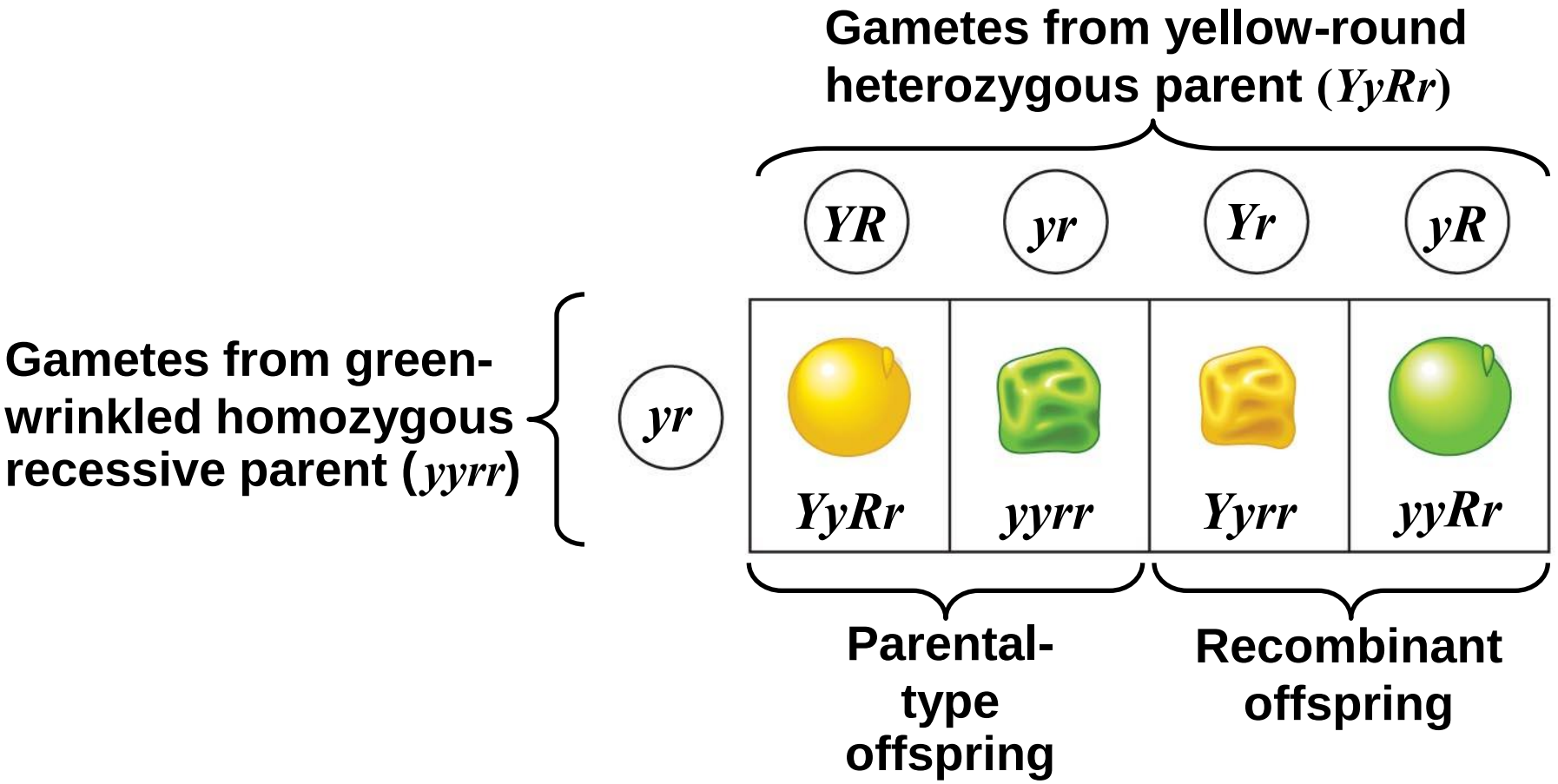
Genetic Recombination and Linkage

- The genetic findings of Mendel and Morgan relate to the chromosomal basis of recombination

Recombination of Unlinked Genes: Independent Assortment of Chromosomes

- Mendel observed that combinations of traits in some offspring differ from either parent
- Offspring with a phenotype matching one of the parental phenotypes are called **parental types**
- Offspring with nonparental phenotypes (new combinations of traits) are called **recombinant types**, or **recombinants**
- A 50% frequency of recombination is observed for any two genes on different chromosomes

Fig. 15-UN2

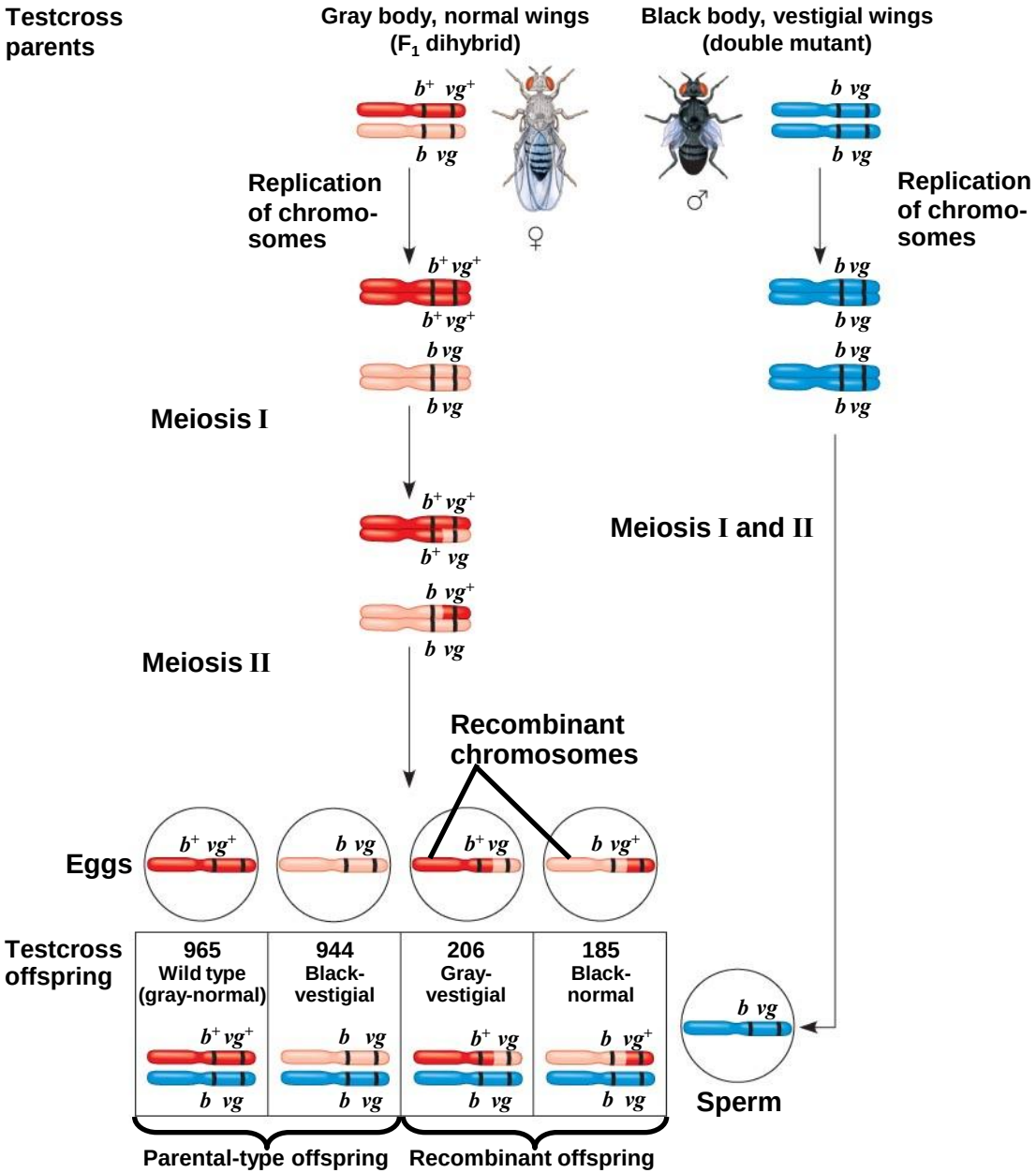


Recombination of Linked Genes: Crossing Over

- Morgan discovered that genes can be linked, but the linkage was incomplete, as evident from recombinant phenotypes
- Morgan proposed that some process must sometimes break the physical connection between genes on the same chromosome
- That mechanism was the **crossing over** of homologous chromosomes

Crossing Over

Fig. 15-10



$$\text{Recombination frequency} = \frac{391 \text{ recombinants}}{2{,}300 \text{ total offspring}} \times 100 = 17\%$$

Fig. 15-10a

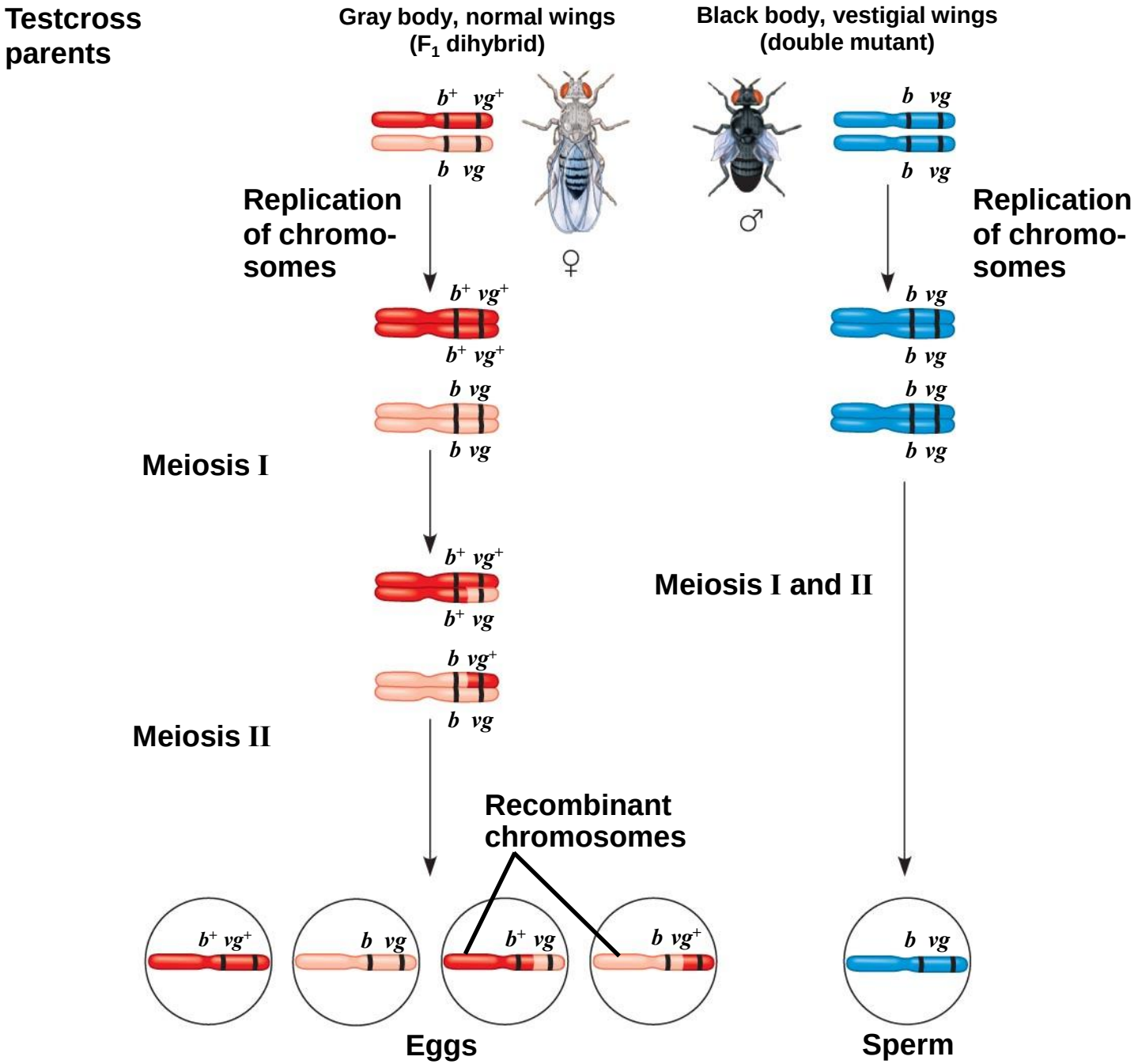
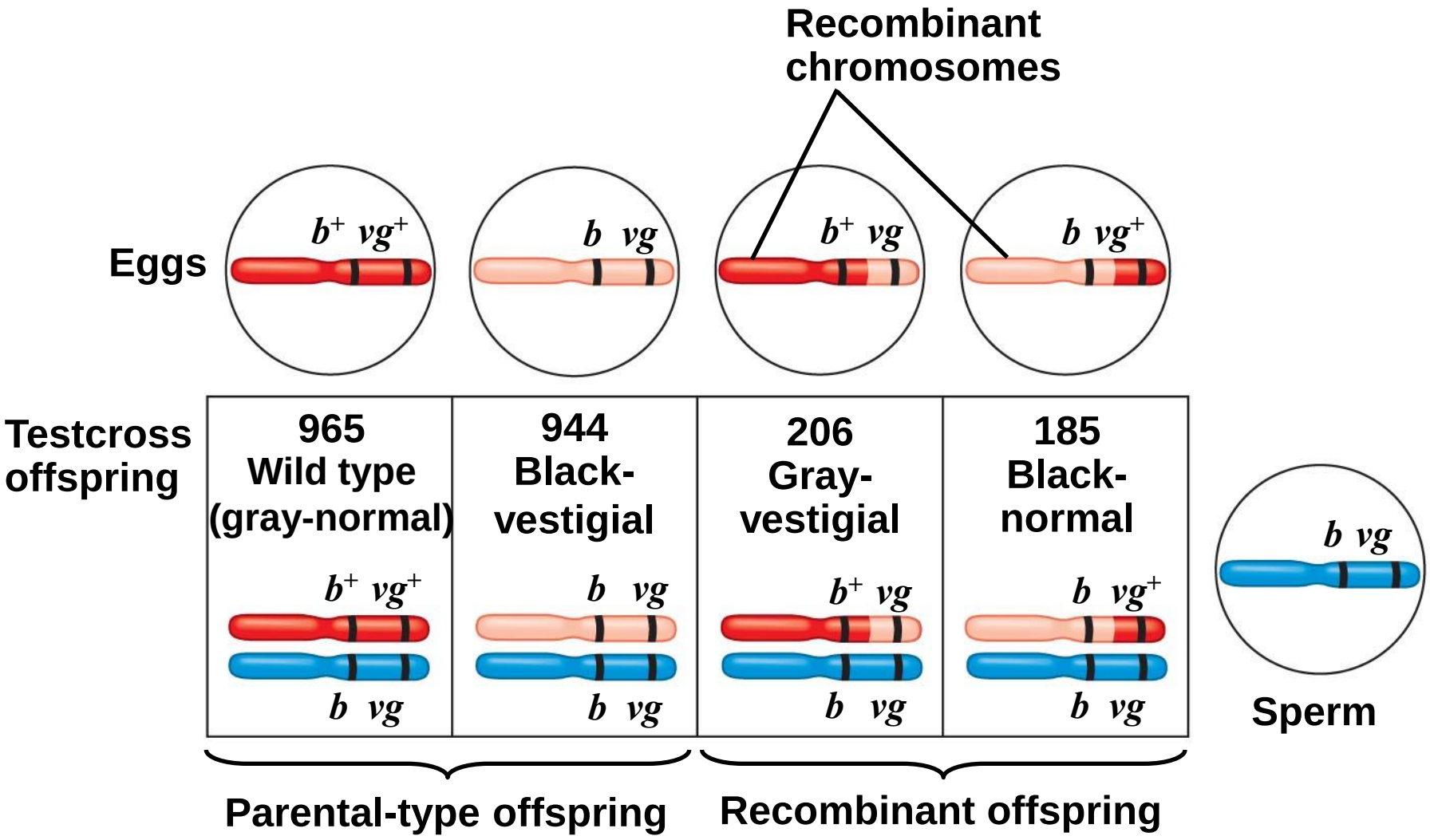


Fig. 15-10b



$$\text{Recombination frequency} = \frac{391 \text{ recombinants}}{2{,}300 \text{ total offspring}} \times 100 = 17\%$$

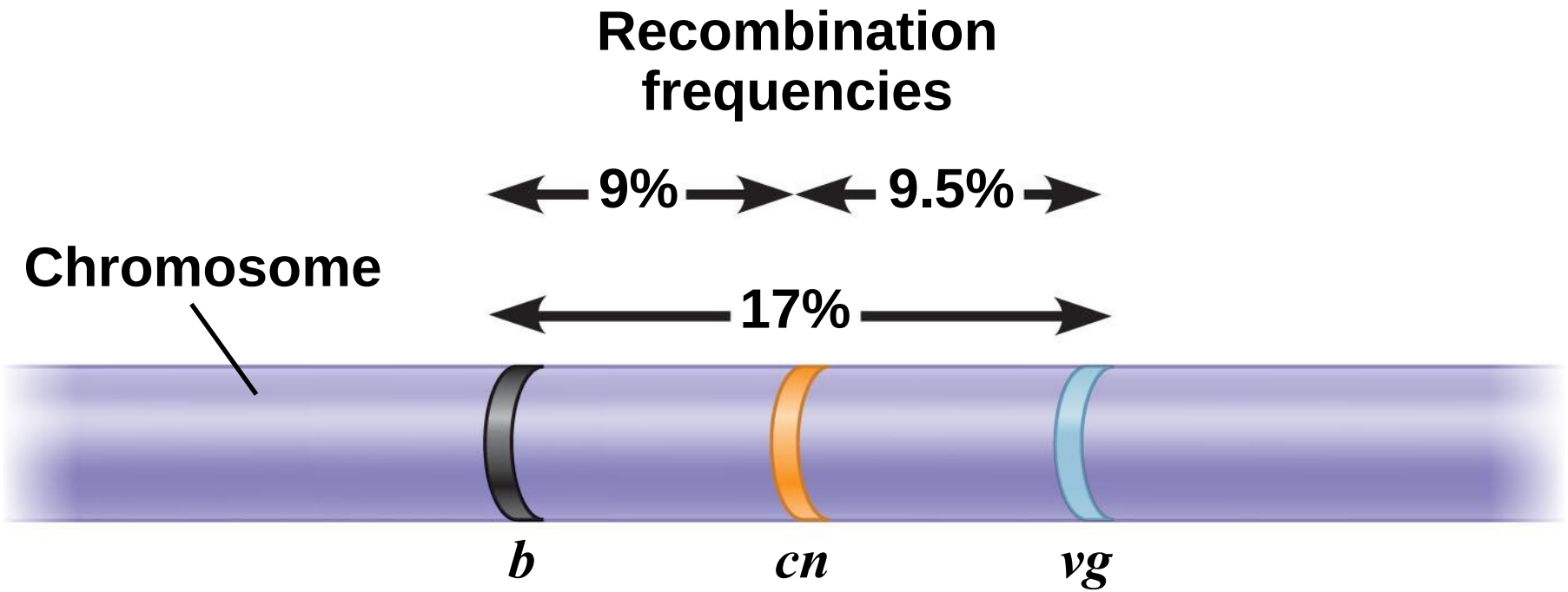
Mapping the Distance Between Genes Using Recombination Data: *Scientific Inquiry*

- Alfred Sturtevant, one of Morgan's students, constructed a **genetic map**, an ordered list of the genetic loci along a particular chromosome
- Sturtevant predicted that *the farther apart two genes are, the higher the probability that a crossover will occur between them and therefore the higher the recombination frequency*

- A **linkage map** is a genetic map of a chromosome based on recombination frequencies
- Distances between genes can be expressed as **map units**; one map unit, or centimorgan, represents a 1% recombination frequency
- Map units indicate relative distance and order, not precise locations of genes

Fig. 15-11

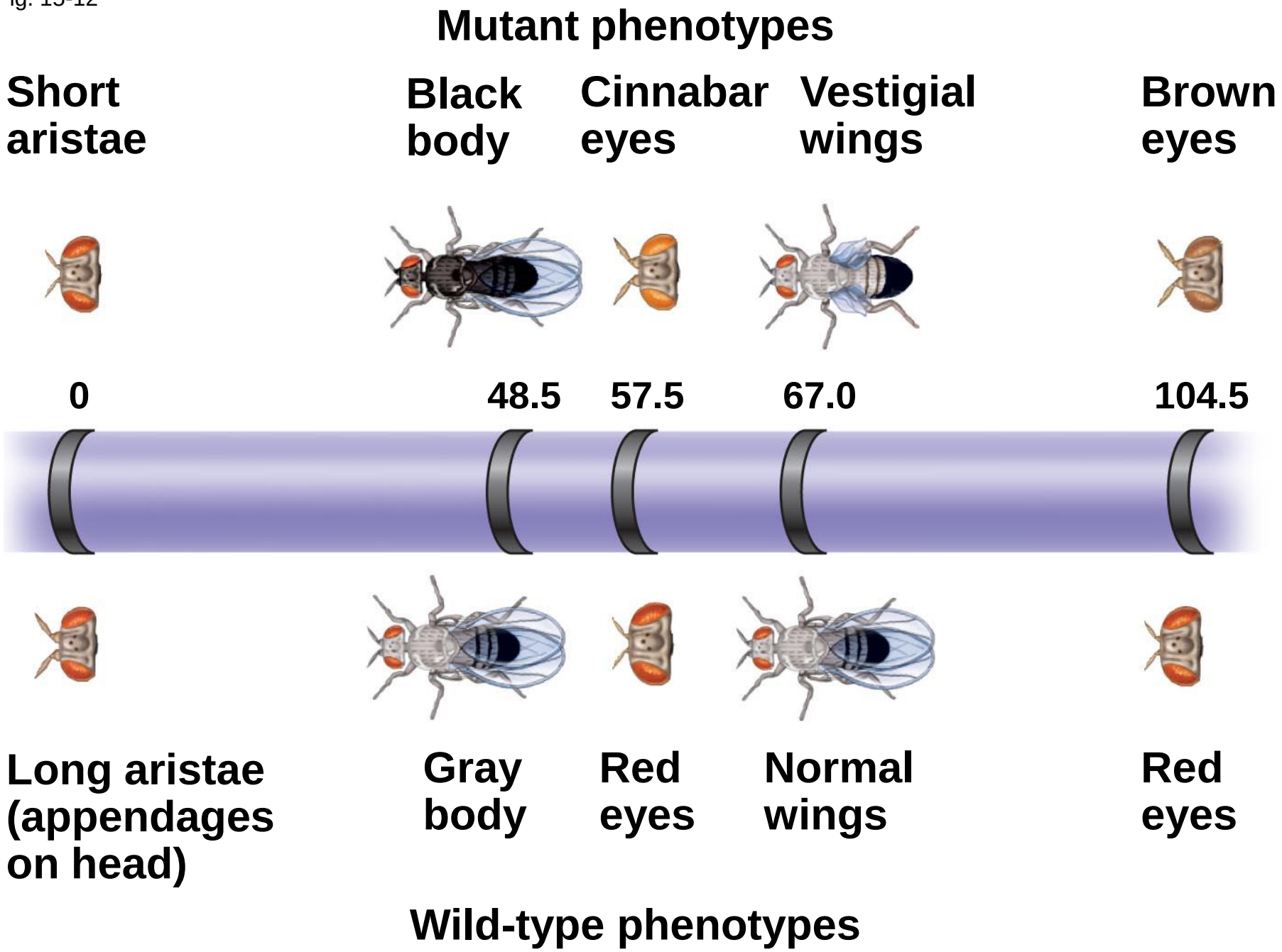
RESULTS



- Genes that are far apart on the same chromosome can have a recombination frequency near 50%
- Such genes are physically linked, but genetically unlinked, and behave as if found on different chromosomes

- Sturtevant used recombination frequencies to make linkage maps of fruit fly genes
- Using methods like chromosomal banding, geneticists can develop cytogenetic maps of chromosomes
- **Cytogenetic maps** indicate the positions of genes with respect to chromosomal features

Fig. 15-12



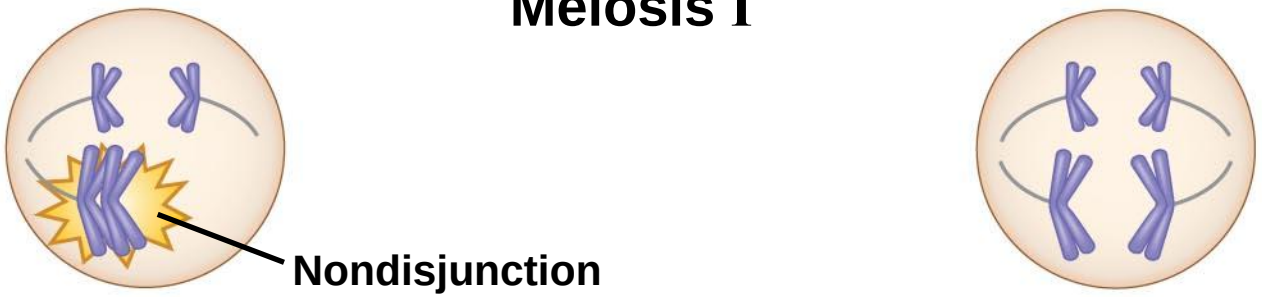
Concept 15.4: Alterations of chromosome number or structure cause some genetic disorders

- Large-scale chromosomal alterations often lead to spontaneous abortions (miscarriages) or cause a variety of developmental disorders

Abnormal Chromosome Number

- In **nondisjunction**, pairs of homologous chromosomes do not separate normally during meiosis
- As a result, one gamete receives two of the same type of chromosome, and another gamete receives no copy

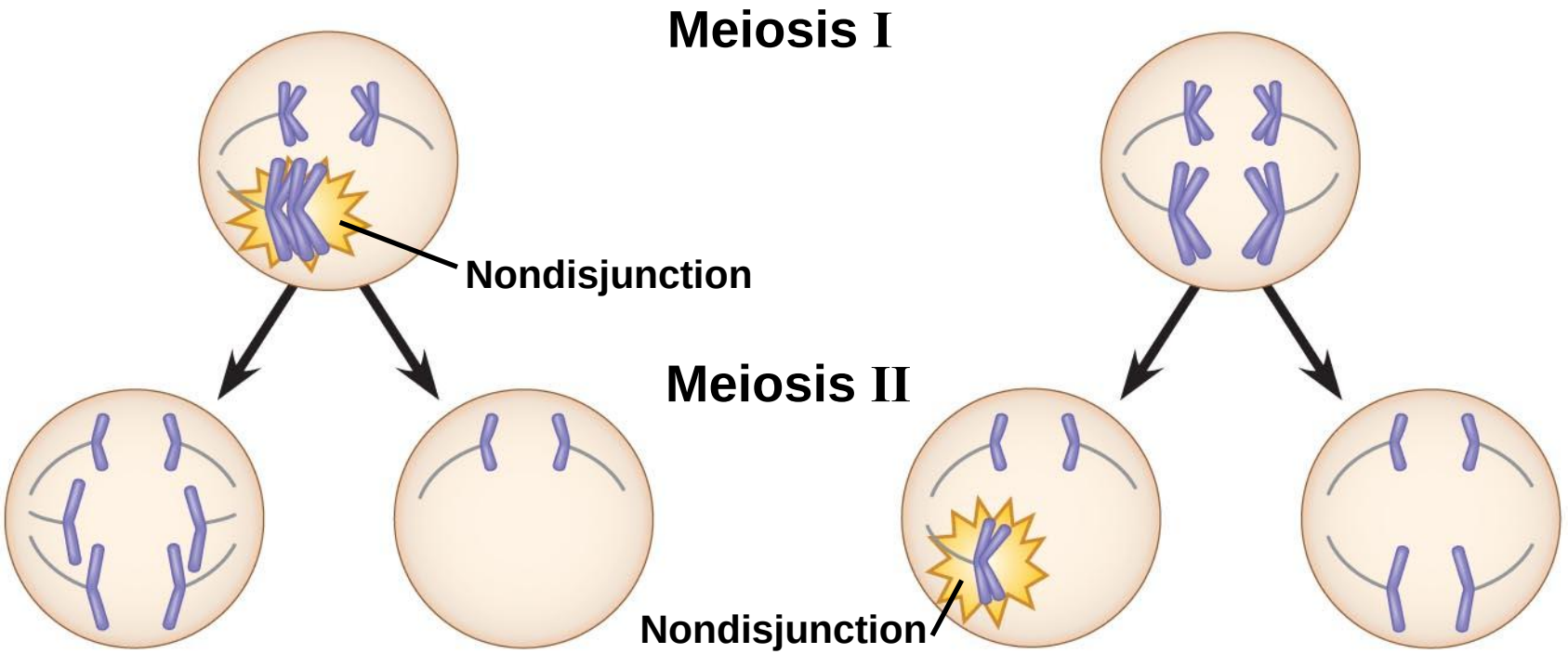
Fig. 15-13-1



(a) Nondisjunction of homologous chromosomes in meiosis I

(b) Nondisjunction of sister chromatids in meiosis II

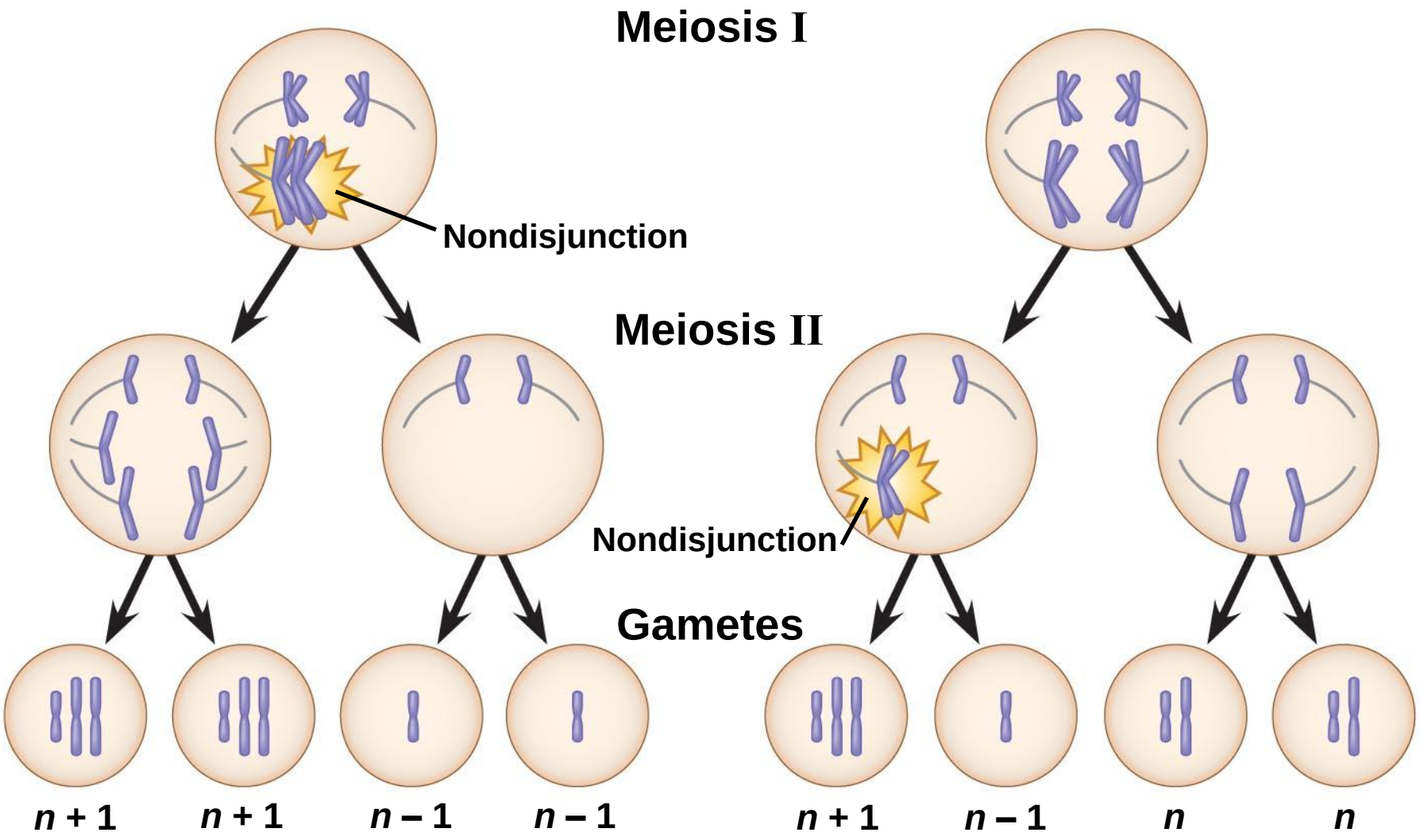
Fig. 15-13-2



(a) Nondisjunction of homologous chromosomes in meiosis I

(b) Nondisjunction of sister chromatids in meiosis II

Fig. 15-13-3



(a) Nondisjunction of homologous chromosomes in meiosis I

(b) Nondisjunction of sister chromatids in meiosis II

- **Aneuploidy** results from the fertilization of gametes in which nondisjunction occurred
- Offspring with this condition have an abnormal number of a particular chromosome

- A **monosomic** zygote has only one copy of a particular chromosome
- A **trisomic** zygote has three copies of a particular chromosome

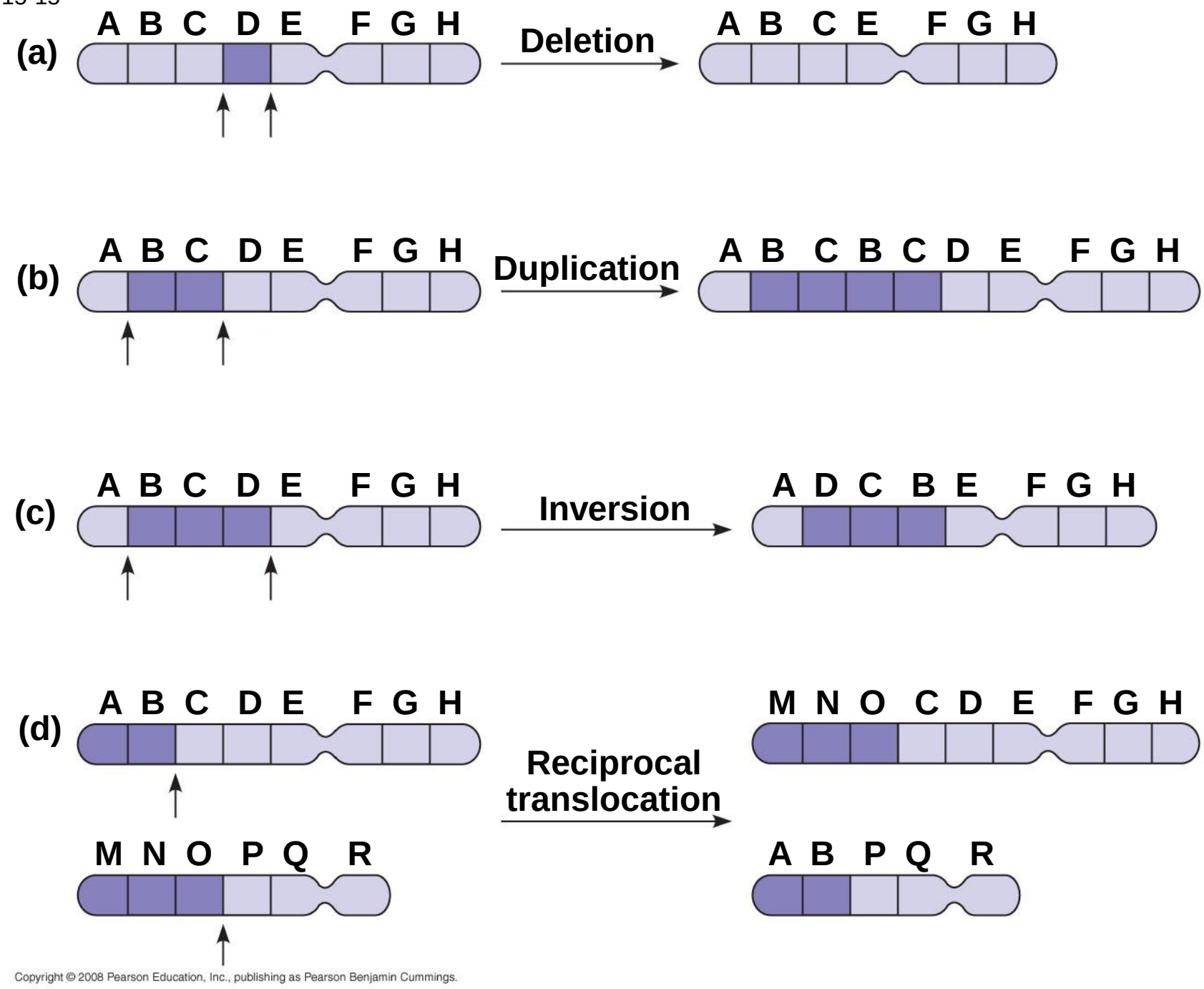
- **Polyploidy** is a condition in which an organism has more than two complete sets of chromosomes
  - Triploidy (3*n*) is three sets of chromosomes
  - Tetraploidy (4*n*) is four sets of chromosomes
- Polyploidy is common in plants, but not animals
- Polyploids are more normal in appearance than aneuploids

Fig. 15-14

Alterations of Chromosome Structure

- Breakage of a chromosome can lead to four types of changes in chromosome structure:
  - **Deletion** removes a chromosomal segment
  - **Duplication** repeats a segment
  - **Inversion** reverses a segment within a chromosome
  - **Translocation** moves a segment from one chromosome to another

Fig. 15-15



Human Disorders Due to Chromosomal Alterations

- Alterations of chromosome number and structure are associated with some serious disorders
- Some types of aneuploidy appear to upset the genetic balance less than others, resulting in individuals surviving to birth and beyond
- These surviving individuals have a set of symptoms, or syndrome, characteristic of the type of aneuploidy

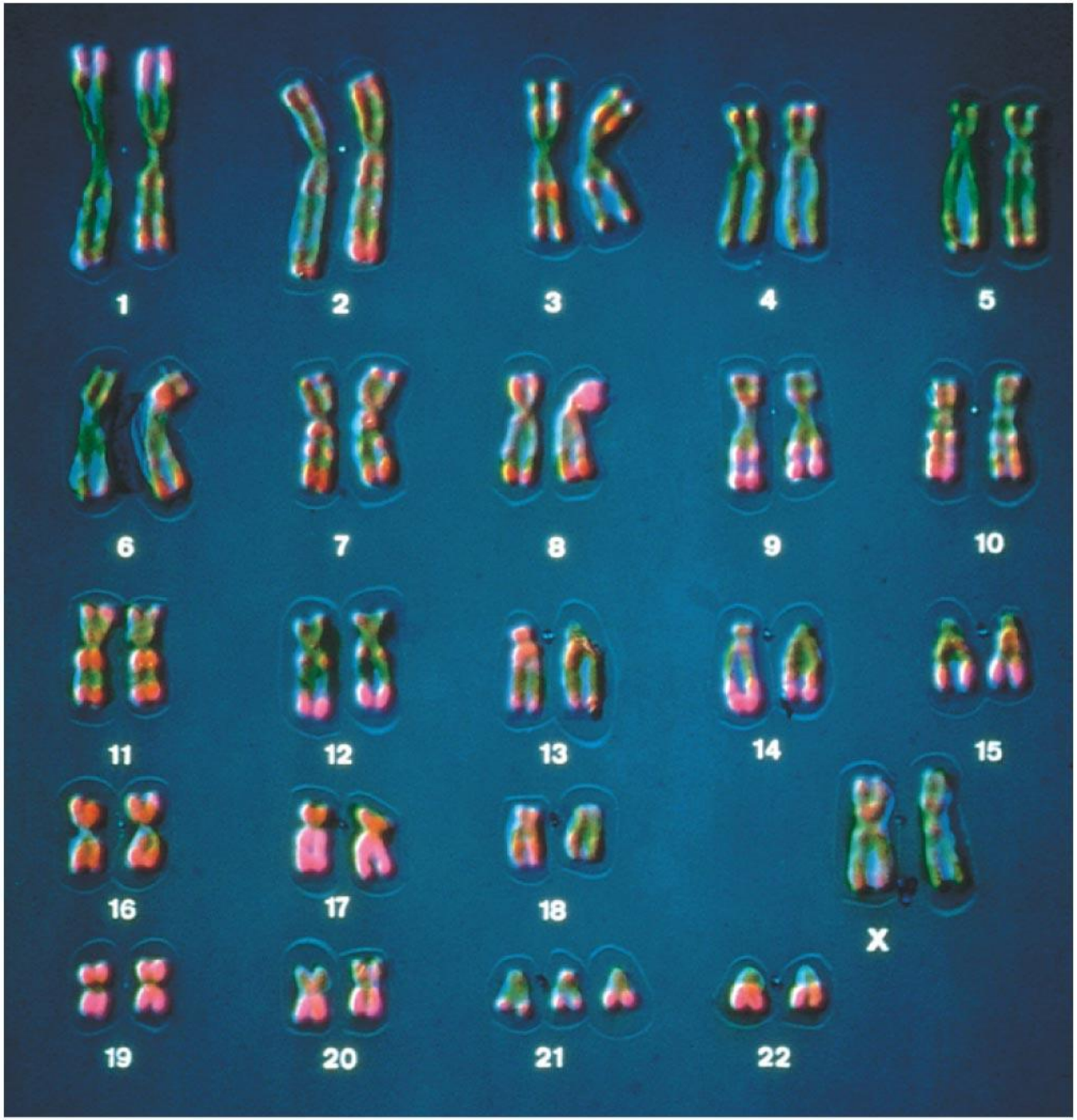
Down Syndrome (Trisomy 21)

- **Down syndrome** is an aneuploid condition that results from three copies of chromosome 21
- It affects about one out of every 700 children born in the United States
- The frequency of Down syndrome increases with the age of the mother, a correlation that has not been explained

Fig. 15-16

Fig. 15-16a

Fig. 15-16b



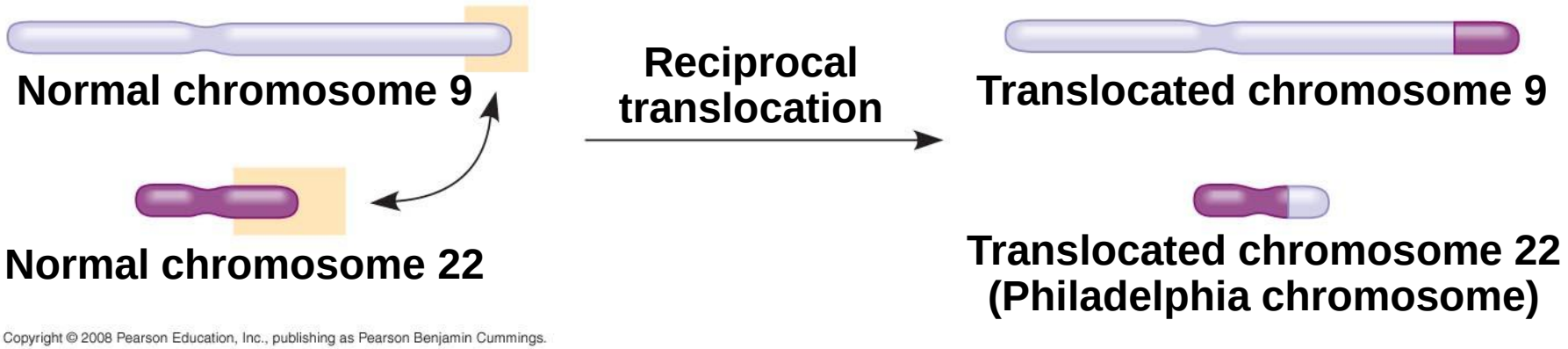
Aneuploidy of Sex Chromosomes

- Nondisjunction of sex chromosomes produces a variety of aneuploid conditions
- *Klinefelter syndrome* is the result of an extra chromosome in a male, producing XXY individuals
- Monosomy X, called *Turner syndrome*, produces X0 females, who are sterile; it is the only known viable monosomy in humans

Disorders Caused by Structurally Altered Chromosomes

- The syndrome *cri du chat* (“cry of the cat”), results from a specific deletion in chromosome 5
- A child born with this syndrome is mentally retarded and has a catlike cry; individuals usually die in infancy or early childhood
- Certain cancers, including *chronic myelogenous leukemia* (CML), are caused by translocations of chromosomes

Fig. 15-17



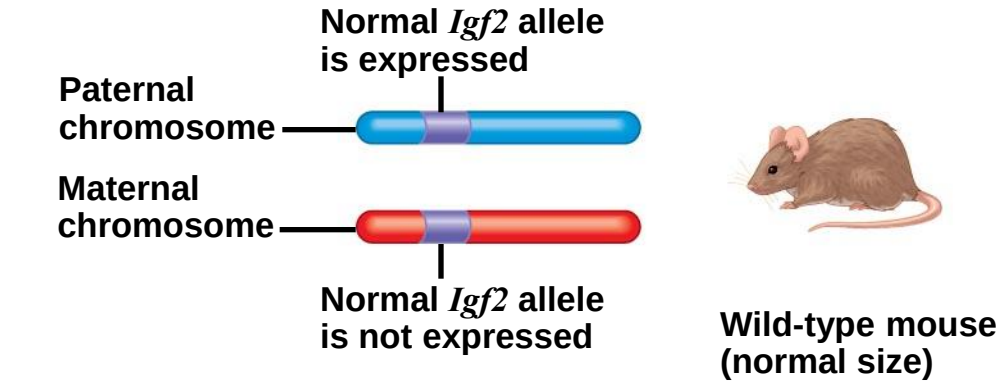
Concept 15.5: Some inheritance patterns are exceptions to the standard chromosome theory

- There are two normal exceptions to Mendelian genetics
- One exception involves genes located in the nucleus, and the other exception involves genes located outside the nucleus

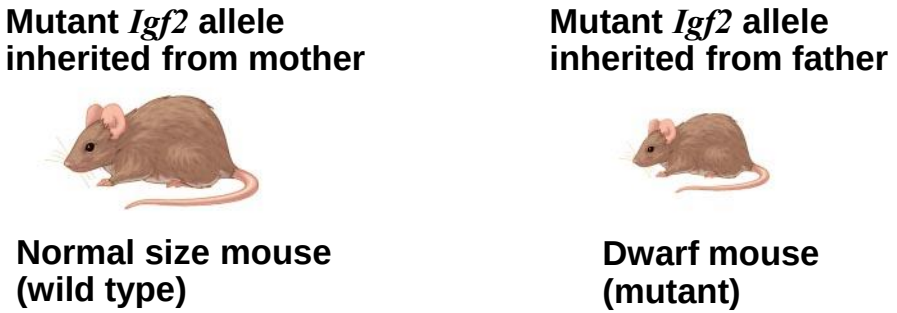
Genomic Imprinting

- For a few mammalian traits, the phenotype depends on which parent passed along the alleles for those traits
- Such variation in phenotype is called **genomic imprinting**
- Genomic imprinting involves the silencing of certain genes that are “stamped” with an imprint during gamete production

Fig. 15-18

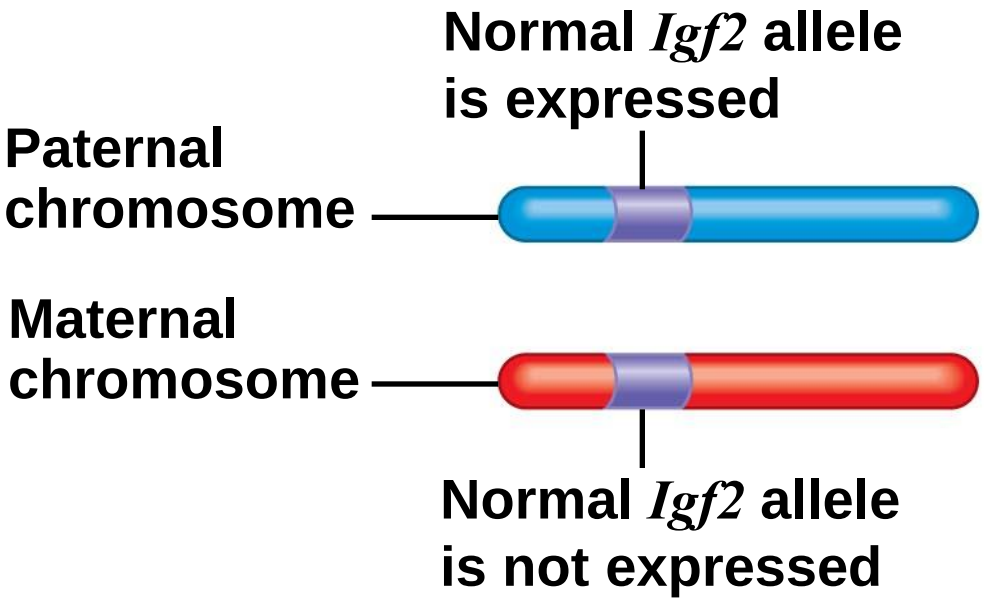


(a) Homozygote



(b) Heterozygotes

Fig. 15-18a



Wild-type mouse (normal size)

(a) Homozygote

Fig. 15-18b

Mutant *Igf2* allele inherited from mother

Normal size mouse (wild type)

Normal *Igf2* allele is expressed

Mutant *Igf2* allele is not expressed

Mutant *Igf2* allele inherited from father

Dwarf mouse (mutant)

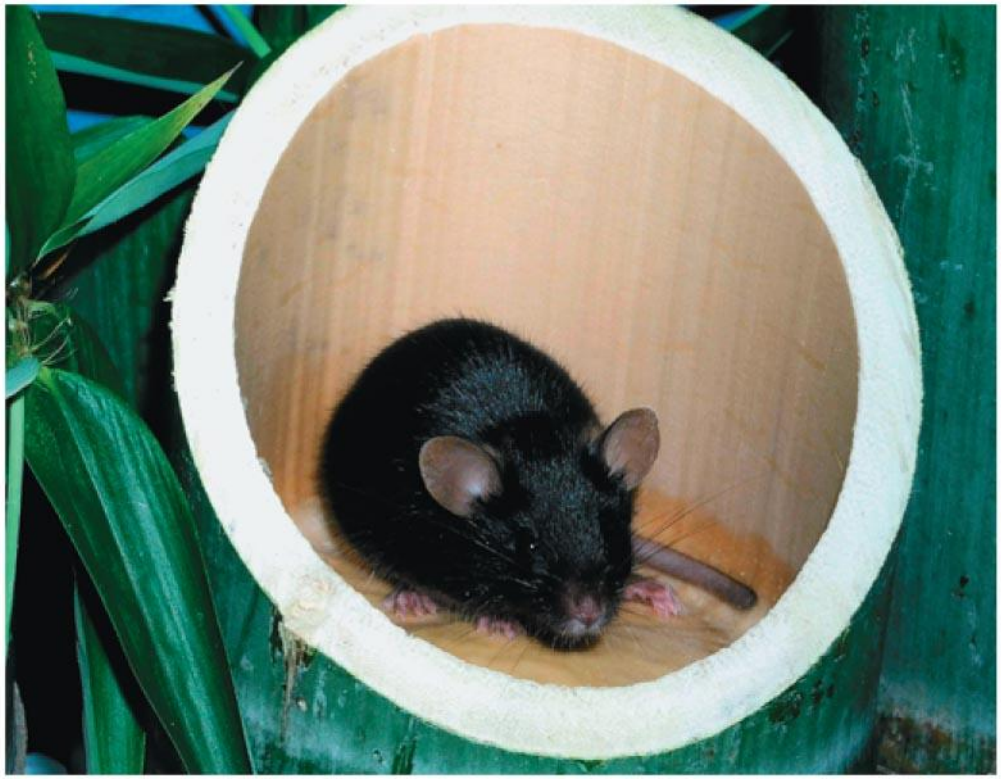
Mutant *Igf2* allele is expressed

Normal *Igf2* allele is not expressed

(b) Heterozygotes

- It appears that imprinting is the result of the methylation (addition of $–CH_3$) of DNA
- Genomic imprinting is thought to affect only a small fraction of mammalian genes
- Most imprinted genes are critical for embryonic development

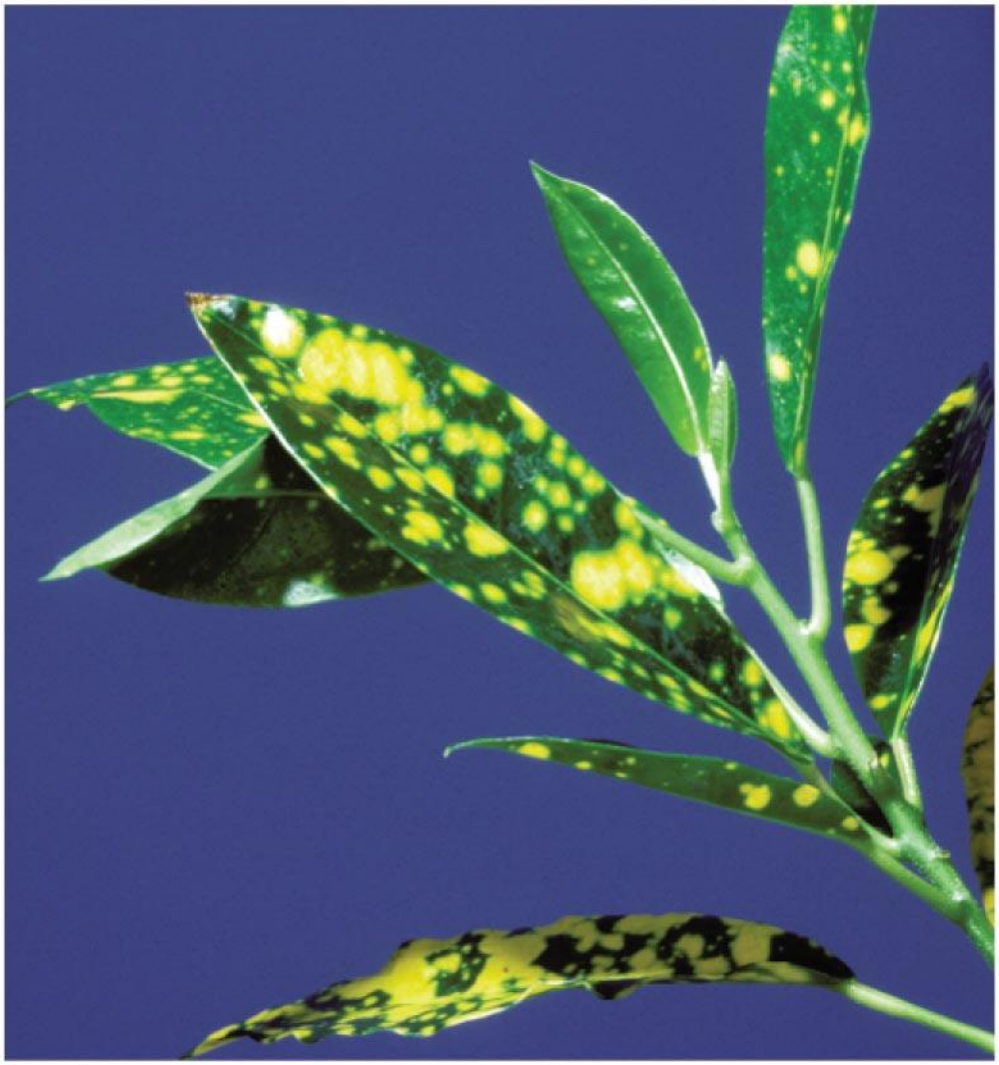
Fig. 15-UN3



Inheritance of Organelle Genes

- *Extranuclear genes* (or *cytoplasmic genes*) are genes found in organelles in the cytoplasm
- Mitochondria, chloroplasts, and other plant plastids carry small circular DNA molecules
- Extranuclear genes are inherited maternally because the zygote's cytoplasm comes from the egg
- The first evidence of extranuclear genes came from studies on the inheritance of yellow or white patches on leaves of an otherwise green plant

Fig. 15-19



- Some defects in mitochondrial genes prevent cells from making enough ATP and result in diseases that affect the muscular and nervous systems
  - For example, mitochondrial myopathy and Leber's hereditary optic neuropathy

Fig. 15-UN4

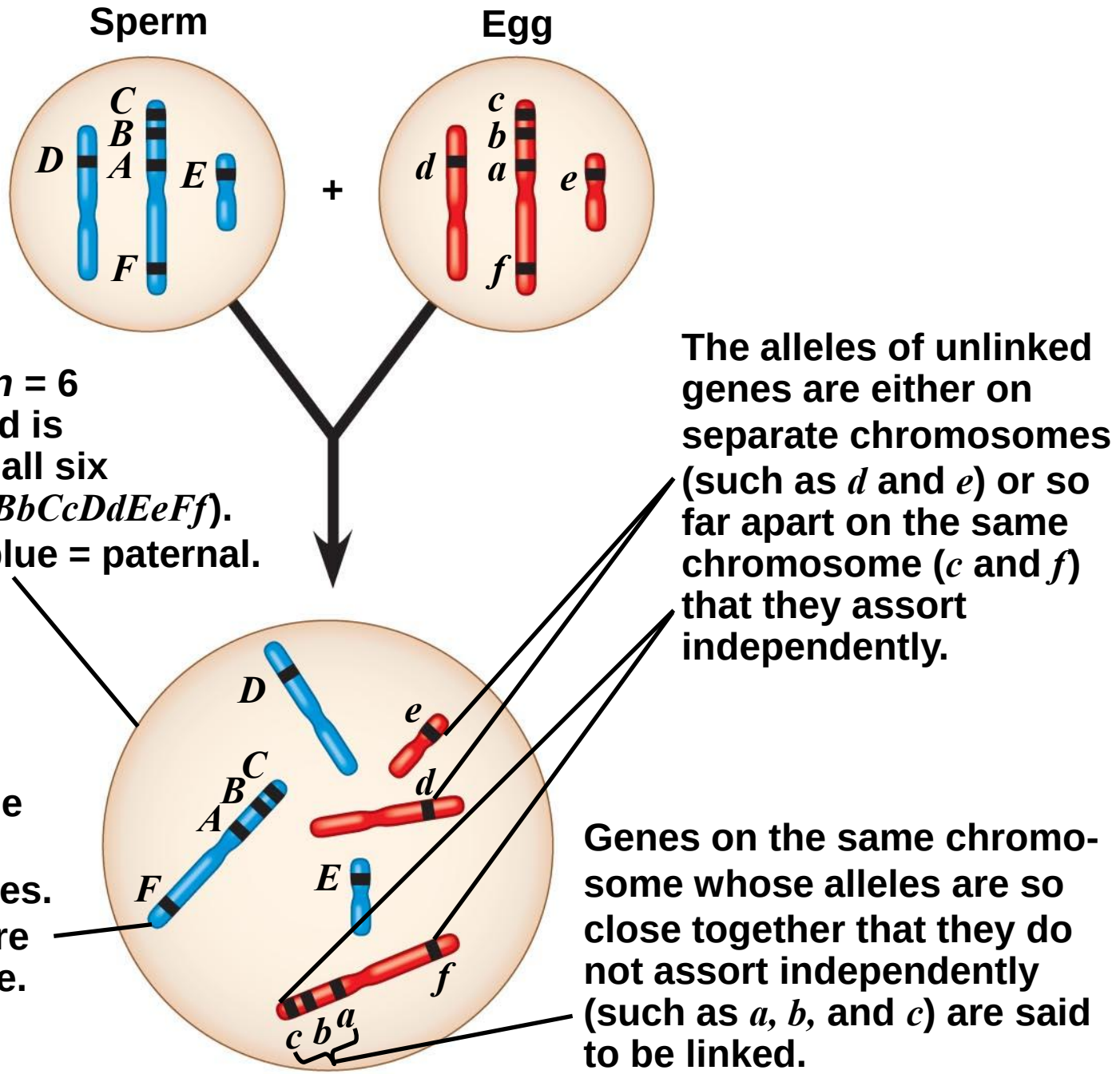


Fig. 15-UN5

Fig. 15-UN6

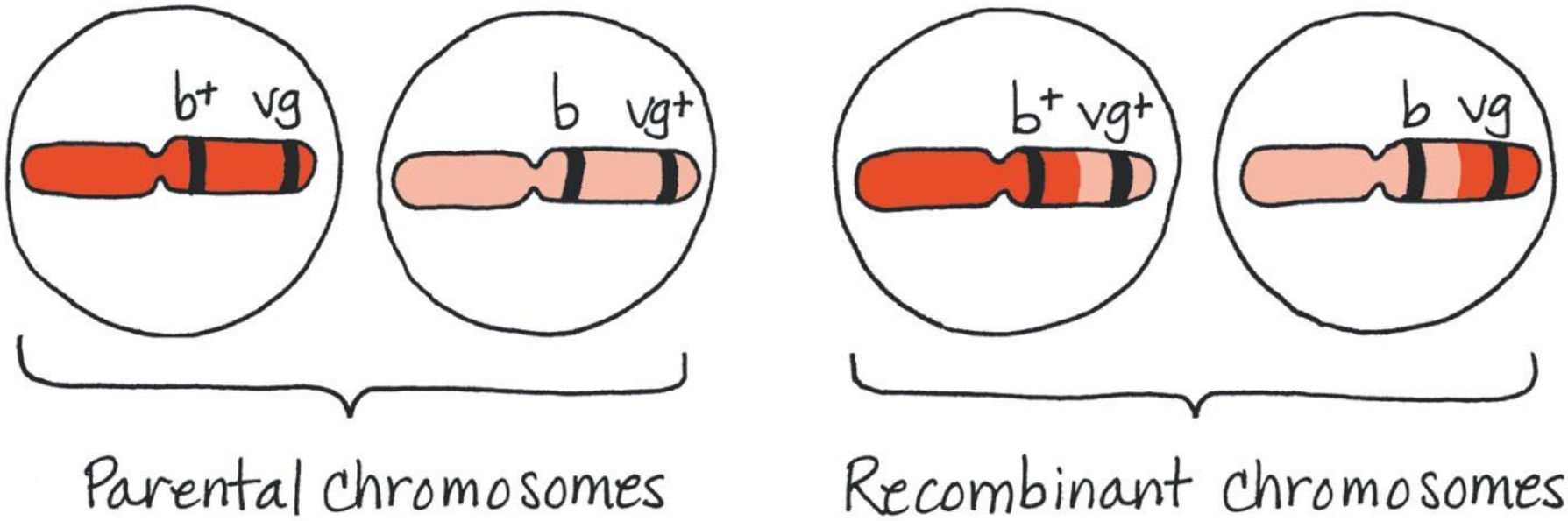


Fig. 15-UN7

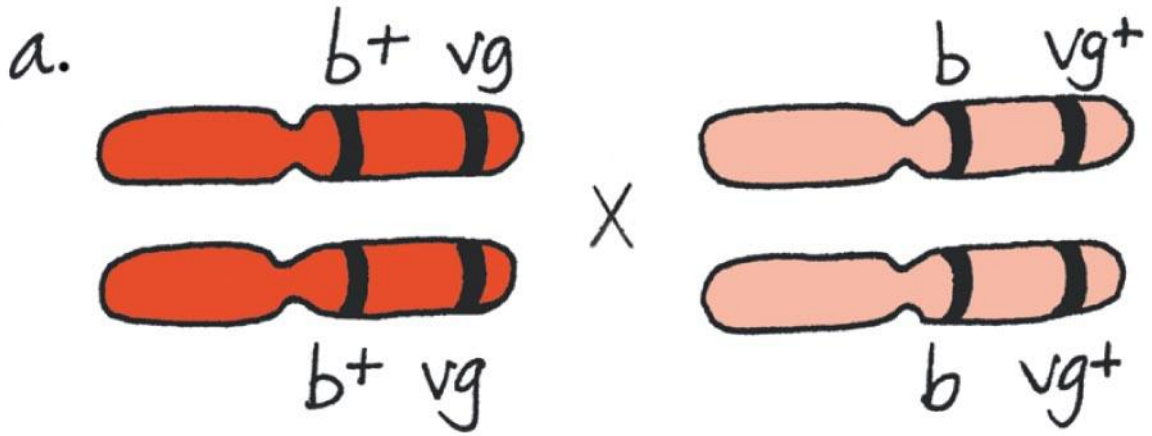


Fig. 15-UN8

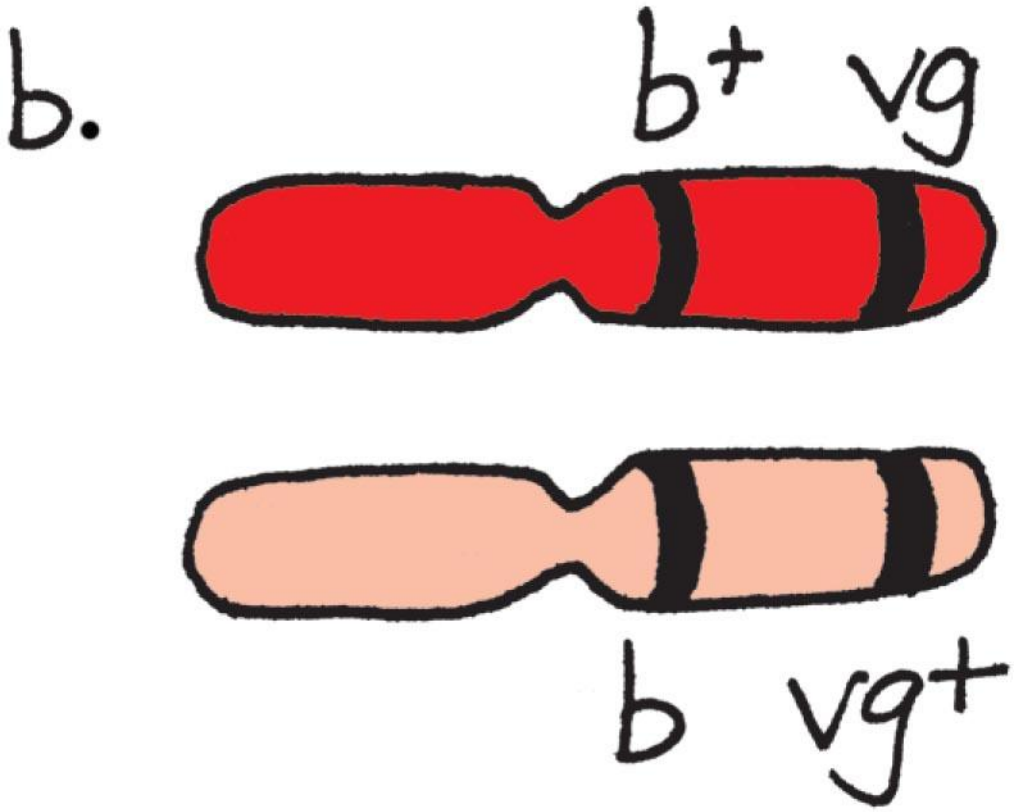
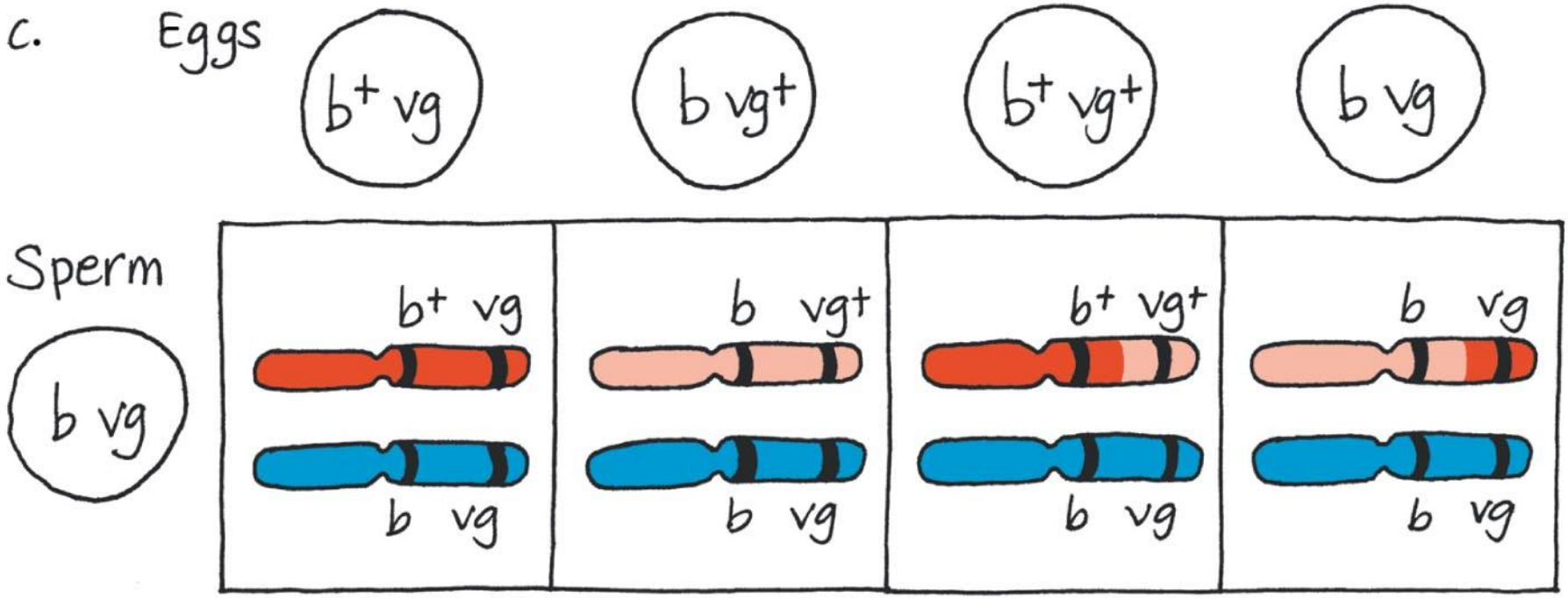


Fig. 15-UN9



You should now be able to:

1. Explain the chromosomal theory of inheritance and its discovery
2. Explain why sex-linked diseases are more common in human males than females
3. Distinguish between sex-linked genes and linked genes
4. Explain how meiosis accounts for recombinant phenotypes
5. Explain how linkage maps are constructed

6. Explain how nondisjunction can lead to aneuploidy
7. Define trisomy, triploidy, and polyploidy
8. Distinguish among deletions, duplications, inversions, and translocations
9. Explain genomic imprinting
10. Explain why extranuclear genes are not inherited in a Mendelian fashion