Chapter 15

The Chromosomal Basis of Inheritance

PowerPoint® Lecture Presentations for

Biology

Eighth Edition

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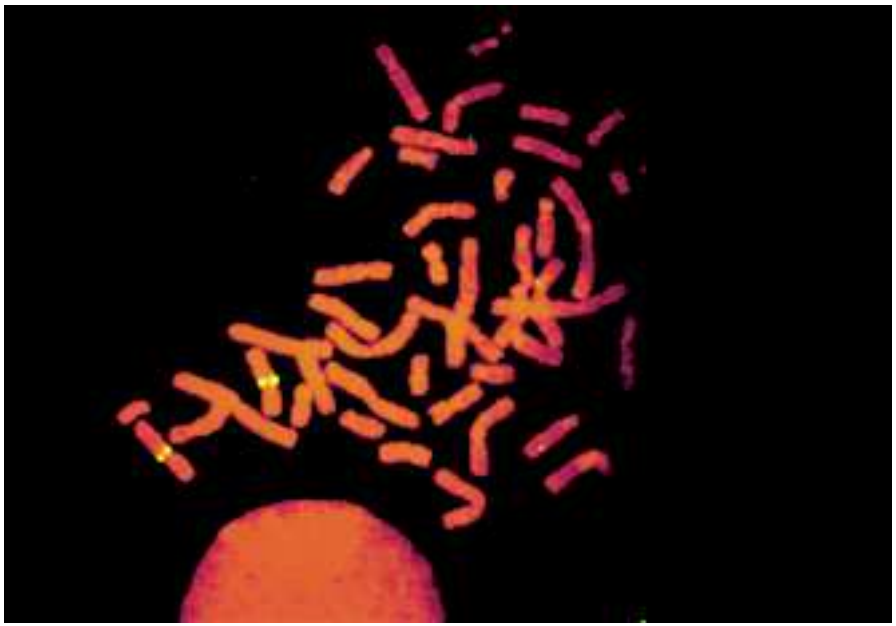
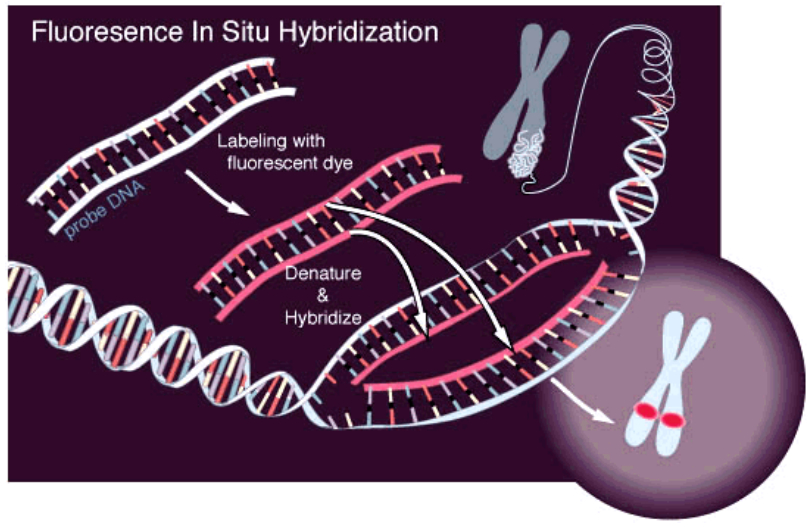
Overview: Locating Genes Along Chromosomes

- 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

Locating Genes on Chromosomes

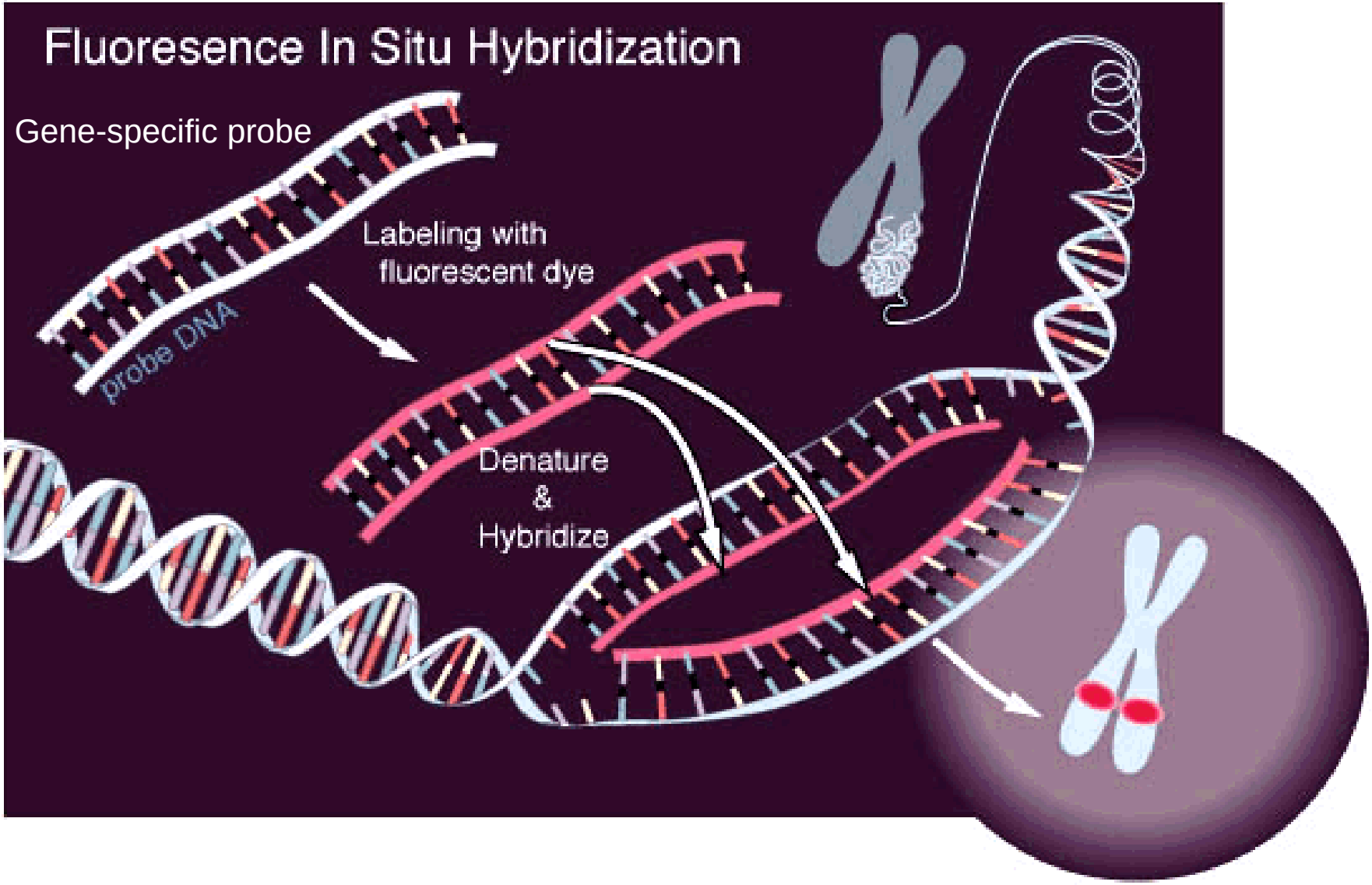
- Genes
  - Are located on chromosomes
  - Can be visualized using certain techniques





FISH (Fluorescent *in situ* hybridization)

Figure 15.1


Fluoresence In Situ Hybridization
Gene-specific probe
probe DNA
Labeling with
fluorescent dye
Denature
&
Hybridize

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. 15-2a

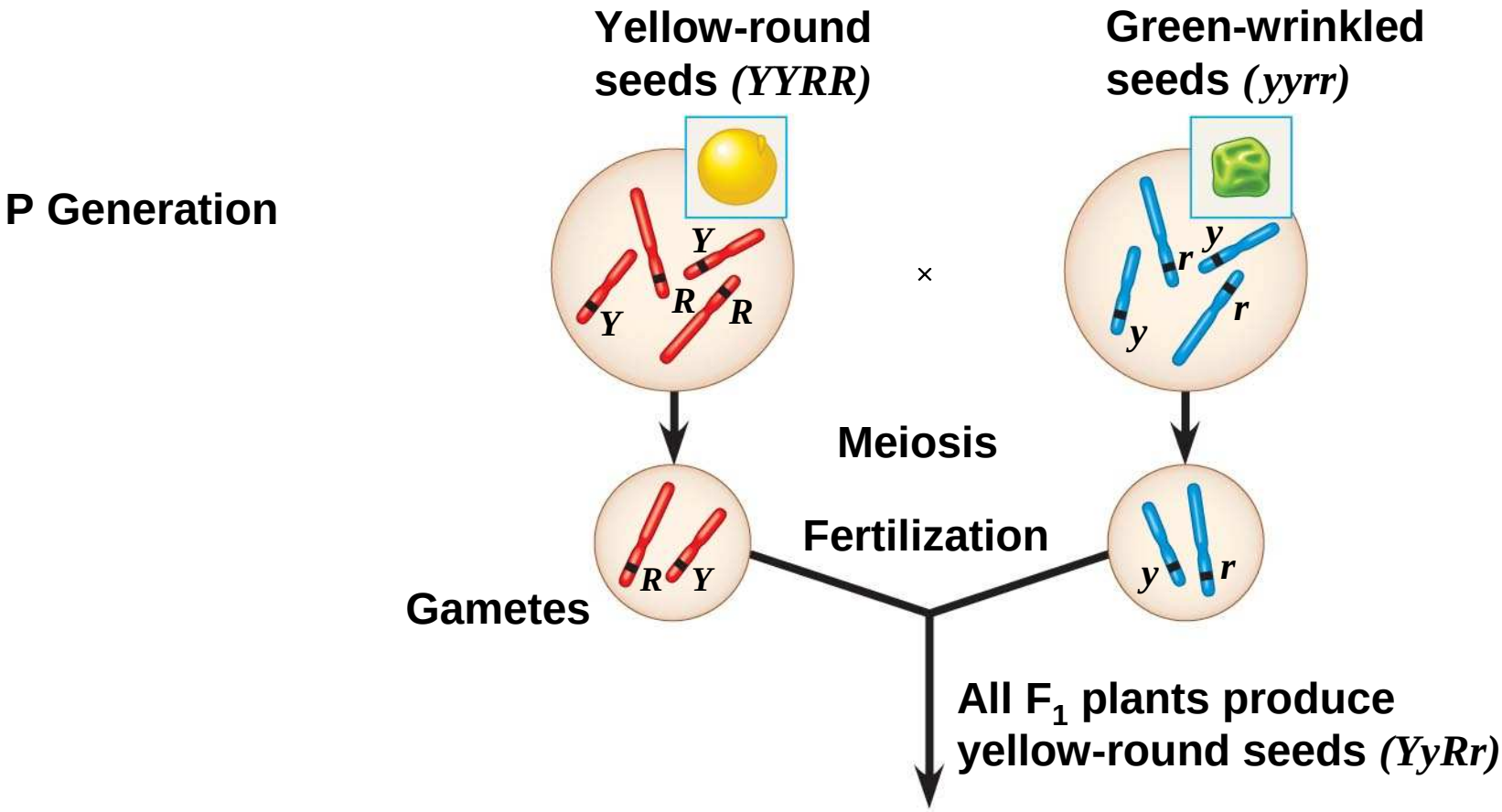


Fig. 15-2b

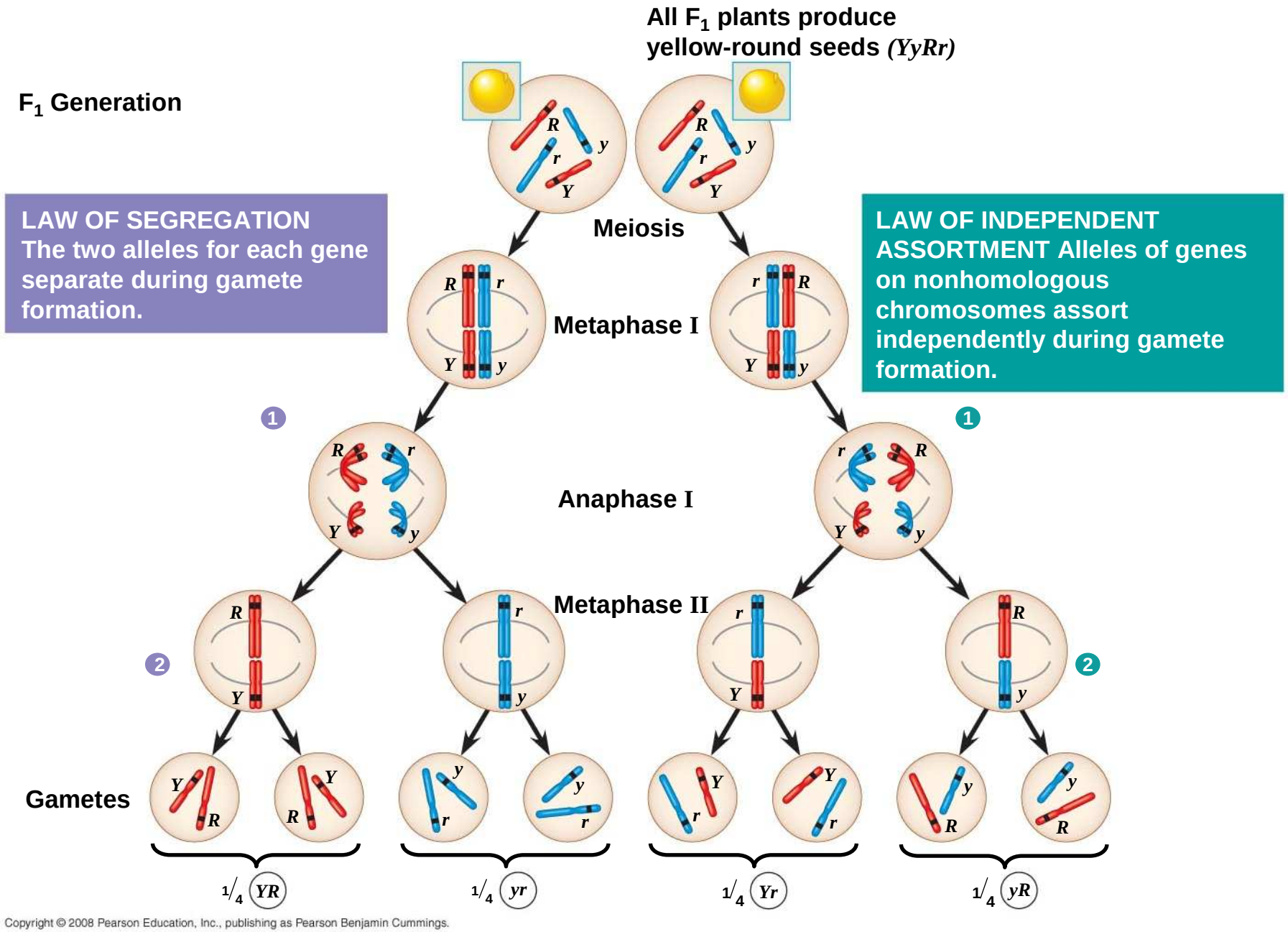
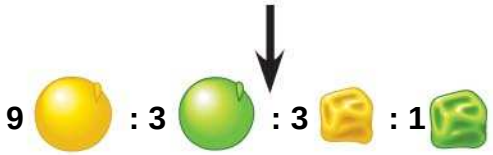


Fig. 15-2c

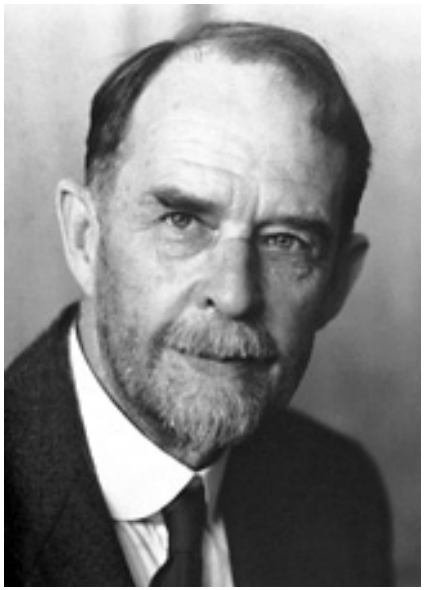
F_2 Generation

3

An $F_1 \times F_1$ cross-fertilization



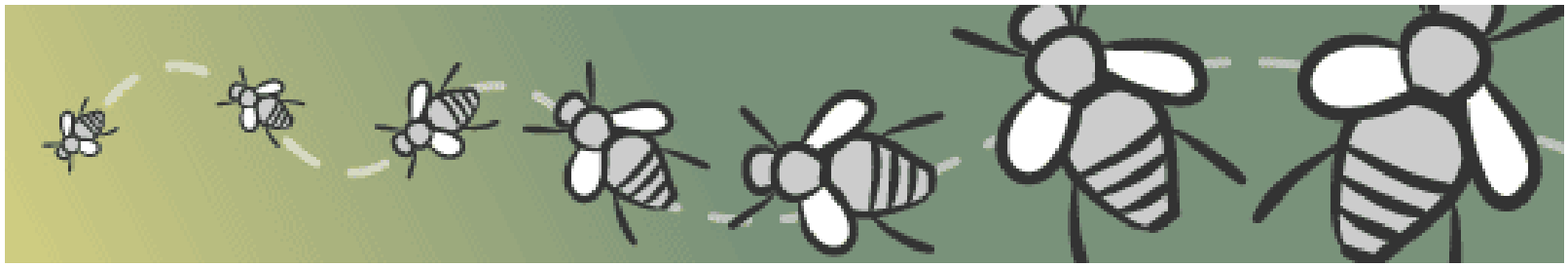
Morgan's Experimental Evidence: *Scientific Inquiry*



Thomas Hunt Morgan

- Provided convincing evidence that chromosomes are the location of Mendel's heritable factors

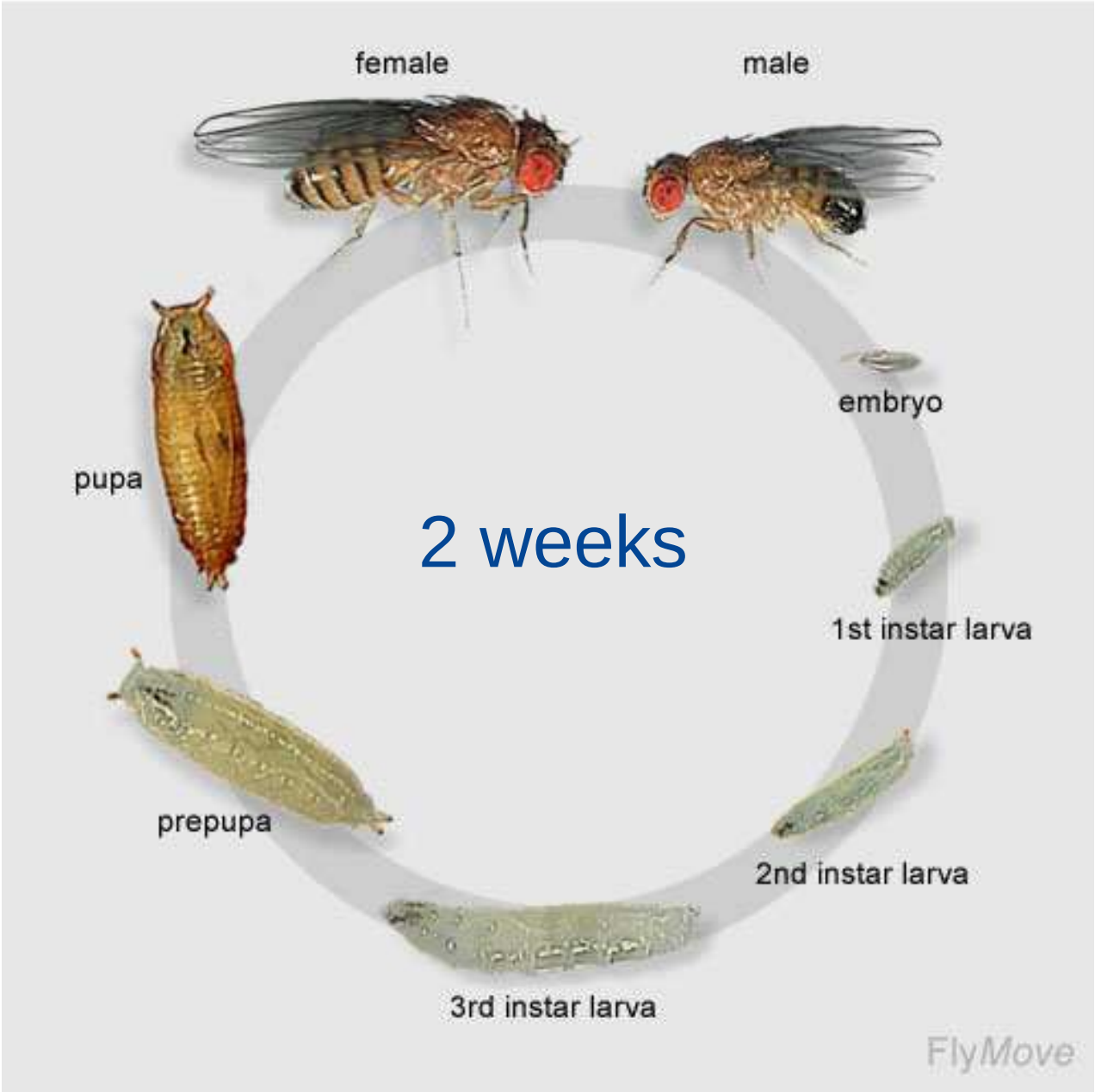
Morgan's Choice of Experimental Organism



Morgan worked with fruit flies

- Because they breed at a high rate
- A new generation can be bred every two weeks
- They have only four pairs of chromosomes

The life cycle of *Drosophila melanogaster*

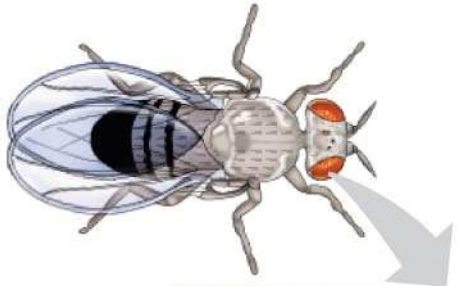


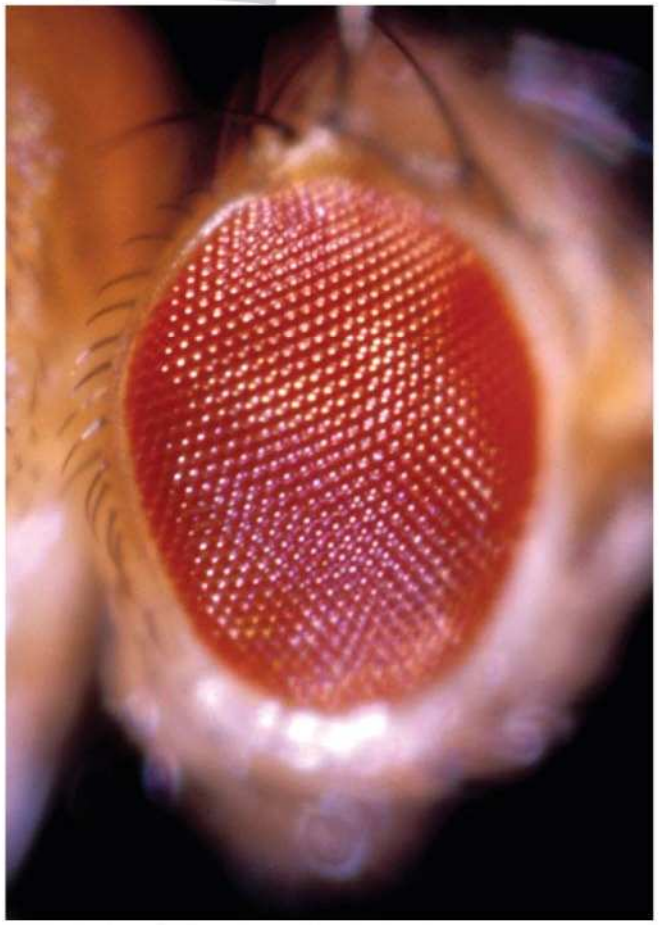
Wild type vs. Mutant phenotype

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

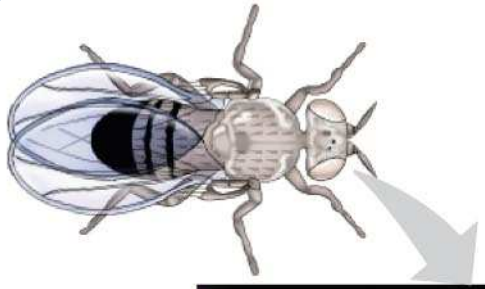
Fig. 15-3

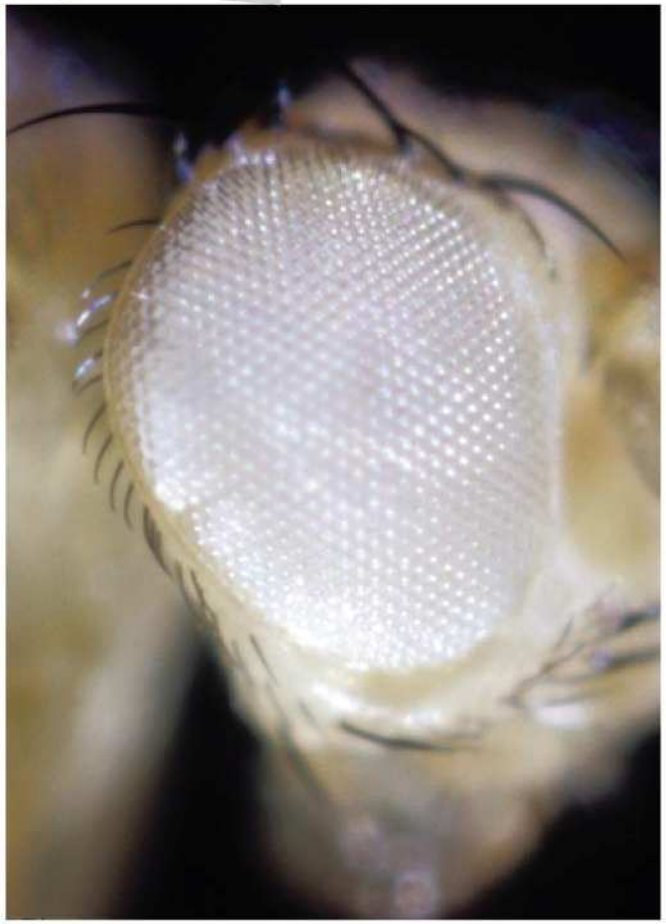
Wild-type





Morgan’s first mutant





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. 15-4a

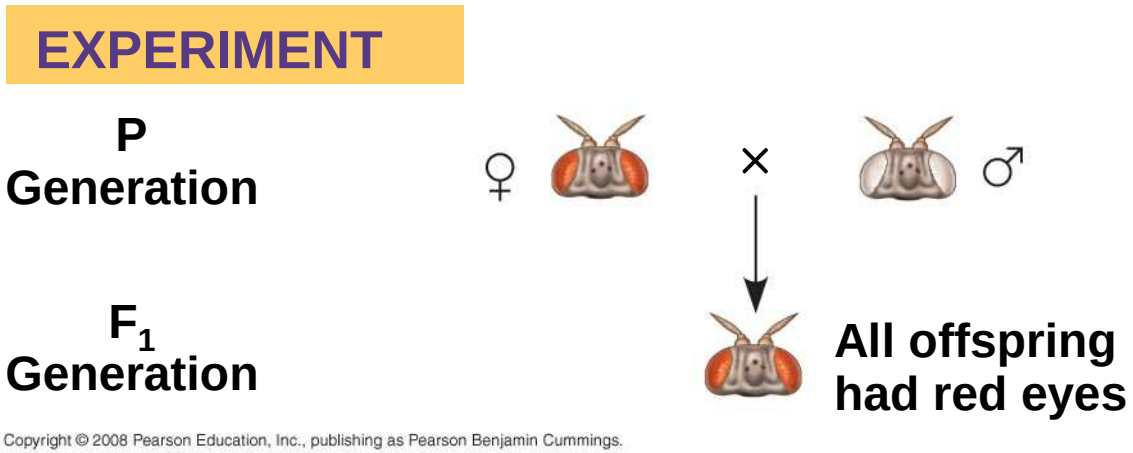


Fig. 15-4b

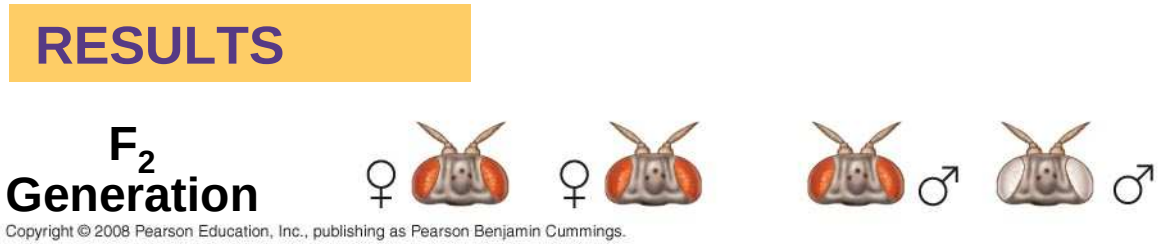
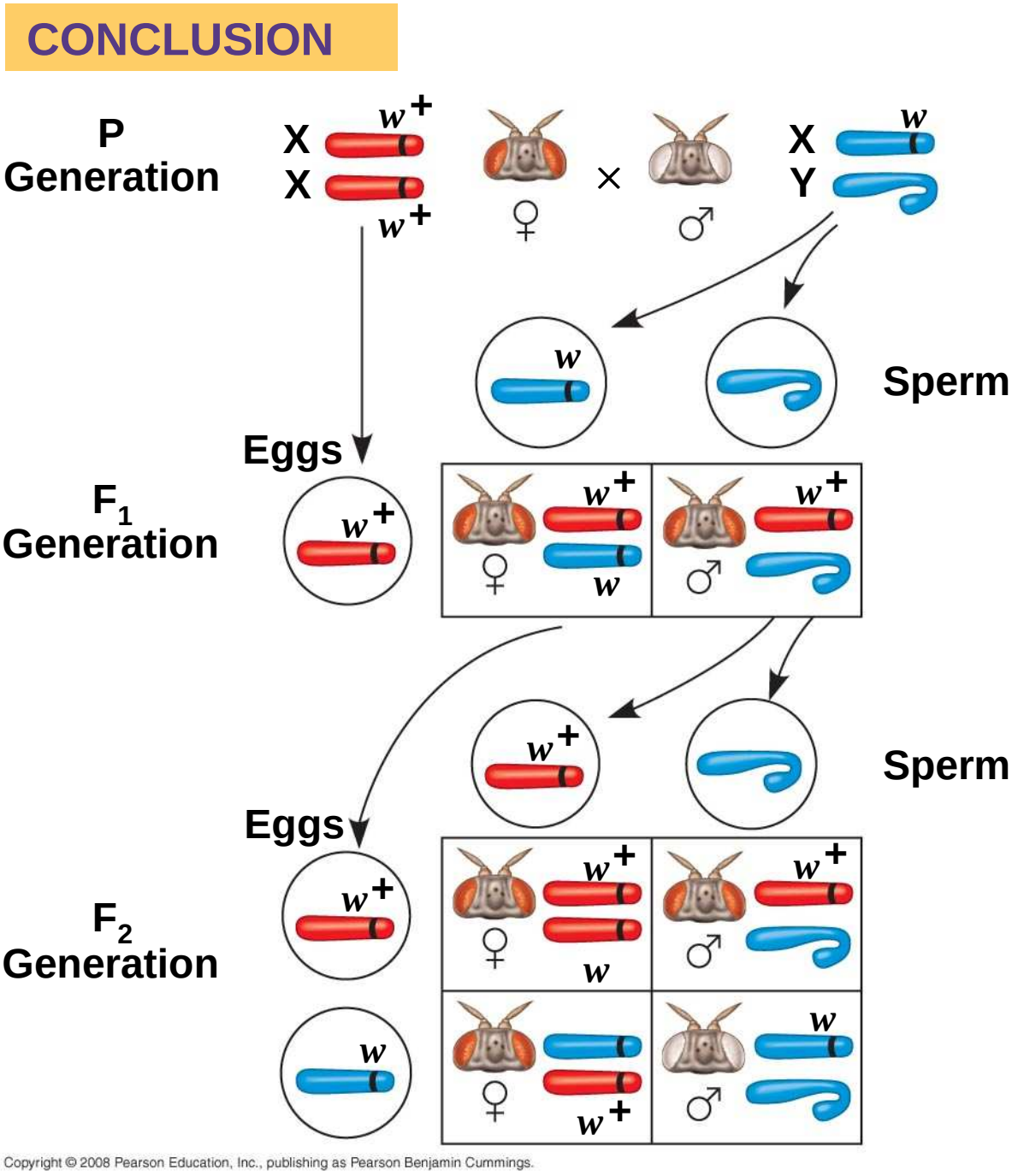


Fig. 15-4c



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

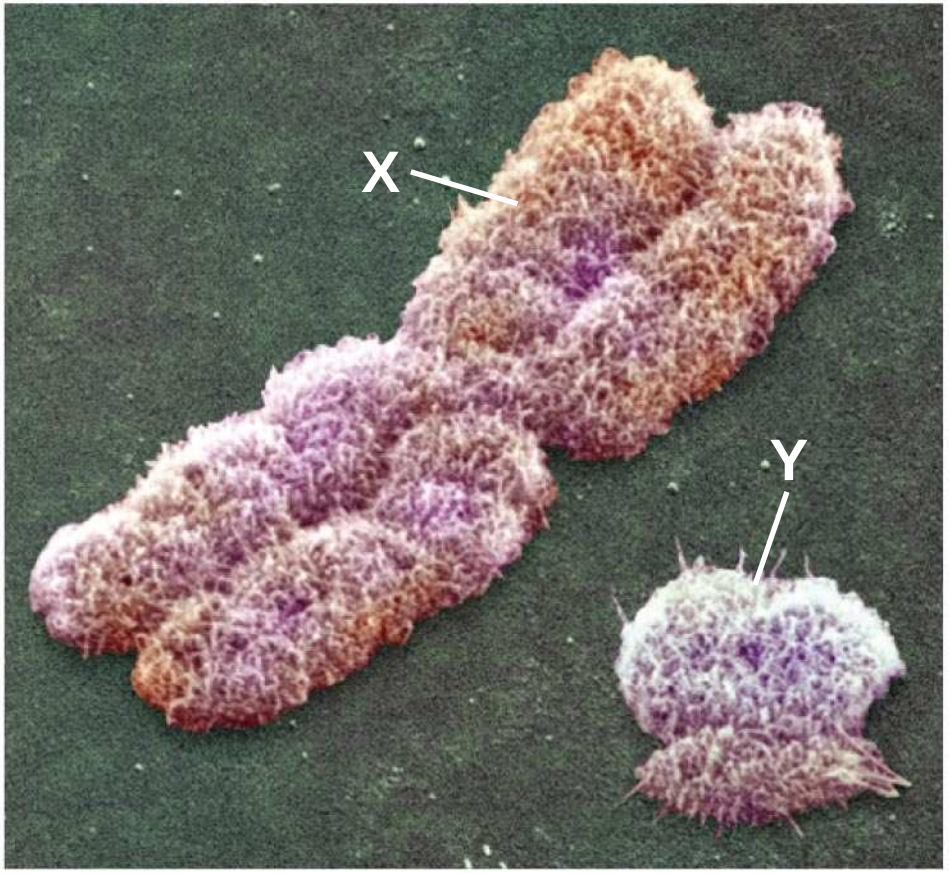
Hermaphrodite in Louvre (1619)

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

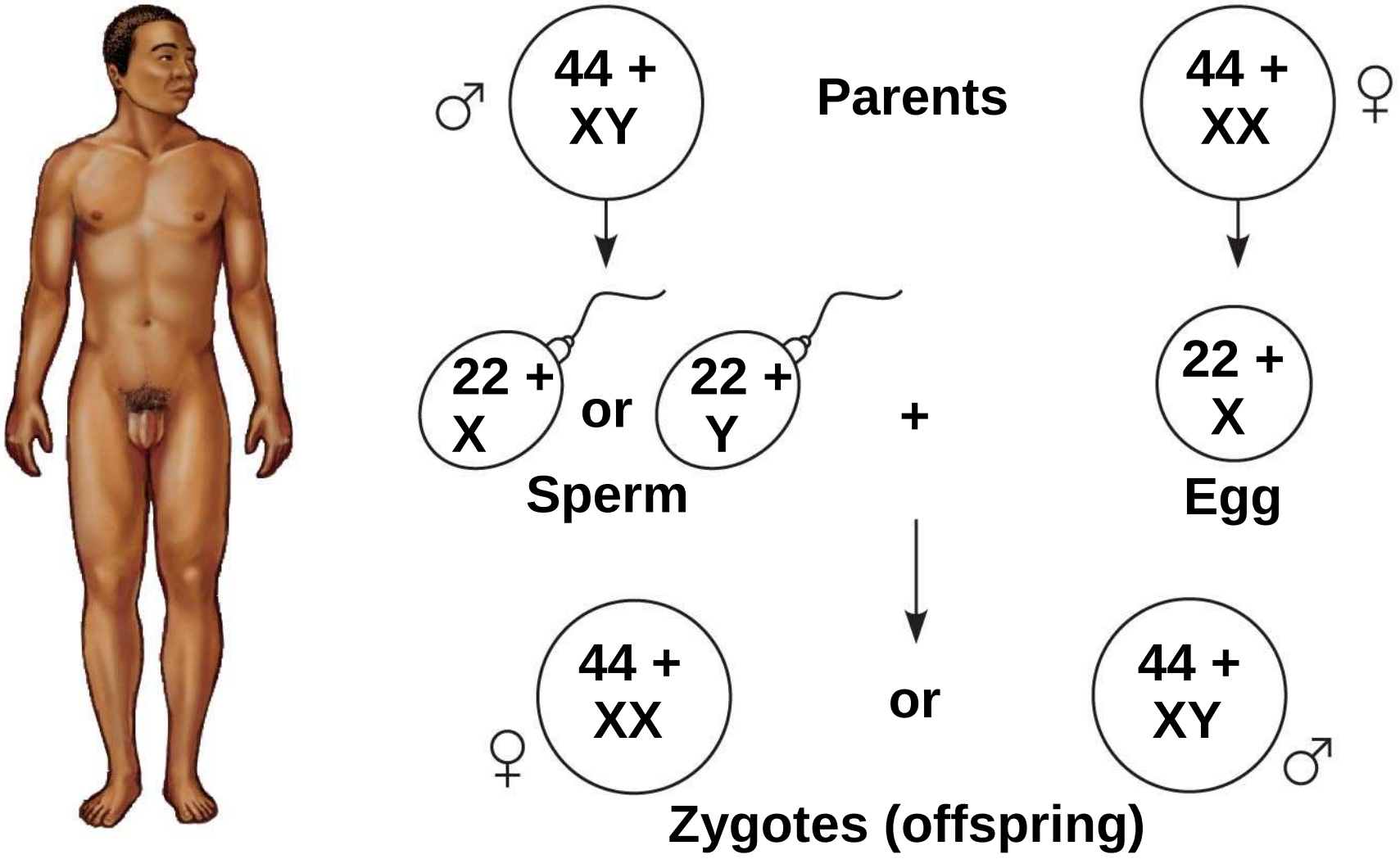
Human sex chromosomes



XX vs. XY

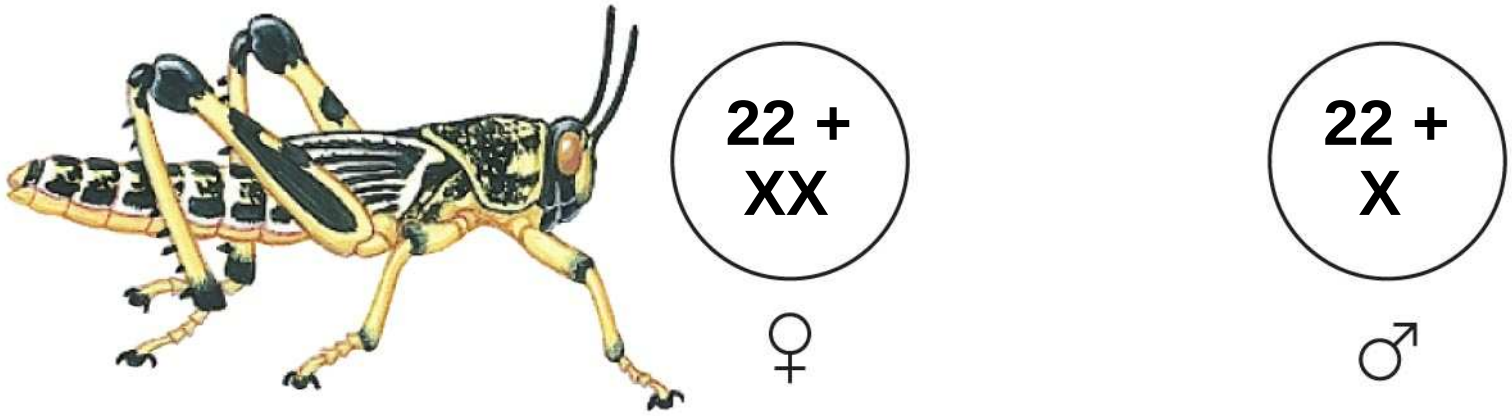
- Females are XX, and males are XY
- Each ovum contains an X chromosome, while a sperm may contain either an X or a Y chromosome – X-Y system
- Other animals have different methods of sex determination
  - X-0 system; Z-W system; Haplo-diploid system

Fig. 15-6a



(a) The X-Y system

Fig. 15-6b



(b) The X-0 system

Fig. 15-6c

76 + ZW

♀

76 + ZZ

♂

(c) The Z-W system

Fig. 15-6d

32
(Diploid)

♀

16
(Haploid)

♂

(d) The haplo-diploid system

Inheritance of Sex-Linked Genes

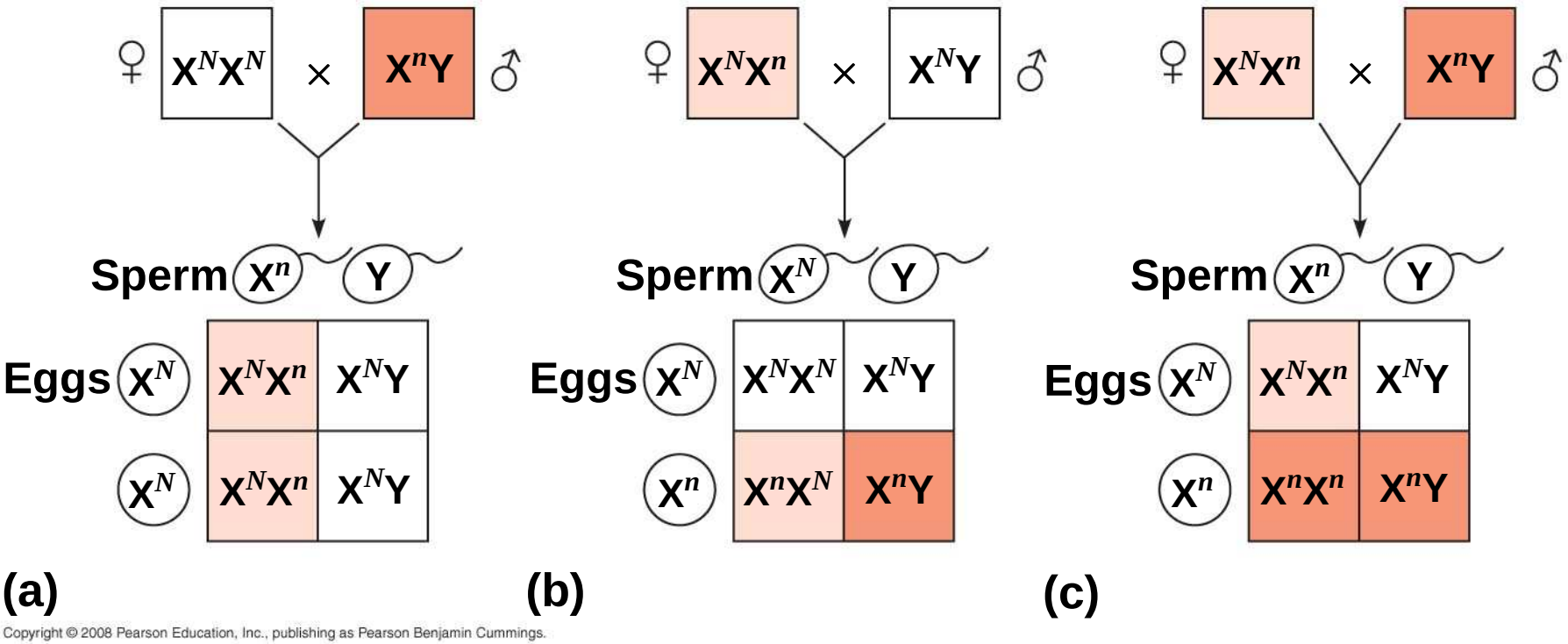
- The sex chromosomes have genes for many characters unrelated to sex
- A gene located on either sex chromosome is called a **sex-linked gene**
- In humans, sex-linked usually refers to a gene on the larger X chromosome

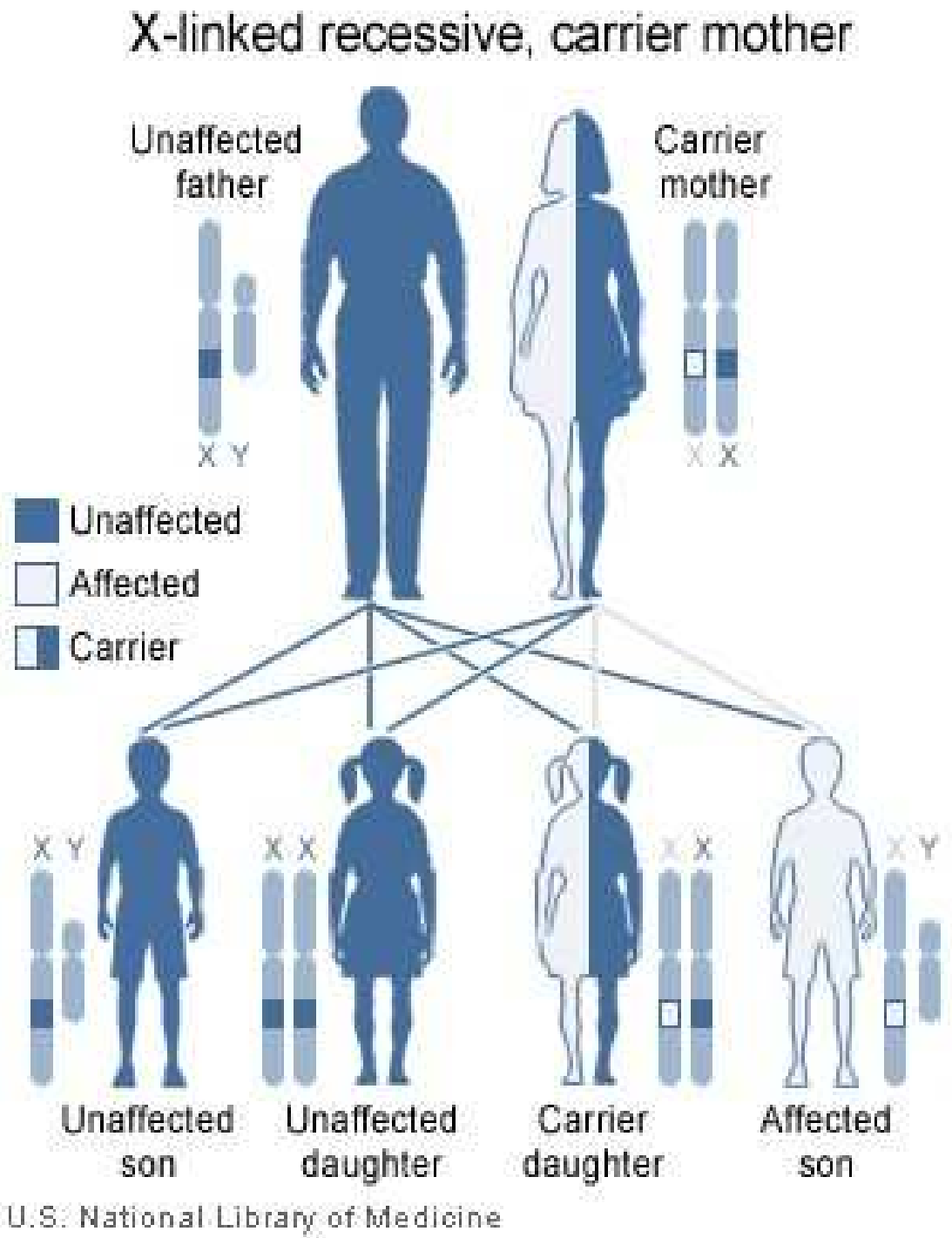
Sex-linked recessive disorders in males

- 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

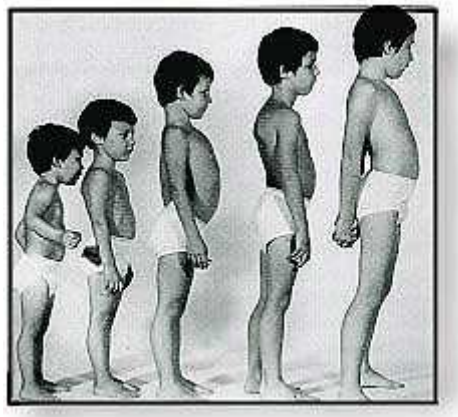
The transmission of sex-linked recessive traits




X-linked recessive, carrier mother
Unaffected father
Carrier mother
X Y
X X
Unaffected
Affected
Carrier
X Y
X X
X X
X Y
Unaffected son
Unaffected daughter
Carrier daughter
Affected son
U.S. National Library of Medicine

X chromosome diseases

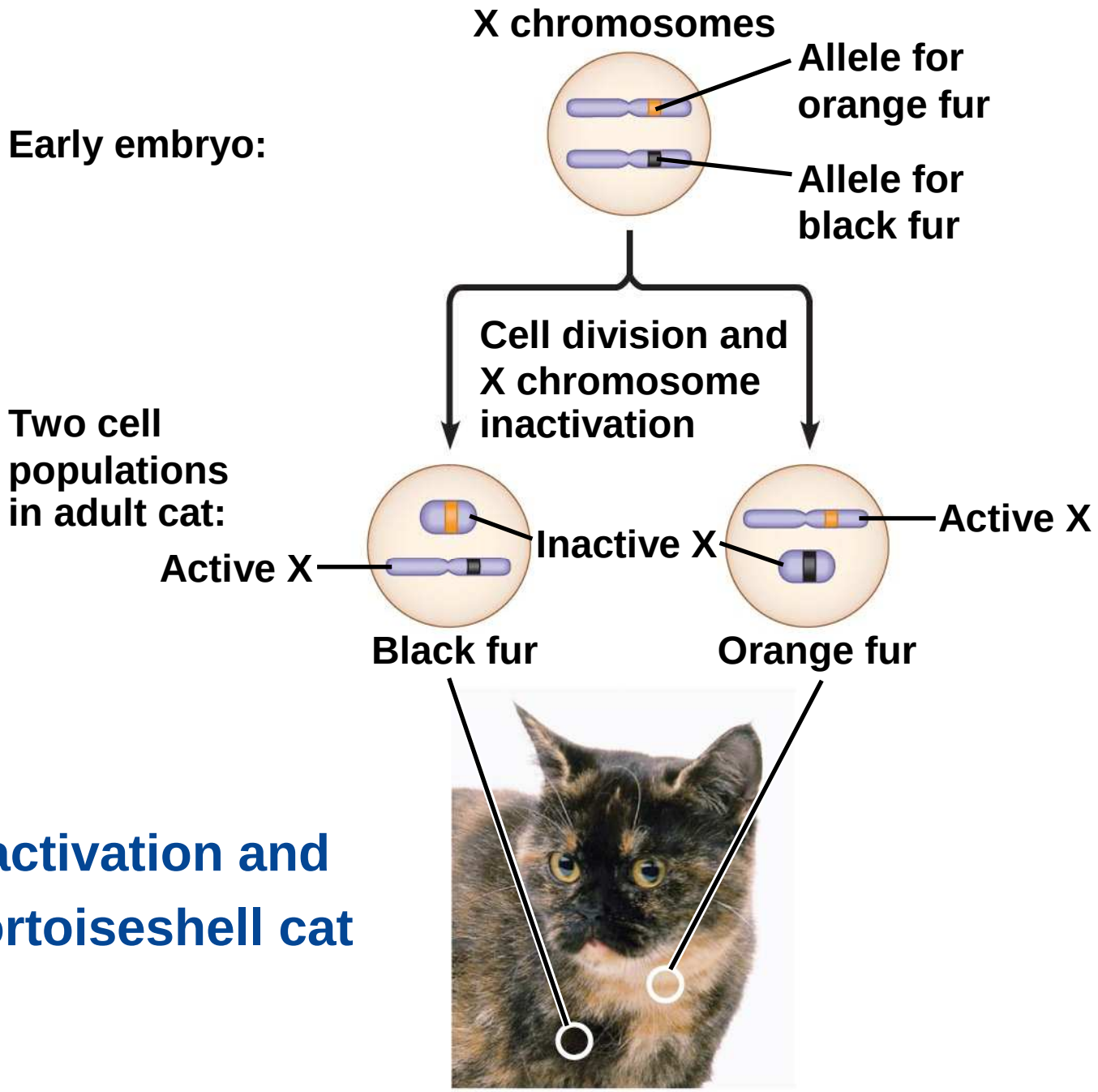
- Some disorders caused by recessive alleles on the X chromosome in humans:
  - Color blindness
  - **Duchenne muscular dystrophy** (杜顯氏/裘馨氏 肌肉萎縮症)
  - **Hemophilia** (血友病)



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



X inactivation and the tortoiseshell cat

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

How does linkage between two genes affect inheritance of characters?

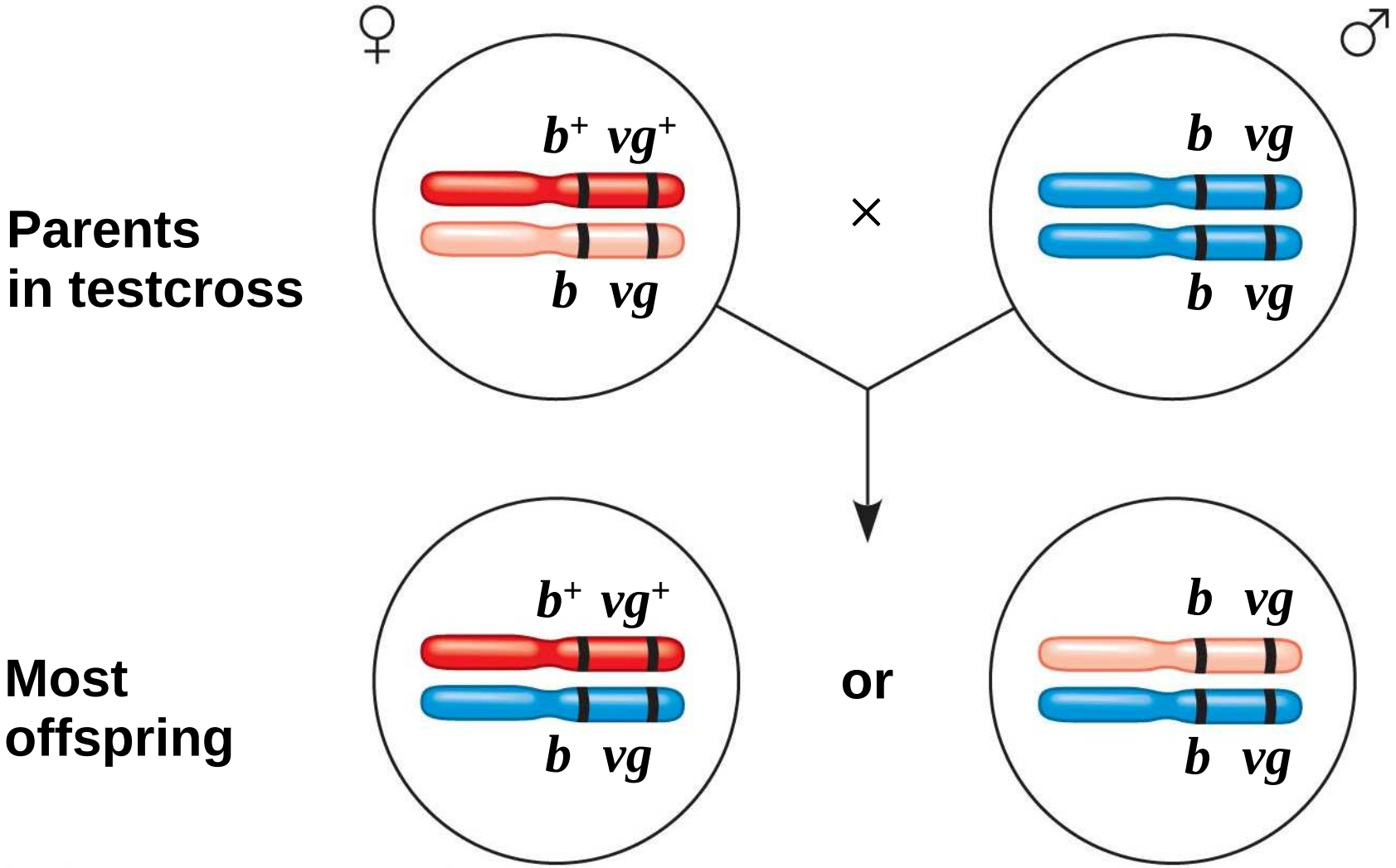


Fig. 15-9-1

EXPERIMENT

P Generation (homozygous)

Wild type (gray body, normal wings)

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

×

Double mutant (black body, vestigial wings)

$b \ b \ vg \ vg$

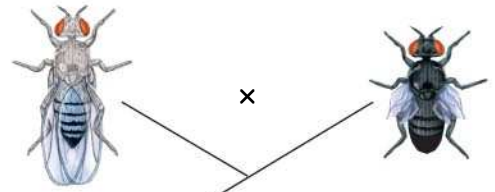
Fig. 15-9-2

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

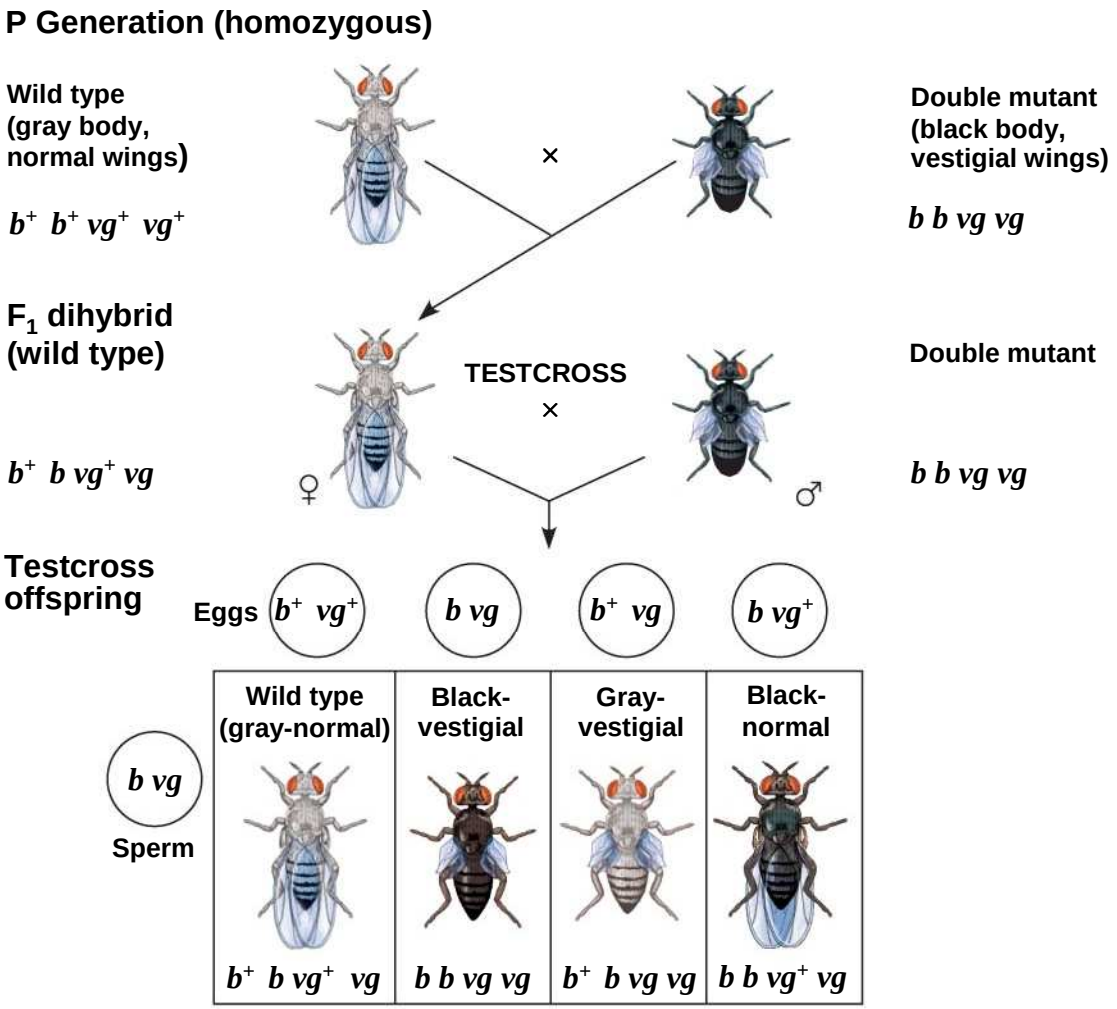


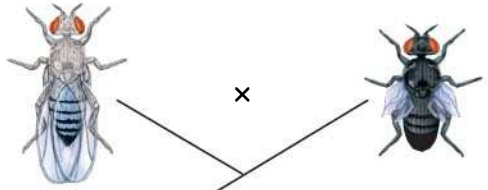
Fig. 15-9-4

EXPERIMENT

P Generation (homozygous)

Wild type (gray body, normal wings)

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



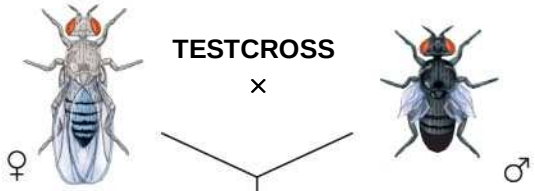
Double mutant (black body, vestigial wings)

b b vg vg

F_1 dihybrid (wild type)

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

TESTCROSS



Double mutant

b b vg vg

Testcross offspring

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

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**
	965	**:**	**944**	**:**	**206**	**:**	**185**

RESULTS

Parental phenotypes inherited together

- 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

Genetic recombination

- 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

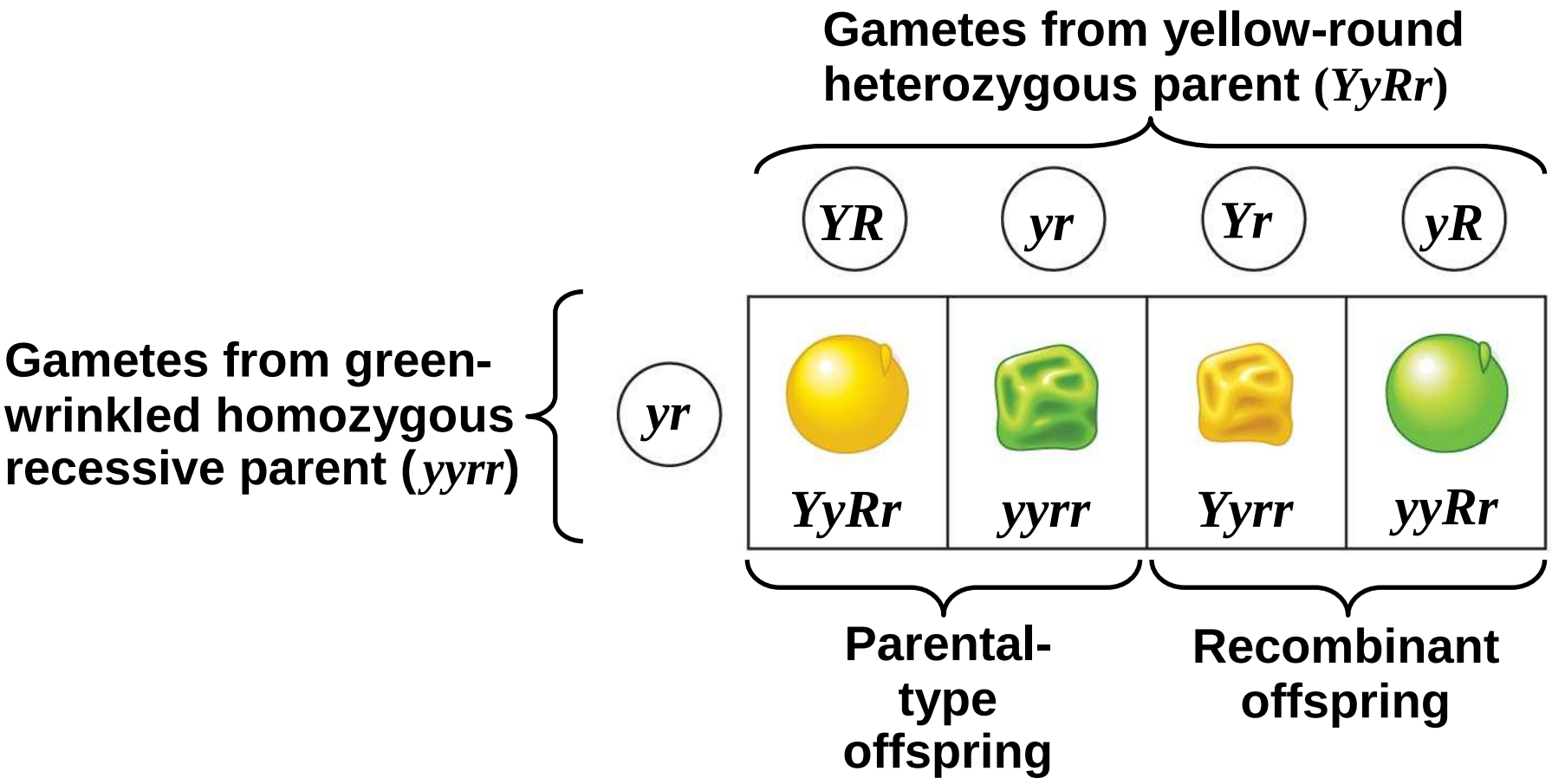
- The genetic findings of Mendel and Morgan relate to the chromosomal basis of recombination

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

Independent Assortment of Chromosomes



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

PLAY Animation: Crossing Over

Fig. 15-10a

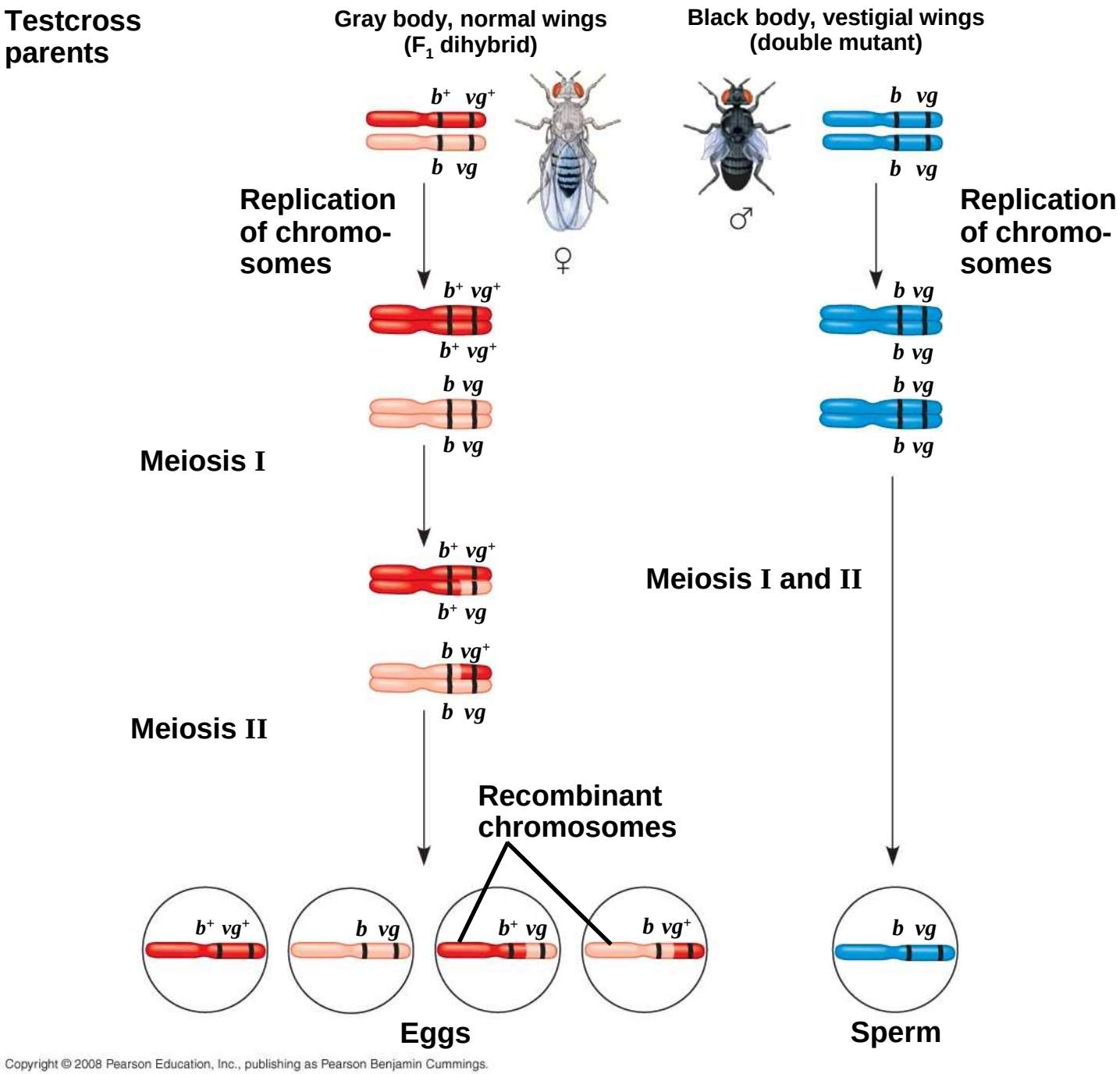
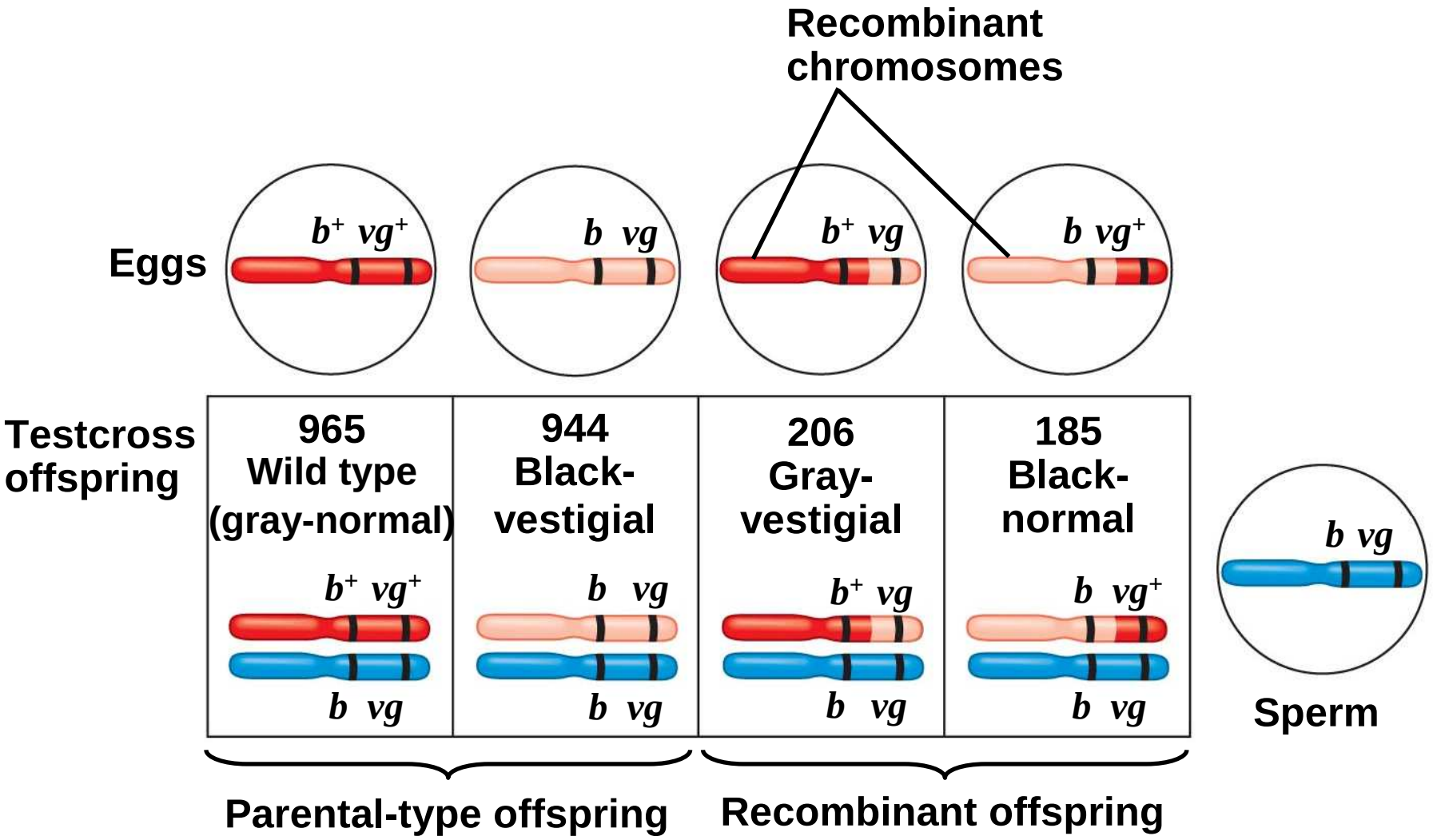


Fig. 15-10b



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

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

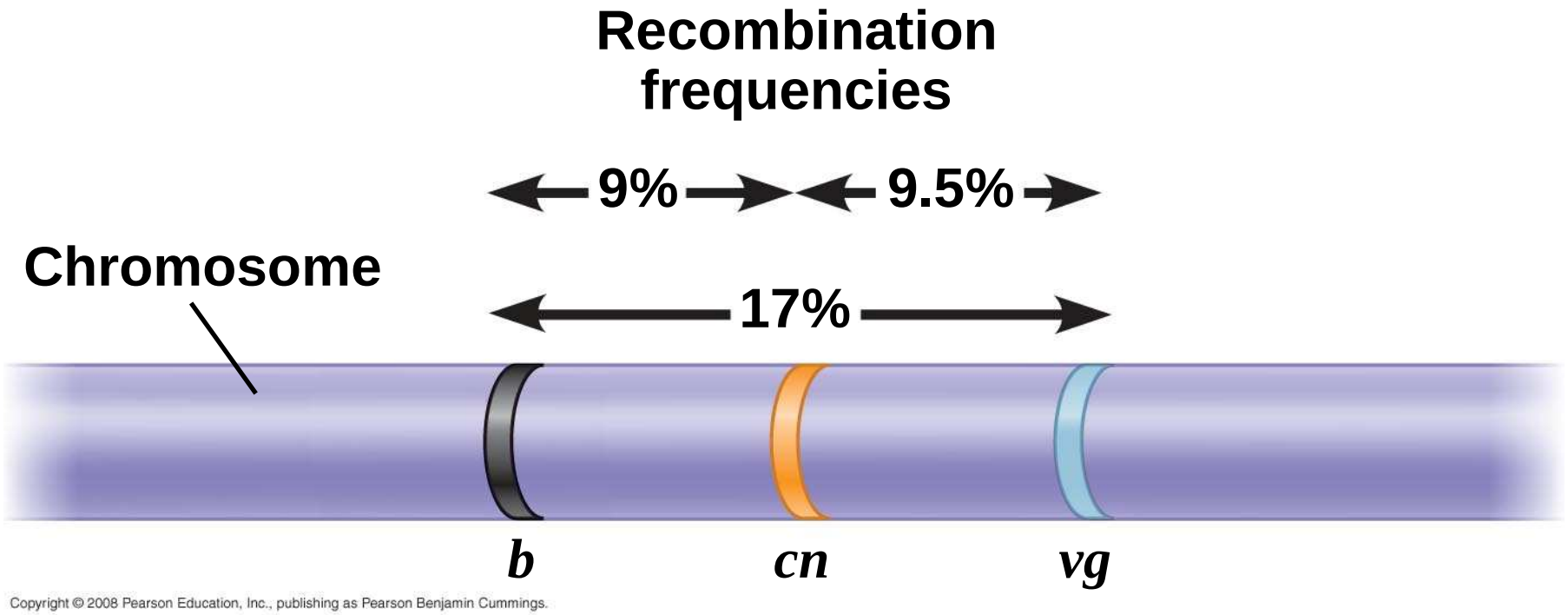
- Alfred Sturtevant, one of Morgan's students, constructed a **genetic map**, an ordered list of the genetic loci along a particular chromosome
- Sturtevant predicted that *the farther apart two genes are, the higher the probability that a crossover will occur between them and therefore the higher the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

Constructing a Linkage Map

- 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



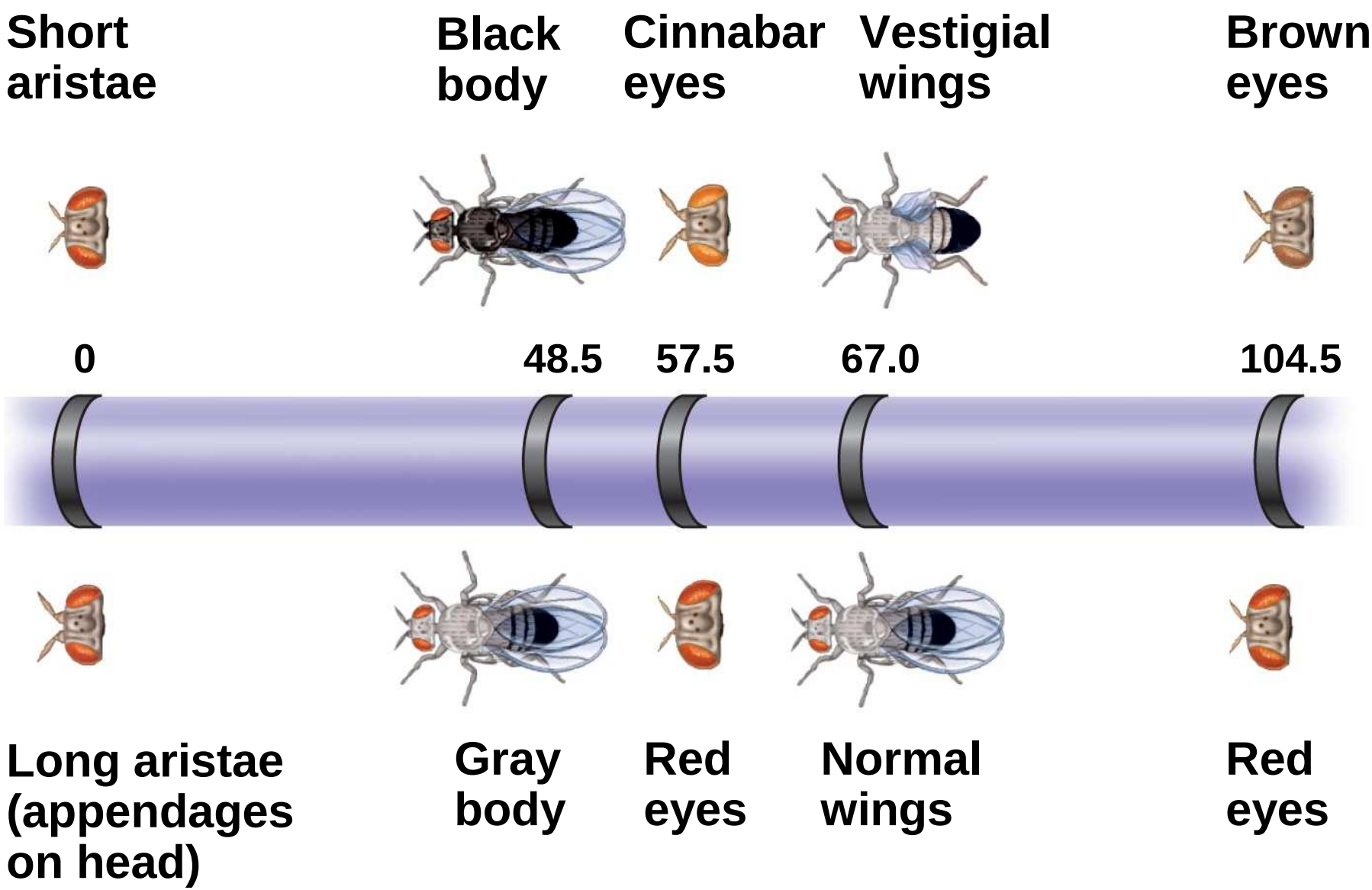
Physically linked may be genetically unlinked

- 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

Mutant phenotypes



Wild-type phenotypes

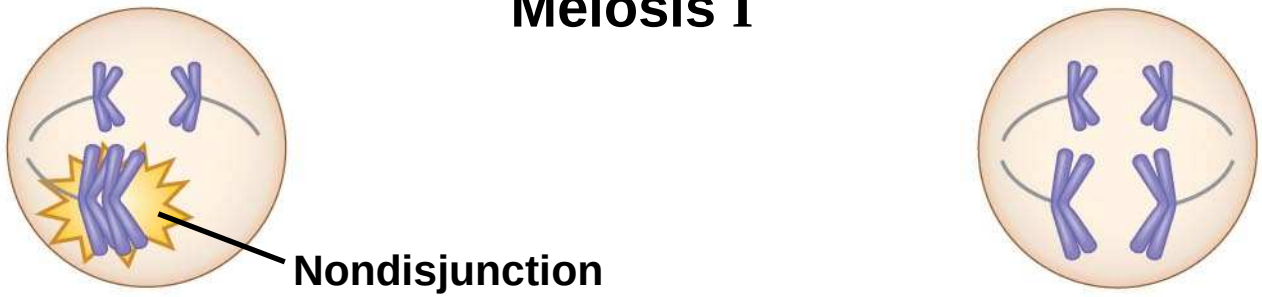
Concept 15.4: Alterations of chromosome number or structure cause some genetic disorders

- 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

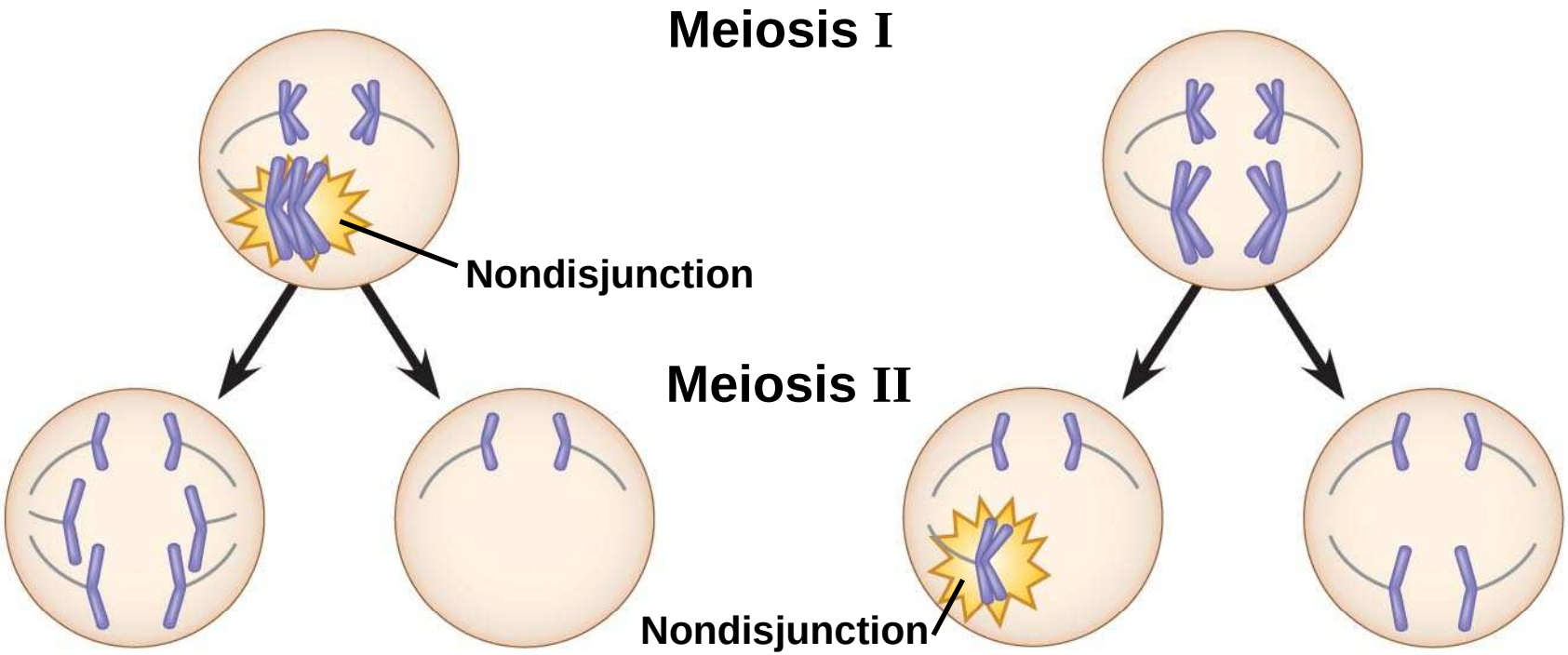
Fig. 15-13-1



(a) Nondisjunction of homologous chromosomes in meiosis I

(b) Nondisjunction of sister chromatids in meiosis II

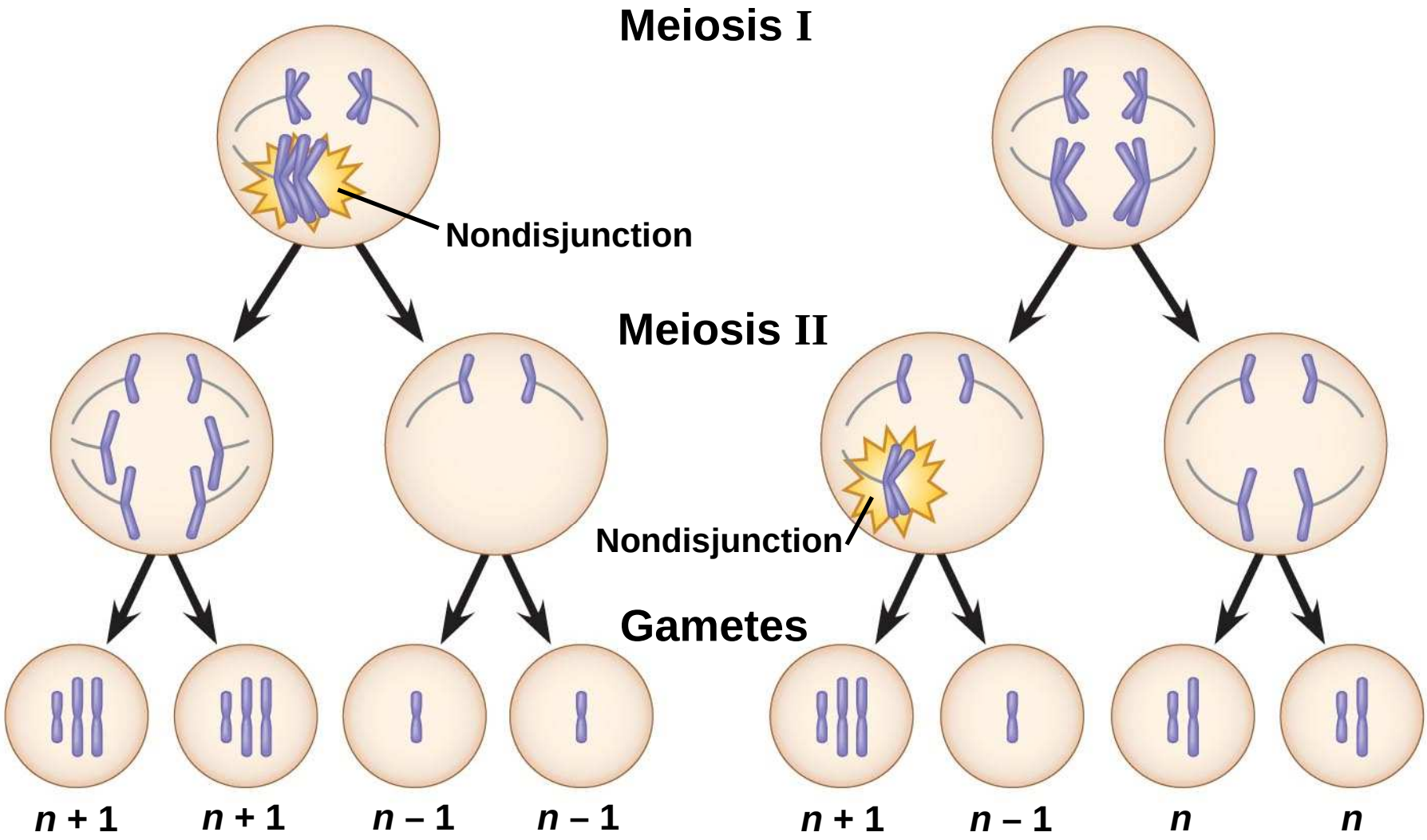
Fig. 15-13-2



(a) Nondisjunction of homologous chromosomes in meiosis I

(b) Nondisjunction of sister chromatids in meiosis II

Fig. 15-13-3



Abnormal chromosome number

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

Too few vs. too many

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

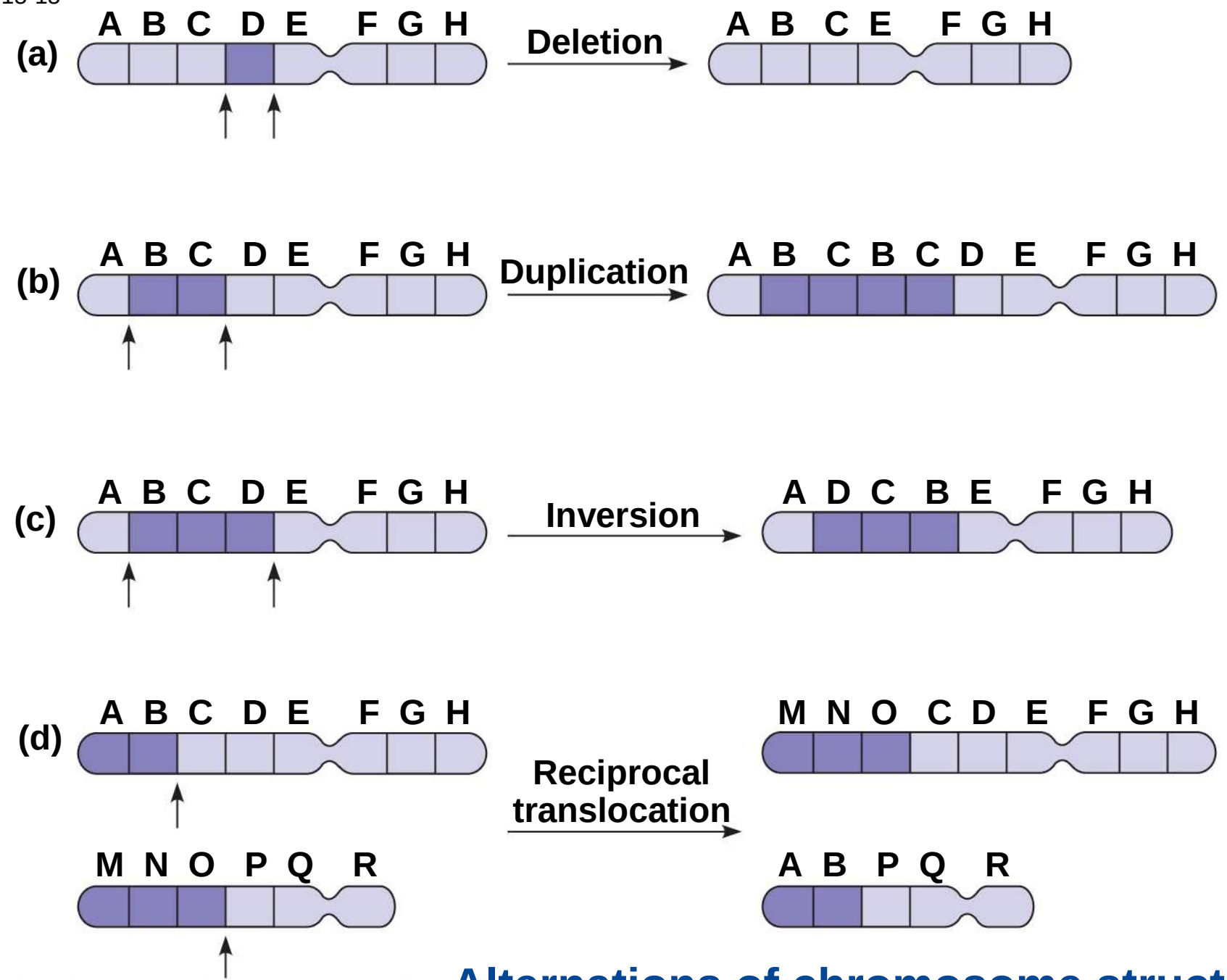
Abnormal chromosome number

- **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

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



Alternations of chromosome structure

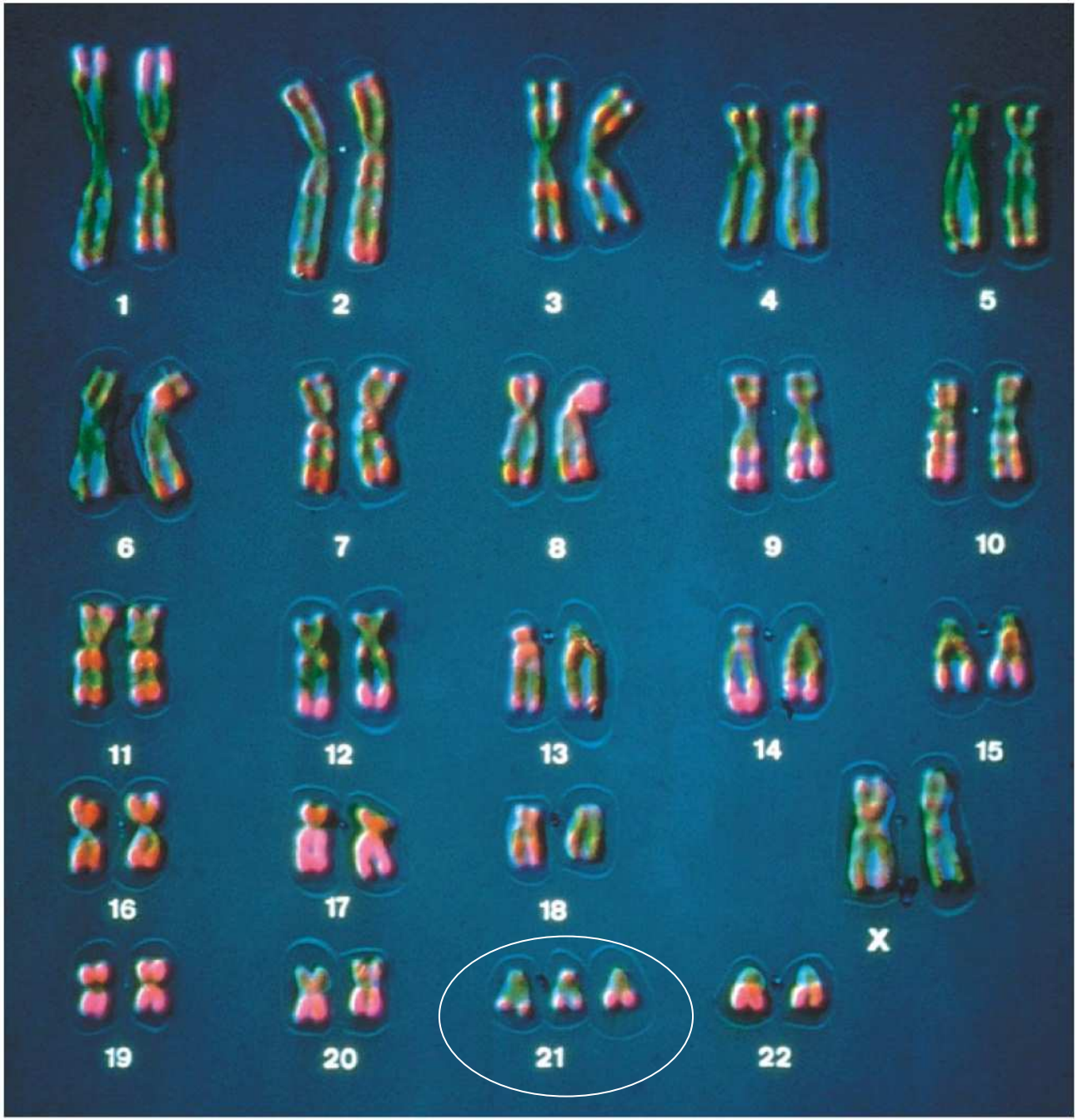
Human Disorders Due to Chromosomal Alterations

- 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. 15-16a



Aneuploidy of Sex Chromosomes

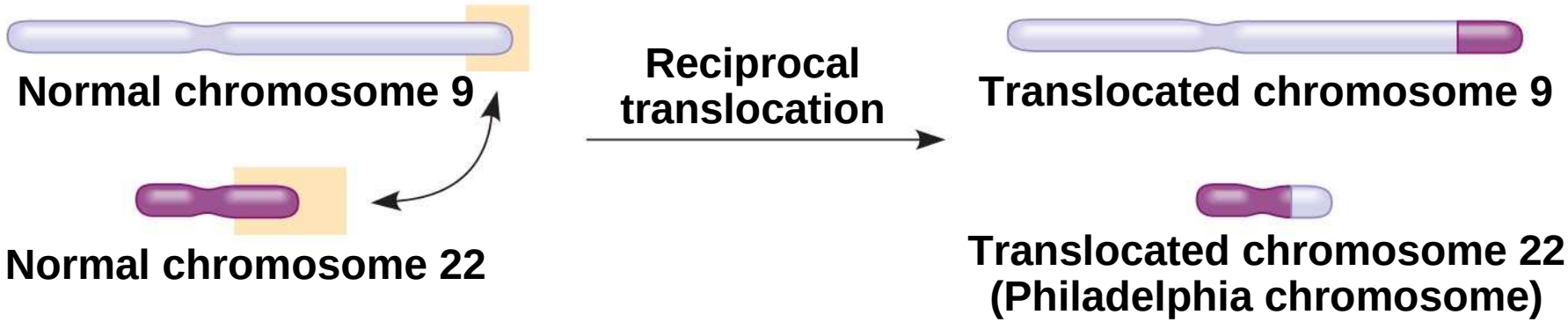
- Nondisjunction of sex chromosomes produces a variety of aneuploid conditions
- *Klinefelter syndrome* is the result of an extra chromosome in a male, producing **XXY** individuals
- Monosomy X, called *Turner syndrome*, produces **X0** females, who are sterile; it is the only known viable monosomy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

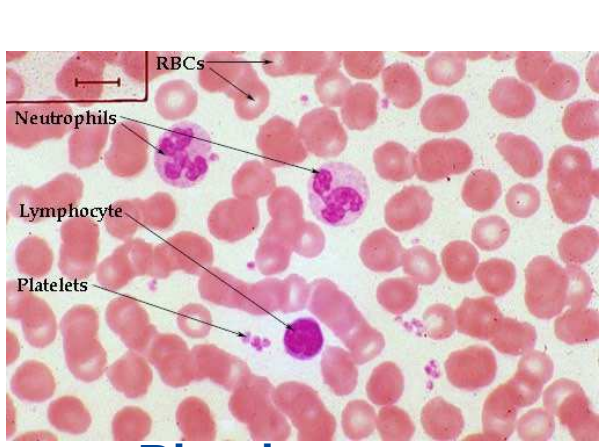
Disorders Caused by Structurally Altered Chromosomes

- 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 (貓哭症); individuals usually die in infancy or early childhood
- Certain cancers, including *chronic myelogenous leukemia* (CML), are caused by translocations of chromosomes

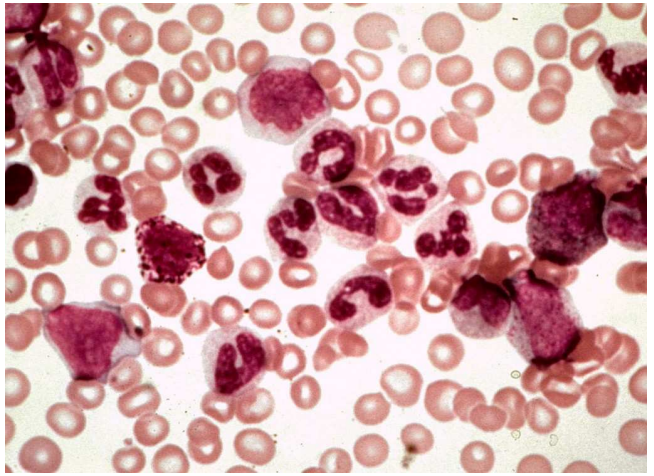
Fig. 15-17

Translocation associated with chronic myelogenous leukemia (CML)





Blood smear



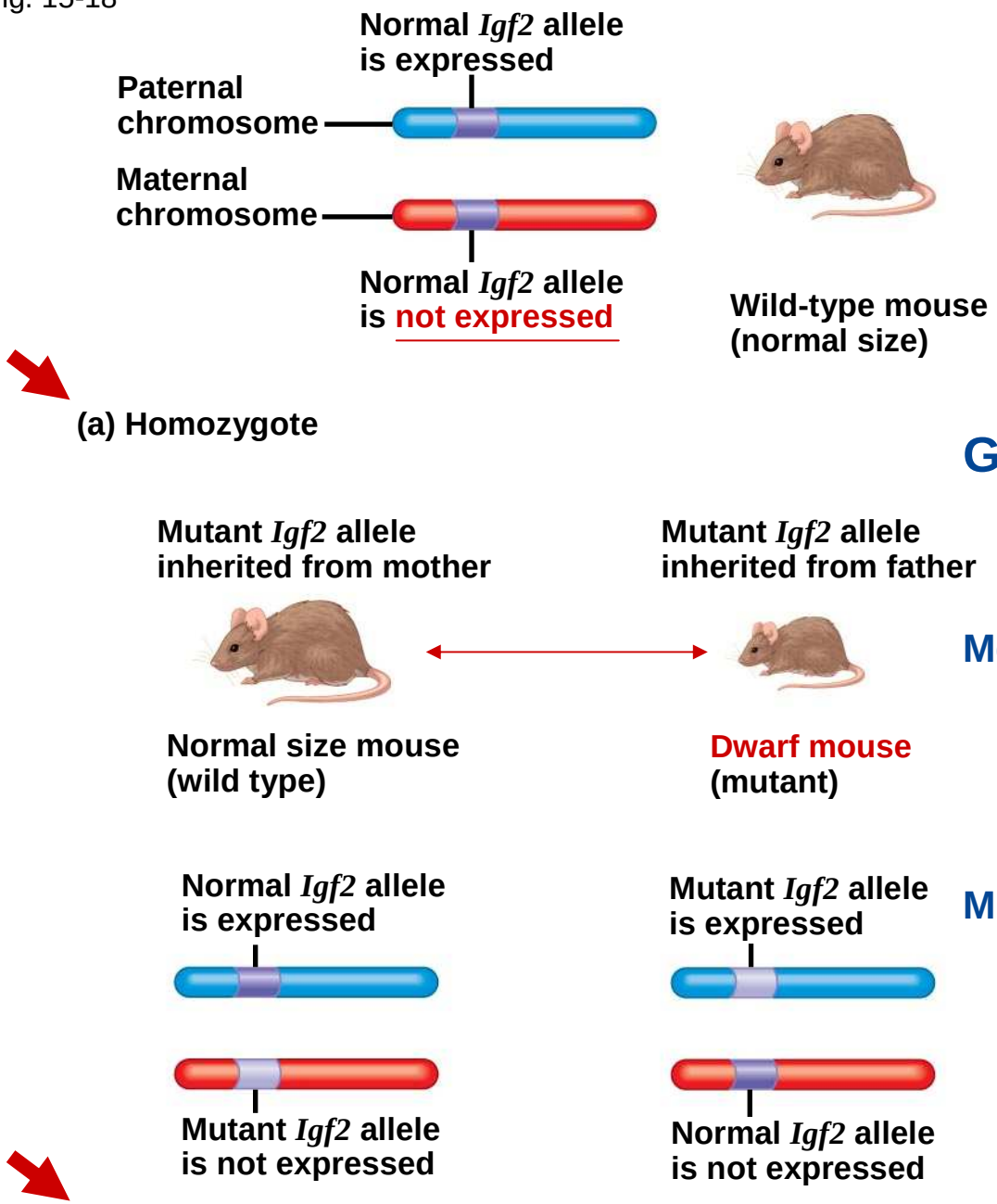
Concept 15.5: Some inheritance patterns are exceptions to the standard chromosome theory

- 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



Genomic imprinting of the mouse *Igf2* gene

Methylation of certain cytosines on the paternal chromosome leads to expression of the paternal *Igf2* allele

Mutant phenotype is seen only when the father contributed the mutant allele

Fig. 15-18a

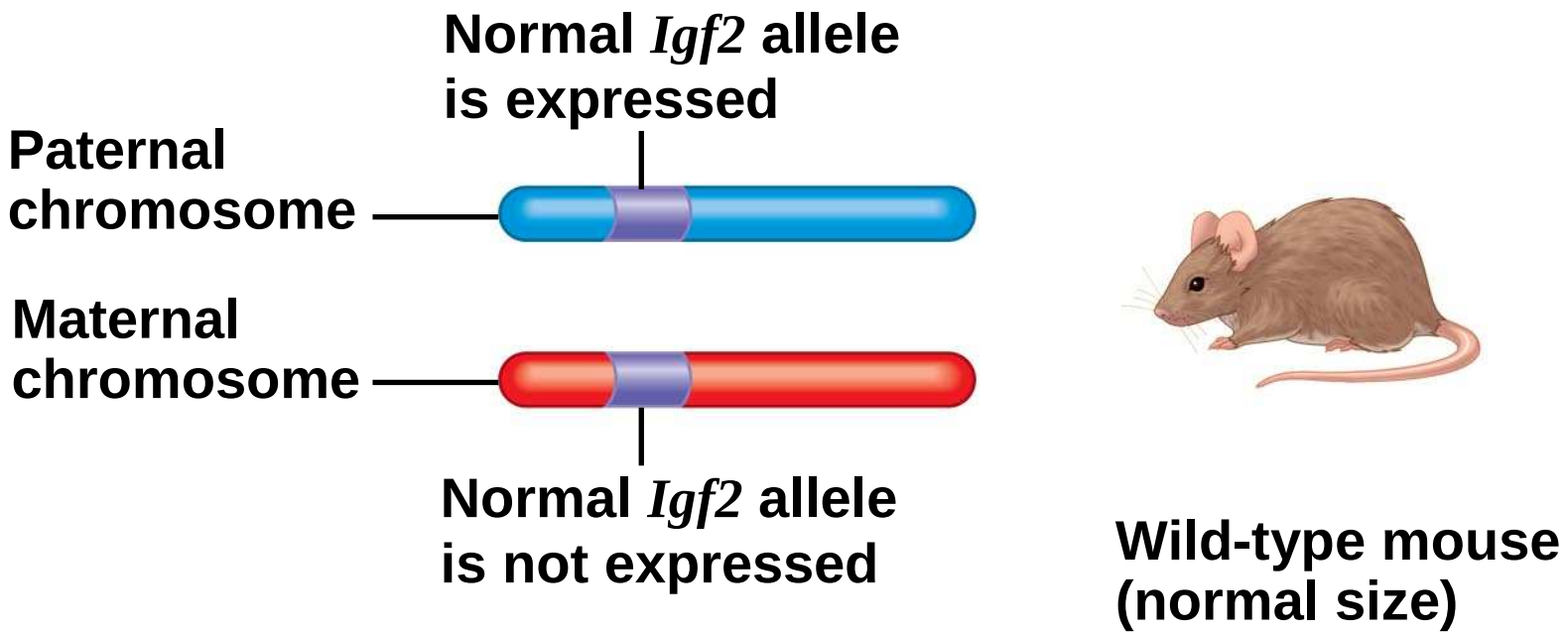


Fig. 15-18b

Mutant *Igf2* allele inherited from mother

Normal size mouse (wild type)

Mutant *Igf2* allele inherited from father

Dwarf mouse (mutant)

Normal *Igf2* allele is expressed

Mutant *Igf2* allele is not expressed

Mutant *Igf2* allele is expressed

Normal *Igf2* allele is not expressed

(b) Heterozygotes

Imprinting and DNA methylation

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

Inheritance of Organelle Genes

- *Extranuclear genes* (or *cytoplasmic genes*) are genes found in organelles in the cytoplasm
- Mitochondria, chloroplasts, and other plant plastids (植物色質體) 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

Variegated (striped or spotted) leaves from *Croton dioicus* *(巴豆)* – mutations in pigment genes located in plastids

Mitochondria diseases

- 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 (線粒體肌病) and Leber's hereditary optic neuropathy (雷伯氏遺傳性視神經萎縮症)

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