

LECTURE PRESENTATIONS

For CAMPBELL BIOLOGY, NINTH EDITION

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Chapter 15

The Chromosomal Basis of Inheritance



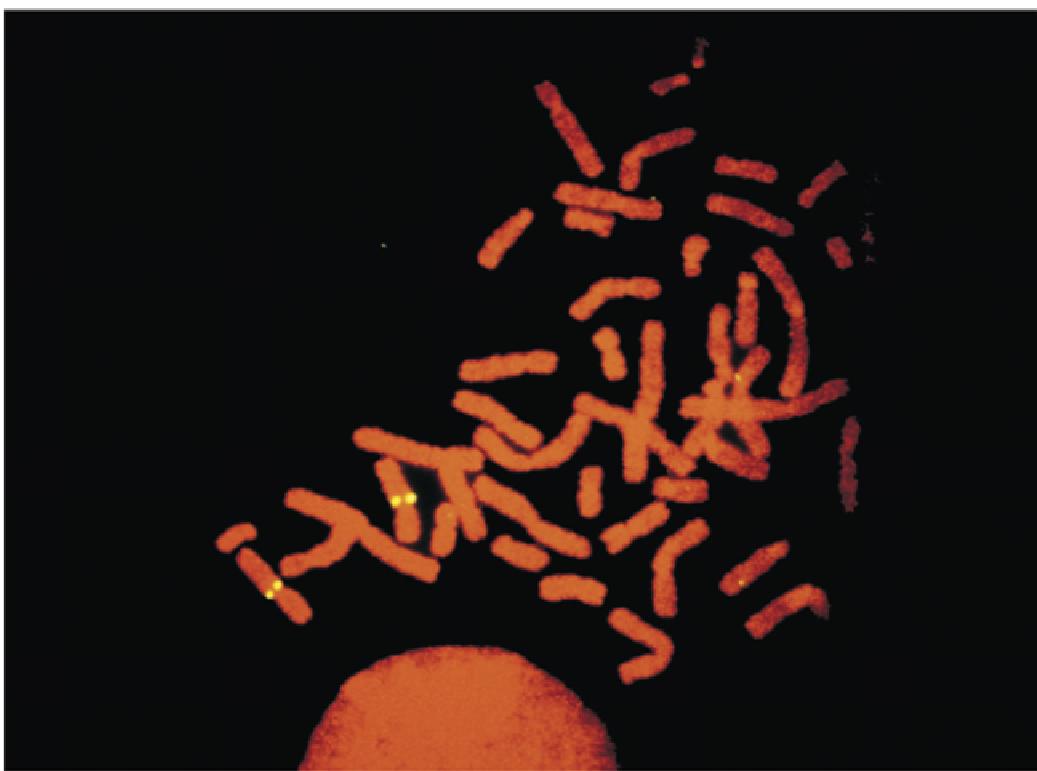
Lectures by
Erin Barley
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Overview: Locating Genes Along Chromosomes

- Mendel's "hereditary factors" were genes
- 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

Figure 15.1



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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 can account for Mendel's laws of segregation and independent assortment

Figure 15.2

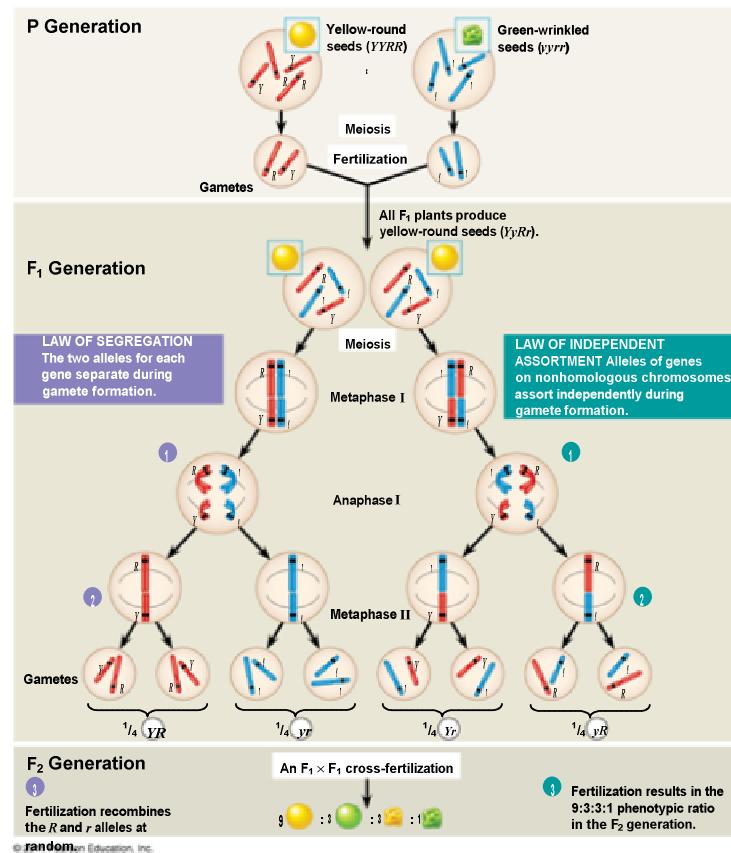


Figure 15.2a

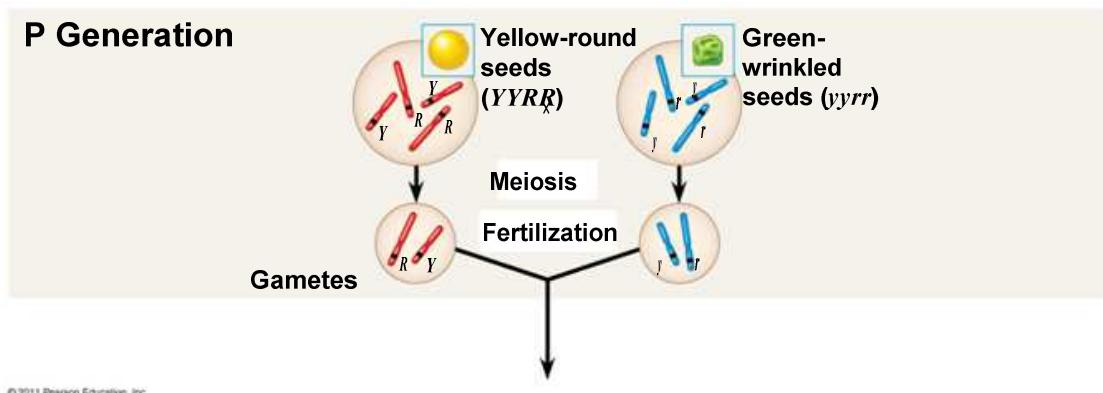
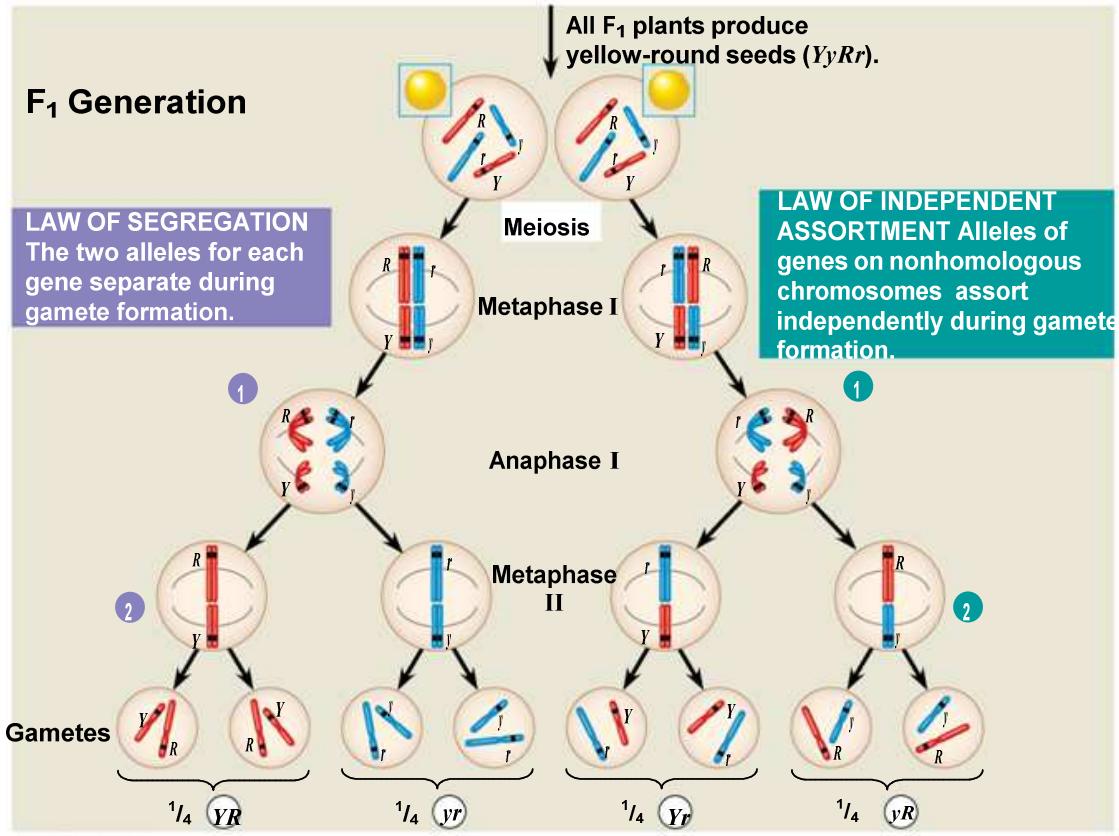
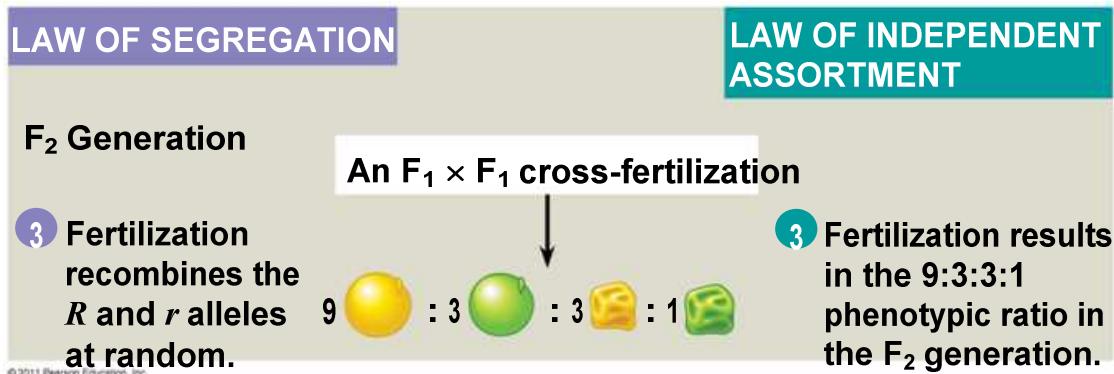


Figure 15.2b



Equal odds of the 4 possible allele combinations = independent assortment

Figure 15.2c



Morgan's Experimental Evidence: *Scientific Inquiry*

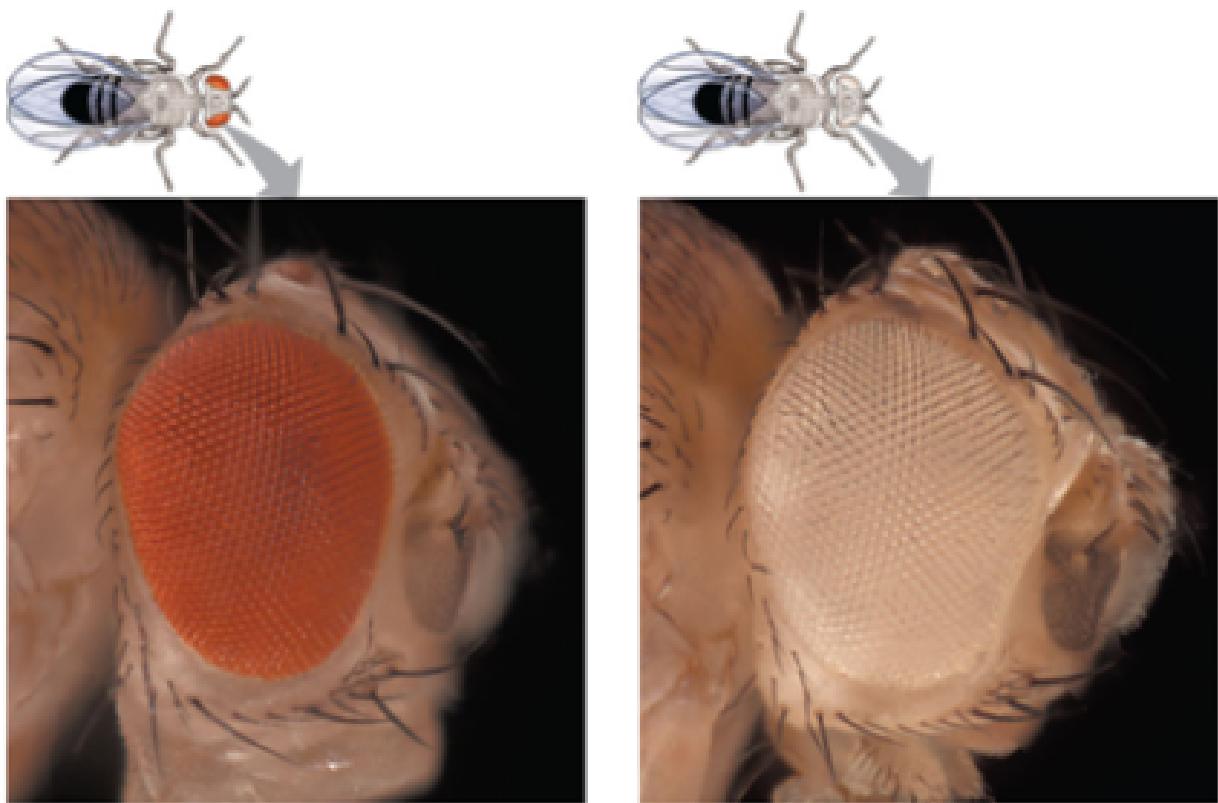
- The first solid evidence associating a specific gene with a specific chromosome came from Thomas Hunt Morgan, an embryologist
- Morgan's experiments with fruit flies provided convincing evidence that chromosomes are the location of Mendel's heritable factors

Morgan's Choice of Experimental Organism

- Several characteristics make fruit flies a convenient organism for genetic studies
 1. They produce many offspring
 2. A generation can be bred every two weeks
 3. 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

Figure 15.3



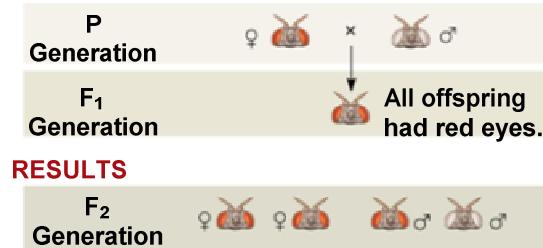
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Correlating Behavior of a Gene's Alleles with Behavior of a Chromosome Pair

- In one experiment, Morgan mated male flies with white eyes (mutant) with female flies with red eyes (wild type)
- The F₁ generation all had red eyes
- The F₂ 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

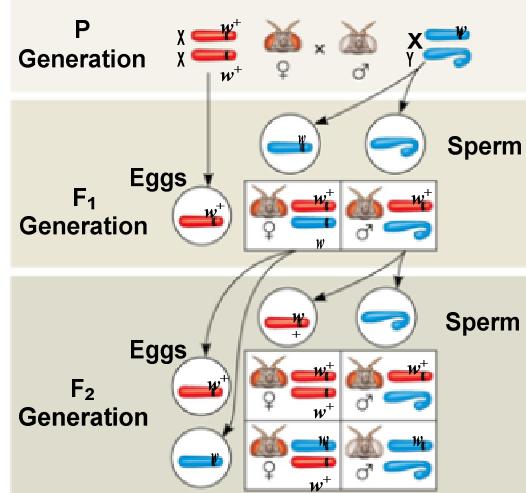
Figure 15.4

EXPERIMENT



Eye color = sex linked

CONCLUSION

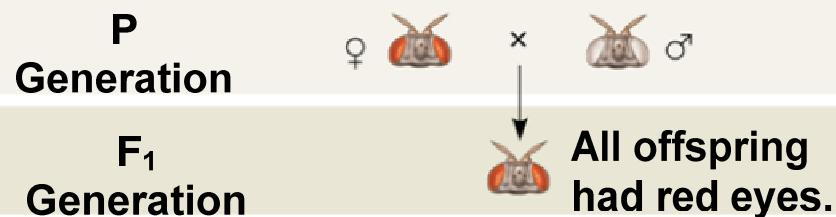


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Figure 15.4a

Eye color = sex linked

EXPERIMENT



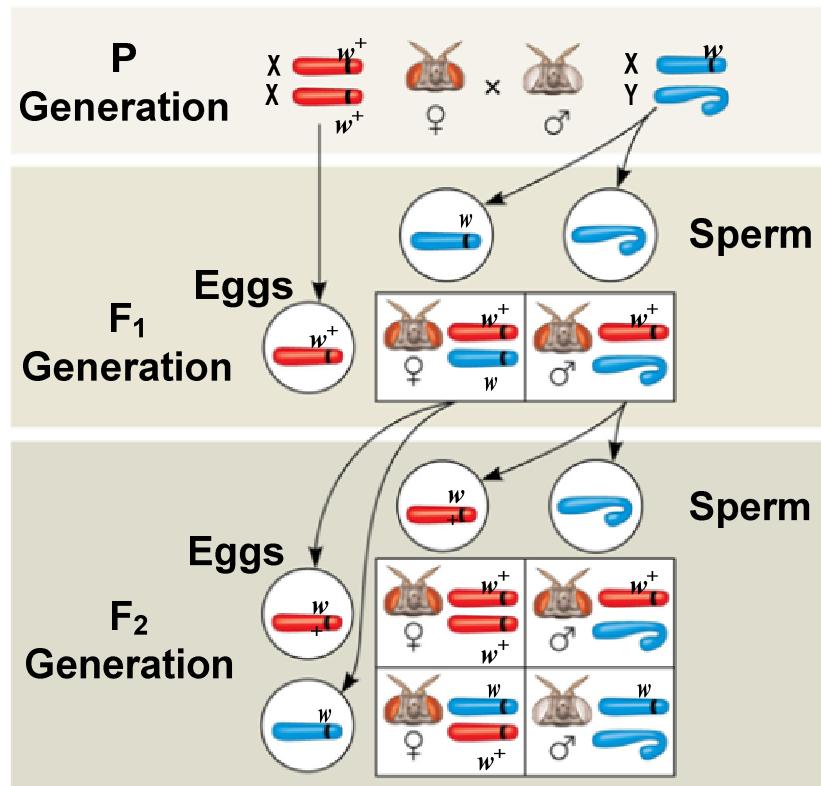
RESULTS



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Figure 15.4b

CONCLUSION



Eye color = sex linked

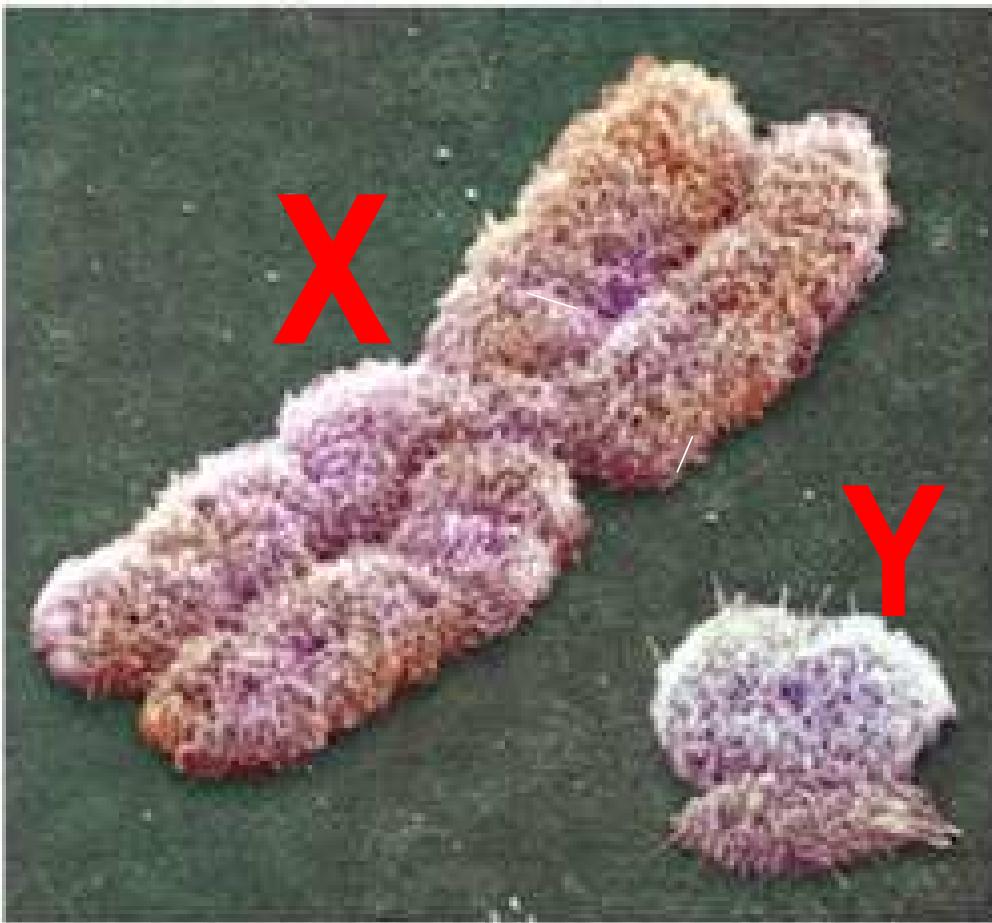
Concept 15.2: Sex-linked genes exhibit unique patterns of inheritance

- 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 corresponding regions of the X chromosome
- The *SRY* gene on the Y chromosome codes for a protein that directs the development of male anatomical features

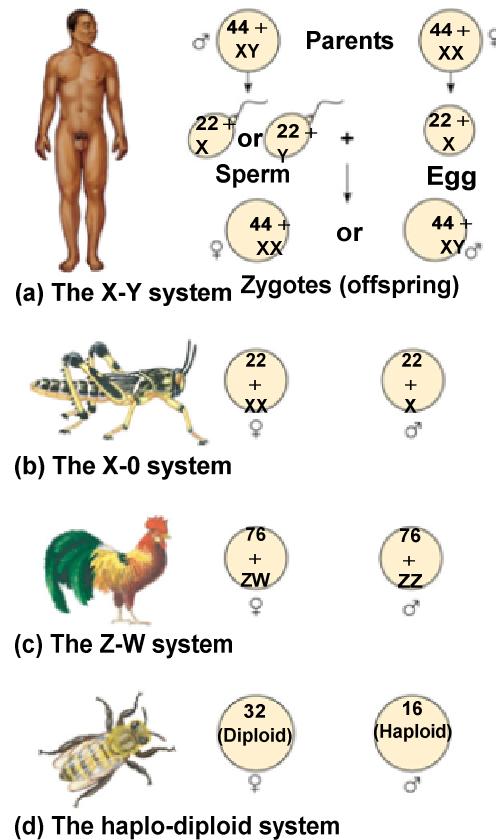
Figure 15.5



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- 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

Figure 15.6



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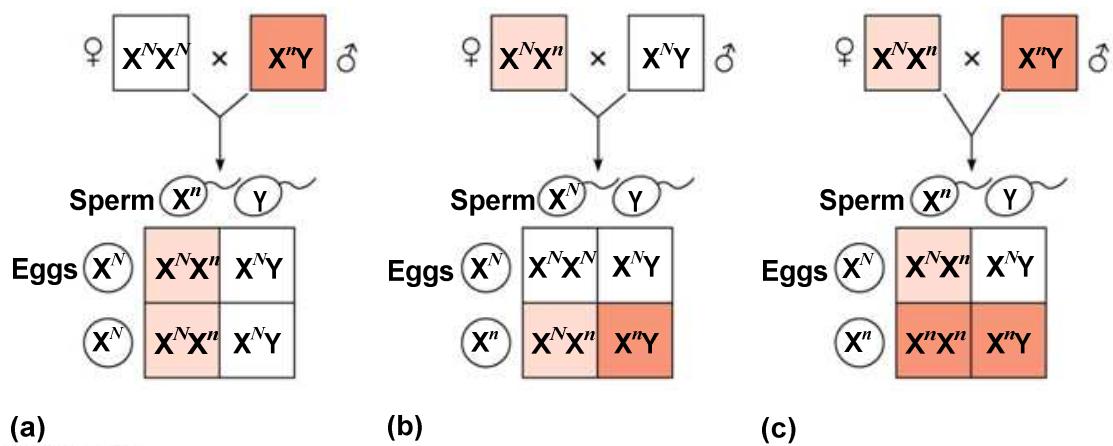
- A gene that is located on either sex chromosome is called a **sex-linked gene**
- Genes on the Y chromosome are called Y-linked genes; there are few of these
- Genes on the X chromosome are called **X-linked genes**

Inheritance of X-Linked Genes

- X chromosome have genes for many characters unrelated to sex, whereas the Y chromosome mainly encodes genes related to sex determination

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

Figure 15.7



(a)

(b)

(c)

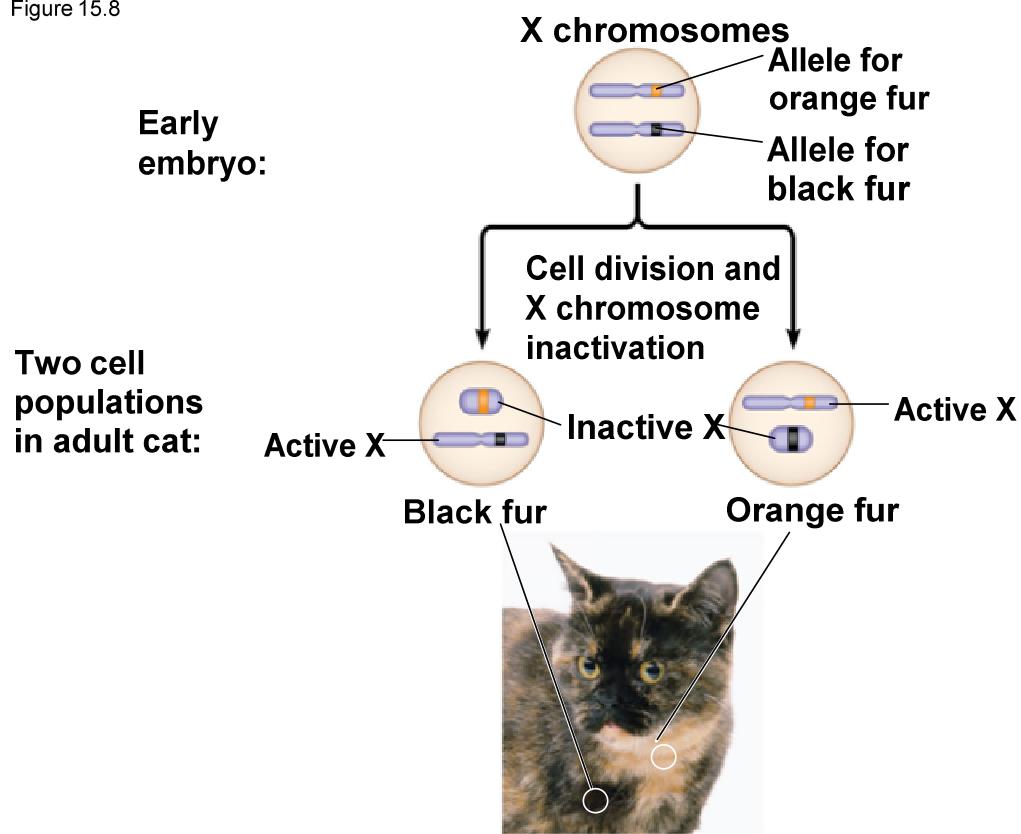
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- Some disorders caused by recessive alleles on the X chromosome in humans:
 1. Color blindness (mostly X-linked)
 2. Duchenne muscular dystrophy
 3. Hemophilia

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

Figure 15.8



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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 (except the Y chromosome)
- 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

Figure 15.9-4

EXPERIMENT

P Generation (homozygous)

Wild type
(gray body, normal wings)

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



Double mutant
(black body,
vestigial wings)

$b b vg vg$

F₁ dihybrid
(wild type)

$b^+ b vg^+ vg$



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
$b^+ b vg^+ vg$				

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

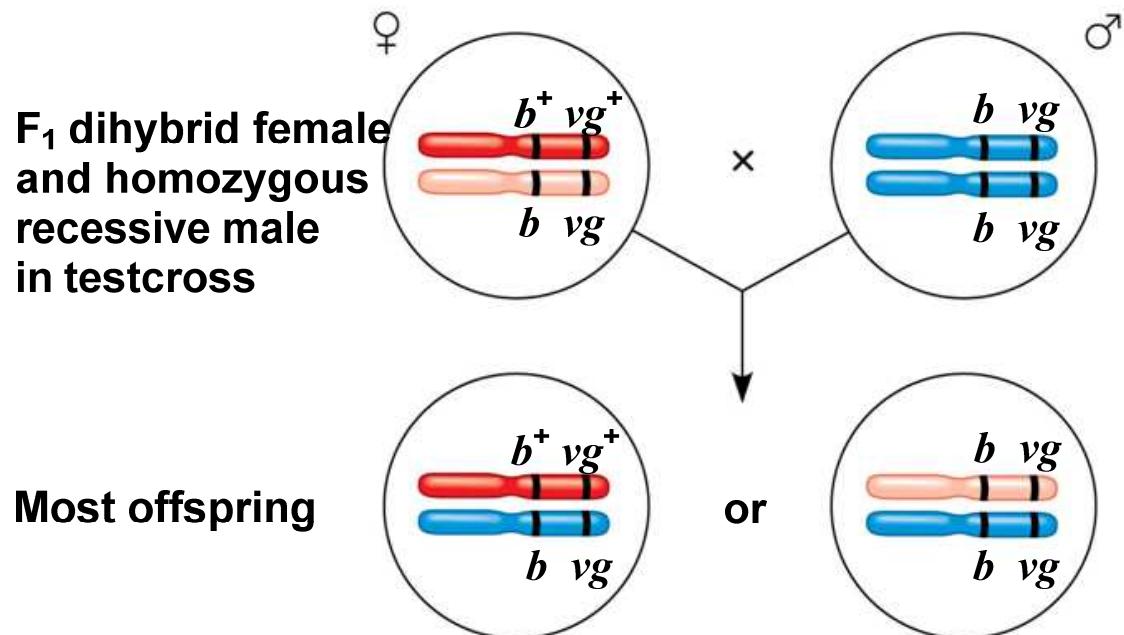
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965 : 944 : 206 : 185

Why are the results this way?

- 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 (alleles assort independently)

Figure 15.UN01



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- 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

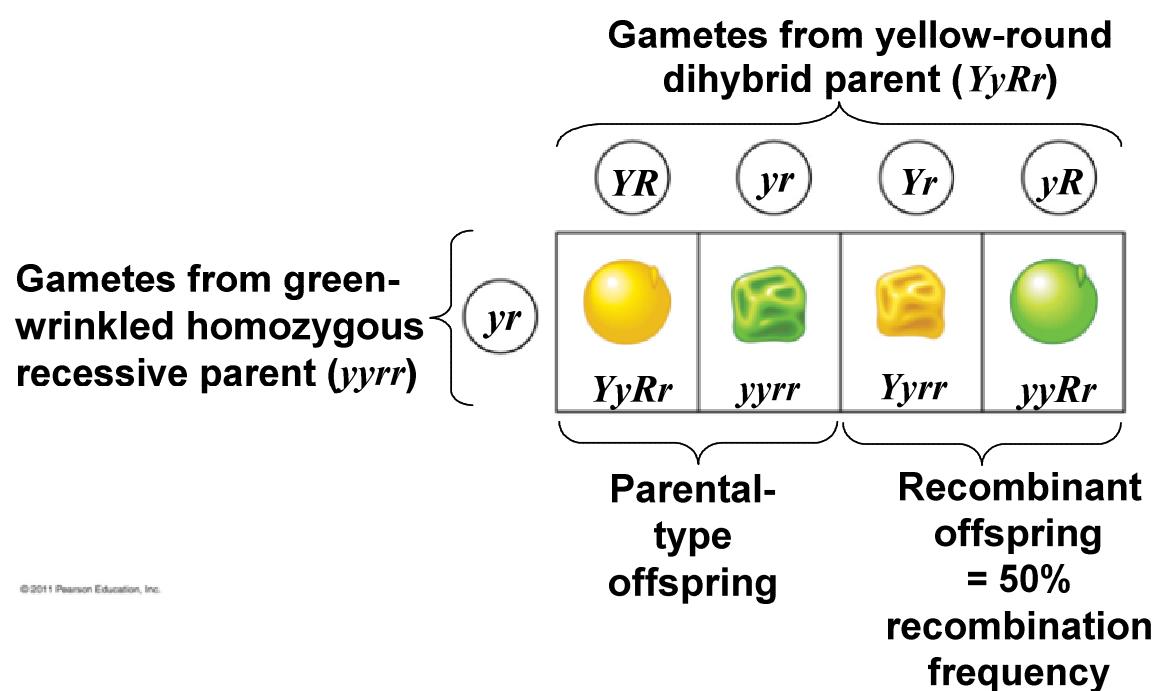
Genetic Recombination and Linkage

- 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

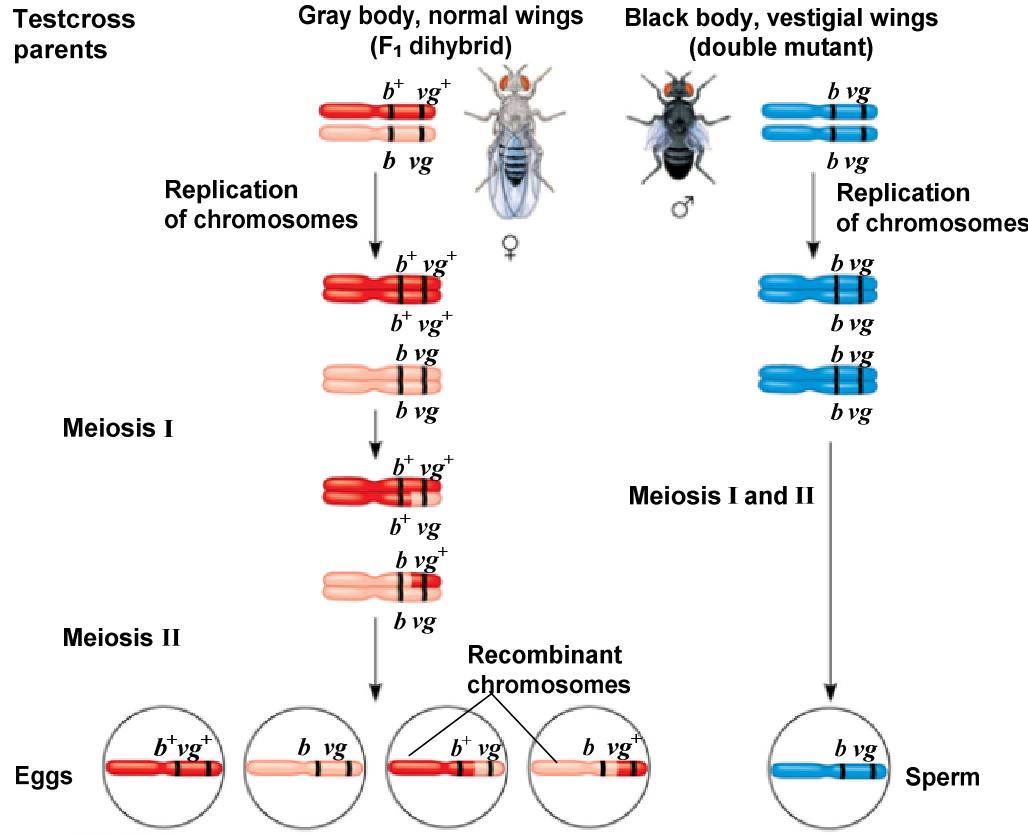
Figure 15.UN02



Recombination of Linked Genes: Crossing Over

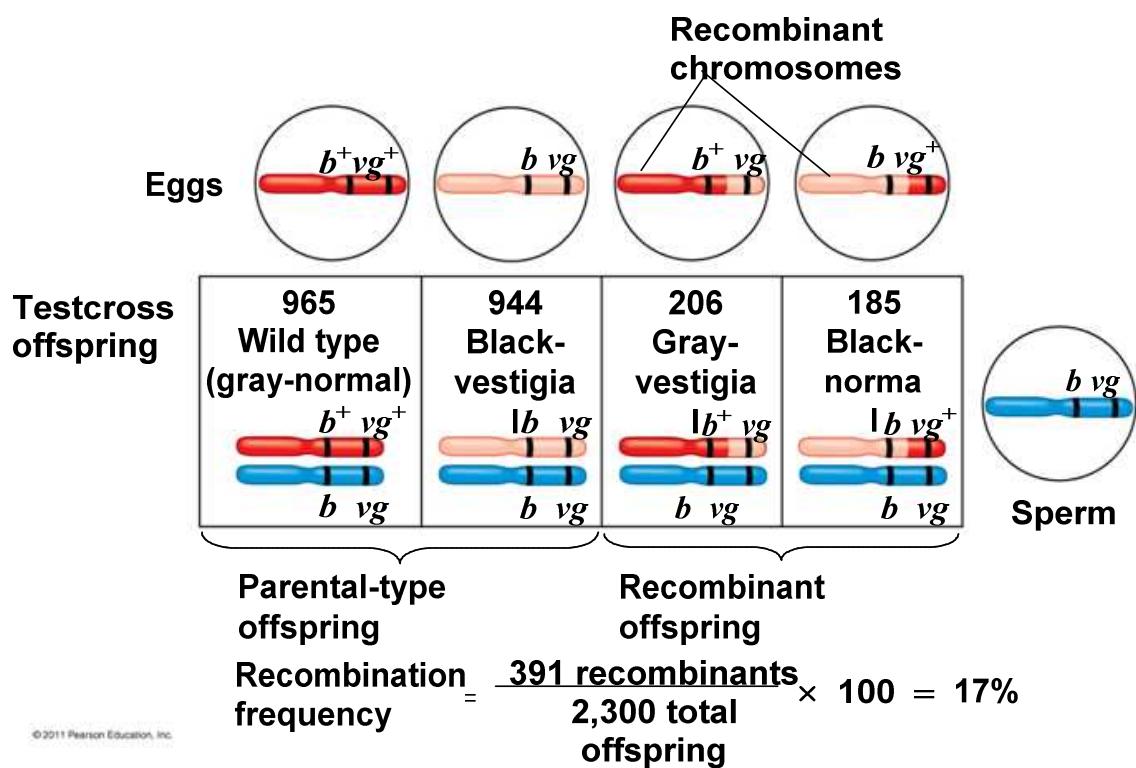
- Morgan discovered that genes can be linked, but the linkage was incomplete, because some recombinant phenotypes were observed
- He proposed that some process must occasionally break the physical connection between genes on the same chromosome
- That mechanism was the **crossing over** of homologous chromosomes

Figure 15.10a



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Figure 15.10b



New Combinations of Alleles: Variation for Normal Selection

- Recombinant chromosomes bring alleles together in new combinations in gametes
- Random fertilization increases even further the number of variant combinations that can be produced
- This abundance of genetic variation is the raw material upon which natural selection works

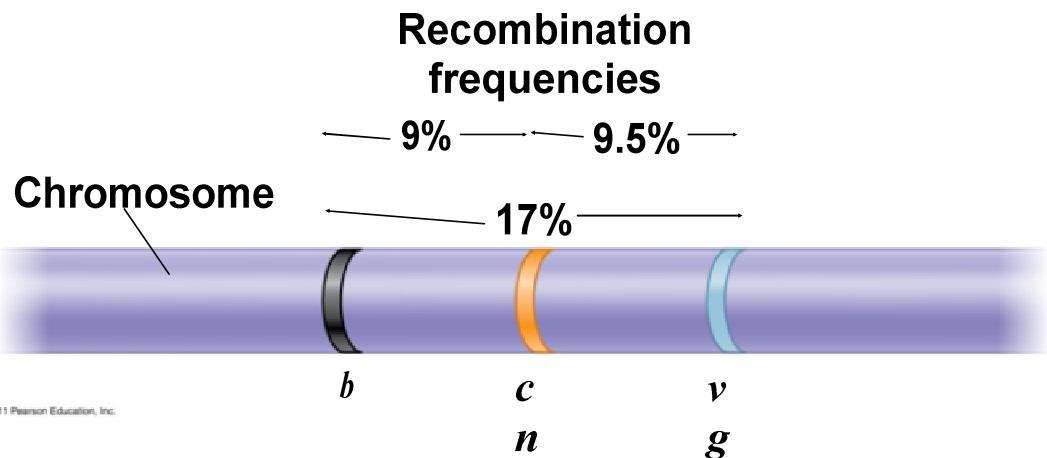
Mapping the Distance Between Genes Using Recombination Data: *Scientific Inquiry*

- 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

Figure 15.11

RESULTS

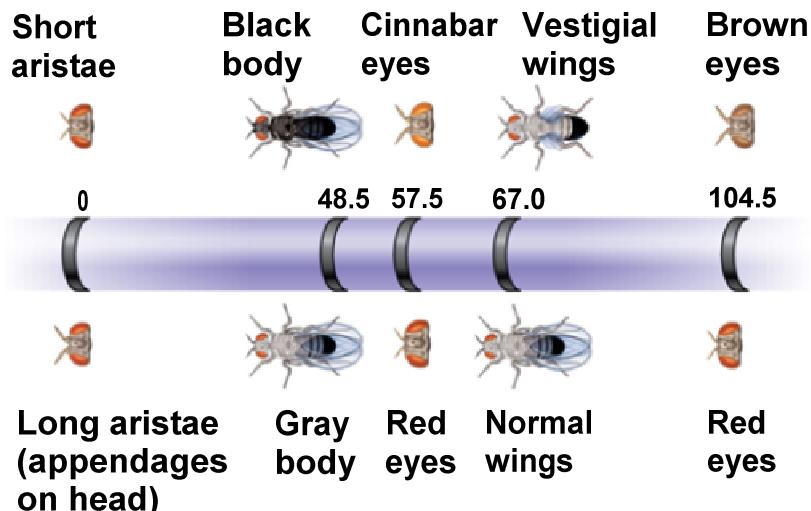


- Genes that are far apart on the same chromosome can have a recombination frequency near 50%
- Such genes are physically linked, but genetically unlinked, and behave as if found on different chromosomes

- 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

Figure 15.12

Mutant phenotypes



Wild-type phenotypes

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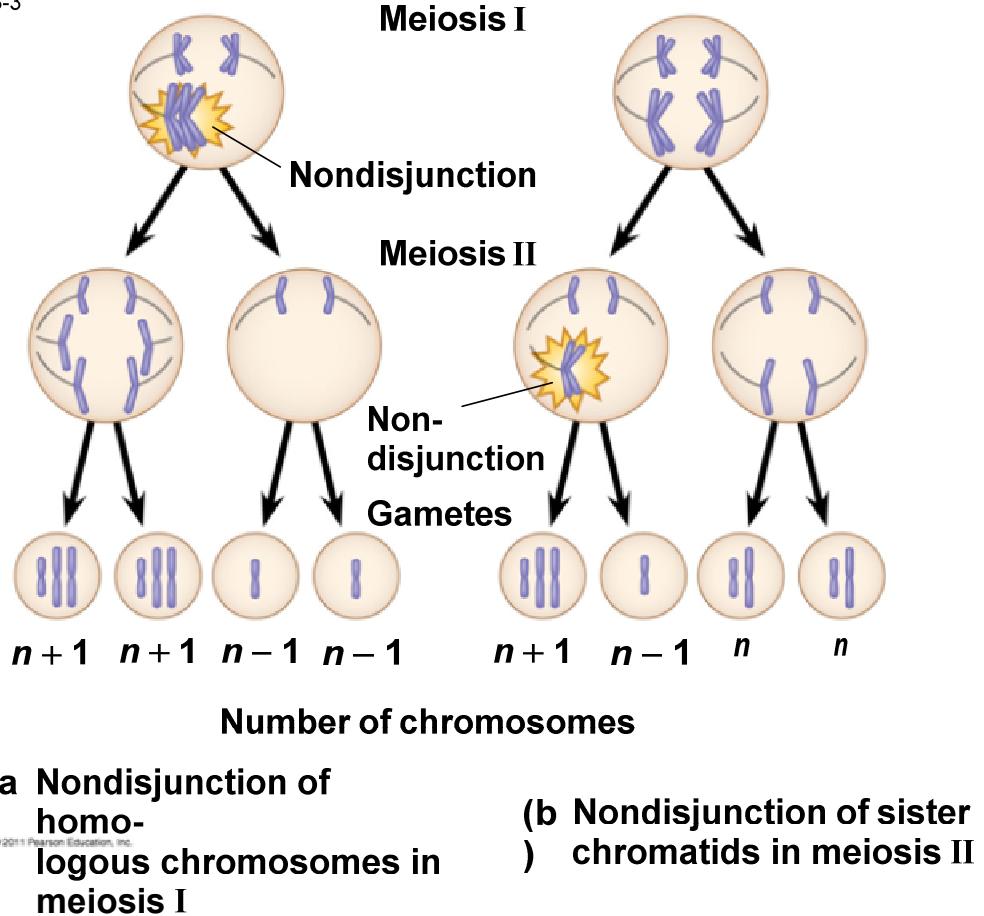
Concept 15.4: Alterations of chromosome number or structure cause some genetic disorders

- Large-scale chromosomal alterations in humans and other mammals often lead to spontaneous abortions (miscarriages) or cause a variety of developmental disorders
- Plants tolerate such genetic changes better than animals do

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

Figure 15.13-3



- **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

- **Polyplody** is a condition in which an organism has more than two complete sets of chromosomes
 - Triploidy ($3n$) is three sets of chromosomes
 - Tetraploidy ($4n$) 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
 - 1. Deletion** removes a chromosomal segment
 - 2. Duplication** repeats a segment
 - 3. Inversion** reverses orientation of a segment within a chromosome
 - 4. Translocation** moves a segment from one chromosome to another

Figure 15.14

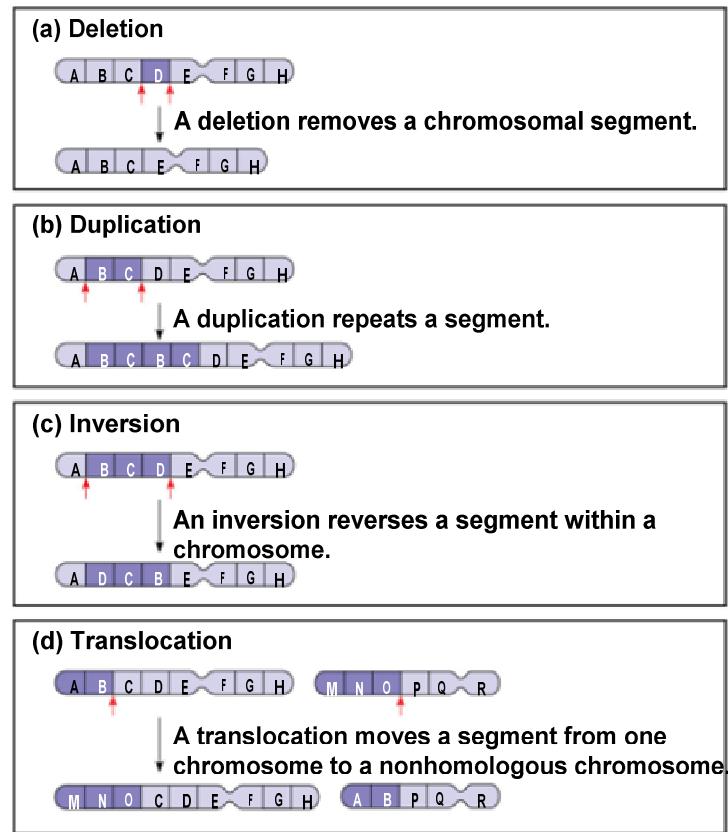
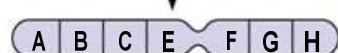


Figure 15.14a

(a) Deletion



A deletion removes a chromosomal segment.



(b) Duplication



A duplication repeats a segment.



Figure 15.14b

(c) Inversion



An inversion reverses a segment within a chromosome.



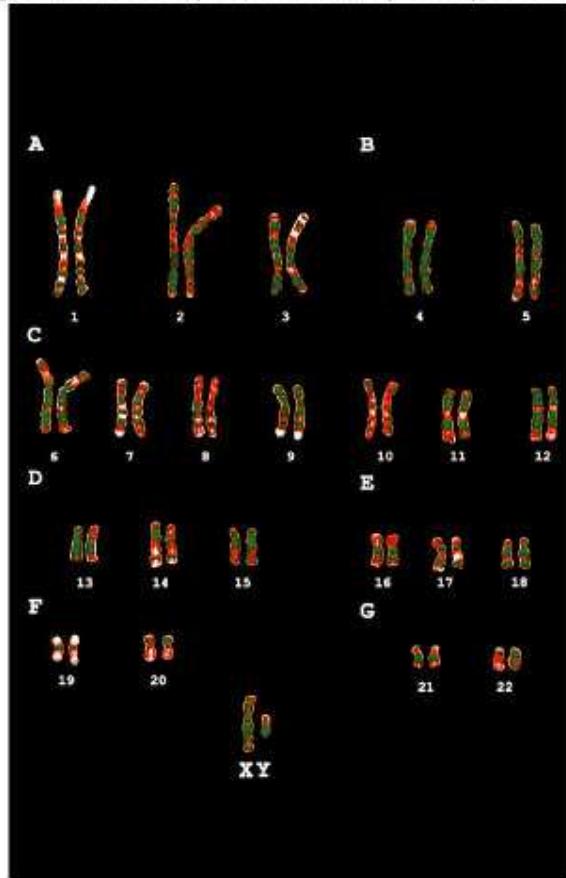
(d) Translocation



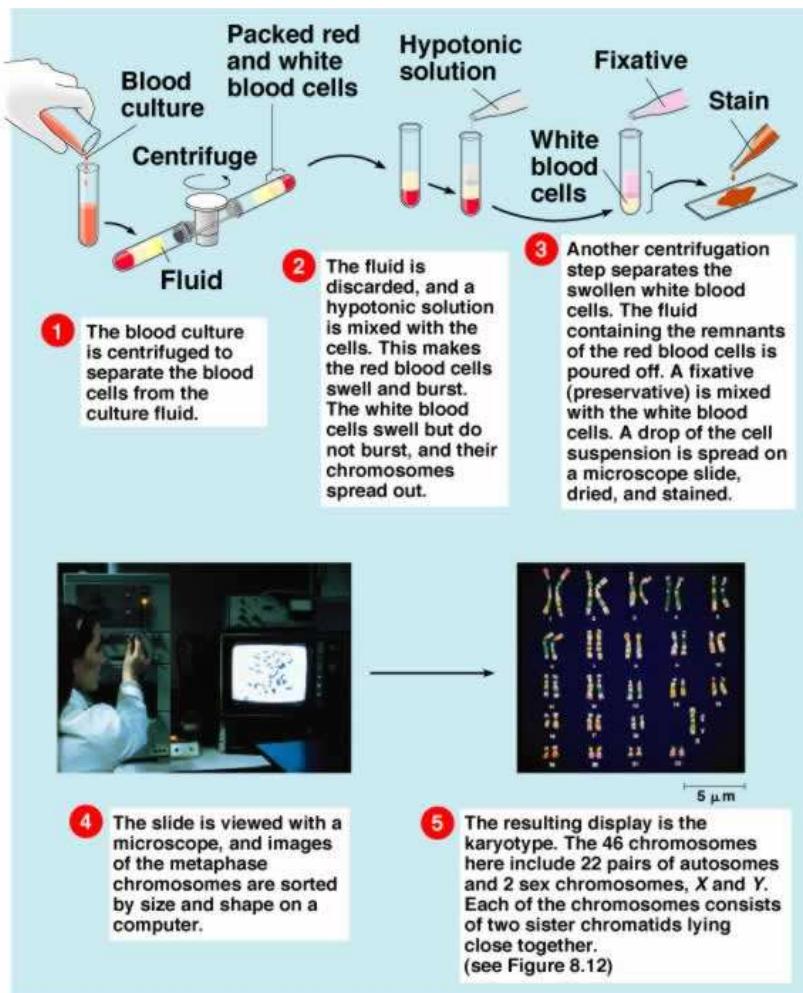
A translocation moves a segment from one chromosome to a nonhomologous chromosome.



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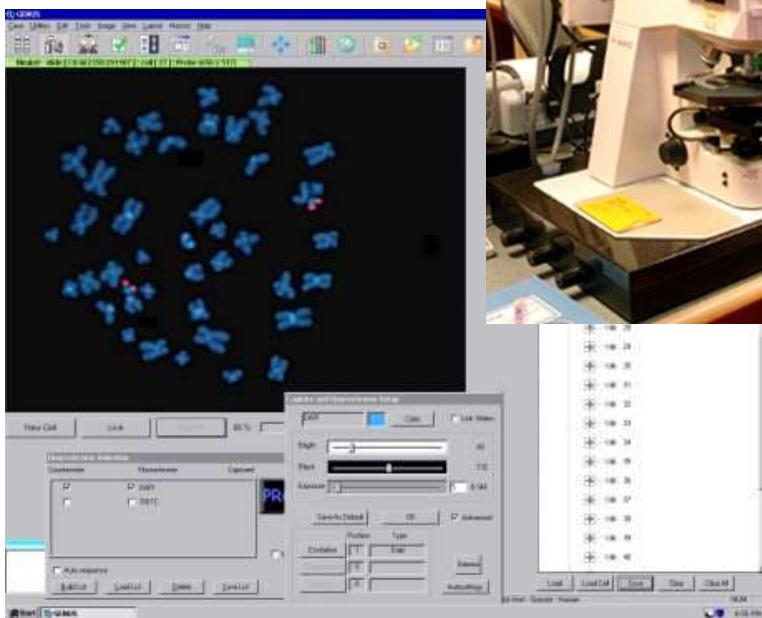


Human Karyotype



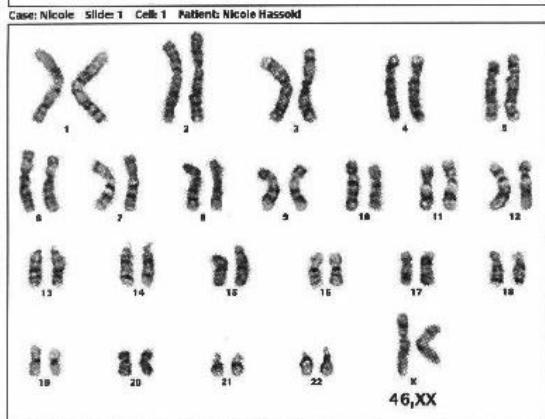
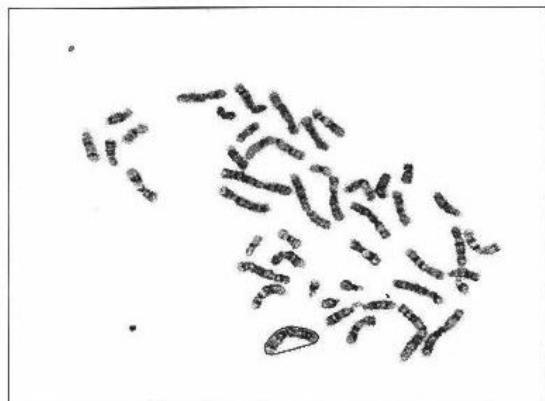
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Karyotyping Computer



Genetix's Genus FISH workstation

**St. Jude Children's Research Hospital
Cytogenetics Laboratory**



Male or Female?



Male or Female? What else do you notice?



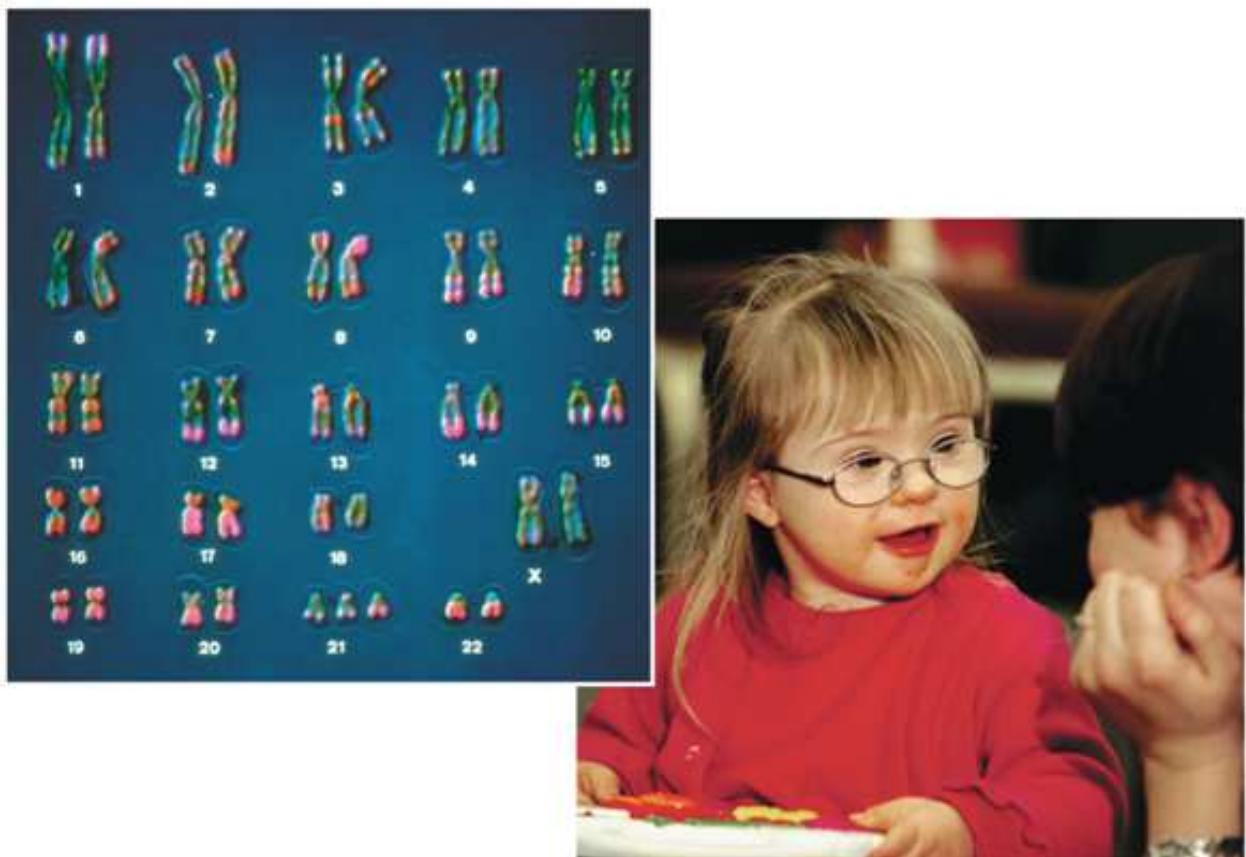
Human Disorders Due to Chromosomal Alterations

- 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

Figure 15.15

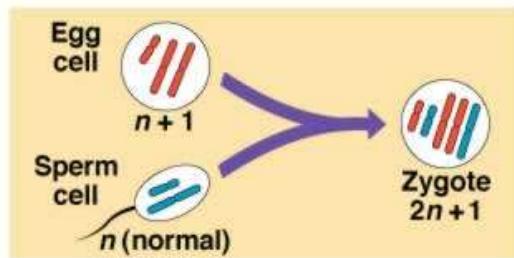
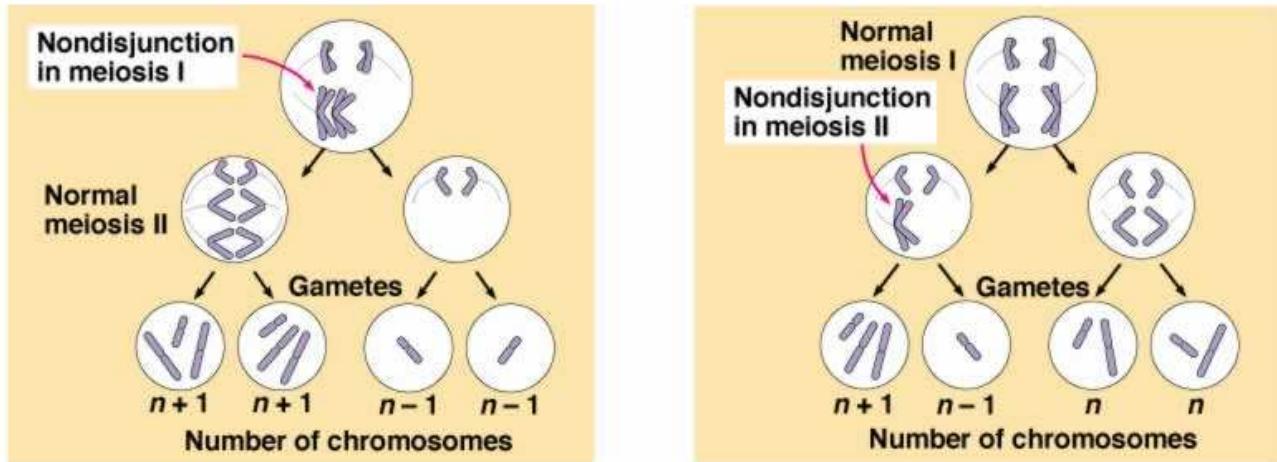


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Alterations in Chromosome Number

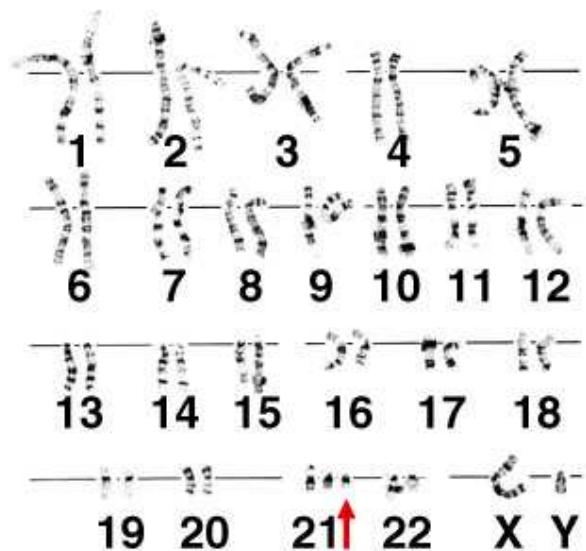
- Failure of chromosomes to separate correctly during meiosis I or II is called **primary nondisjunction**.
 - Down Syndrome caused by **trisomy 21**
 - 1 in 1700 for mothers < 20.
 - 1 in 1400 for mothers >20<30.
 - 1 in 750 for mothers >30<35.
 - 1 in 16 for mothers >45.

Nondisjunction

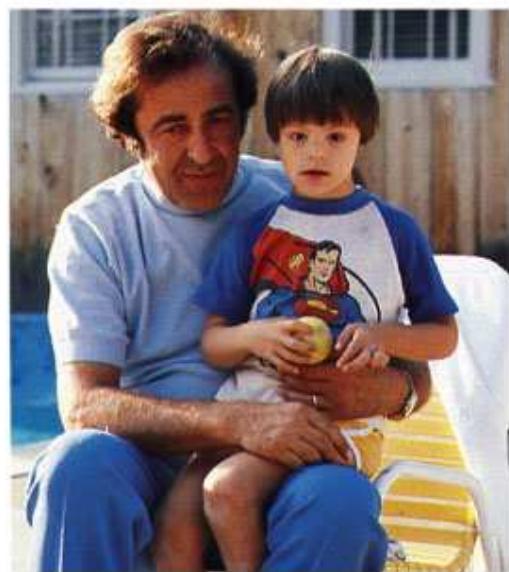


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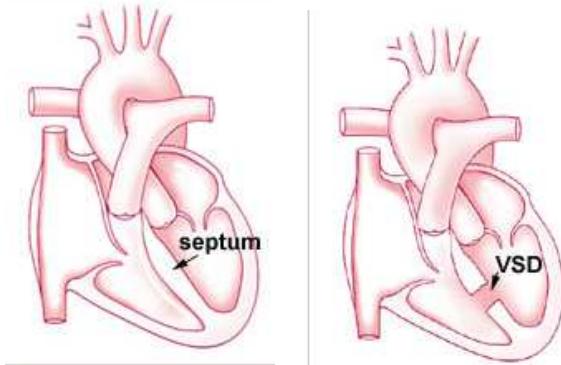
(a)



(b)

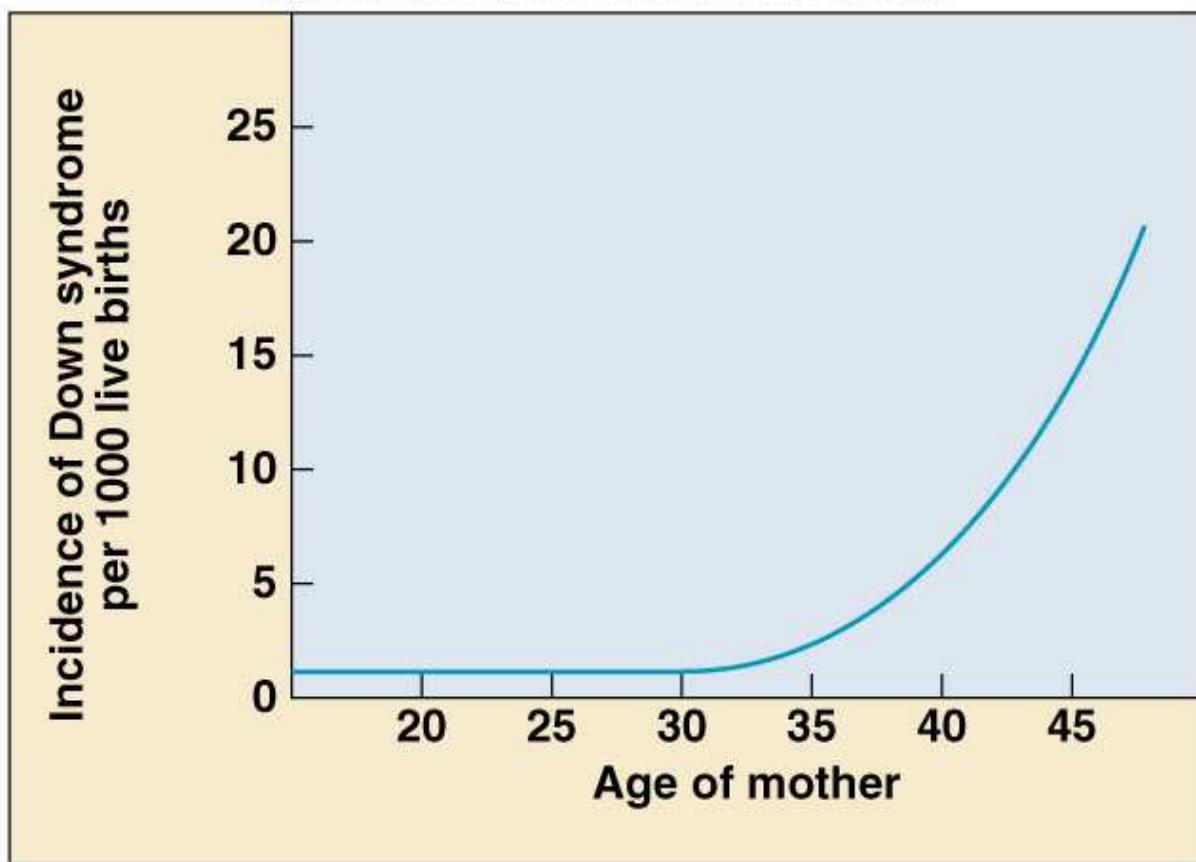


Down Syndrome produces mild to severe mental retardation and is also characterized by an increased susceptibility to many diseases and a higher frequency of birth defects.

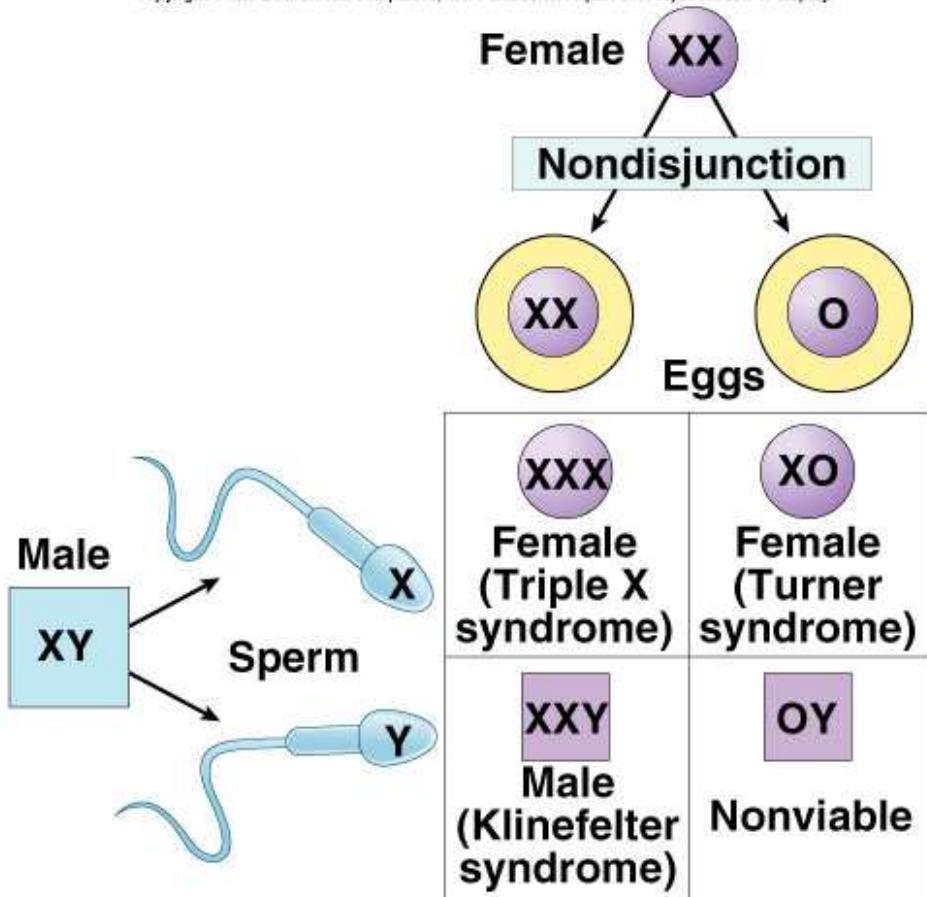


Ventricular Septal Defect

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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

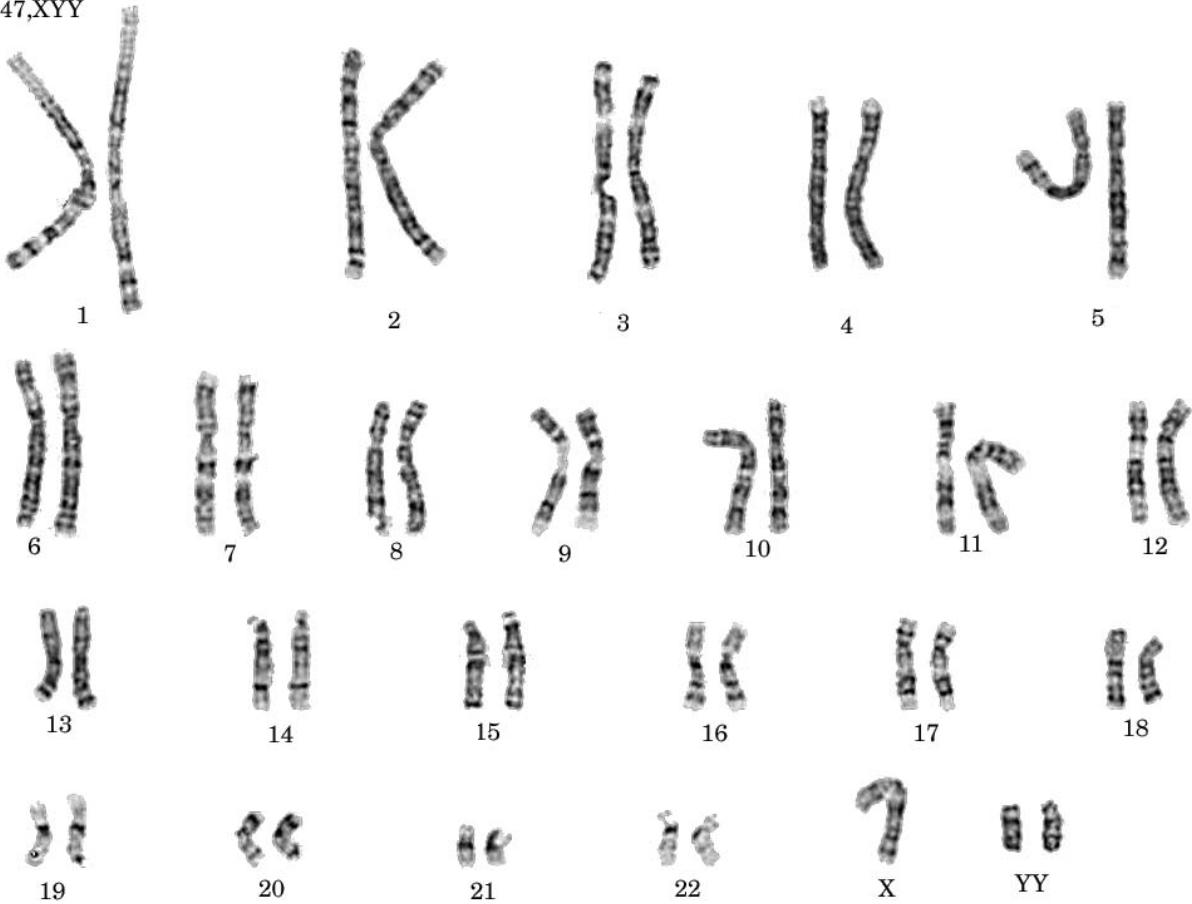
The X is needed for survival!

Nondisjunction in Sex Chromosomes

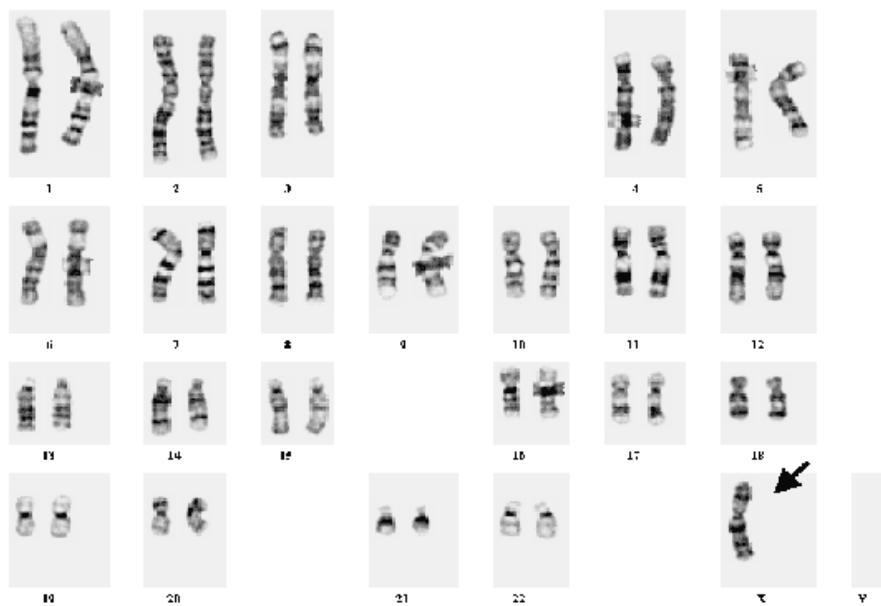
- Presence of an X is needed
- Presence of a Y makes a male
- X Chromosome
 - XXY yields Klinefelter syndrome
 - sterile male
 - female body characteristics
 - 1 in 500 males
 - XO yields Turner syndrome
 - O is a lack of a chromosome
 - short stature, webbed neck, undeveloped sex organs
 - 1 in 5000 females

- XXX yields Metafemales
 - has 1 functional X and 2 Barr bodies
 - sterile but normal in other respects
- Y Chromosome
 - XYY - Jacob syndrome
 - 1 in 1000 males
 - suggested that XYY may be antisocial

47,XYY



Sex Chromosome disorders: Turner's Syndrome. 45XO



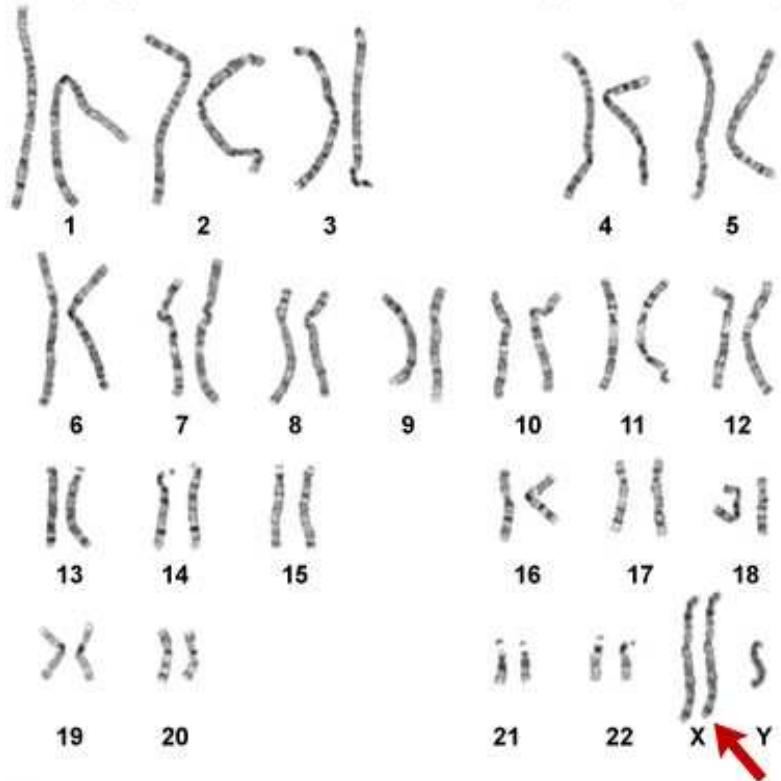


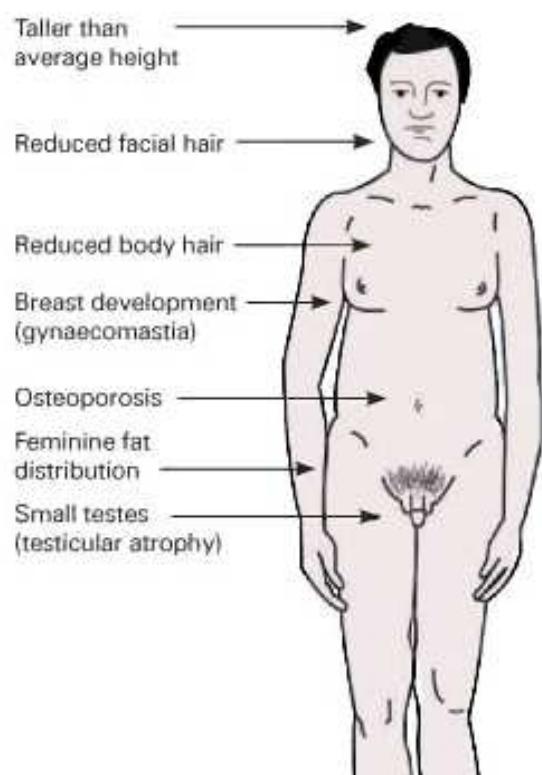
Inherits only one X chromosome.

XO

Sterile and exhibit webbing of skin in the neck region.

Karyotype from a male with Klinefelter syndrome (47,XXY)





**Also reported with
genotypes of XXXY or
XXXXY.**

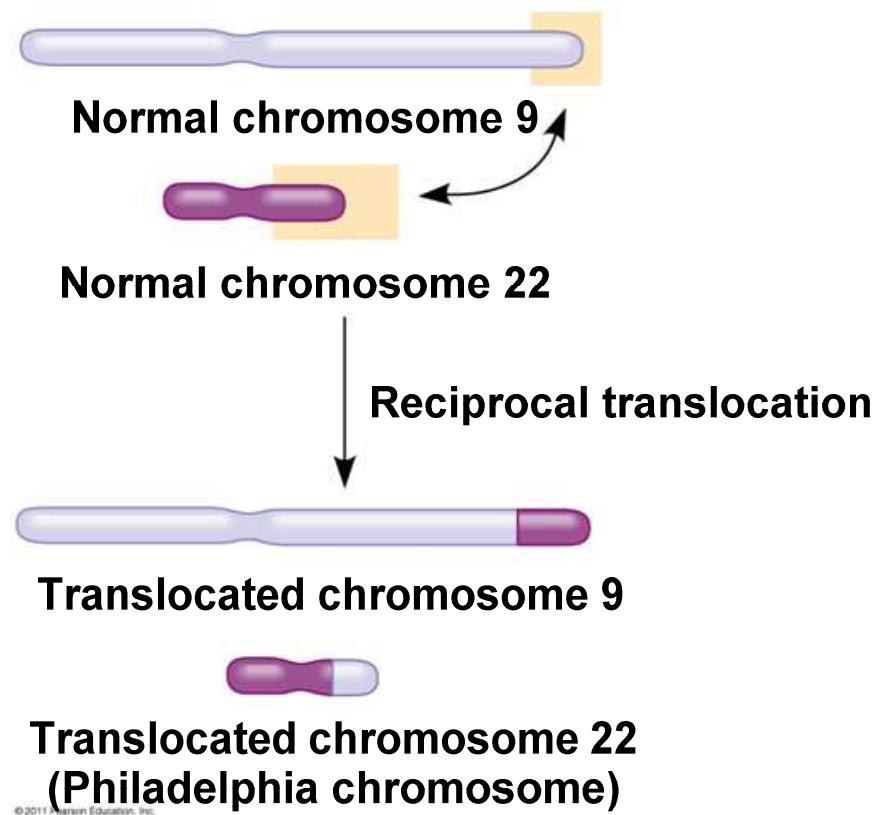
TERMINOLOGY FOR VARIATION IN CHROMOSOME NUMBERS

Term	Explanation
Aneuploidy	$2n \pm x$ chromosomes
Monosomy	$2n - 1$
Trisomy	$2n + 1$
Tetrasomy, pentasomy, etc.	$2n + 2, 2n + 3$, etc.
Euploidy	Multiples of n
Diploidy	$2n$
Polyplody	$3n, 4n, 5n, \dots$
Triploidy	$3n$
Tetraploidy, pentaploidy, etc.	$4n, 5n$, etc.
Autopolyplody	Multiples of the same genome
Allopolyploidy (Amphidiploidy)	Multiples of different genomes

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

Figure 15.16



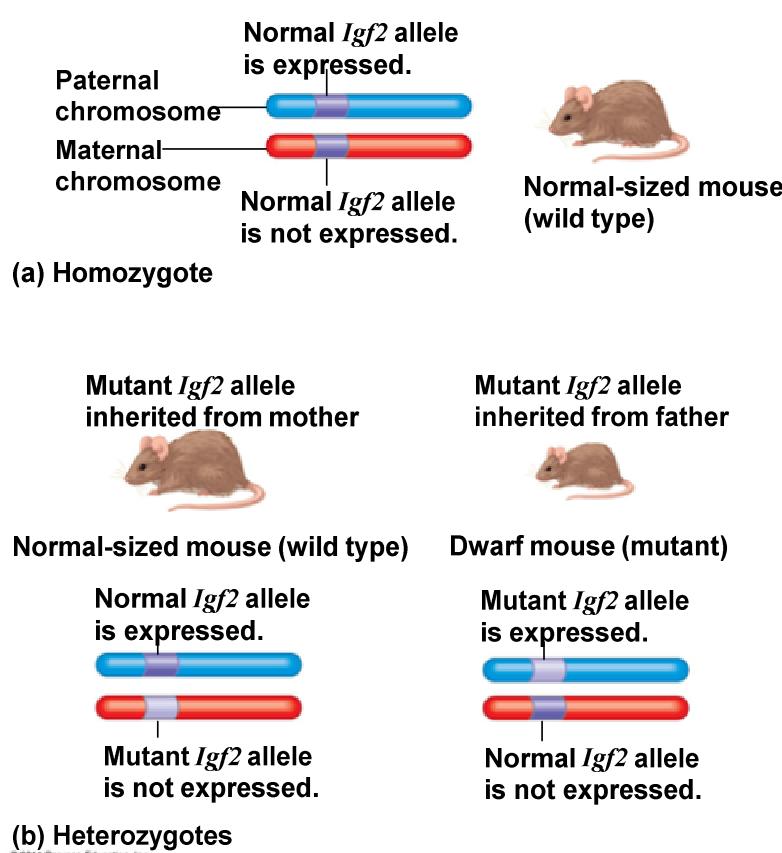
Concept 15.5: Some inheritance patterns are exceptions to standard Mendelian inheritance

- 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
- In both cases, the sex of the parent contributing an allele is a factor in the pattern of inheritance

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

Figure 15.17



- It appears that imprinting is the result of the methylation (addition of $-\text{CH}_3$) of cysteine nucleotides
 - 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 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

Figure 15.18



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- 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

Figure 15.UN03

