

Molecular and Cellular Biology (MCB)

BB101

LECTURE-5

18/ 1/ 2018
19/ 1/ 2018

Chromosomal & Molecular basis of Inheritance

Sanjeeva Srivastava, Ph.D.

Associate Professor

Biosciences and Bioengineering, IIT Bombay

Outline

1. Genetics & Probability
2. Chromosomal basis of inheritance
3. Molecular basis of inheritance

- Genetics and Probability
- Chromosomal basis of Inheritance
- Molecular basis of Inheritance

Genetics and Rules of Probability

Basics: Probability

- Probability is a measure of the expectation that an event will occur (probability is always between 0 – 1)

- To determine the probability of any genotype in offspring of two heterozygote – *multiply the individual probability of a specific allele from egg & sperm*

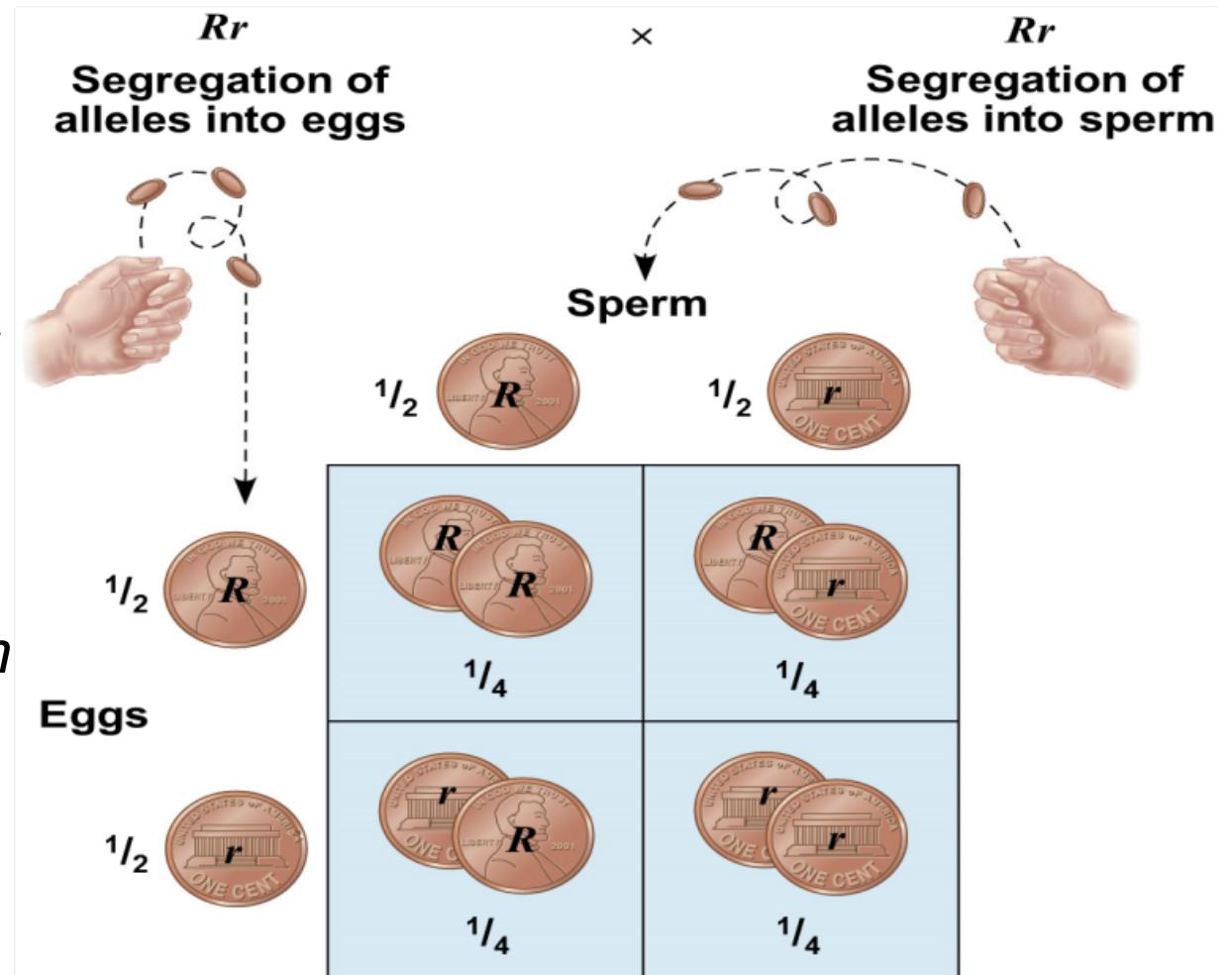
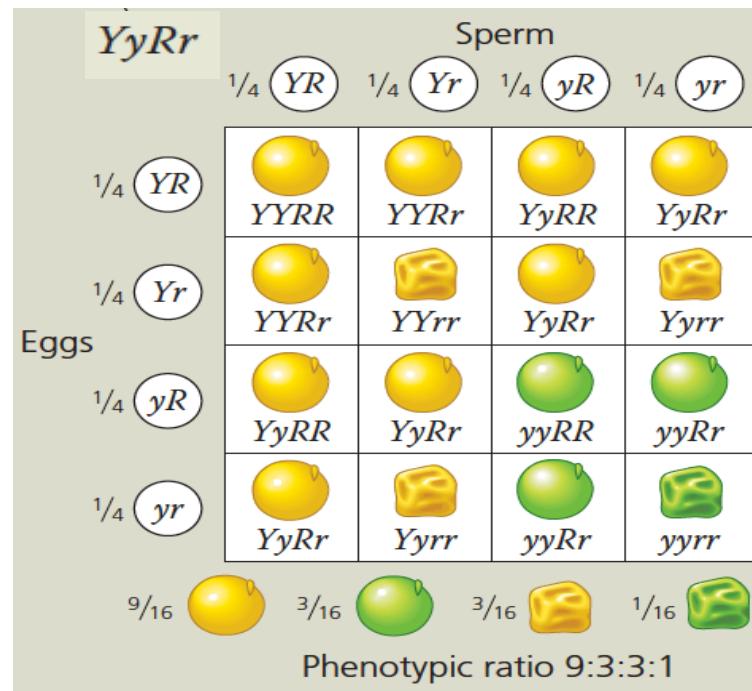


Figure 14.9

4

Genetics and Rules of Probability

- Remember, Law of Independent Assortment - each allelic pair segregates independently during gamete formation.
- Therefore, a dihybrid or multicharacter cross is equivalent to two or more independent monohybrid crosses happening simultaneously.
- Consider dihybrid cross between $YyRr$ heterozygotes or monohybrid cross of Yy plants (seed color) or Rr plants (seed shape).



Consider each gene separately

Genetics and Rules of Probability

Seed color

Y y

	YY	Yy
Y	YY	Yy
y	Yy	yy

$\frac{1}{4} YY, \frac{1}{2} Yy, \frac{1}{4} yy$

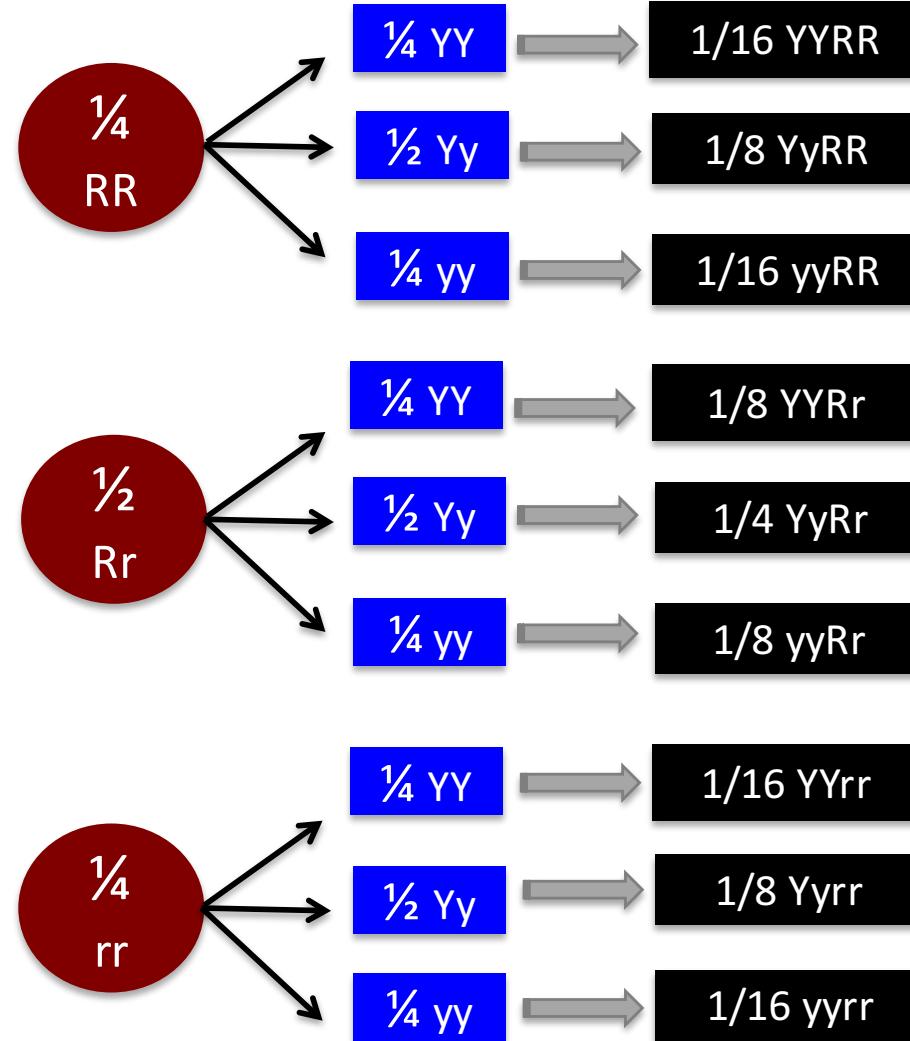
Seed shape

R r

	RR	Rr
R	RR	Rr
r	Rr	rr

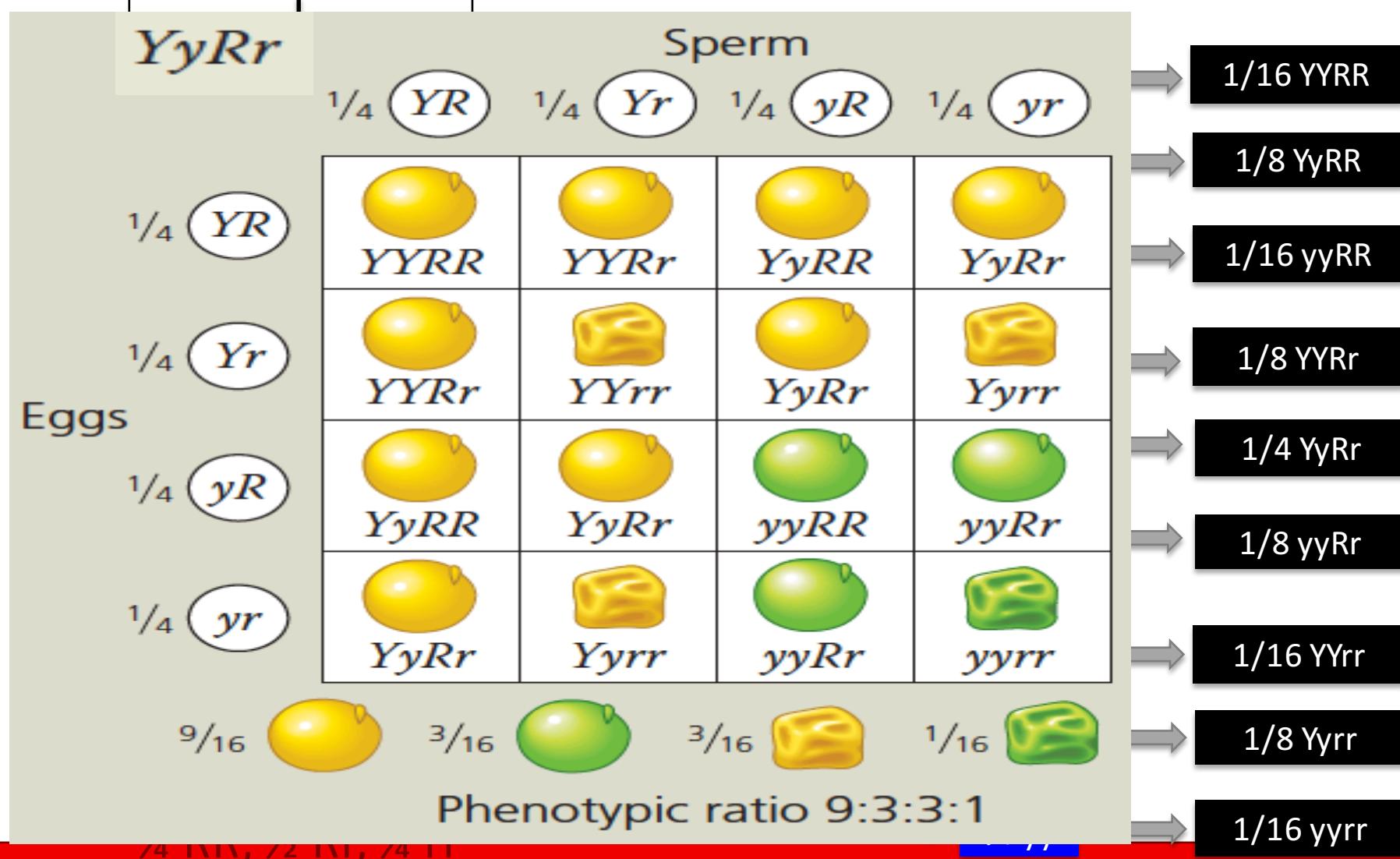
$\frac{1}{4} RR, \frac{1}{2} Rr, \frac{1}{4} rr$

- Probability of F2 genotype $YYRR ? = \frac{1}{4} (YY) \times \frac{1}{4} (RR) = 1/16$
- Probability of F2 genotype $YyRR ? = \frac{1}{2} (Yy) \times \frac{1}{4} (RR) = 1/8$



Genetics and Rules of Probability

- Probability of F2 genotype YYRR ? = $\frac{1}{4}$ (YY) X $\frac{1}{4}$ (RR) = 1/16
- Probability of F2 genotype YyRR ? = $\frac{1}{2}$ (Yy) X $\frac{1}{4}$ (RR) = 1/8



Genetics Examples

- What is the probability of having an Albino child, if both the parents are heterozygous for the albinism?

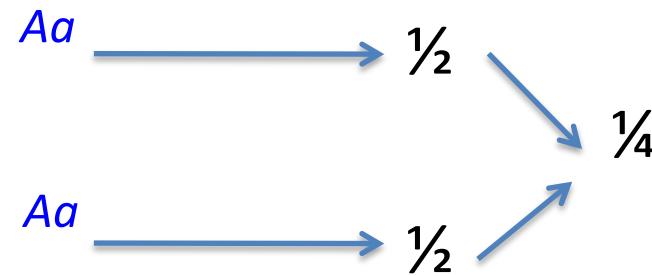
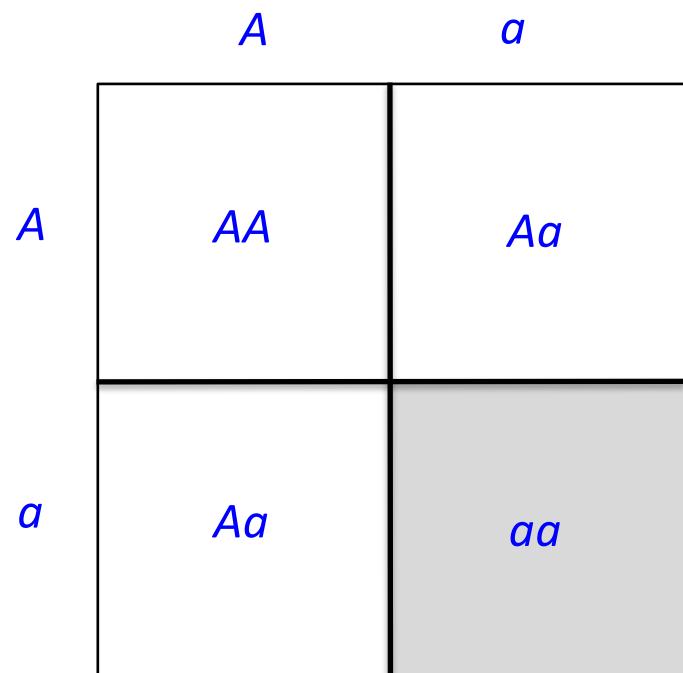
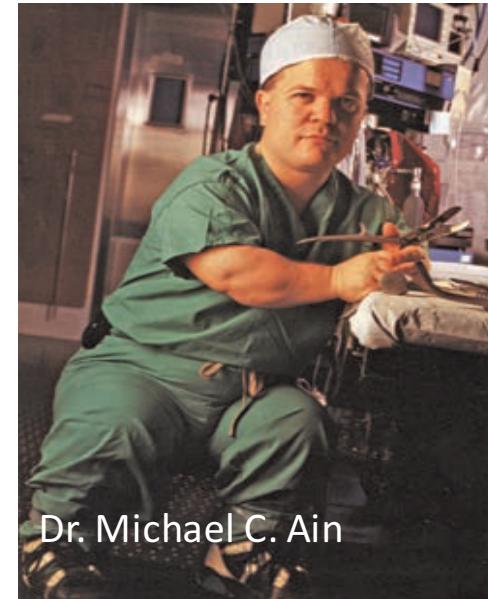


Figure 14.18

Genetics Examples

- Achondroplasia (dwarfism) is due to a dominant allele. What is the probability of having a child with disease if one parent is homozygous recessive and the other is heterozygous?

	D	d
d	Dd Dwarf	dd Normal
d	Dd Dwarf	dd Normal



$\frac{1}{2}$

Figure 14.18

- Genetics and Probability ✓
- Chromosomal basis of Inheritance
- Molecular basis of Inheritance

Chromosomal basis of Inheritance

What are the heritable factors defined by Mendel?

Chromosomal Basis of Mendel's Laws

- Chromosome theory of inheritance – genes are located on chromosomes & behavior of chromosomes during meiosis accounts for Mendel's laws of segregation & independent assortment

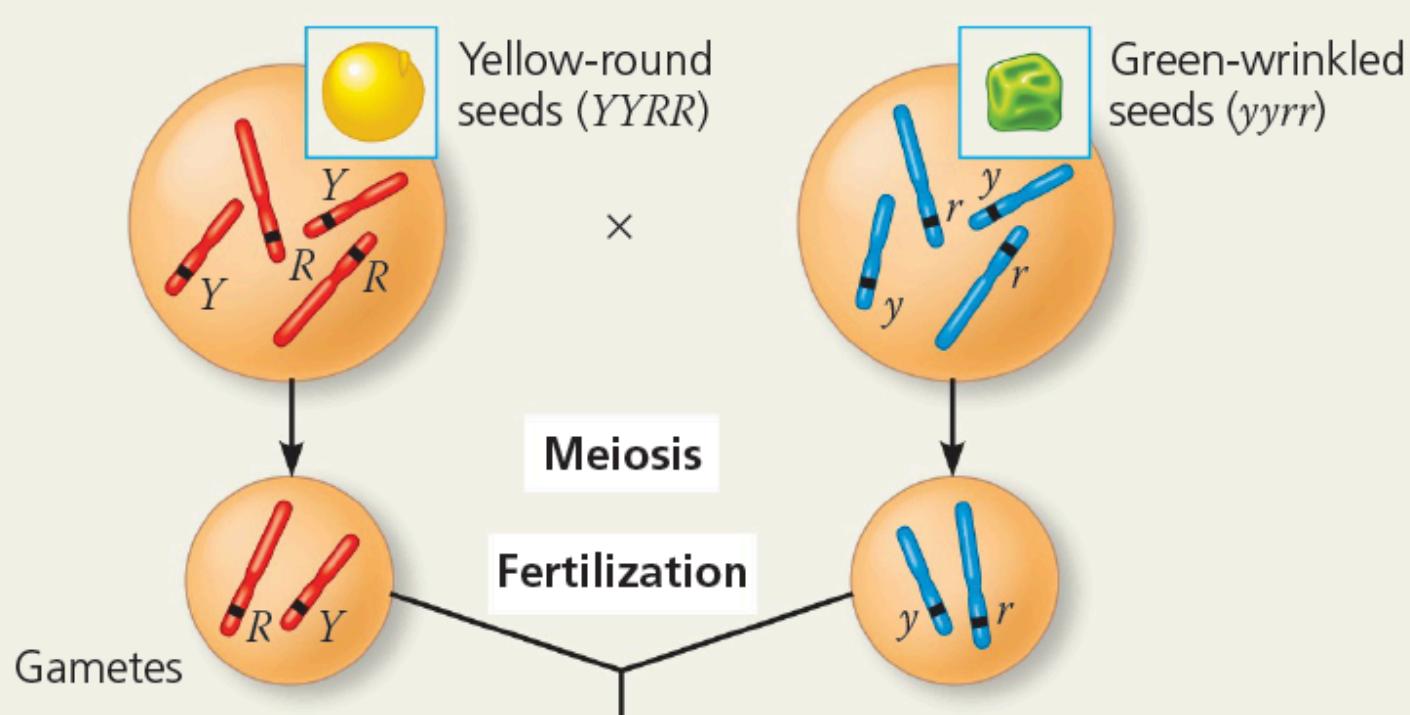


Figure 15.2
11

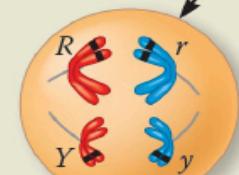
Chromosomal Basis of Mendel's laws

F₁ Generation

LAW OF SEGREGATION

The two alleles for each gene separate during gamete formation. As an example, follow the fate of the long chromosomes (carrying R and r). Read the numbered explanations below.

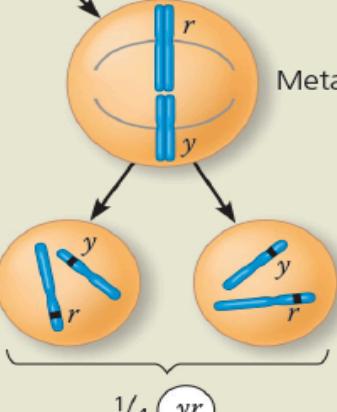
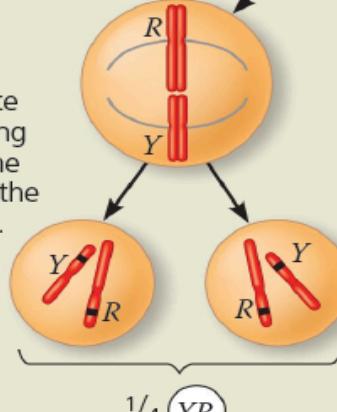
- 1 The R and r alleles segregate at anaphase I, yielding two types of daughter cells for this locus.



Anaphase I

- 2 Each gamete gets one long chromosome with either the R or r allele.

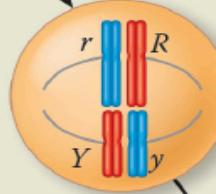
Gametes



All F₁ plants produce yellow-round seeds (YyRr).

Meiosis

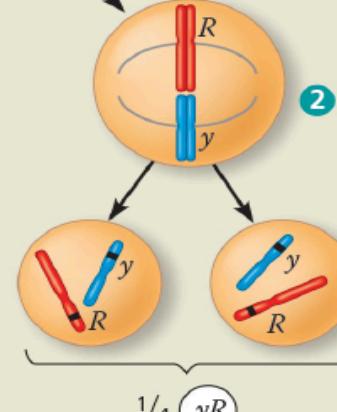
Two equally probable arrangements of chromosomes at metaphase I



LAW OF INDEPENDENT ASSORTMENT

Alleles of genes on nonhomologous chromosomes assort independently during gamete formation. As an example, follow both the long and short chromosomes along both paths. Read the numbered explanations below.

- 1 Alleles at both loci segregate in anaphase I, yielding four types of daughter cells, depending on the chromosome arrangement at metaphase I. Compare the arrangement of the R and r alleles relative to the Y and y alleles in anaphase I.



- 2 Each gamete gets a long and a short chromosome in one of four allele combinations.

Chromosomal Basis of Mendel's Laws

- Results of Mendel's dihybrid crosses can be correlated with the behavior of chromosomes during meiosis.
- During meiosis homologous chromosomes separate and alleles segregate.
- The behavior of chromosomes during meiosis in F1 generation and subsequent random fertilization give rise to the F2 phenotypic ratio observed by Mendel.

Mendelian Inheritance has its Physical Basis in Behavior of Chromosomes

Morgan independently tested Mendel's experiment

Morgan's Experiment: Genes are Associated with a Specific Chromosome



Thomas Hunt Morgan
Columbia University

Morgan's experiment provided evidence that chromosomes are indeed the location of Mendel's heritable factors

Morgan's Choice of Experimental Organism

- Phenotype for most commonly observed character in natural populations (e.g. red eyes in *Drosophila*), is called wild type.
- Traits alternatives to the wild type (e.g. white eyes in *Drosophila*), are called mutant phenotypes.



Figure 15.3

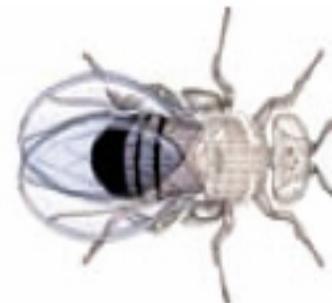
Morgan's Choice of Experimental Organism

Wild-type w^+
Red



$X^{w+} X^{w+}$

Mutant w
White

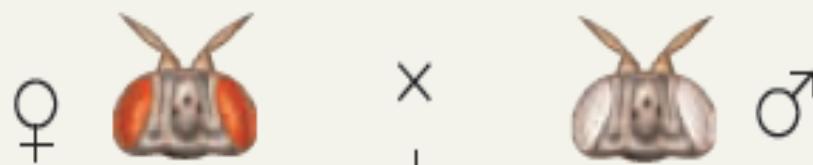


$X^w Y$

In a cross between a wild-type female fruit fly and a mutant white-eyed male, what color eyes will the F1 and F2 offspring have?

Experiment – wild-type (red-eyed) female mating with mutant (white-eyed) male

P
Generation

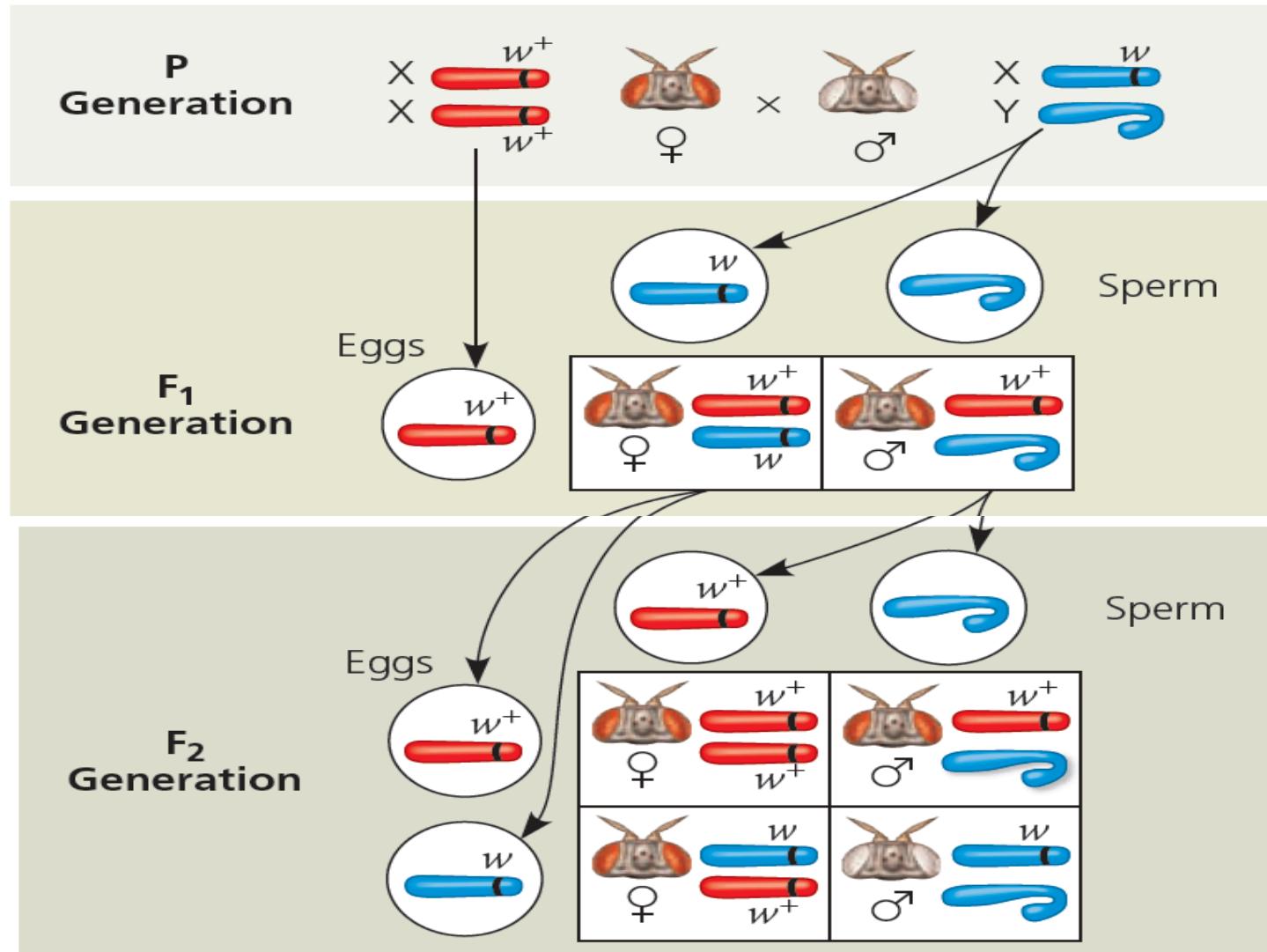


F₁
Generation



All offspring had red eyes.

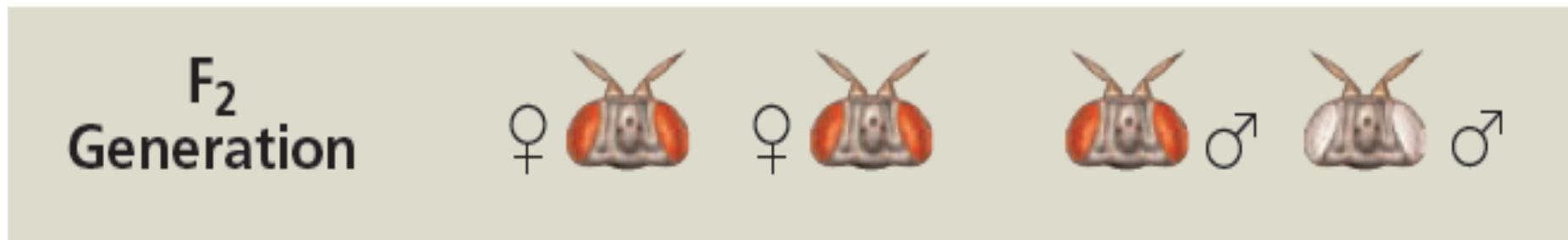
Morgan Supported Chromosome Theory of Inheritance



A specific gene is carried on a specific chromosome

In a cross between a wild-type female fruit fly and a mutant white-eyed male, what color eyes will the F1 and F2 offspring have?

- F1 red-eyed female mating to an F1 red-eyed male

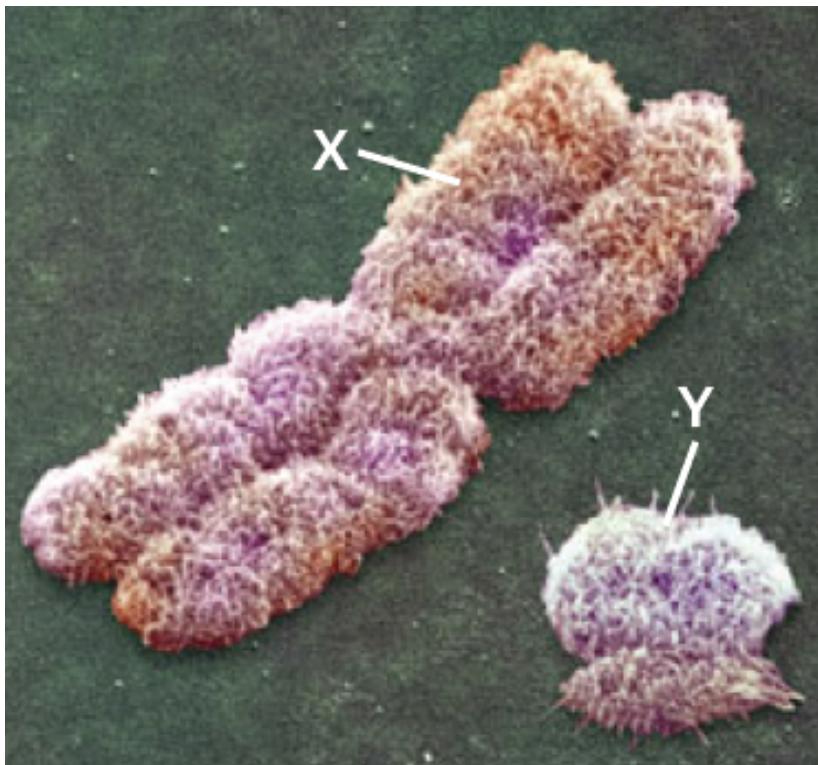


- The mutant white-eye trait (w) is recessive to wild-type red-eye trait (w+)
- Interestingly, the recessive trait (white eyes) was expressed only in males in F2 generation
- Therefore, Morgan concluded that eye-color gene is located on X chromosome and there is no corresponding locus on Y chromosome

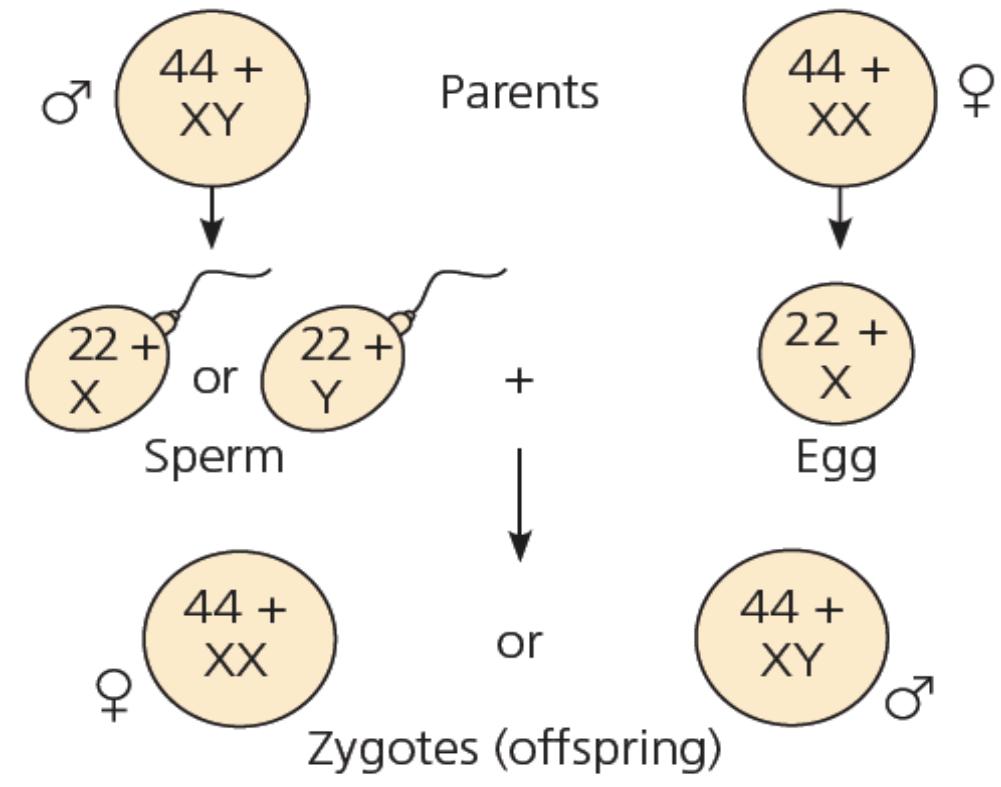
Conclusion:

Morgan's experiment provided evidence that chromosomes are indeed the location of Mendel's heritable factors

Chromosomal Basis of Sex in Human



Human Sex Chromosomes



- Sex of an offspring depends on whether sperm cell contains an X or a Y chromosome

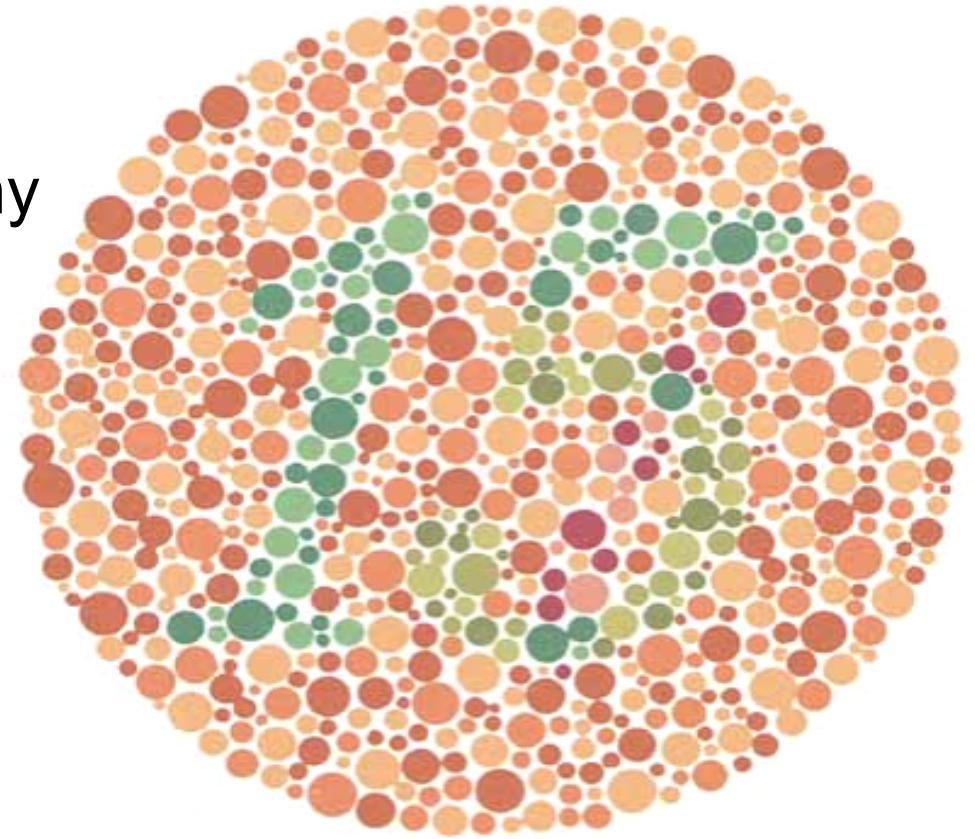
Figure 15.6

Sex-linked Inheritance

- Sex-linked gene - a gene located on either sex chromosome
- Y-linked genes - those located on the Y chromosome (~ 78 genes), mainly help determine sex
- X-linked genes - those located on the X chromosome (~ 1,100 genes), genes for many characters but unrelated to sex

Examples of Sex-linked Traits And Disorders

- Red-green Colour blindness
- Duchenne muscular dystrophy
- Night blindness
- Hemophilia



Transmission of X-linked Recessive Traits: Red-green Color Blindness

Red-green Color Blindness: X-linked Disorder

N = dominant allele for normal color vision
(carried on X chromosome)

n = recessive allele having a mutation for
color blindness



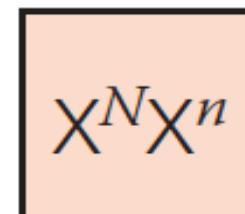
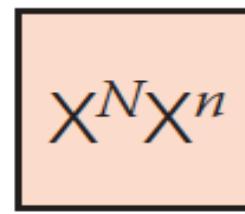
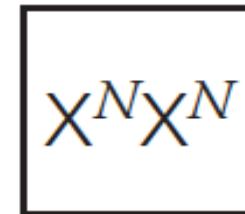
Unaffected individuals



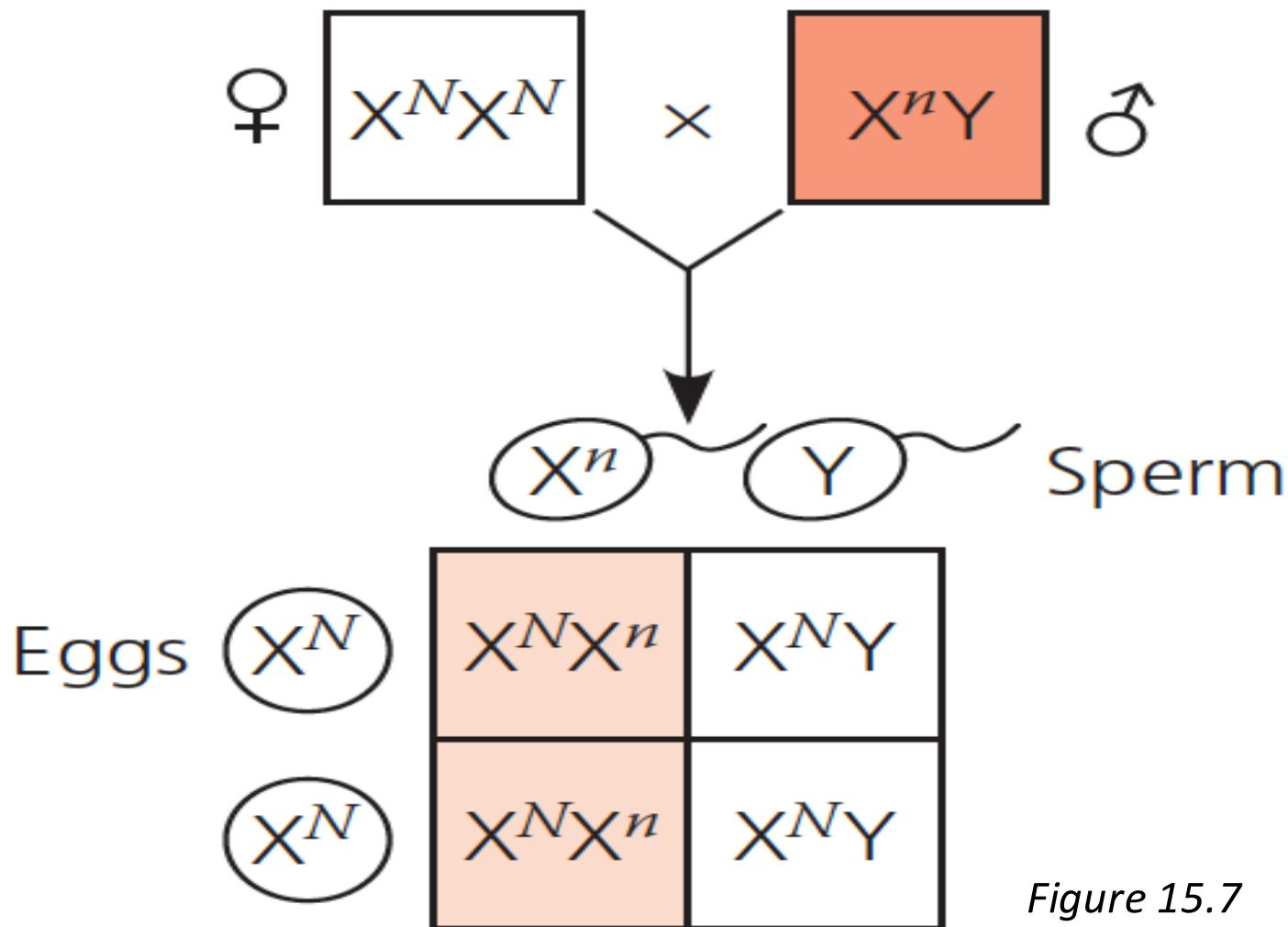
Carriers



Color-blind individuals

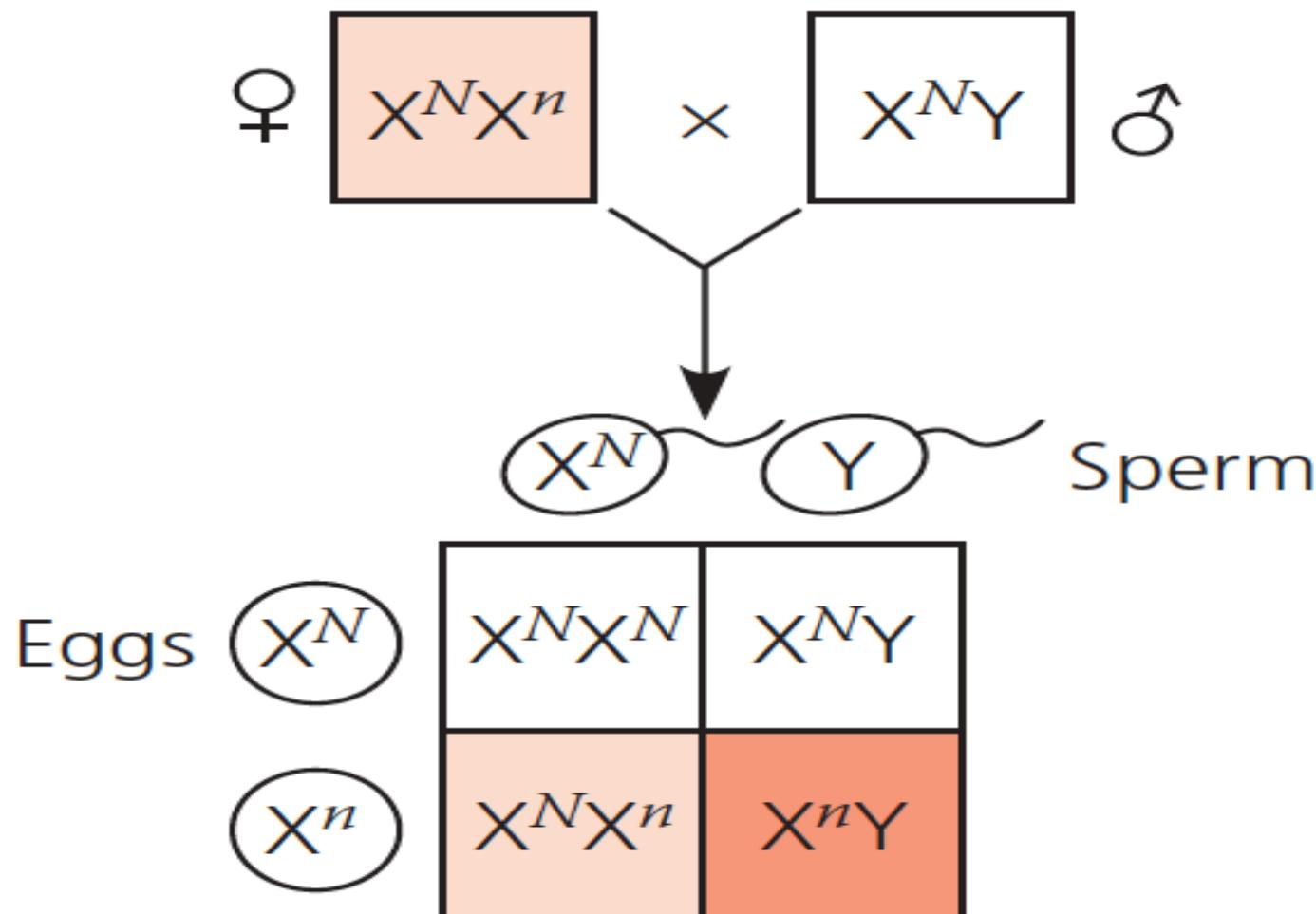


Red-green Color Blindness: X-linked Disorder



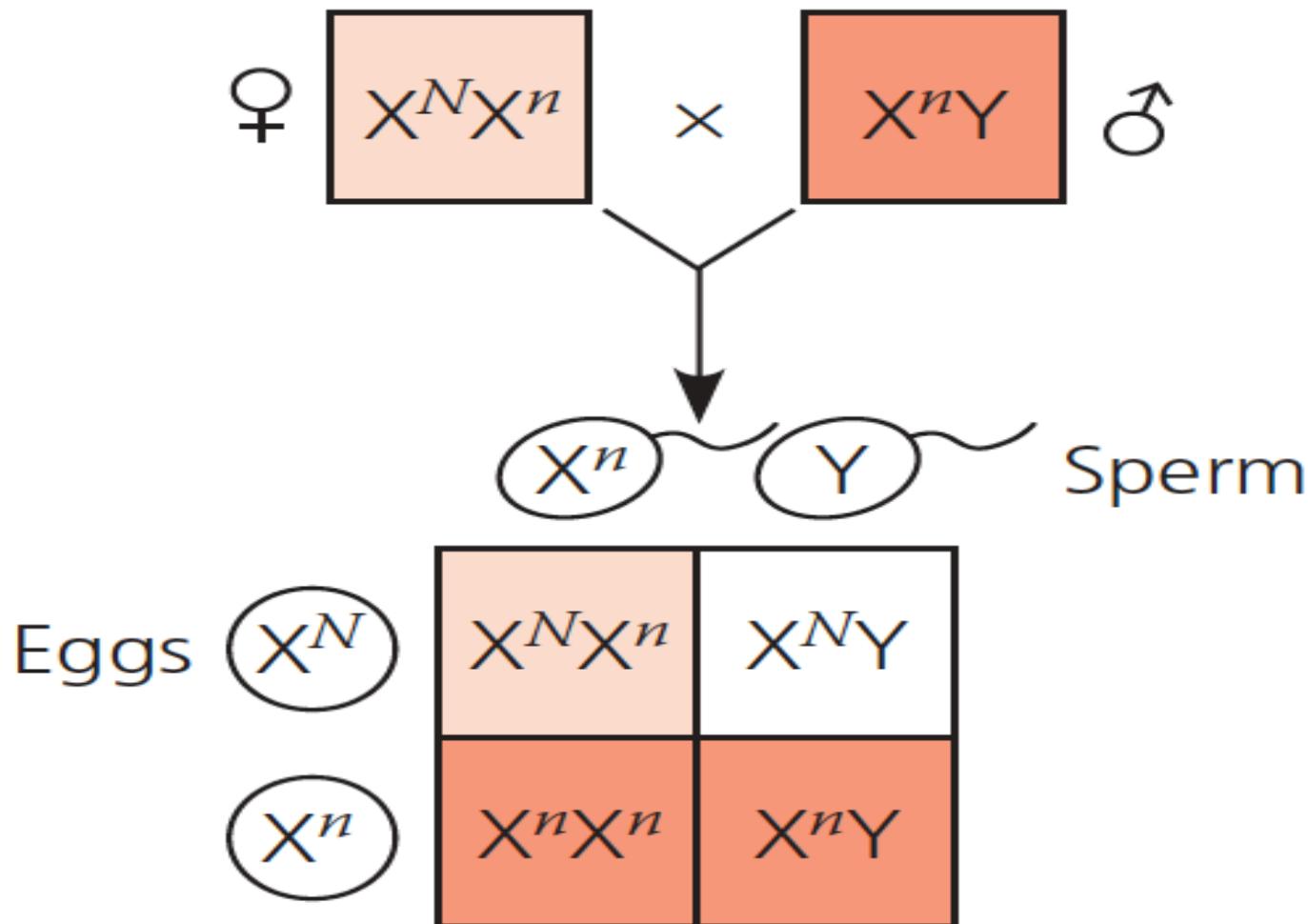
- A color-blind father will transmit mutant allele to all daughters

If a Carrier Mates with a Male Having Normal Color Vision



- 50% chance that each daughter will be a carrier like her mother and a 50% chance that each son will have the disorder

If a Carrier Mates with a Color-blind Male



- There is a 50% chance that each child will have the disorder, regardless of sex.
- Daughters having normal color vision will be carriers.

Fathers pass X-linked alleles to all of their daughters but to none of their sons.

Mothers can pass X-linked alleles to both sons and daughters.

Any male receiving the recessive allele from his mother will express the trait.

Therefore, far more males than females have X-linked recessive disorders.

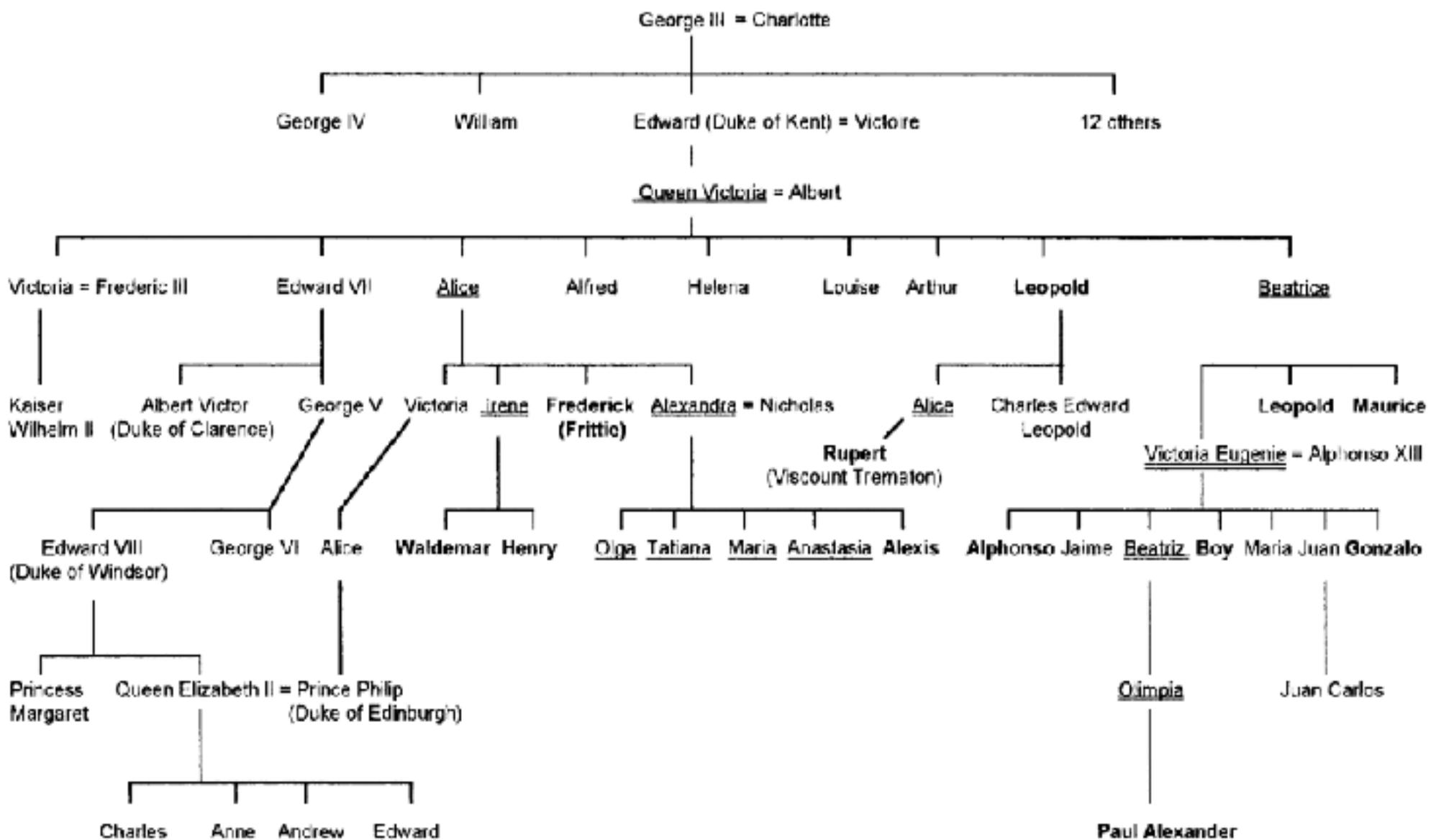
X-linked Recessive Disorder: Hemophilia

- Absence of one or more of the proteins required for blood clotting.
- When a person with hemophilia is injured, bleeding is prolonged because a firm clot is slow to form.
- Small cuts in the skin are usually not a problem, but bleeding in the muscles or joints can be painful and can lead to serious damage

Hemophilia and Royal Family of Europe

- Queen Victoria of England is known to have passed the allele to several of her descendants.
- Intermarriage with royal family members of other nations, such as Spain and Russia, further spread this X-linked trait.

Example: Royal Families of Europe And Hemophilia



British Journal of Haematology, 1999, 105, 25–32

33

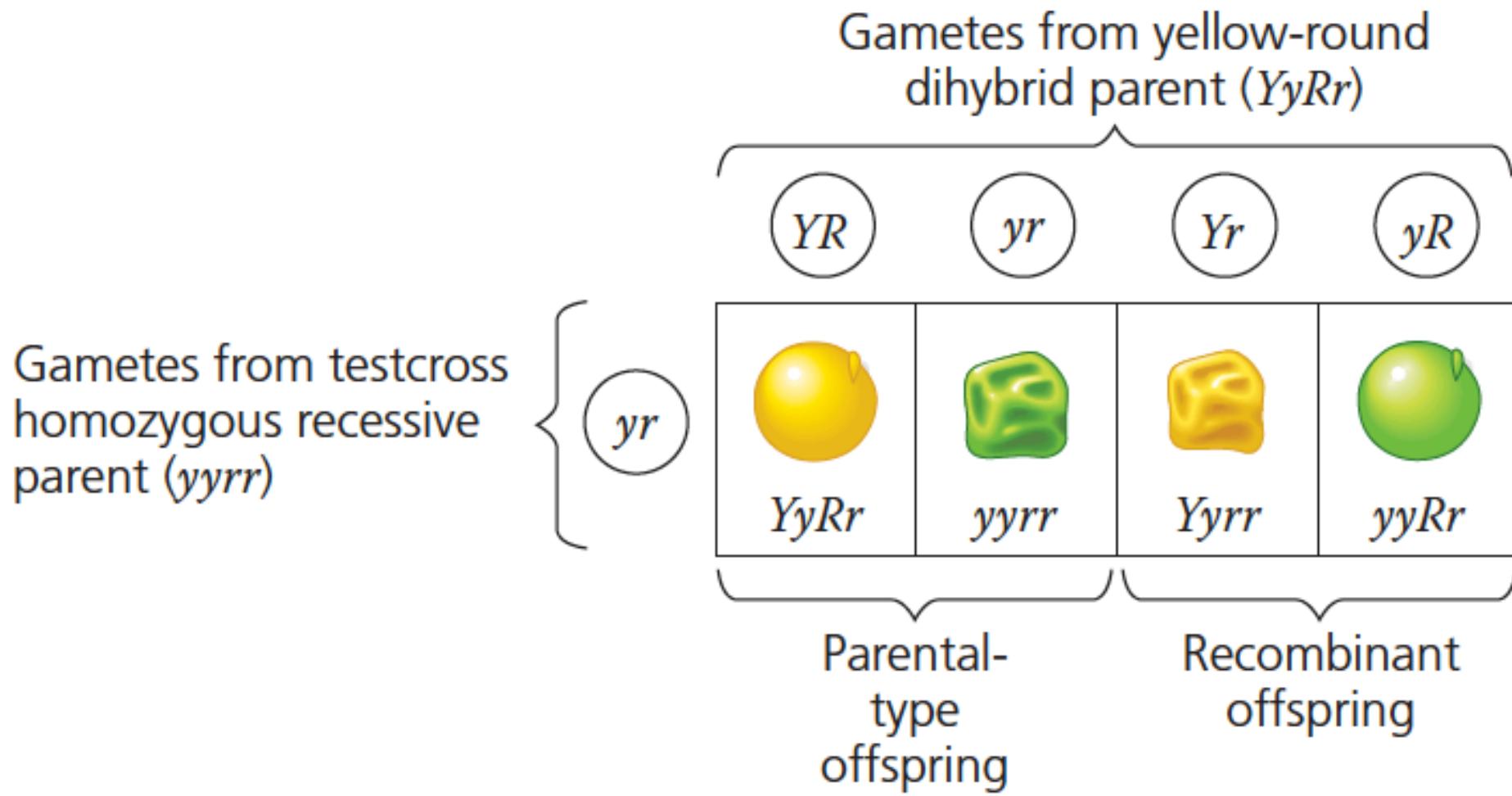
The genetic basis of the mutation, and how it resulted in a nonfunctional blood-clotting factor, is now understood..

Today, people with hemophilia are treated as needed with intravenous injections of the protein that is missing

Genetic Recombination and Linkage

The production of offspring with combinations of traits that differ from those found in either P generation parent

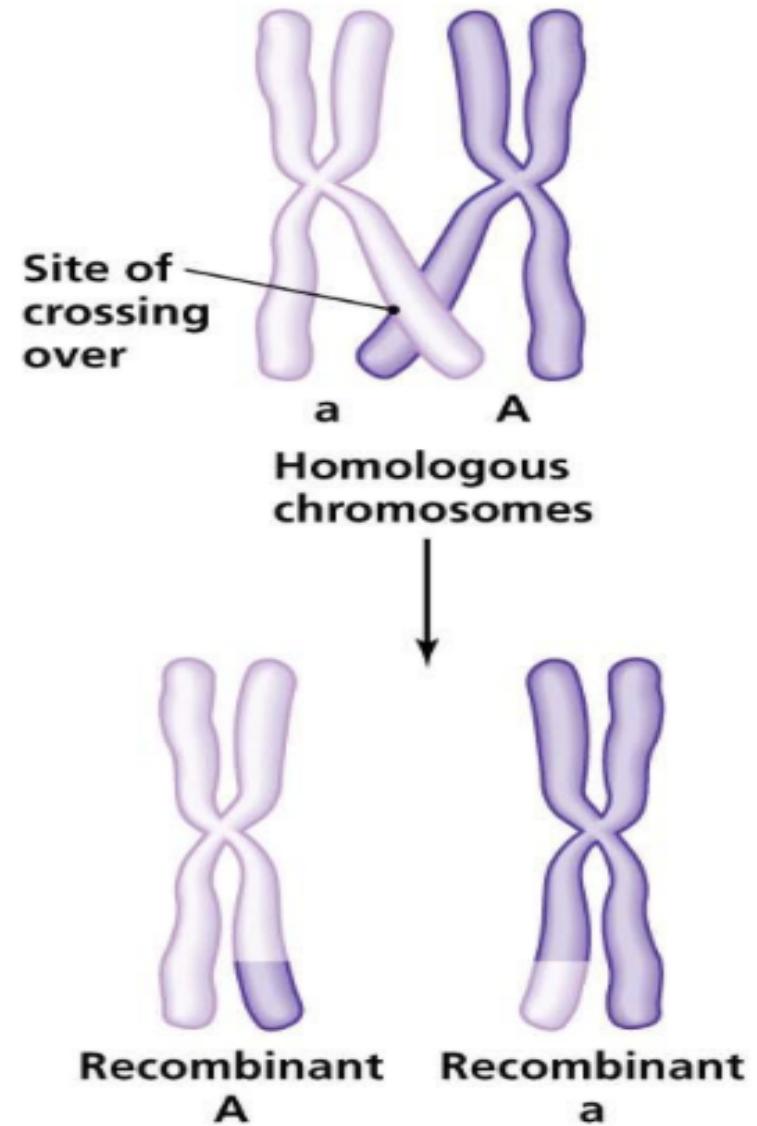
Recombination of Unlinked Genes: Independent Assortment of Chromosomes



Two non-parental phenotypes were found among the offspring. Since these offspring have new combinations of seed shape and color, they are called **recombinant types, or recombinants**.

Recombination and Linkage

- **Recombination** is the exchange of nucleotide sequences between two homologous DNA molecules (identical or nearly identical to one another).
- In **crossing over**, short sequences of DNA on chromosome tetrads are exchanged.



Recombination Of Linked Genes: Crossing Over

- Replicated chromosomes are paired up in the prophase of meiosis I.
- A set of proteins conducts the exchange of corresponding segments of two non-sister chromatids by a process called “crossing over”.

How does Linkage between two genes affect Inheritance of Characters?

Morgan's Experiment on Flies



Wild type
(gray body,
normal wings)

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



Double mutant
(black body,
vestigial wings)

$b b vg vg$

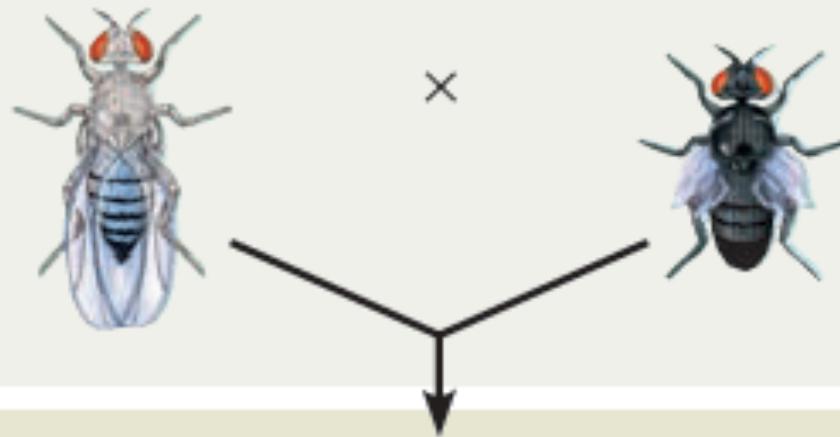
How does linkage between two genes affect inheritance of characters?

P Generation

(homozygous)

Wild type
(gray body,
normal wings)

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



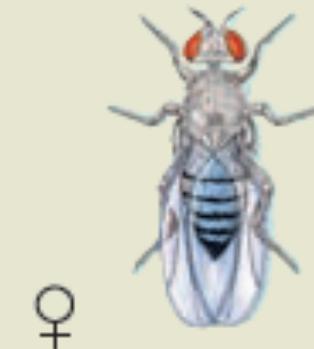
Double mutant
(black body,
vestigial wings)

$b b vg vg$

F₁ dihybrid testcross

Wild-type F₁ dihybrid
(gray body, normal wings)

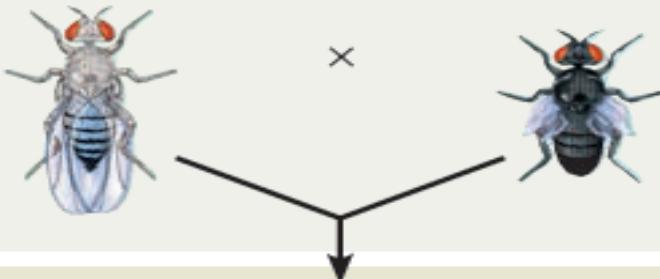
$b^+ b vg^+ vg$



How does linkage between two genes affect inheritance of characters? – TEST CROSS

P Generation (homozygous)

Wild type
(gray body,
normal wings)
 $b^+ b^+ vg^+ vg^+$

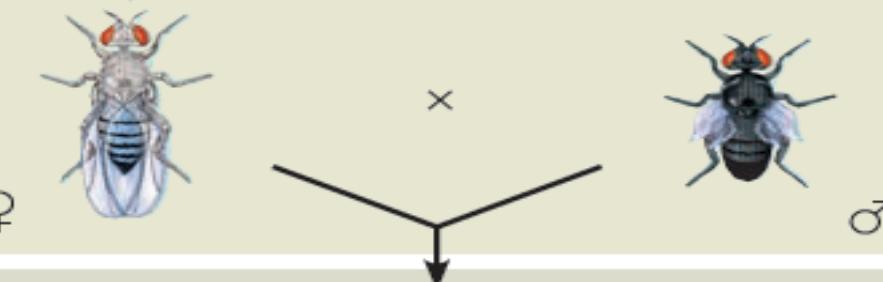


Double mutant
(black body,
vestigial wings)
 $b b vg vg$

F₁ dihybrid testcross

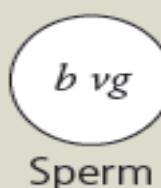
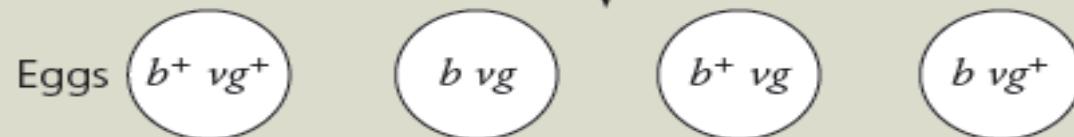
Wild-type F₁ dihybrid
(gray body, normal wings)

$b^+ b vg^+ vg$



Homozygous
recessive (black
body, vestigial
wings)
 $b b vg vg$

Testcross offspring



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

How does linkage between two genes affect inheritance of characters?

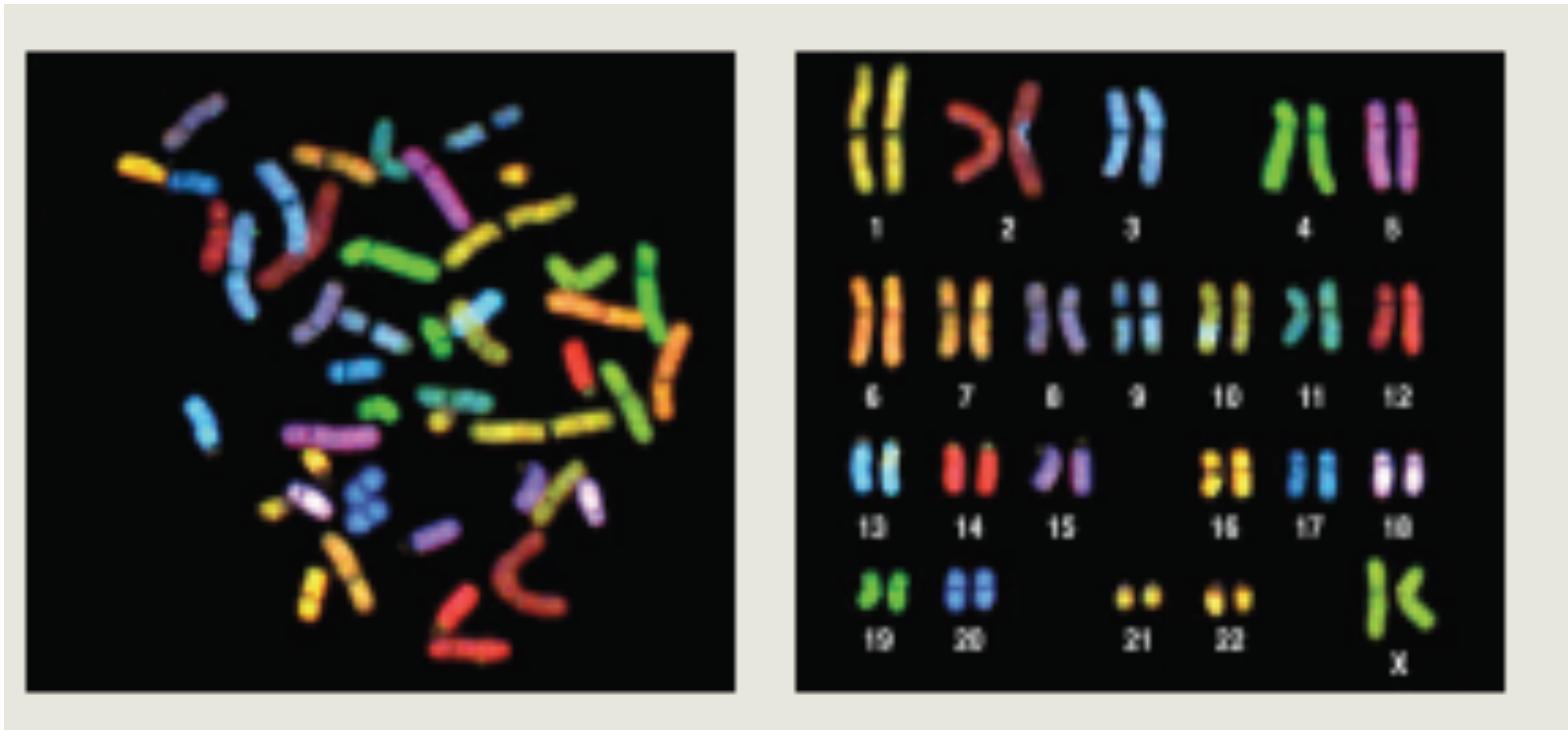
- Since **most offspring had a parental phenotype**, Morgan concluded that genes for body color & wing size are genetically linked on same chromosome.
- However, the production of a **relatively small number of offspring with non-parental phenotypes** indicated that *some mechanism occasionally breaks the linkage* between specific alleles of genes on the same chromosome.

Alterations of chromosome number or structure cause some genetic disorders

Physical and chemical disturbances, as well as errors during meiosis, can damage chromosomes

Eukaryotic Genomes are Organized into Chromosomes

- Humans have 23 pairs of chromosomes: 22 pairs of autosomes and one pair of sex chromosomes (X and Y)
- Image below shows a spread of human chromosomes, each ‘painted’ with a different color; on the right these are organized into a karyotype



45

Alterations of Chromosome Structure

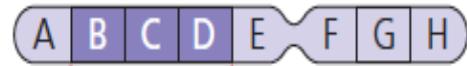
DELETION



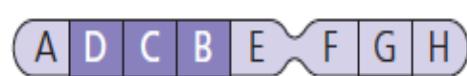
A **deletion** removes a chromosomal segment.



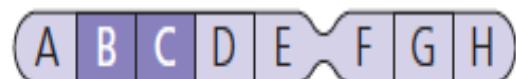
INVERSION



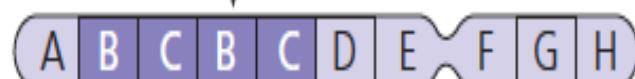
An **inversion** reverses a segment within a chromosome.



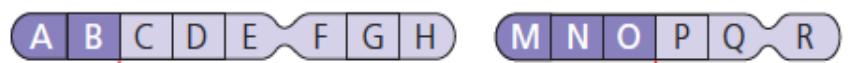
DUPLICATION



A **duplication** repeats a segment.



TRANSLOCATION



A **translocation** moves a segment from one chromosome to a nonhomologous chromosome. In a reciprocal translocation, the most common type, nonhomologous chromosomes exchange fragments.



Less often, a nonreciprocal translocation occurs: A chromosome transfers a fragment but receives none in return (not shown).

Figure 15.14

Aneuploidy: Abnormalities in Chromosome Number



Down's Syndrome:
Trisomy 21



Edwards Syndrome:
Trisomy 18

Down's syndrome is usually the result of an extra chromosome 21, so that each body cell has a total of 47 chromosomes. Cells are trisomic for chromosome 21, Down syndrome is often called *trisomy 21*



Patau syndrome:
Trisomy 13



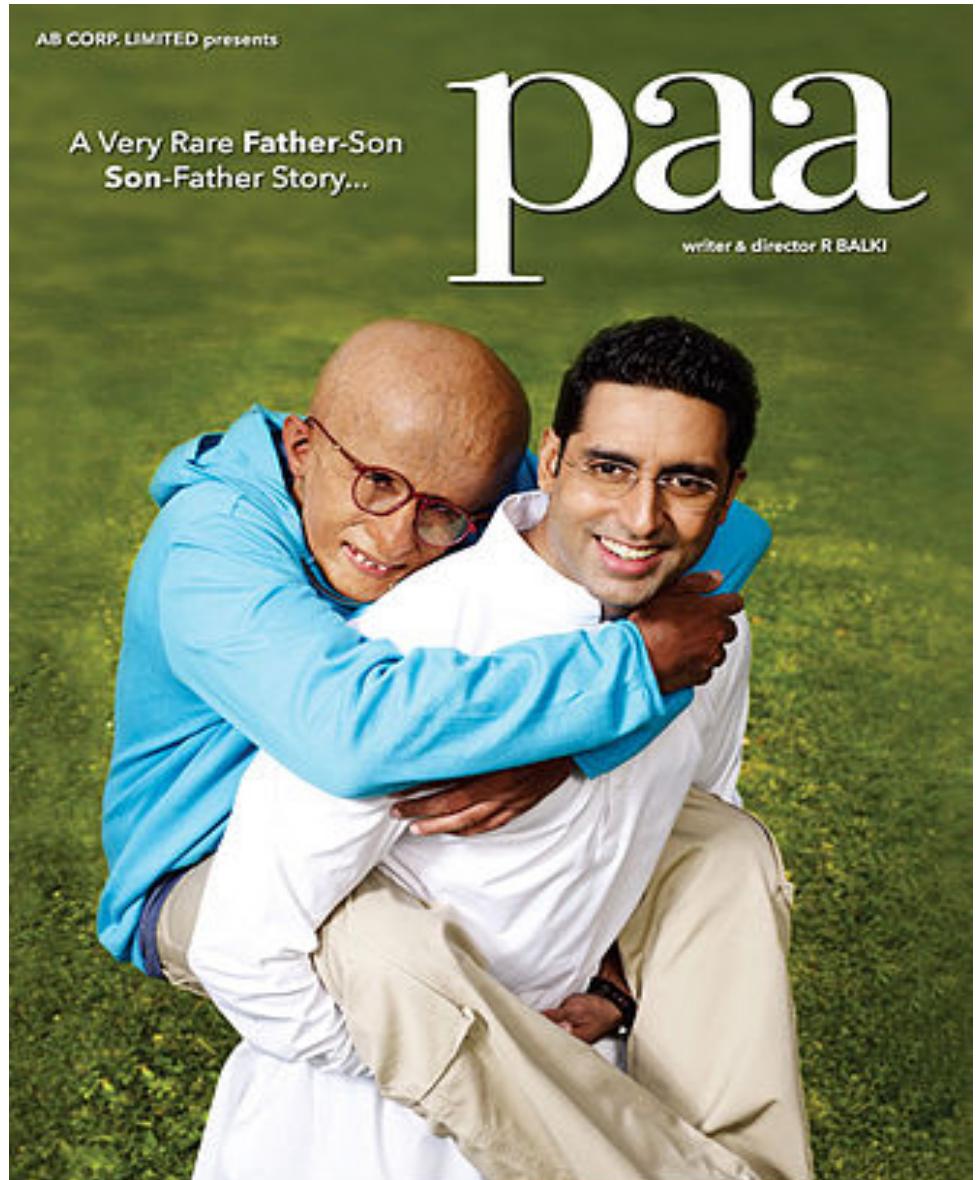
Turners Syndrome: Absence of one or both copies of X chromosome

Figure 15.15

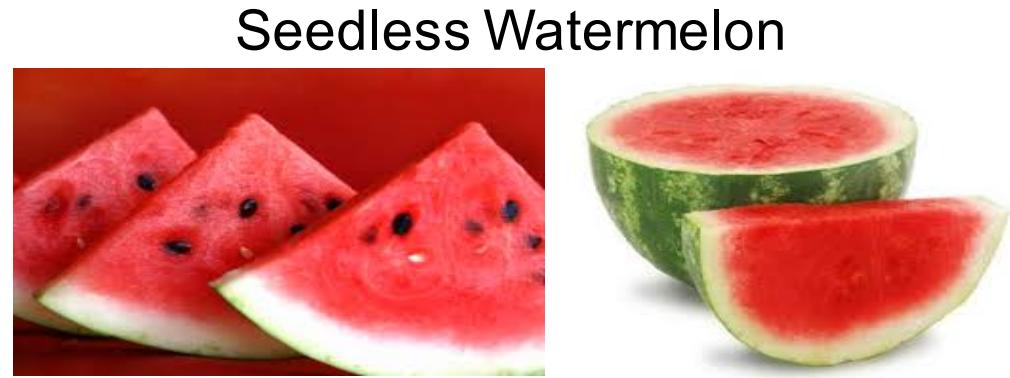
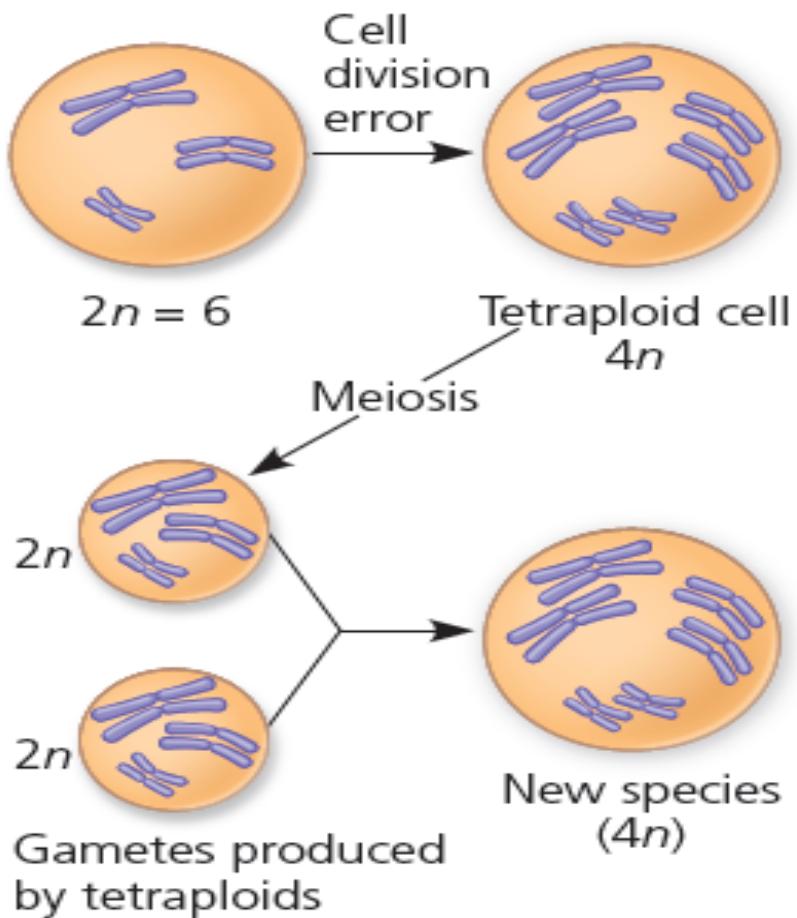
47

Food for thought: Genetic Tests

- Progeria or ***Hutchinson-Gilford Progeria Syndrome:***
- Gene responsible for HGPS is called LMNA (or Lamin A). There is a genetic test to identify it.



Polyplody: Complete set of Chromosomes in Multiple Number ($2n$, $4n$, $6n$ etc.)



Wheat variety giving more yield



- In general, polyploids are nearly normal in appearance than aneuploids
- One extra (or missing) chromosome disrupts genetic balance more than does an entire extra set of chromosomes

Figure 24.9

49

- Genetics and Probability ✓
- Chromosomal basis of Inheritance ✓
- Molecular basis of Inheritance



Molecular basis of Inheritance

Can a genetic trait be transferred between different bacterial strains?

*Two strains of the bacterium **Streptococcus pneumoniae***

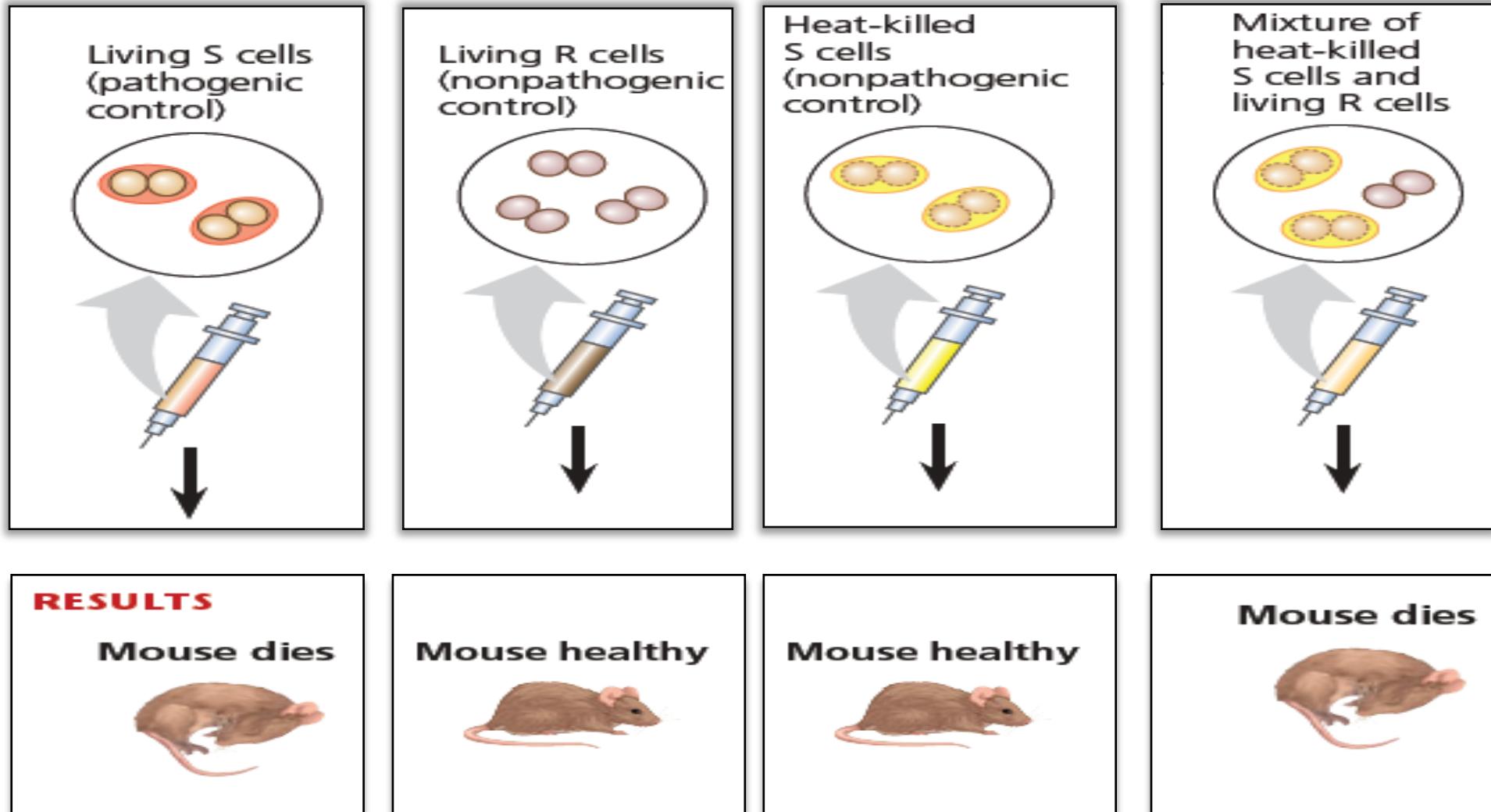
S strain (Smooth strain - presence of a capsule) causing pneumonia

R strain (Rough strain - absence of a capsule) not causing pneumonia

Transformation - change in genotype and phenotype due to the assimilation of external DNA by a cell

Griffith's Experiment (1928)

The 'Transforming principle/factor'



The living R bacteria was transformed into pathogenic S bacteria by a **heritable substance from dead S cells that enabled R cells to make capsules**

Figure 16.2

Summary

- Probability rules govern Mendelian inheritance and it could be used to solve the complex genetics problems
- Chromosomal basis of inheritance: classical genetics experiments

References

- Campbell Biology - Reece, Urry, Cain, Wasserman, Minorsky, Jackson 10th Edition, Cummings
- *Video contents*

- <https://www.youtube.com/watch?v=bmQwMlhCUM>
- <https://www.youtube.com/watch?v=H1HaR47Dqfw>



Next Lecture
DNA Tools and Biotechnology