

# Bioscience & Bioengineering 101: BB101

How did we get from Mendel's traits and alleles to DNA?

*Chromosomal basis of Inheritance*

## Lecture – 4

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BSBE, IIT Bombay



Like the one ring of power in Tolkien's "Lord of the Rings," **deoxyribonucleic acid (DNA)** is the master molecule of every cell. <https://science.howstuffworks.com/life/cellular-microscopic/dna.htm>

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# Outline

- Mendelian Genetics: Examples & Deviation (from previous lecture)
  - Pleiotropy; Sickle-cell disease (an illustration)
- Chromosomal basis of Inheritance
  - Morgan's Experiment: Genes association with specific chromosome
  - Sex-linked Inheritance
  - Genetic Recombination and Linkage
- Molecular basis of Inheritance
  - Griffith, Hershey and Chase; Meselson and Stahl experiments

- Mendelian Genetics Examples ✓
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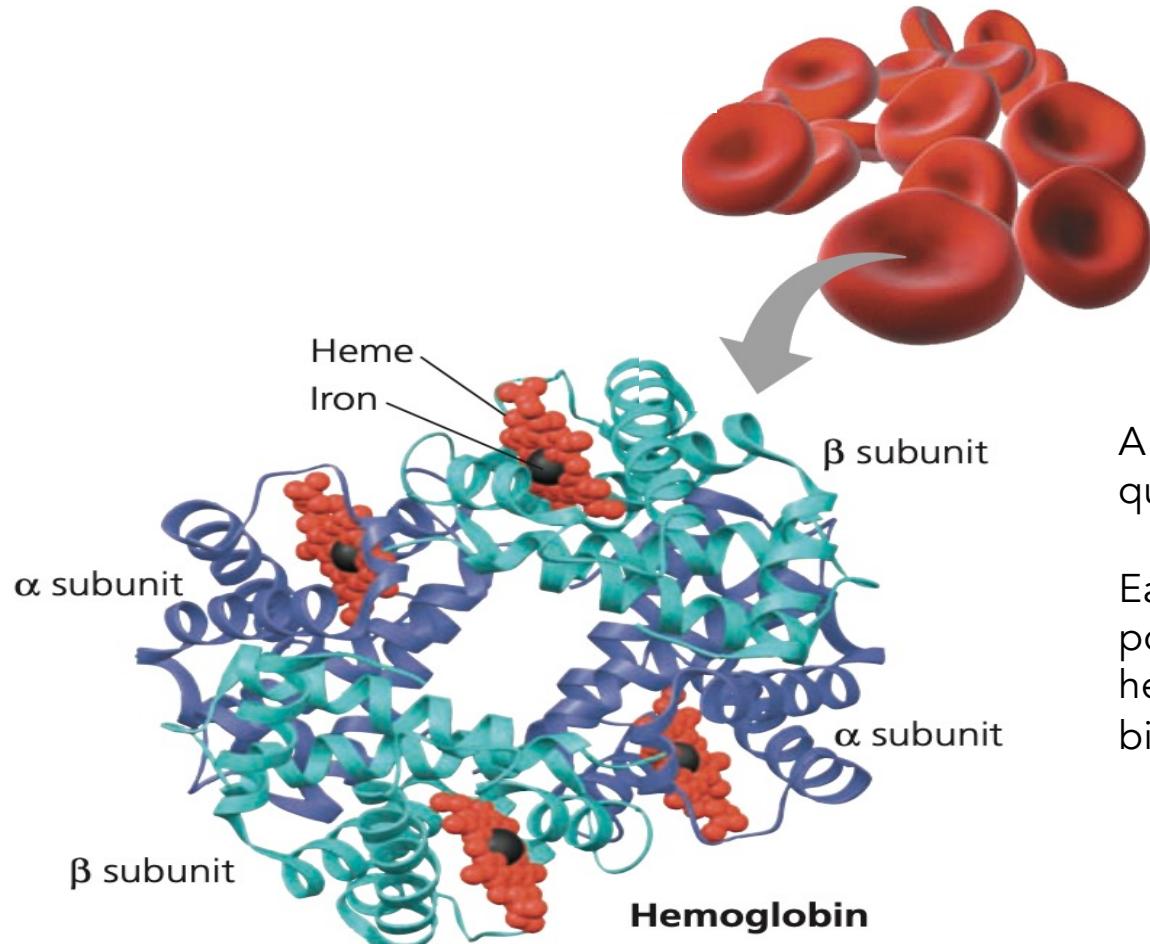
# Pleiotropy

*Mendelian inheritance relied on fact that each gene affects only one phenotypic character.. Is this always true?*

# Pleiotropy

- Pleiotropy describes multiple phenotypic effects from same gene
- Examples - Sickle-cell disease, Cystic fibrosis
- The pleiotropic alleles are responsible for the multiple symptoms associated with these hereditary diseases

# Hemoglobin



A globular protein with quaternary structure

Each subunit has a non-polypeptide component, called heme, with an iron atom that binds oxygen

## Sickle-Cell Disease: How is it Caused?

- The  $\beta$ -chain of haemoglobin (HbA) and sickle-cell anemia (HbS) differ at amino acid residue 6.



HbA  $\beta$ -chain: Val—His—Leu—Thr—Pro—*Glu*—Glu—Lys



HbS  $\beta$ -chain: Val—His—Leu—Thr—Pro—*Val*—Glu—Lys.

- Caused by the substitution of a single amino acid in hemoglobin protein
- Mutation causes red blood cells to develop a crescent or “sickle” shape
- Sickled RBCs restrict the flow in blood vessels and limit oxygen delivery to the body’s tissues, leading to severe pain and organ damage known as *vaso-occlusive crises*

# A single amino acid substitution in a protein causes sickle-cell disease

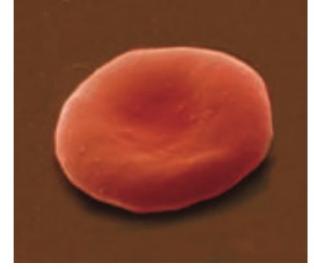
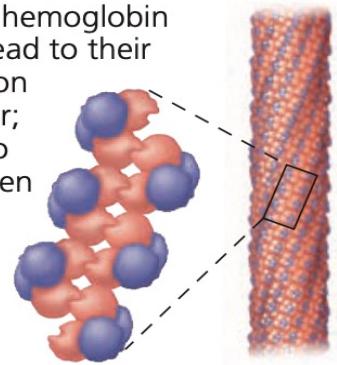
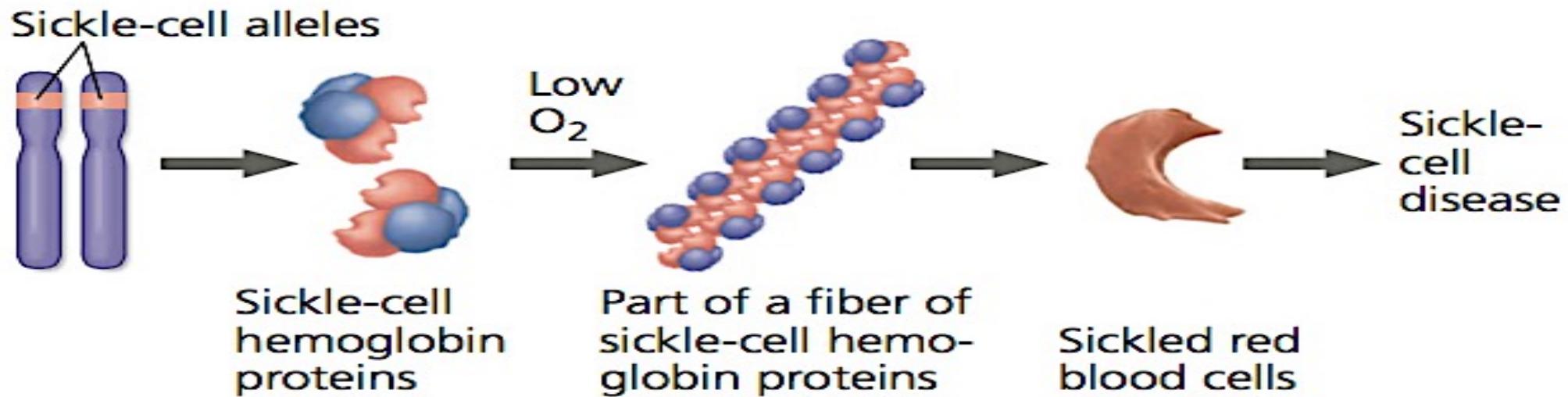
	Primary Structure	Secondary and Tertiary Structures	Quaternary Structure	Function	Red Blood Cell Shape
Normal hemoglobin	1 Val 2 His 3 Leu 4 Thr 5 Pro 6 Glu 7 Glu	Normal $\beta$ subunit	Normal hemoglobin $\beta$ $\alpha$	Normal hemoglobin proteins do not associate with one another; each carries oxygen.	Normal red blood cells are full of individual hemoglobin proteins.  5 $\mu\text{m}$
Sickle-cell hemoglobin	1 Val 2 His 3 Leu 4 Thr 5 Pro <b>6 Val</b> 7 Glu	Sickle-cell $\beta$ subunit	Sickle-cell hemoglobin $\beta$ $\alpha$	Hydrophobic interactions between sickle-cell hemoglobin proteins lead to their aggregation into a fiber; capacity to carry oxygen is greatly reduced. 	Fibers of abnormal hemoglobin deform red blood cell into sickle shape.  5 $\mu\text{m}$

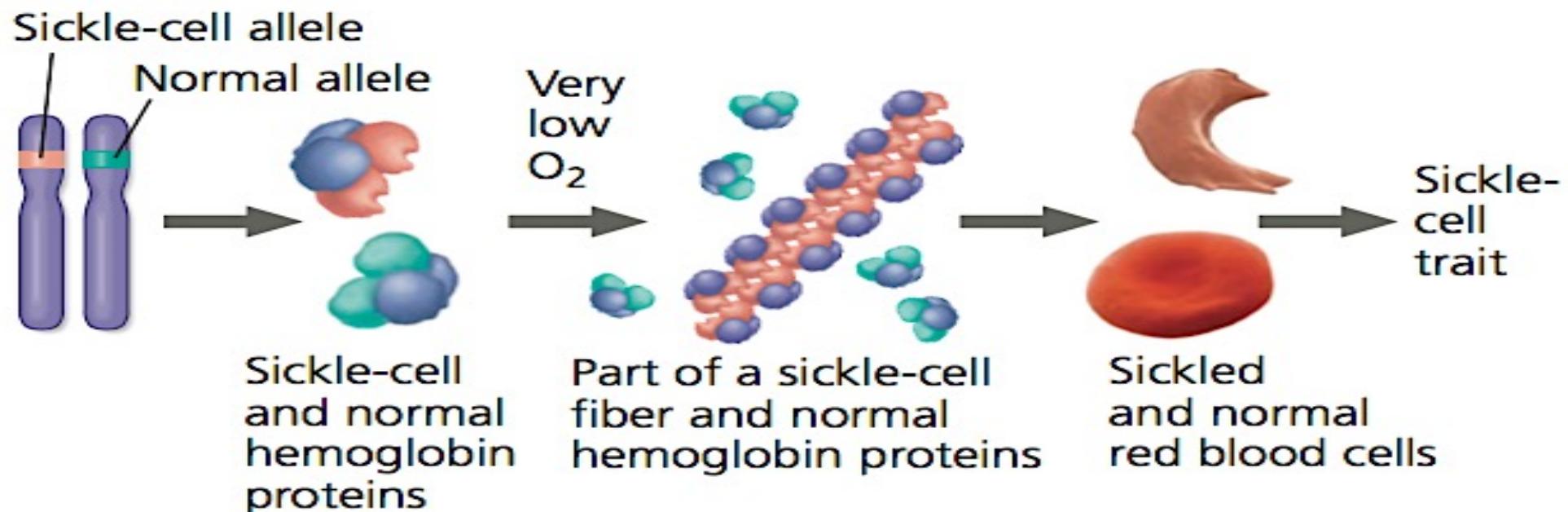
Figure 5.19

## Sickle-Cell Disease (homozygous condition)



In homozygous all hemoglobin is sickle-cell (abnormal):  
weakness, anemia, pain & fever

# Sickle-Cell Disease (heterozygous condition)



Heterozygote with sickle-cell trait: Some symptoms when blood oxygen is very low

Figure 14.17

# Sickle-Cell Disease: A Genetic Disorder with Evolutionary Implications

**Why sickle-cell allele confers an advantage to heterozygotes in Africa?**



*Sickled red blood cell*

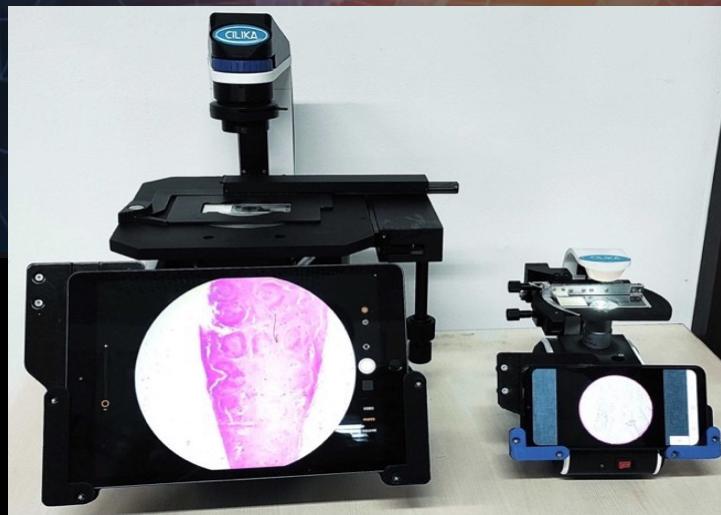


*Normal red blood cell*

- A single copy of the sickle-cell allele reduces the frequency and severity of malaria attacks
- Malaria parasite spends part of its life cycle in RBC and presence of heterozygous sickle-cell hemoglobin results in lower parasite densities & hence reduced malaria

# Prof. Debjani Paul licences her Sickle Cell Diagnosis technology

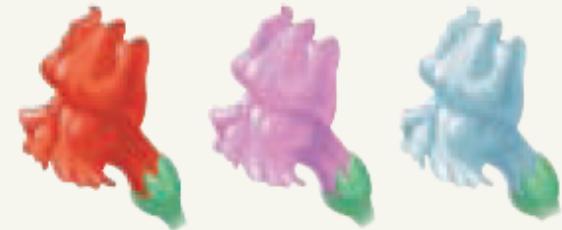
May 3, 2023



# Mendelian Genetics for a Single Gene

Relationship among alleles of a single gene	Description	Example
<b>Complete dominance of one allele</b>	Heterozygous phenotype same as that of homozygous dominant	$PP$  $Pp$ 
<b>Codominance</b>	Both phenotypes expressed in heterozygotes	$I^A I^B$ 
<b>Multiple alleles</b>	In the population, some genes have more than two alleles	ABO blood group alleles $I^A, I^B, i$

## Mendelian Genetics for a Single Gene (2)

Relationship among alleles of a single gene	Description	Example
<b>Incomplete dominance of either allele</b>	Heterozygous phenotype intermediate between the two homozygous phenotypes	 $C^R C^R$ $C^R C^W$ $C^W C^W$
<b>Pleiotropy</b>	One gene affects multiple phenotypic characters	Sickle-cell disease

- Mendelian Genetics Examples ✓
- Pleiotropy; Sickle-cell disease (an illustration) ✓
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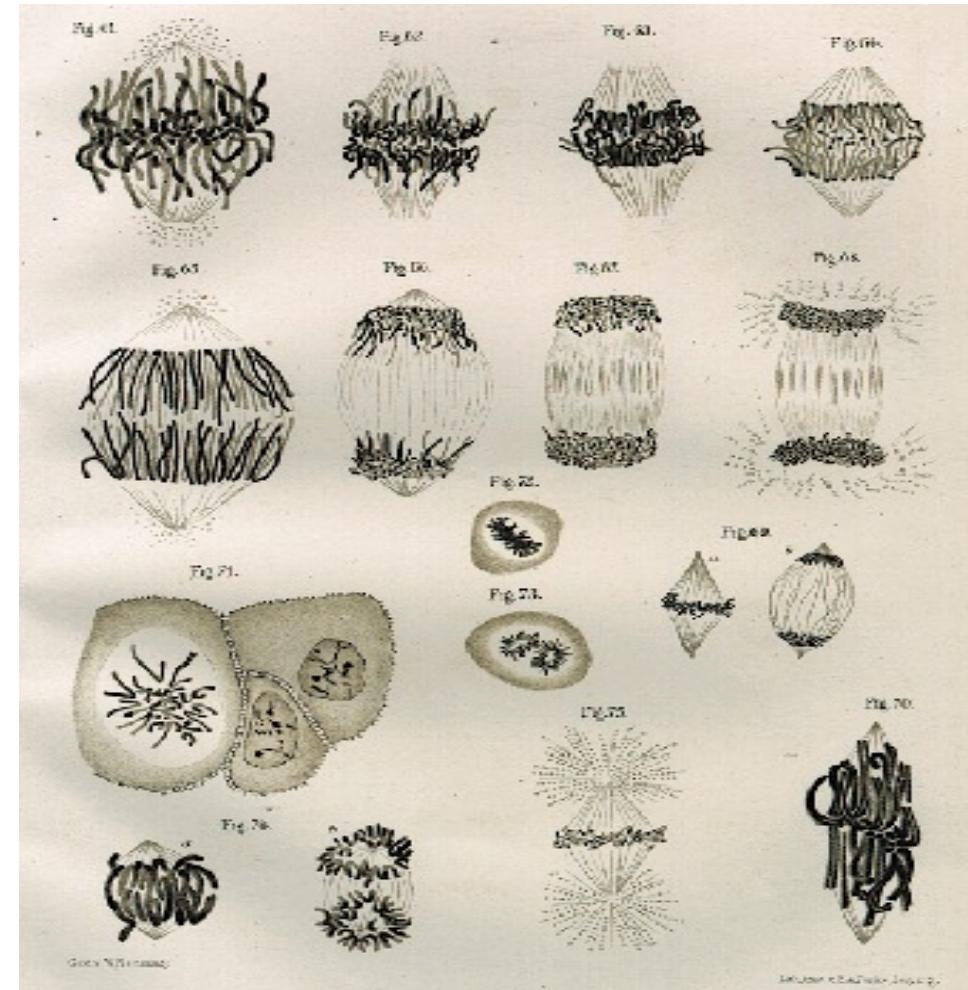
## Chromosomal basis of Inheritance

# Mendel's results were explained when chromosomes were discovered

- Around 20 years after Mendel's experiments, Walther **Flemming** used stains to visualize cells and found strands of material that could be stained (called "**chromatin**").
- These turned out to be *chromosomes* and they were the '*units*' that Mendel had predicted. Pea plants have 2 copies of each chromosome.
- Yes, he drew gorgeous pictures of his microscopy studies.

Drawing of mitosis by Walther Flemming.

Flemming, W. Zellsubstanz, Kern und Zelltheilung (F. C. W. Vogel, Leipzig, 1882).



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Mendelian Inheritance has its Physical Basis in Behavior of Chromosomes

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



Thomas Hunt Morgan  
Columbia University



# Cross of Fruit Fly

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

Wild-type  $w^+$   
Red



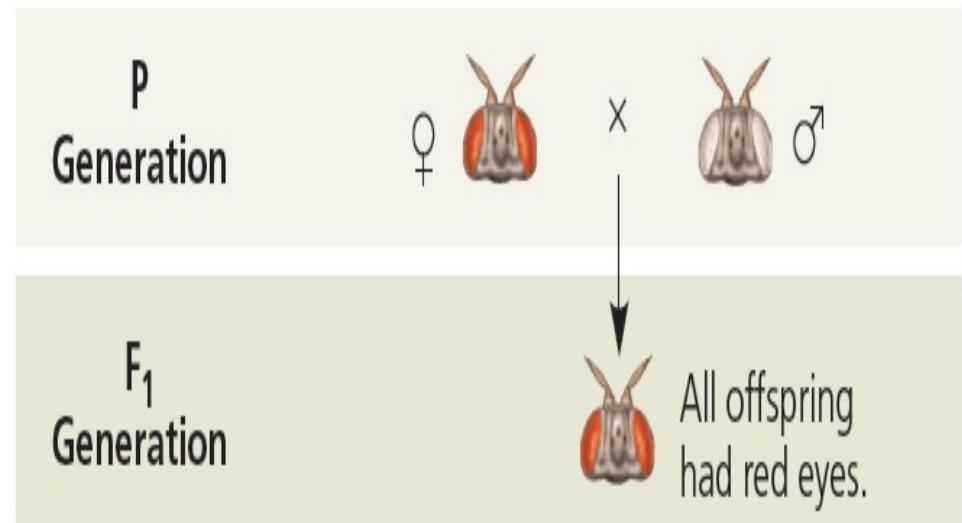
$X^{w+} \times X^{w+}$

Mutant  $w$   
White

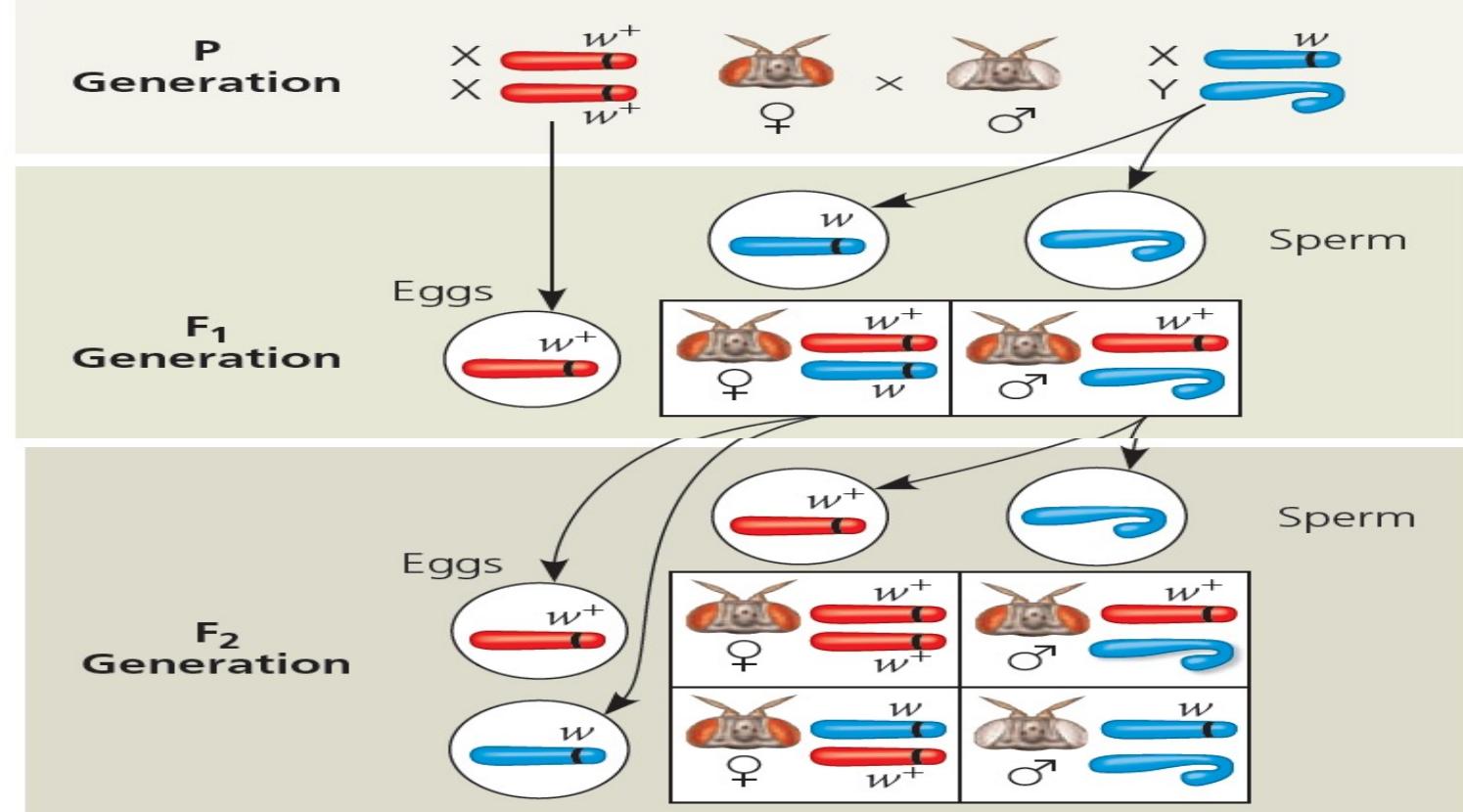


$X^w \times Y$

Wild-type (red-eyed) female mating  
with mutant (white-eyed) male



# Morgan Supported Chromosome Theory of Inheritance



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

- Mendelian Genetics Examples ✓
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- **Sex-linked Inheritance**
- Genetic Recombination and Linkage
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## 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

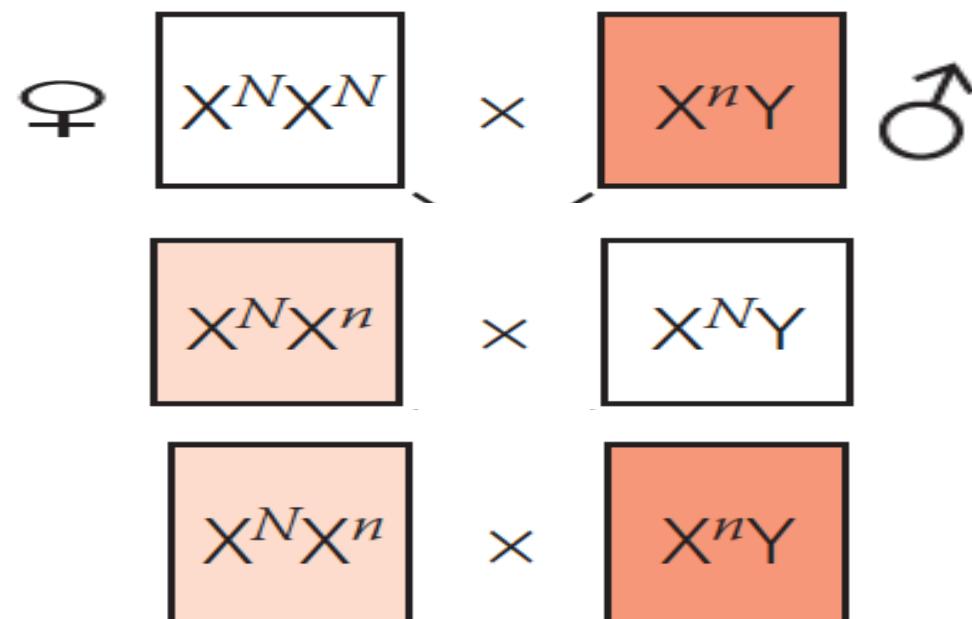
# Red-green Color Blindness: X-linked Disorder

$N$  = dominant allele for normal color vision

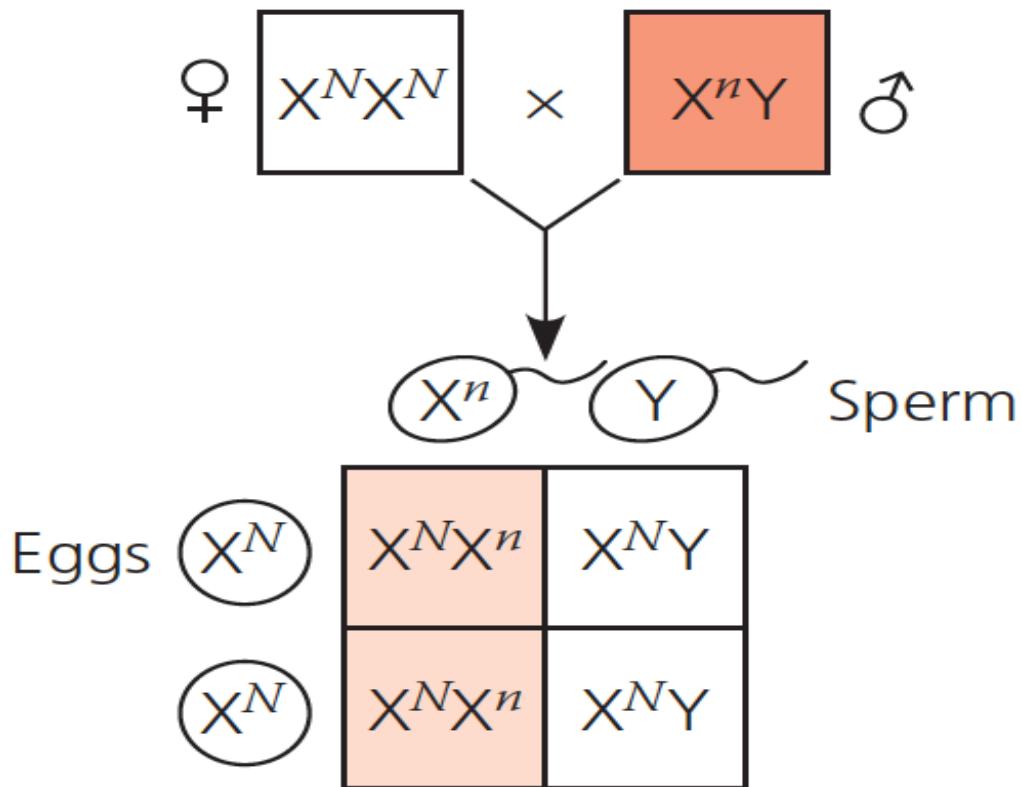
(carried on X chromosome)

$n$  = recessive allele having a mutation for color blindness

- Unaffected individuals
- Carriers
- Color-blind individuals

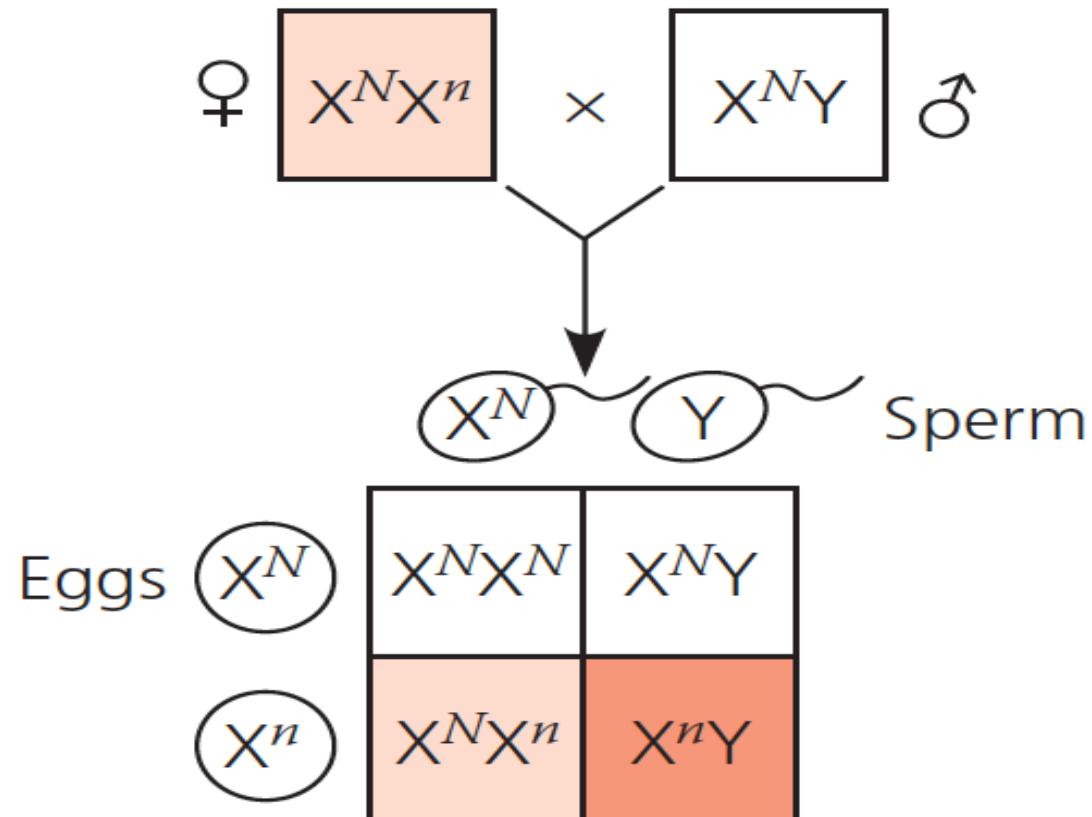


# Red-green Color Blindness: X-linked Disorder



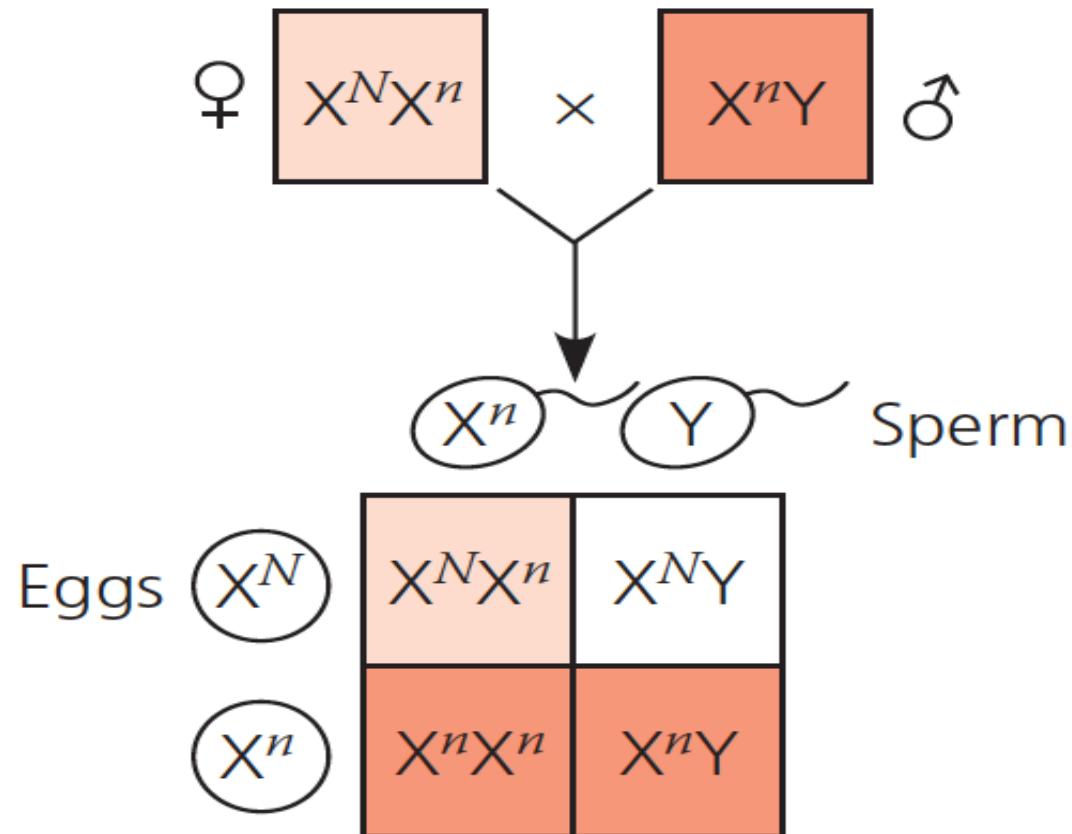
- A color-blind father will transmit mutant allele to all daughters

# Red-green Color Blindness: X-linked Disorder



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

# Red-green Color Blindness: X-linked Disorder



- 50% chance, each child will have disorder; Daughters having normal color vision will be carriers.

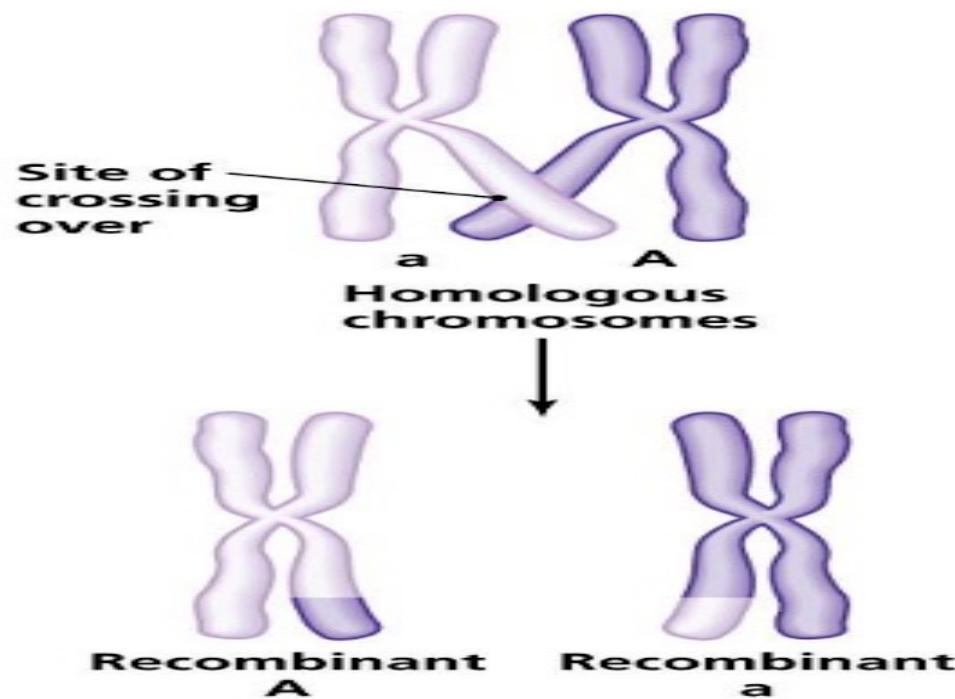
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# Genetic Recombination and Linkage

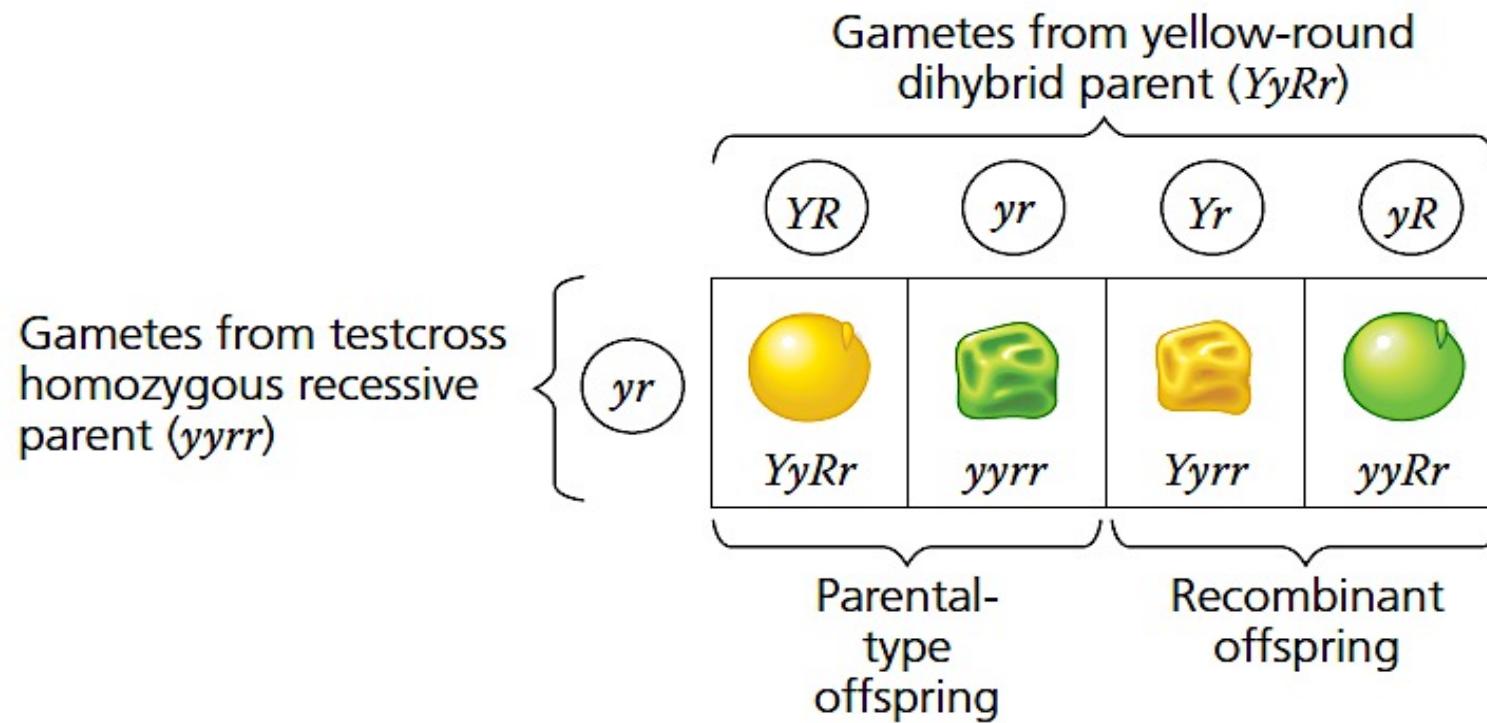
*The production of offspring with combinations of traits that differ from those found in either P generation parent*

# 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.

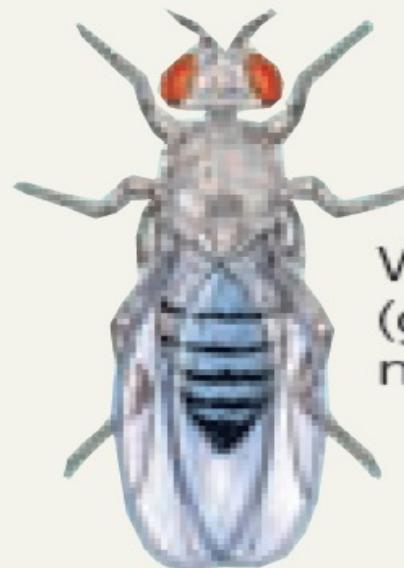


# Recombination of Unlinked Genes: *Independent Assortment of Chromosomes*



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

# How does Linkage between two genes affect Inheritance of Characters? Morgan's Fly Experiments



Wild type  
(gray body,  
normal wings)

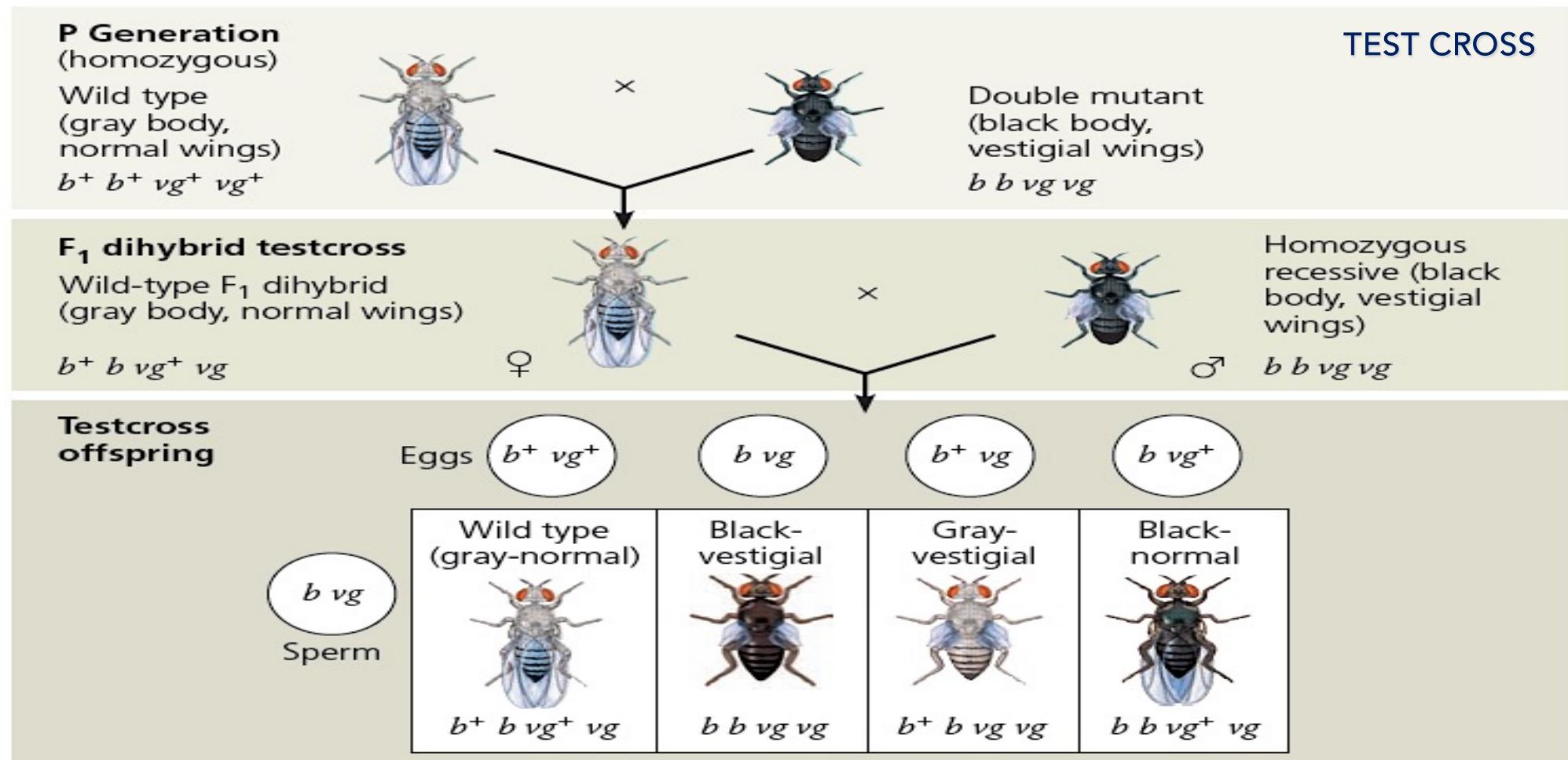
$b^+ b^+ vg^+ vg^+$

Double mutant  
(black body,  
vestigial wings)



$b b vg vg$

# How does Linkage between 2 genes affect Inheritance of characters?

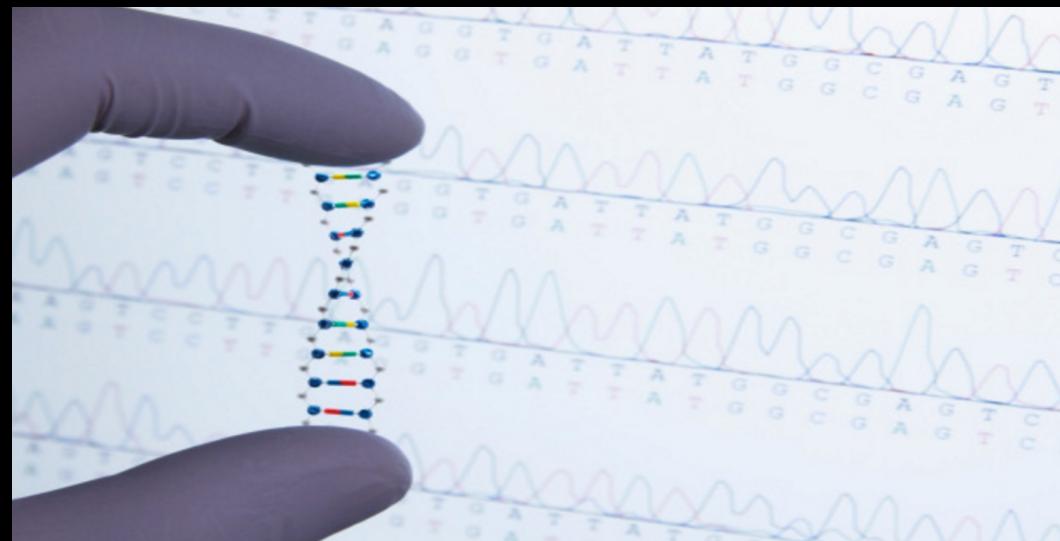


# How does Linkage between 2 genes affect Inheritance of characters?

- 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.

# Challenges & Advances in Healthcare Technology

Dr Suvin Shetty MD  
Laboratory Director  
Dr L H Hiranandani Hospital

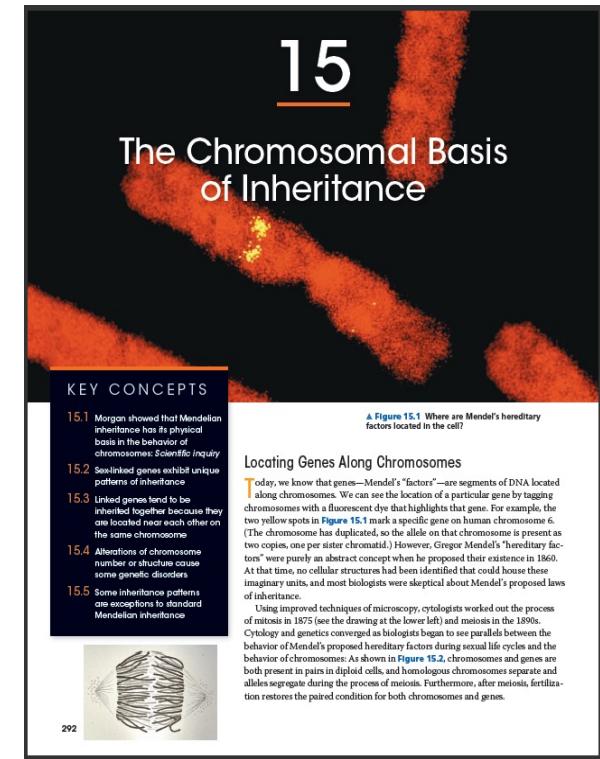


# Summary

- Morgan's Experiment: The lecture covered Morgan's experiment on fruit flies, which provided crucial insights into the principles of inheritance, especially regarding sex-linked traits.
- Sex-Linked Inheritance: The concept of sex-linked inheritance was discussed. This involves the inheritance patterns of genes located on the sex chromosomes (X and Y) and how they are passed down from one generation to the next.
- Genetic Recombination and Linkage: The lecture delved into the processes of genetic recombination and linkage. These phenomena are essential for understanding how genes are inherited, especially when they are located on the same chromosome.
- In the next class, further details about the molecular basis of inheritance would be explored, specifically discussing the experiments conducted by Griffith, Hershey & Chase, and Meselson & Stahl. These experiments are pivotal in understanding the molecular mechanisms underlying genetic inheritance.

# References

- Campbell Biology - Reece, Urry, Cain, Wasserman, Minorsky, Jackson 10th Edition, Cummings
- Acknowledgment
  - Cover images – getty images



## Next Lecture...

*Molecular basis of inheritance & Flow of information*