KARPAGAM ACADEMY OF HIGHER EDUCATION

Class: II M.Sc Microbiology **COURSE NAME: Inheritance Biology**

Subject **code: 17MBU504B** **BATCH – 2017-2020**

LECTURE PLAN

Semester – V

17MBU504B **INHERITANCE BIOLOGY** **(3H – 3C)**

Instruction Hours / week: L: 3 T: 0 P: 0 **Marks:** Internal: **40** External: **60** Total: **100**
End Semester Exam: 3 Hours

SCOPE

This paper imparts knowledge on the different aspects of genetics and pedigree analysis.

OBJECTIVE

- To make students understand the principles of Genetics and inheritance biology.

Unit I

Historical developments: Model organisms in genetic analyses and experimentation: *Escherichia coli*, *Saccharomyces cerevisiae*, *Neurospora crassa*, *Caenorhabditis elegans Drosophila melanogaster*, *Arabidopsis thaliana.*

Unit II

Mendel's Laws: Dominance, segregation, independent assortment, deviation from Mendelian inheritance, Rediscovery of Mendel's principles, Chromosome theory of inheritance: Allele, multiple alleles, pseudoallele, complementation tests, Extensions of Mendelian genetics: Allelic interactions, concept of dominance, recessiveness, Incomplete dominance and co-dominance, Multiple alleles, Epistasis, penetrance and expressivity.

Unit III

Linkage and recombination of genes, Cytological basis of crossing over, Crossing over at four-strand stage, Molecular mechanism of crossing over, mapping Homologous and non-homologous recombination, including transposition, site-specific recombination.

Unit IV

Rules of extra nuclear inheritance, Organelle heredity - Chloroplast mutations in *Chlamydomonas*, mitochondrial, mutations in *Saccharomyces*, Maternal effects – Shell coiling in *Limnaea peregra* Infectious heredity - Kappa particles in *Paramecium.* Pedigree analysis, lod score for linkage testing, karyotypes, genetic disorders. Polygenic inheritance, heritability and its measurements, QTL mapping.

Unit V

Structural organization of chromosomes - centromeres, telomeres and repetitive DNA, Packaging DNA molecules into chromosomes, Concept of euchromatin and heterochromatin, Normal and abnormal karyotypes of human chromosomes, Chromosome banding, Giant chromosomes: Polytene and lampbrush chromosomes, Variations in chromosome structure: Deletion, duplication, inversion and translocation, Variation in chromosomal number and structural abnormalities -

Klinefelter syndrome, Turner syndrome, Down syndrome

SUGGESTED READINGS

1. Gardner EJ, Simmons MJ, Snustad DP (2008). Principles of Genetics. 8th Ed. Wiley-India.
2. Snustad DP, Simmons MJ (2011). Principles of Genetics. 6th Ed. John Wiley and Sons Inc.
3. Weaver RF, Hedrick PW (1997). Genetics. 3rd Ed. McGraw-Hill Education.
4. Klug WS, Cummings MR, Spencer CA, Palladino M (2012). Concepts of Genetics. 10th Ed. Benjamin Cummings.
5. Griffith AJF, Wessler SR, Lewontin RC, Carroll SB. (2007). Introduction to Genetic Analysis. 9th Ed. W.H.Freeman and Co., New York.
6. Hartl DL, Jones EW (2009). Genetics: Analysis of Genes and Genomes. 7th Ed, Jones and Bartlett Publishers.
7. Russell PJ. (2009). *i* Genetics - A Molecular Approach. 3rd Ed, Benjamin Cummings.

LECTURE PLAN

UNIT I

UNIT I S. No	Duration	Topic	Reference
1	1	Inheritance Biology-Introduction	W1, W1a, T1
2	1	Inheritance Biology Introduction	W1, W1a, T1
3	1	Model organism – E. coli	W2
4	I	Model organism of E. coli	W2
5	1	Model organism of s. cervisiae	W3
6	1	Model organism of Neurospora	W7
7	1	Model organism of C. elecans	W4
8	1	Model organism of Drosophila	W5
9	1	Model organism of Arabidopsis thaliana	W6
10	1	Unit revision	
Total Hrs: 10			

References:

T1. Gardner EJ, Simmons MJ, Snustad (2008). Principles of genetics. 8th Ed. Wiley,-India.
W1. www.yourgenome.org
W1a.Basic biology.net
W2.www.interchopen.com, www.study.com/accademy/
W3. Ncbi.nlm.nih.gov, https://onlinelibraty.wiely.com
W4. Yourgenome.org., www.socmucimm.org.
W5. Modencode.sciencemag.org, www.news-madeical.net
W6.nsf.gov, www.arabidopsis.org.
W7.www.en.m.wikpedia.org, www.fgsc.net.

KARPAGAM ACADEMY OF HIGHER EDUCATION

Class: III B.Sc Microbiology **COURSE NAME: Inheritance Biology**

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LECTURE PLAN

UNIT II

UNIT I S. No	**Duration**	**Topic**	**Reference**
1	1	Mendels laws	W1
2	1	Dominance, segregation, independent assortment, and mendelian inheritance	W2-4
3	1	Rediscovery of mendels principle	W5
4	1	Chromosome theory of inheritance	W6
5	1	Allele, multiple alles, Pseudoalle	W7
6	1	Complementation test	W7
7	1	Extension of Mendelian genetics-allele interaction	W7
8	1	Concept of dominance recessiveness, dominance and codominance	W1-4
9	1	Multiple alles, epistasis	W1-4
10		Penetrance and expressivity	W8
11		Unit revision	
Total Hrs: 11			

W1. www.byjus.com/
W2. www.khanacademy.org.
W3. WWW.thoughco.com,
W4. www.nature.com
W5. www.genome.gov
W6. https:en.wikipedia.org
W7.www.genetic.org
W8. WWW.nature.com, www.couses.lumenlearing.com/wm-biology1/

KARPAGAM ACADEMY OF HIGHER EDUCATION

Class: III B.Sc Microbiology **COURSE NAME: Inheritance Biology**

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LECTURE PLAN

UNIT III

UNIT I S. No	**Duration**	**Topic**	**Reference**
1	1	Linkage and recombination of genes	
2	1	Cytological basis of crossing over	
3	1	Crossing over at four stand stage	
4	1	Molecular mechanism of crossing over	
5	1	Mappling homologus	
7	1	Non-homologus recombination	
8	1	Including transposition, side specific recombination	
9	1	Unit revision	
Total Hrs: 9			

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LECTURE PLAN

UNIT IV

UNIT I S. No	Duration	Topic	Reference
1	1	Rule of extra nuclear inheritance	
2	1	Organelle herdidty	
3	1	Chloroplast mutation is chlamydononas	
4	I	Mitochondiral, mutation in saccharomyces	
5	1	Meternal effect	
6	1	Shell coiling in Limnaeo perega infections	
7	1	Heridity-kappa particles in paramecium	
8	1	Pedigree analysis.. lod score for linkage testing	
9	1	Karyotypes, genetic disorders	
10	1	Polygenic inheritance, heritability and its measurements	
11	1	QTL mapping	
12	1	Unit revision	
Total Hrs: 12			

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LECTURE PLAN

UNIT I S. No	**Duration**	**Topic**	**Reference**
1	1	Structural organization of chromosomes- entromere, telomeres	
2	1	Repetitive DNA, packing DNA molecules into chromosomes	
3	1	Concept of euchromatin and heterochromatin	
4	I	Normal and abnormal karyotypesin human chromosomes	
5	1	Chromosome banding	
6	1	Giant chromosomes	
7	1	Polytene and lampbrush chromosomes	
8	1	Variations in chromosome structure-deletion. Duplication, inversion	
9	1	Translocation, variation in chromosomal number	
10	1	Structural abnormalties- klienfelters syndrome	
11	1	Turner syndrome, down syndrome	
12	1	Unit revision	
Total Hrs: 9			

UNIT V

Unit 1

The evolution of present-day cells from a common ancestor has important implications for cell and molecular biology as an experimental science. Because the fundamental properties of all cells have been conserved during evolution, the basic principles learned from experiments performed with one type of cell are generally applicable to other cells. On the other hand, because of the diversity of present-day cells, many kinds of experiments can be more readily undertaken with one type of cell than with another. Model organisms have always been at the forefront of genetics. The initial choice of an organism for research is based on some feature of that organism that lends itself particularly well to the study of a genetic process that the researcher is interested.

Model Organism of E. coli:

Model Organism of E. coli is comparative simplicity, prokaryotic cells (bacteria) are ideal models for studying many fundamental aspects of biochemistry and molecular biology. The most thoroughly studied species of bacteria is *E. coli*, which has long been the favored organism for investigation of the basic mechanisms of molecular genetics. *E. coli* has been especially useful to molecular biologists because of both its relative simplicity and the ease with which it can be propagated and studied in the laboratory. The genome of *E. coli*, for example, consists of approximately 4.6 million base pairs and encodes about 4000 different proteins. Important findings and Nobel Prizes in biology have been developed in *E. coli*. For instance, cracking the genetic code, unveiling the nature of DNA replication, the groundbreaking advances on gene organization and regulation or as we love to call 'the operon', important evidence for the basis of mutations and ultimately to the evolution of organisms, and finally, the achievement of a genetically modified organism that skyrocketed several applications of the enormous capacity for manipulating this organism, rendering *E. coli* as a key player in biotechnology.

Type and morphology

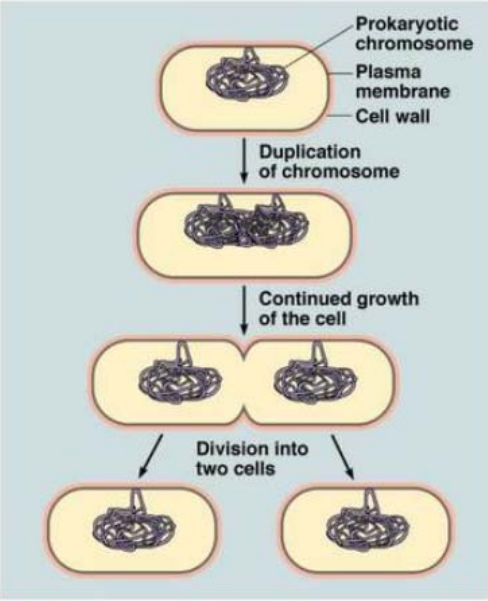
E. coli is a Gram-negative, facultative anaerobe (that makes ATP by aerobic respiration if oxygen is present, but is capable of switching to fermentation or anaerobic respiration if oxygen is absent) and nonsporulating bacterium. Cells are typically rod-shaped, and are about 2.0 μmlong and 0.25–1.0 μm in diameter, with a cell volume of 0.6–0.7 μm.

E. coli stains Gram-negative because its cell wall is composed of a thin peptidoglycan layer and an outer membrane. During the staining process, *E. coli* picks up the color of the counterstain safranin and stains pink. The outer membrane surrounding the cell wall provides a barrier to certain antibiotics such that *E. coli* is not damaged by penicillin.

Strains that possess flagella are motile. The flagella have a peritrichous arrangement. It also attaches and effaces to the microvilli of the intestines via an adhesion molecule known as intimin.

Cell cycle

The bacterial cell cycle is divided into three stages. The B period occurs between the completion of cell division and the beginning of DNA replication. The C period encompasses the time it takes to replicate the chromosomal DNA. The D period refers to the stage between the conclusion of DNA replication and the end of cell division.[27] The doubling rate of *E. coli* is higher when more nutrients are available. However, the length of the C and D periods do not change, even when the doubling time becomes less than the sum of the C and D periods. At the fastest growth rates, replication begins before the previous round of replication has completed, resulting in multiple replication forks along the DNA and overlapping cell cycles



Plasmid and the E. coli revolution

Without a doubt, plasmids are the most important tools not only for the manipulation of *E. coli* but also the foundation for the genetic engineering of many organisms, cloning and sequencing, generation of mutants, and many applications in molecular biology. Plasmids are extrachromosomal molecules that are self-replicative and sometimes provide interesting features to its host. The term was first coined by Joshua Lederberg in 1952 referring to genetic elements in bacteria that remained as an independent molecule from the chromosome at any stage of their replication cycle. In nature, many bacteria contain self-replicating DNA molecules that can be harnessed for molecular biology applications. *E. coli* plasmids were the first ones to be extensively modified for such purposes.

Some exceptional features of plasmids are they can be used in systems where replication origins (check compatibility first) and selection markers can coexist in the same cell, which can

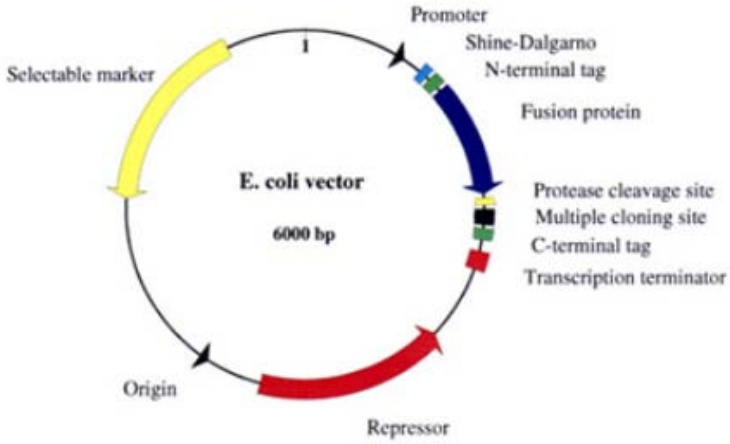
be extremely useful for the coexpression of four different proteins in the same cell (e.g., the four plasmid system developed by Dykxhoorn group, which are compatible between them; the broad diversity of selection markers and partitioning control elements; cloning capacity, which is an important feature for cloning large fragments required for synthetic biology applications or metabolic engineering; reporter proteins useful for selecting positive clones; recombination or assembly technology for easier cloning methods, and the ability to be transferred from one host to another like the case of the OriV from RK2 plasmid.

Escherichia coli plasmids

Name	Type of element	Characteristics
ColE1	Replication origin	Generates 15–20 copies of each plasmid molecule. Colicin production. Related to plasmids that confer immunity to phage infections. Found in low copy plasmids such as pBR322. There are mutations in this replication origin that leads to high copy number plasmids, such as pUC series that can render up to 700 copies per cell.
p15A	Replication origin	Low copy number replication origin, estimated in 18–22 copies per cell. This type of replication origin is often found in pACYC and its derivative vectors
pMB1	Replication origin	Versatile replication origin. The original sequence generates 15–20 copies per cell, but a mutant version can lead up to 700 copies per cell. This plasmid contains the *Eco*RI restriction-modification system
pSC101	Replication origin	Five copies per cell.
R6K	Replication origin	15–20 copies per cell. Requires the π protein from the gene *pir* for replication. This origin of replication is functional in diverse bacterial species
Amp^r, Kan^r, Cm^r, Tet^r among other	Selection markers	Elements required for the selection and maintenance of plasmids in bacterial hosts. Here are listed the resistance cassettes for Ampicillin, Kanamycin, Chloramphenicol, and Tetracycline, which are the most common selection markers. For additional markers, RAC database contains the information regarding antibiotic resistance traits and their sequence or iGEM website for sequence modules bearing the proper syntax for synthetic constructs

LacZ, CcdB, Green Fluorescent protein (GFP), etc	Additional elements required for positive clone selection, reporter protein fusions among others	Plasmids have been modified so that they contain multiple cloning sites with diverse unique restriction sites, counter selection for positive clone selection. Additional elements such as filamentous origins for single-stranded DNA generation for sequencing of high G+C templates or site-directed mutagenesis

Linear plasmids are common in bacteria (particularly in actinobacteria), but thus far, only N15 plasmid prophage has been isolated from *E. coli* and is an impediment for generating knockouts using linear DNA (see Section 3). Recently, a linear plasmid was created to clone unstable fragments bearing repetitive sequences without showing size bias during cloning, active promoter sequences, or sequences with A + T content. As part of the information needed for plasmid manipulation, databases and repositories are also relevant for the manipulation and selection of the right plasmid for the applications you want to further exploit.



Genome modifications to understand E. coli

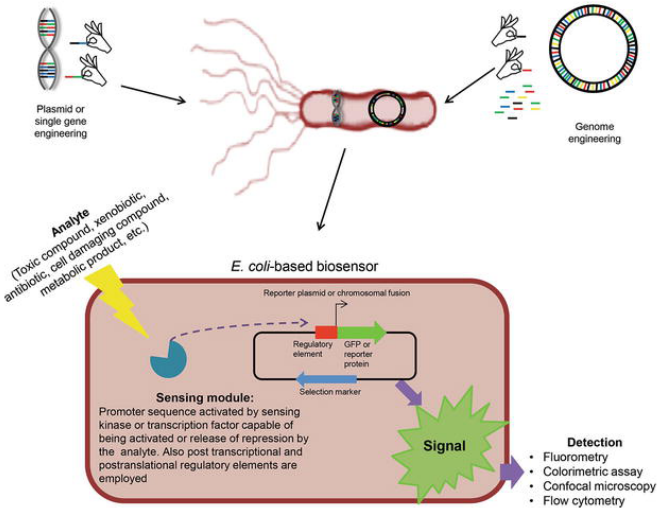
In *E. coli*, several tools for genome modification have been developed. Some of the most important methods involve either the generation of deletion mutants by removing specific genes, one outstanding case is the use of the lambda Red system for inhibiting linear DNA degradation and by homologous recombination, the deletion of specific genes using PCR-derived selection marker cassettes with homologous sequences with target gene.

Lambda Red-based method have yielded a total of 4288 genes mutated without lethality (Keio collection), 303 genes were unable to be deleted, from which 37 are of unknown function. This experimental evidence has pointed out one very important aspect of genome structure and function. Larger genomic editions are needed to understand how far we can delete redundant or nonessential sequences. By using Cre/lox recombination, substantial genomic fragments can be

deleted or sequentially removed, rendering the nonessential regions (regardless the genes present) from the genome. All these methods rely on basic bacterial genetics founded with *E. coli*, such as transposon-based integration of recombination sequences, λ-recombination of PCR products integrating deletion module cassettes, and the gene-specific knockout methods. Mutations can then be transferred from one strain to the other to generate multiple deletions at once, and other technologies are still limited to either whole genome synthesis with previous knowledge on the structure of the genome.

E. coli based biosensors. Tools for many applications

In biotechnology, biosensors are broadly defined as any device based on biological part, cell, tissue, or protein complex that are linked to a mechanical sensor or analytical receptor that provides a measurable signal proportional to the analyte in the reaction. *E. coli*-based biosensors using plasmid or chromosomal constructs are useful for the detection of environmental traits or hazards or measuring cellular processes as any standard reporter system.



Plasmid vectors with all the possible modifications can lead to almost endless combinations. For practical applications, there are commercial vectors that can be used for such purposes or as mentioned in the previous sections, plasmid methods are powerful enough for fast and robust biosensor design. In the literature, there are several reports where *E. coli*-based biosensors have been successful for detecting different traits: oxidants, DNA damaging compounds, membrane-damaging compounds, protein-damaging compounds, aromatic compounds, xenobiotics, antibiotic panels using reporter strains without antibiotic selection, etc.

3. Genetic engineering and synthetic biology of E. coli

New biological parts (genes, promoter sequence, terminators, etc.), devices (gene networks), and modules (biosynthetic pathways) are only limited by our imagination and the drive to create them. Also, without the advancement of methods for analyzing large amounts of

data, bioinformatics, codon optimization software, genome mining, and user-friendly databases, synthetic biology creations are permeating in many laboratories around the world. With this in mind, we will review the current technologies for synthetic genes and genomes, and how this technology can be applied in generating novel regulatory circuits and even whole genomes.

Proteome

Several studies have investigated the proteome of *E. coli*. By 2006, 1,627 (38%) of the 4,237 open reading frames (ORFs) had been identified experimentally. The 4,639,221–base pair sequence of Escherichia coli K-12 is presented. Of 4288 protein-coding genes annotated, 38 percent have no attributed function. Comparison with five other sequenced microbes reveals ubiquitous as well as narrowly distributed gene families; many families of similar genes within *E. coli* are also evident.

Interactome

The interactome of *E. coli* has been studied by affinity purification and mass spectrometry (AP/MS) and by analyzing the binary interactions among its proteins.

Protein complexes. A 2006 study purified 4,339 proteins from cultures of strain K-12 and found interacting partners for 2,667 proteins, many of which had unknown functions at the time. A 2009 study found 5,993 interactions between proteins of the same *E. coli* strain, though these data showed little overlap with those of the 2006 publication.

Binary interactions: Systematic yeast two-hybrid screens with most *E. coli* proteins, and found a total of 2,234 protein-protein interactions. This study also integrated genetic interactions and protein structures and mapped 458 interactions within 227 protein complexes.]

therapeutic use

Nonpathogenic *E. coli* strain Nissle 1917, (Mutaflor) and *E. coli* O83:K24:H31 (Colinfant) are used as probiotic agents in medicine, mainly for the treatment of various gastrointestinal diseases, including inflammatory bowel disease.

Saccharomyces cerevisiae

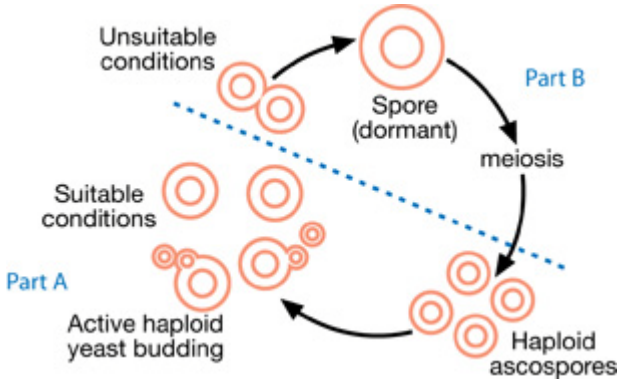
Saccharomyces cerevisiae is one of the long-time classic model organisms that remains highly relevant today. As one of the simplest eukaryotes (containing membrane bound organelles), and indeed the first eukaryotic organism to be sequenced with a genome size of ~12 Mbp, it can be used for studies of common pathways in higher organisms such as humans. In addition to important applications within the food industry and biotechnology areas. As yeast share the same cell division processes with humans, S. cerevisiae is well established for studies of cell division and cancer research applications. Yeasts have simple nutritional requirements and can be easily grown in standard lab conditions.

The genome of the most frequently studied yeast, *Saccharomyces cerevisiae*, consists of 12 million base pairs of DNA and contains about 6000 genes. Although the yeast genome is approximately three times larger than that of *E. coli*, it is far more manageable than the genomes of more complex eukaryotes, such as humans. Yet even in its simplicity, the yeast cell exhibits the typical features of eukaryotic cells. It contains a distinct nucleus surrounded by a nuclear membrane, its genomic DNA is organized as 16 linear chromosomes, and its cytoplasm contains a cytoskeleton and subcellular organelles.

Yeasts can be readily grown in the laboratory and can be studied by many of the same molecular genetic approaches that have proved so successful with *E. coli*. Although yeasts do not replicate as rapidly as bacteria, they still divide as frequently as every 2 hours and can easily be grown as colonies from a single cell. Consequently, yeasts can be used for a variety of genetic manipulations similar to those that can be performed using bacteria. These features have made yeast cells the most approachable eukaryotic cells from the standpoint of molecular biology. Yeast mutants have been important in understanding many fundamental processes in eukaryotes, including DNA replication, transcription, RNA processing, protein sorting, and the regulation of cell division, as will be discussed in subsequent chapters. The unity of molecular cell biology is made abundantly clear by the fact that the general principles of cell structure and function revealed by studies of yeasts apply to all eukaryotic cells.

Life Cycle:

The cell cycle, *S. cerevisiae* cells bud to produce new offspring. Whereas both haploid and diploid yeast can use this vegetative lifecycle, haploid cells (gametes) are also capable of fusing to form diploid cells. In heterothallic strains, there are two distinct haploid mating types – **a** and α – that remain haploid when cultured separately. However, these gametes are capable of fusing when mixed together. In contrast, homothallic strains can switch mating types. Thus it is difficult to maintain haploid cultures of homothallic yeast, as some cells will switch to the opposite mating type and fuse with other members of the population (part A and B).



Metabolic and Pathway Engineering

Due to its rapid growth, genetic tractability, and an abundance of prior research on its physiology and metabolism, *S. cerevisiae* is a popular choice for conversion into a "cell factory" (Nielsen, Larsson, Van Maris, & Pronk, **2013**). Two common strategies for metabolic engineering in budding yeast are (1) modification of endogenous pathways via gene deletion or overexpression and (2) heterologous expression of genes from other organisms.

***S. cerevisiae* has developed as a model organism because it scores favorably on a number of these criteria.**

- As a single-cell organism, *S. cerevisiae* is small with a short generation time (doubling time 1.25–2 hours at 30 °C or 86 °F) and can be easily cultured. These are all positive characteristics in that they allow for the swift production and maintenance of multiple specimen lines at low cost.
- *S. cerevisiae* divides with meiosis, allowing it to be a candidate for sexual genetics research.
- *S. cerevisiae* can be transformed allowing for either the addition of new genes or deletion through homologous recombination. Furthermore, the ability to grow *S. cerevisiae* as a haploid simplifies the creation of gen knockout strains.
- As a eukaryote, *S. cerevisiae* shares the complex internal cell structure of plants and animals without the high percentage of non-coding DNA that can confound research in higher eukaryotes.
- *S. cerevisiae* research is a strong economic driver, at least initially, as a result of its established use in industry.

collection	Description and representative use(s)
Deletion Collection(Giaever et al., 2002)	Nearly all non-essential genes replaced with kanMX selectable marker (Fig. 2B) Screen for phenotype of interest in haploid, homozygous diploid, or heterozygous deletion strains
GFP Clone Collection(Huh et al., 2003)	Over 4,000 genes tagged at C-terminus with GFP (Fig. 2C) Localization and/or expression studies
TAP Tagged ORFs(Ghaemmaghami et al., 2003)	Over 4,000 genes tagged at the C-terminus with the tandem affinity purification tag Protein detection and/or purification
ORF Collection(Gelperin et al., 2005)	Roughly 5,000 ORFs cloned into plasmids and epitope tagged; expression is under control of the *GAL1* promoter Protein purification Phenotypic analysis of the effects of overexpression

GST Tagged ORF Collection (Sopko et al., 2006)	Similar to above, but ORFs have a different epitope tag
DAmP Collection(Breslow et al., 2008)	The 3′ untranslated regions of over 800 essential genes have been disrupted with the kanMX selectable marker, destabilizing the corresponding mRNAs and reducing gene expression (Fig. 2D) Allows study of essential gene function
Tet-Regulated Collection(Mnaimneh et al., 2004)	The promoters of 800 essential genes have been replaced with a promoter that can be shut off with the addition of doxycycline. Allows study of essential gene function

In the study of aging

S. cerevisiae has been highly studied as a model organism to better understand aging for more than five decades and has contributed to the identification of more mammalian genes affecting aging than any other model organism. Some of the topics studied using yeast are calorie restriction, as well as in genes and cellular pathways involved in senescence. The two most common methods of measuring aging in yeast are Replicative Life Span, which measures the number of times a cell divides, and Chronological Life Span, which measures how long a cell can survive in a non-dividing stasis state.

Meiosis, recombination and DNA repair

S. cerevisiae reproduces by mitosis as diploid cells when nutrients are abundant. However, when starved, these cells undergo meiosis to form haploid spores.[38]

Evidence from studies of *S. cerevisiae* bear on the adaptive function of meiosis and recombination. Mutations defective in genes essential for meiotic and mitotic recombination in *S. cerevisiae* cause increased sensitivity to radiation or DNA damaging chemicals.[39][40] For instance, gene *rad52* is required for both meiotic recombination[41] and mitotic recombination.[42] *Rad52* mutants have increased sensitivity to killing by X-rays, Methyl methanesulfonate and the DNA cross-linking agent 8-methoxypsoralen-plus-UVA, and show reduced meiotic recombination.[40][41][43] These findings suggest that recombination repair during meiosis and mitosis is needed for repair of the different damages caused by these agents.

Genome sequencing

S. cerevisiae was the first eukaryotic genome to be completely sequenced. The *S. cerevisiae* genome is composed of about 12,156,677 base pairs and 6,275 genes, compactly organized on 16 chromosomes. Only about 5,800 of these genes are believed to be functional. It is estimated at least 31% of yeast genes have homologs in the human genome.

Gene function and interactions

The availability of the *S. cerevisiae* genome sequence and a set of deletion mutants covering 90% of the yeast genom have further enhanced the power of *S. cerevisiae* as a model for understanding the regulation of eukaryotic cells. A project underway to analyze the genetic interactions of all double-deletion mutants through synthetic genetic array analysis will take this research one step further. The goal is to form a functional map of the cell's processes.

Synthetic yeast genome project

The international Synthetic Yeast Genome Project (Sc2.0 or *Saccharomyces cerevisiae version 2.0*) aims to build an entirely designer, customizable, synthetic *S. cerevisiae* genome from scratch that is more stable than the wild type. In the synthetic genome all transposons, repetitive elements and many introns are removed, all UAG stop codons are replaced with UAA, and transfer RNA genes are moved to a novel neochromosome. As of March 2017, 6 of the 16 chromosomes have been synthesized and tested. No significant fitness defects have been found.

Other tools in yeast research

Approaches that can be applied in many different fields of biological and medicinal science have been developed by yeast scientists. These include yeast two-hybrid for studying protein interactions and tetrad analysis. Other resources, include a gene deletion library including ~4,700 viable haploid single gene deletion strains. A GFP fusion strain library used to study protein localisation and a TAP tag library used to purify protein from yeast cell extracts.

Brewing/ Baking

Saccharomyces cerevisiae is used in brewing beer, when it is sometimes called a top-fermenting or top-cropping yeast. It is so called because during the fermentation process its hydrophobic surface causes the flocs to adhere to CO_2 and rise to the top of the fermentation vessel. Top-fermenting yeasts are fermented at higher temperatures than the lager yeast *Saccharomyces pastorianus*, and the resulting beers have a different flavor than the same beverage fermented with a lager yeast. *S. cerevisiae* is used in baking; the carbon dioxide generated by the fermentation is used as a leavening agent in bread and other baked goods. Historically, this use was closely linked to the brewing industry's use of yeast, as bakers took or bought the barm or yeast-filled foam from brewing ale from the brewers (producing the barm cake); today, brewing and baking yeast strains are somewhat different.

Systematic gene names for Baker's yeast	
Example gene name	**YGL118W**
Y	the Y to show this is a yeast gene
G	chromosome on which the gene is located

L	left or right arm of the chromosome
118	sequence number of the gene/ORF on this arm, starting at the centromere
W	whether the coding sequence is on the Watson or Crick stran

Uses in aquaria

Owing to the high cost of commercial CO_2 cylinder systems, CO_2 injection by yeast is one of the most popular DIY approaches followed by aquaculturists for providing CO_2 to underwater aquatic plants. The yeast culture is, in general, maintained in plastic bottles, and typical systems provide one bubble every 3–7 seconds. Various approaches have been devised to allow proper absorption of the gas into the water.

Neurospora crassa

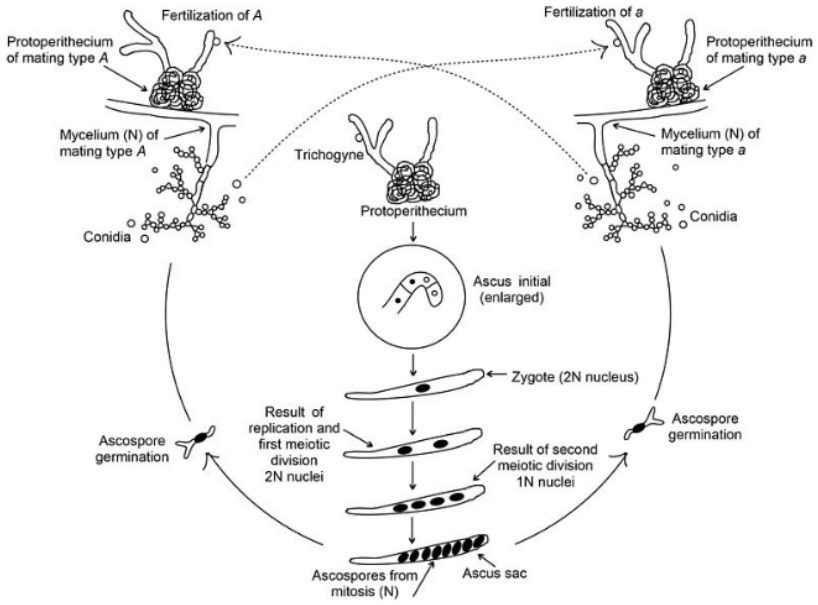
Neurospora crassa is a type of red bread mold of the phylum Ascomycota. The genus name, meaning "nerve spore" in Greek, refers to the characteristic striations on the spores. *N. crassa* is used as a model organism because it is easy to grow and has a haploid life cycle that makes genetic analysis simple since recessive traits will show up in the offspring. Analysis of genetic recombination is facilitated by the ordered arrangement of the products of meiosis in *Neurospora* ascospores.

First developed as an experimental organism by Dodge in the late 1920s and about 10 years later was adopted by Beadle and Tatum for their famous “one gene–one protein” studies linking biochemistry and genetics (Davis and de Serres 1970). Beadle and Tatum selected *Neurospora*, in part, because this organism grows fast and is easy to propagate on defined growth media, and because genetic manipulations, such as mutagenesis, complementation tests, and mapping are simple. Although not as widely studied as some other model eukaryotes, *Neurospora* continues to attract researchers because of its moderate complexity and because it is well suited for a variety of genetic, biochemical, developmental, and subcellular studies. *Neurospora* has been especially useful for studies of photobiology, circadian rhythms, population biology, morphogenesis, mitochondrial import, DNA repair and recombination, DNA methylation, and other epigenetic processes.

Life Cycle

Sexual fruiting bodies (perithecia) can only be formed when two mycelia of different mating type come together (see Figure). Like other Ascomycetes, *N. crassa* has two mating types that, in this case, are symbolized by *A* and *a*. There is no evident morphological difference between the *A* and *a* mating type strains. Both can form abundant protoperithecia, the female reproductive structure (see Figure). Protoperithecia are formed most readily in the laboratory when growth occurs on solid (agar) synthetic medium with a relatively low source of nitrogen. Nitrogen

starvation appears to be necessary for expression of genes involved in sexual development. The protoperithecium consists of an ascogonium, a coiled multicellular hypha that is enclosed in a knot-like aggregation of hyphae. A branched system of slender hyphae, called the trichogyne, extends from the tip of the ascogonium projecting beyond the sheathing hyphae into the air. The sexual cycle is initiated (i.e. fertilization occurs) when a cell (usually a conidium) of opposite mating type contacts a part of the trichogyne. Such contact can be followed by cell fusion leading to one or more nuclei from the fertilizing cell migrating down the trichogyne into the ascogonium. Since both *A* and *a* strains have the same sexual structures, neither strain can be regarded as exclusively male or female. However, as a recipient, the protoperithecium of both the *A* and *a*strains can be thought of as the female structure, and the fertilizing conidium can be thought of as the male participant.



Structure genetic analysis

Above features *N. crassa* was found to be very useful for the study of genetic events occurring in individual meioses. Mature asci from a perithecium can be separated on a microscope slide and the spores experimentally manipulated. These studies usually involved the separate culture of individual ascospores resulting from a single meiotic event and determining the genotype of each spore. Studies of this type, carried out in several different laboratories, established the phenomenon of "gene conversion".

Regulation

A description of the regulation of *frq* and FRQ requires a description of the clock cycle. The molecular basis of the circadian oscillator in *Neurospora* begins with two protein complexes.

One is the FFC, the negative element complex composed of two copies of FRQ, FRH, and Casein kinase 1 as well as, probably, other less strongly bound proteins.[16] The other complex which acts as the positive element in the feedback loop includes WC-1 and WC-2; they are GATA transcription factors that, together, form the heterodimeric WCC via their PAS domains.[21] When WCC is released from the FFC negative element complex during subjective night, it binds to the clock-box within frequency (*frq*) gene promoter and activates *frq* transcription.[22][23] It has recently been shown that the Histone H3 Lysine 36 Methyltransferase, SET-2, is responsible for methylation of the *frq* gene to establish a chromatin state that will allow for transcription of *frq* by the WCC.

Mutation

Forward genetics has been used to create *Neurospora* clock mutants with varied periods of conidiation. Although nine alleles have been described as having come from forward genetics, sequence analysis subsequent to the cloning of *frq* showed that *frq*[2] ,*frq*[4], and *frq*[6] shared the same single base change, and likewise *frq*[7] and *frq*[8] had the same single base change, so the redundant alleles have been dropped.[37] The periods of various *frq* mutants that arose from forward screens are as follows when measured at 25°C, although it should be noted that because *frq*[3] and *frq*[7] result in clocks with altered temperature compensation, periods will be different at other temperatures:

Period of *frq* mutants at 25˚C

Mutant	*frq*[1]	*frq*[2]	*frq*[3	*frq*[7]	*frq*[9]
Period (hr)	16.5	19.3	24.0	29.0	Arrhythmic

Adaptive function of mating type

That mating in *N. crassa* can only occur between strains of different mating type suggests that some degree of outcrossing is favored by natural selection. In haploid multicellular fungi, such as *N. crassa*, meiosis occurring in the brief diploid stage is one of their most complex processes. The haploid multicellular vegetative stage, although physically much larger than the diploid stage, characteristically has a simple modular construction with little differentiation. In *N. crassa*, recessive mutations affecting the diploid stage of the life cycle are quite frequent in natural populations. These mutations, when homozygous in the diploid stage, often cause spores to have maturation defects or to produce barren fruiting bodies with few ascospores (sexual spores). The majority of these homozygous mutations cause abnormal meiosis (e.g. disturbed chromosome pairing or disturbed pachytene or diplotene). The number of genes affecting the diploid stage was estimated to be at least 435[15] (about 4% of the total number of 9,730 genes). Thus, outcrossing, promoted by the necessity for union of opposite mating types, likely provides

the benefit of masking recessive mutations that would otherwise be deleterious to sexual spore formation.

DNA methylation in Neurospora

Neurospora revealed itself to be an excellent system to study the control and function of DNA methylation. Some model eukaryotes, including the nematode *Caenorhabditis elegans* and the yeasts *S. cerevisiae* and *S. pombe*, lack detectable DNA methylation and isolated reports of DNA methylation in another model organism, *Drosophila melanogaster*, remain controversial. In some organisms such as mammals, DNA methylation is essential for viability, complicating certain analyses. In *N. crassa* DNA, ~1.5% of the cytosines are methylated, but this methylation is dispensable, facilitating genetic studies. Although one must be cautious when extrapolating from one system to another, at least some aspects of DNA methylation appear conserved. For example, all known DNA methyltransferases (DMTs), the enzymes that methylate cytosine residues, including those from both prokaryotes and eukaryotes, show striking homology in their catalytic domains. Findings from *Neurospora*, *Arabidopsis*, mice, and other systems in the last decade have revealed important similarities and interesting differences in the control and function of DNA methylation, demonstrating the value of performing investigations in multiple model systems. Discovery of DNA methylation in *Neurospora* initially attracted interest because it was not limited to symmetrical sites, such as CpG dinucleotides or CpNpG trinucleotides. Riggs, and Holliday and Pugh had proposed an attractive model for the "inheritance" or "maintenance" of methylation patterns that relied on the symmetrical nature of methylated sites observed in animals. Although results of a variety of in vitro and in vivo studies have supported the "maintenance methylase" model, mechanisms for maintenance methylation that do not rely on faithful copying at symmetrical sites can be imagined and may be operative in a variety of organisms

Rip, a genome defense system with both genetic and epigenetic aspects

A detailed analysis of progeny from crosses of *Neurospora* transformants. It was noticed that duplicated sequences, whether native or foreign, and whether genetically linked or unlinked, were subjected to numerous polarized transition mutations (G:C to A:T) in the haploid genomes of the special heterokaryotic cells resulting from fertilization. When the stability of a gene was tested when it was unique in the genome or else combined with an unlinked homolog, it was found that RIP is not simply repeat-*associated*; it is truly repeat-*induced*. In a single passage through the sexual cycle, up to ~30% of the G:C pairs in duplicated sequences can be mutated. Frequently (but not invariably), the sequences that are altered by RIP become methylated de

novo. It is likely that the mutations arising from RIP occur by enzymatic deamination of 5-methylcytosines (5mC) or by deamination of Cs followed by DNA replication.

FRQ-less Oscillator (FLO)

A number of identifiably distinct oscillators outside of the FRQ/WCC system have been discovered; however, none of these FRQ-less oscillations (FLOs) satisfy the characteristics to be classified as circadian oscillators. The circadian FRQ-WCC Oscillator (FWO) has been shown, via luciferase reporting, to continue running even when a FLO (the CDO or choline deficiency oscillator that controls conidiation under conditions of choline limitation) controls conidiation. In the *frq[9]* mutant *Neurospora crassa*, a non-temperature compensated rhythm of conidiospore development was still observed in constant darkness (DD). The period for *frq* null mutants varied from 12 to 35 hours but could be stabilized by the addition of farnesol or geraniol. However, this mechanism is not well understood.

Evolution

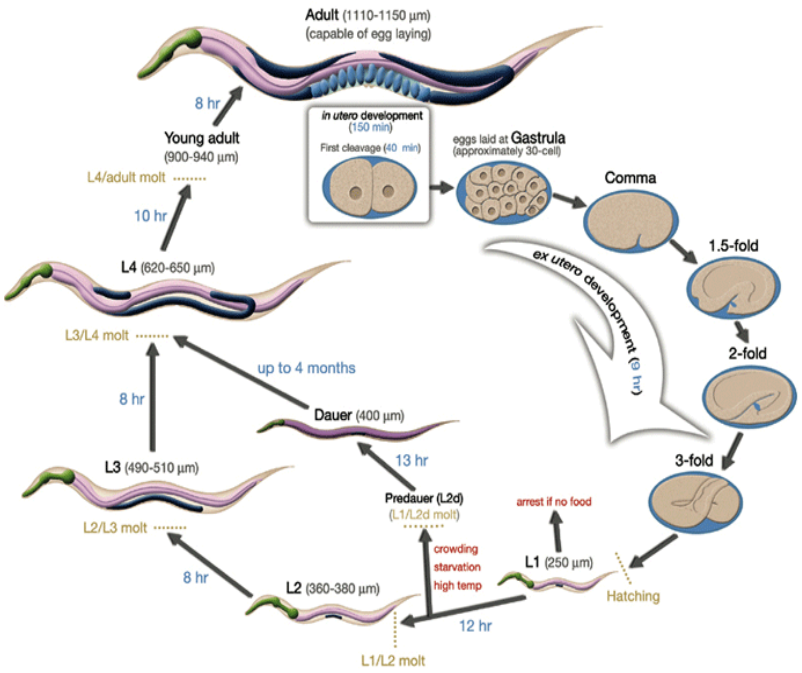
Nonetheless bona fide FRQ-based circadian cocks have been found in organisms other than *Neurospora* both within the *Sordariacea*, for instance, in the salient fungal pathogen Botrytis, and also as far afield as Pyronema within the Pezizomycetes, an early-diverging lineage of filamentous ascomycetes. *Frq* was even found in non-Dikarya group of fungi. The finding of *frq* and conserved circadian clock mechanism inside non-Dikarya, Arbuscular Mycorrhizal Fungi expanded the evolutionary history of this gene in Fungal kingdom, *frq* seems to diverge very quickly during its evolution. A part of the reason why the FRQ primary amino acid sequence diverges so quickly may be because it is an Intrinsically Disordered Protein and as a result lacks the structural constraints that limit sequence changes. Since codon optimization of the *frq* gene results in impaired circadian feedback loop function, *frq* displays non-optimal codon usage bias across its open reading frame in contrast to most other genes. FRQ is an intrinsically disordered protein that is not well conserved, even across fungi.

Caenorhabditis elegans

Caenorhabditis elegans is a microscopic, soil-dwelling roundworm that has been powerfully used as a model organism since the early 1970′s. It was initially proposed as a model for developmental biology because of its invariant body plan, ease of genetic manipulation and low cost of maintenance. Since then C. elegans has rapidly grown in popularity and is now utilized in numerous research endeavors, from studying the forces at work during locomotion to studies of neural circuitry.

Caenorhabditis elegans Development and Reproduction

Ceanorhabditis elegans is a powerful tool to help understand how organisms develop from a single cell into a vast interconnected array of functioning tissues. Early work in C. elegans traced the complete cell lineage and structure at the electron microscopy level, allowing researchers unprecedented insight into the connection between genes, development and disease. Appreciating the stereotyped development and reproductive program of C. elegans is essential to using this model organism to its experimental fullest. This video will give you a peek into the development of a worm from fertilization to hatching, and walk you though the life stages of the newly hatched larvae on its journey to reproductive maturity. The video will detail how the major axes are established, which founder cells give rise to what tissues in the developing embryo and how to discriminate between the four larval stages. Finally, you will learn how to set up a genetic cross and well visit a few applications that manipulate the development and reproduction of C. elegans to experimental benefit.



Genome study

C. elegans was the first multicellular organism to have its whole genome sequenced. The sequence was published in 1998, although some small gaps were present; the last gap was

finished by October 2002. Neurons of humans and *C. elegans* are almost identical. Both human and *C. elegans* neurons contain a dendrite which extends from the cell to receive neurotransmitters, and extends to the nerve ring or brain for a synaptic connection between neurons. The biggest difference is that *C. elegans* has motor excitatory and inhibitory neurons, known as cholingergic and gabaergic neurons, which simply act as further regulation for the tiny creature. They have no influence on the nervous system besides regulating neuron impulses

Size and gene content

The *C. elegans* genome is about 100 million base pairs long and consists of six chromosomes and a mitochondrial genome. Its gene density is about one gene per five kilo-base pairs. Introns make up 26% and intergenic regions 47% of the genome. Many genes are arranged in clusters and how many of these are operons is unclear. *C. elegans* and other nematodes are among the few eukaryotes currently known to have operons; these include trypanosomes, flatworms (notably the trematode *Schistosoma mansoni*), and a primitive chordate tunicate *Oikopleura dioica*. Many more organisms are likely to be shown to have these operon.

Protein-coding genes

The genome contains an estimated 20,470 protein-coding genes. About 35% of *C. elegans* genes have human homologs. Remarkably, human genes have been shown repeatedly to replace their *C. elegans* homologs when introduced into *C. elegans*. Conversely, many *C. elegans* genes can function similarly to mammalian genes. The number of known RNA genes in the genome has increased greatly due to the 2006 discovery of a new class of *21U-RNA* genes, and the genome is now believed to contain more than 16,000 RNA genes, up from as few as 1,300 in 2005. Scientific curators continue to appraise the set of known genes; new gene models continue to be added and incorrect ones modified or removed. The reference *C. elegans* genome sequence continues to change as new evidence reveals errors in the original sequencing. Most changes are minor, adding or removing only a few base pairs of DNA. For example, the WS202 release of WormBase (April 2009) added two base pairs to the genome sequence.[99] Sometimes, more extensive changes are made as noted in the WS197 release of December 2008, which added a region of over 4,300 bp to the sequence.

Related genomes

In 2003, the genome sequence of the related nematode *C. briggsae* was also determined, allowing researchers to study the comparative genomics of these two organisms. The genome sequences of more nematodes from the same genus e.g., *C. remanei*, *C. japonica* and *C. brenneri*, have also been studied using the shotgun sequencing technique. These sequences have now been completed.

Phylogenetic study

C. elegans is the most basal species in the 'Elegans' group (10 species) of the 'Elegans' supergroup (17 species) in phylogenetic studies. It forms a branch of its own distinct to any other species of the group.

Apoptosis

Programmed cell death (apoptosis) eliminates many additional cells (131 in the hermaphrodite, most of which would otherwise become neurons); this "apoptotic predictability" has contributed to the elucidation of some apoptotic genes. Cell death-promoting genes and a single cell-death inhibitor have been identified.

RNA interference (RNAi)

RNA interference (RNAi) is a relatively straightforward method of disrupting the function of specific genes. Silencing the function of a gene can sometimes allow a researcher to infer its possible function (s). The nematode can be soaked in, injected with, or fed with genetically transformed bacteria that express the double-stranded RNA of interest, the sequence of which complements the sequence of the gene that the researcher wishes to disable. RNAi has emerged as a powerful tool in the study of functional genomics. In *C. elegans*, it has been used to analyse gene functions and the report claims the promise of future findings in the systematic genetic interactions.

Meiosis:

Research into meiosis has been considerably simplified since every germ cell nucleus is at the same given position as it moves down the gonad, so is at the same stage in meiosis. In an early phase of meiosis, the oocytes become extremely resistant to radiation and this resistance depends on expression of genes *rad51* and *atm* that have key roles in recombinational repair. Gene *mre-11* also plays a crucial role in recombinational repair of DNA damage during meiosis. A study of the frequency of outcrossing in natural populations showed that selfing is the predominant mode of reproduction in *C. elegans*, but that infrequent outcrossing events occur at a rate around 1%. Meioses that result in selfing are unlikely to contribute significantly to beneficial genetic variability, but these meioses may provide the adaptive benefit of recombinational repair of DNA damages that arise, especially under stressful conditions.

Ageing

C. elegans has been a model organism for research into ageing; for example, the inhibition of an insulin-like growth factor signaling pathway has been shown to increase adult lifespan threefold;[77][78] while glucose feeding promotes oxidative stress and reduce adult lifespan by a half.[58] In addition *C. elegans* exposed to 5mM lithium chloride (LiCl) showed

lengthened life spans.[79] When exposed to 10μM LiCl, reduced mortality was observed, but not with 1μM

C. elegans Chemotaxis

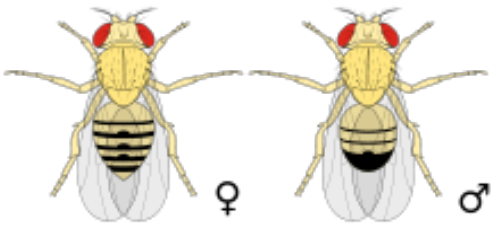
Chemotaxis is a process in which cells or organisms move in response to a chemical stimulus. In nature, chemotaxis is important for organisms to sense and move toward food sources and move away from stimuli that may be toxic or harmful. Chemotaxis is also important at the cellular level. For example, chemotaxis is required for the movement of sperm toward an egg prior to fertilization. In the lab, chemotaxis is frequently examined in the nematode, C. elegans, which is known to migrate towards food sources in soil, but away from toxins such as heavy metals, substances with a low pH, and detergents.

Drosophila melanogaster

Drosophila melanogaster is a species of fly (the taxonomic order Diptera) in the family Drosophilidae. The species is known generally as the **common fruit fly** (though inaccurately[2]) or **vinegar fly**. Starting with Charles W. Woodworth's proposal of the use of this species as a model organism, *D. melanogaster* continues to be widely used for biological research in genetics, physiology, microbial pathogenesis, and life history evolution. As of 2017, eight Nobel prizes had been awarded for research using *Drosophila*.

Physical appearance

Wildtype fruit flies are yellow-brown, with brick-red eyes and transverse black rings across the abdomen. They exhibit sexual dimorphism; females are about 2.5 mm (0.098 in) long; males are slightly smaller with darker backs. Males are easily distinguished from females based on colour differences, with a distinct black patch at the abdomen, less noticeable in recently emerged flies, and the sexcombs (a row of dark bristles on the tarsus of the first leg). Furthermore, males have a cluster of spiky hairs (claspers) surrounding the reproducing parts used to attach to the female during mating. Extensive images are found at FlyBase.

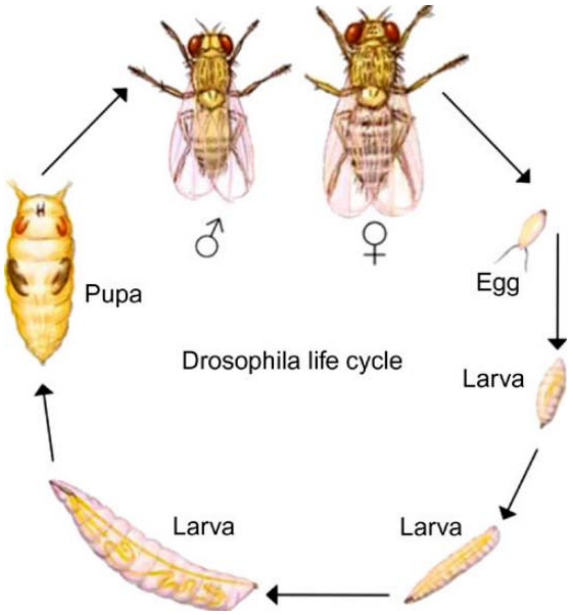


The Life Cycle of *Drosophila* – 12 Days, Lots of Offspring

The female fruit fly, about 3 mm in length, will lay between 750 and 1,500 eggs in her lifetime. The life cycle of the fruit fly only takes about 12 days to complete at room temperature (25°C). After the egg (at a mere half a millimeter in length) is fertilized, the embryo emerges in ~24 hours. The embryo undergoes successive molts to become the first, second, and third instar larva. The larval stages are characterized by consumption of food and resulting growth, followed by the quiescent pupal stage, during which there is a dramatic reorganization of the body plan (metamorphosis) followed by the emergence of the adult fly.

Easy to Grow, Easy to Keep, Easy to Study

Because the flies themselves are quite small (~1 mg), you can raise a *lot* of them at once. Traditionally flies have been raised in quarter-pint milk bottles, using a well-ripened banana as food, although more often a corn-meal agar mixture is now used. Genetic experiments can be done in a shell vial with just a few flies. Thus many different mutant stocks can be maintained, and numerous experiments carried out, in a small lab space. When large amounts of material are needed, large population cages, which hold up to 50,000 flies in a cage that is 1' diameter x 1.5' long, can be used. That means that scientists can collect and harvest hundreds of grams of embryos, larvae, or adults at a time. The material can be frozen in liquid nitrogen, and then used as the starting point for preparing enzymes such as RNA polymerase II, or for purifying chromosomal proteins such as the histones, or for analysis of chromatin structure (see Chromatin module).



Model organism in genetics

D. melanogaster remains one of the most studied organisms in biological research, particularly in genetics and developmental biology.

History of use in genetic analysis

D. melanogaster was among the first organisms used for genetic analysis, and today it is one of the most widely used and genetically best-known of all eukaryotic organisms. All organisms use common genetic systems; therefore, comprehending processes such as transcription and replication in fruit flies helps in understanding these processes in other eukaryotes, including humans. Thomas Hunt Morgan began using fruit flies in experimental studies of heredity at Columbia University in 1910 in a laboratory known as the Fly Room. The Fly Room was cramped with eight desks, each occupied by students and their experiments. They started off experiments using milk bottles to rear the fruit flies and handheld lenses for observing their traits. The lenses were later replaced by microscopes, which enhanced their observations. Morgan and his students eventually elucidated many basic principles of heredity, including sex-linked inheritance, epistasis, multiple alleles, and gene mapping.

There are many reasons the fruit fly is a popular choice as a model organism:

- Its care and culture require little equipment, space, and expense even when using large cultures.
- It can be safely and readily anesthetized (usually with ether, carbon dioxide gas, by cooling, or with products such as FlyNap).
- Its morphology is easy to identify once anesthetized.
- It has a short generation time (about 10 days at room temperature), so several generations can be studied within a few weeks.
- It has a high fecundity (females lay up to 100 eggs per day, and perhaps 2000 in a lifetime).
- Males and females are readily distinguished, and virgin females are easily isolated, facilitating genetic crossing.
- The mature larva has giant chromosomes in the salivary glands called polytene chromosomes, "puffs", which indicate regions of transcription, hence gene activity.
- It has only four pairs of chromosomes - three autosomes, and one pair of sex chromosomes.
- Males do not show meiotic recombination, facilitating genetic studies.
- Recessive lethal "balancer chromosomes" carrying visible genetic markers can be used to keep stocks of lethal alleles in a heterozygous state without recombination due to multiple inversions in the balancer.
- The development of this organism-from fertilized egg to mature adult-is well understood.
- Genetic transformation techniques have been available since 1987.
- Its complete genome was sequenced and first published in 2000.
- Sexual mosaics can be readily produced, providing an additional tool for studying the development and behavior of these flies.

Genetic markers

Genetic markers are commonly used in *Drosophila* research, for example within balancer chromosomes or P-element inserts, and most phenotypes are easily identifiable either with the

naked eye or under a microscope. In the list of a few common markers below, the allele symbol is followed by the name of the gene affected and a description of its phenotype. *(Note: Recessive alleles are in lower case, while dominant alleles are capitalized).*

- Cy^1: Curly; the wings curve away from the body, flight may be somewhat impaired
- e^1: Ebony; black body and wings (heterozygotes are also visibly darker than wild type)
- Sb^1: Stubble; bristles are shorter and thicker than wild type
- w^1: White; eyes lack pigmentation and appear white
- bw: Brown; eye color determined by various pigments combined.
- y^1: Yellow; body pigmentation and wings appear yellow, the fly analog of albinism.

Classic genetic mutations

Drosophila genes are traditionally named after the phenotype they cause when mutated. For example, the absence of a particular gene in *Drosophila* will result in a mutant embryo that does not develop a heart. Scientists have thus called this gene *tinman*, named after the Oz character of the same name.Likewise changes in the *Shavenbaby* gene cause the loss of dorsal cuticular hairs in *Drosophila sechellia* larvae. This system of nomenclature results in a wider range of gene names than in other organisms.

Adh: Alcohol dehydrogenase- *Drosophila melanogaster* can express the alcohol dehydrogenase (*ADH*) mutation, thereby preventing the breakdown of toxic levels of alcohols into aldehydes and ketones. While ethanol produced by decaying fruit is a natural food source and location for oviposit for *Drosophila* at low concentrations (<4%), high concentrations of ethanol can induce oxidative stress and alcohol intoxication.

b: black: The black mutation was discovered in 1910 by Thomas Hunt Morgan. The black mutation results in a darker colored body, wings, veins, and segments of the fruit fly's leg. This occurs due to the fly's inability to create beta-alanine, a beta amino acid. The phenotypic expression of this mutation varies based on the genotype of the individual; for example, whether the specimen is homozygotic or heterozygotic results in a darker or less dark appearance.This genetic mutation is x-linked recessive.

bw: brown: The brown eye mutation results from pteridine (red) pigments inability to be produced or synthesized, due to a point mutation on chromosome II. When the mutation is homozygous, the pteridine pigments are unable to be synthesized because in the beginning of the pteridine pathway, a defective enzyme is being coded by homozygous recessive genes. In all, mutations in the pteridine pathway produces a darker eye color, hence the resulting color of the biochemical defect in the pteridine pathway being brown.

m: miniature: One of the first records of the *miniature* mutation of wings was also made by Thomas Hunt Morgan in 1911. He described the wings as having a similar shape as the wild-type phenotype. However, their *miniature* designation refers to the lengths of their wings, which do not stretch beyond their body and, thus, are notably shorter than the wild-type length. He also noted its inheritance is connected to the sex of the fly and could be paired with the inheritance of other sex-determined traits such as *white* eyes. The wings may also demonstrate other characteristics deviant from the wild-type wing, such as a duller and cloudier color.

se: sepia: The sepia eye color is brown. Ommochromes[brown] and drosopterins [red] are responsible for the typical eye color of *Drosophila melanogaster*. These mutations occur on the third chromosome. When mated with a wild type, flies with red eyes will be dominant over sepia color eyes. They are then classified as a recessive mutation, and can only result when both chromosomes contain the gene for sepia eyes. Sepia colored eyes are not dependent on the sex of the fly. The Sepia eye color decreases sexual activity in males and influences preference of females.

v: vermilion: Vermilion eye color compared to a wild type D. melanogaster is a radiant red. Vermilion eye color mutant is sex-linked recessive gene due to its absence of brown eye pigment. The red pigment is located on the X chromosome.[53] The synthesis of brown pigment is due to the process of converting tryptophane to kynurenine, vermilion flies lack the ability to convert these amino acids blocking the production of brown pigment.

vg: vestigial: A spontaneous mutation, discovered in 1919 by Thomas Morgan and Calvin Bridges. Vestigial wings are those not fully developed and that have lost function. Since the discovery of the vestigial gene in *Drosophila melanogaster*, there have been many discoveries of the vestigial gene in other vertebrates and their functions within the vertebrates.

w: white*: Drosophila melanogaster* wild type typically expresses a brick red eye color. In January 1910, Thomas Hunt Morgan first discovered the white gene and denoted it as *w*. The discovery of the white-eye mutation by Morgan brought about the beginnings of genetic experimentation and analysis of *Drosophila melanogaster*. Hunt eventually discovered that the gene followed a similar pattern of inheritance related to the meiotic segregation of the X chromosome. He discovered that the gene was located on the X chromosome with this information.

y: yellow: The yellow gene is a genetic mutation known as Dmel\y within the widely used data base called flybase. This mutation can be easily identified by the atypical yellow pigment observed in the cuticle of the adult flies and the mouth pieces of the larva. The y mutation comprises the following phenotypic classes: the mutants that show a complete loss of pigmentation from the cuticle (y-type) and other mutants that show a mosaic pigment pattern with some regions of the cuticle (wild type, y2-type). The role of the yellow gene is diverse and is responsible for changes in behaviour, sex-specific reproductive maturation and, epigenetic reprogramming. The y gene is an ideal gene to study as it is visibly clear when an organisim has this gene, making it easier to understand the passage of DNA to offspring.

Immunity

Unlike mammals, *Drosophila* flies only have innate immunity and lack an adaptive immune response. The *D. melanogaster* immune system can be divided into two responses: humoral and cell-mediated. The former is a systemic response mediated through the *Toll* and *imd* pathways, which are parallel systems for detecting microbes. The *Toll* pathway in *Drosophila* is known as the homologue of *Toll-like* pathways in mammals. Spatzle, a known ligand for the *Toll* pathway in flies, is produced in response to Gram-positive bacteria, parasites, and fungal infection. Upon infection, pro-Spatzle will be cleaved by protease SPE (Spatzle processing enzyme) to become active Spatzle, which then binds to the *Toll* receptor located on the cell surface (Fat body, hemocytes) and dimerise for activation of downstream NF-κB signaling pathways.

Behavioral genetics and neuroscience

In 1971, Ron Konopka and Seymour Benzer published "Clock mutants of *Drosophila melanogaster*", a paper describing the first mutations that affected an animal's behavior. Wild-type flies show an activity rhythm with a frequency of about a day (24 hours). They found mutants with faster and slower rhythms, as well as broken rhythms-flies that move and rest in random spurts. Work over the following 30 years has shown that these mutations (and others like them) affect a group of genes and their products that form a biochemical or biological clock. This clock is found in a wide range of fly cells, but the clock-bearing cells that control activity are several dozen neurons in the fly's central brain.

Transgenesis:

It is now relatively simple to generate transgenic flies in Drosophila, relying on a variety of techniques. One approach of inserting foreign genes into the *Drosophila* genome involves P elements. The transposable P elements, also known as transposons, are segments of bacterial

DNA that are transferred into the fly genome. Transgenic flies have already contributed to many scientific advances, e.g., modeling such human diseases as Parkinson's, neoplasia, obesity, and diabetes.

Arabidopsis thaliana

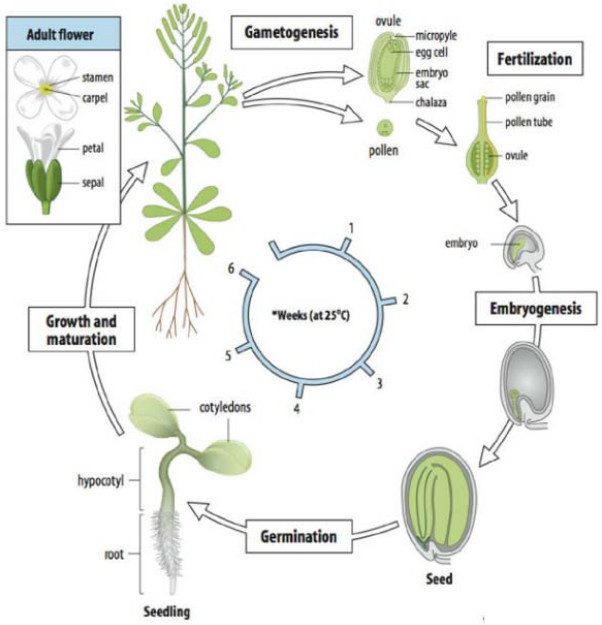
A. thaliana, also known as rockcress or thale cress, is a small plant with white flowers, often considered to be a weed where it is found across Europe, Asia and Africa. However, in plant genetic research it is seen in a much more favourable light, being a very popular model organism for plant studies. *A. thaliana* is easy to look after compared with animal model organisms. It grows quickly, produces many very small seeds, has a small genome ~114.5 Mb and is genetically well characterised due to the volume of work being focused on this plant. As a member of the *Brassicaceae* family it is linked to more important cultivated species such as cabbage, mustard and radish.

The fruit is a siliqua 5–20 mm long, containing 20-30 seeds. Roots are simple in structure, with a single primary root that grows vertically downward, later producing smaller lateral roots. These roots form interactions with rhizosphere bacteria such as *Bacillus megaterium*. *A. thaliana* can complete its entire lifecycle in six weeks. The central stem that produces flowers grows after about three weeks, and the flowers naturally self-pollinate. In the lab, *A. thaliana* may be grown in Petri plates, pots, or hydroponics, under fluorescent lights or in a greenhouse.

Life Cycle:

The plant's small size and rapid lifecycle are also advantageous for research. Having specialized as a spring ephemeral, it has been used to found several laboratory strains that take

about six weeks from germination to mature seed. The small size of the plant is convenient for cultivation in a small space, and it produces many seeds. Further, the selfing nature of this plant assists genetic experiments. Also, as an individual plant can produce several thousand seeds; each of the above criteria leads to *A. thaliana* being valued as a genetic model organism.



Use as a model organism

Botanists and biologists began to research *A. thaliana* in the early 1900s, and the first systematic description of mutants was done around 1945. *A. thaliana* is now widely used for studying plant sciences, including genetics, evolution, population genetics, and plant development. Although *A. thaliana* has little direct significance for agriculture, it has several traits that make it a useful model for understanding the genetic, cellular, and molecular biology of flowering plants.

The first mutant in *A. thaliana* was documented in 1873 by Alexander Braun, describing a double flower phenotype (the mutated gene was likely *Agamous*, cloned and characterized in 1990). However, not until 1943 did Friedrich Laibach (who had published the chromosome number in 1907) propose *A. thaliana* as a model organism. His student, Erna Reinholz, published her thesis on *A. thaliana* in 1945, describing the first collection of *A. thaliana* mutants that they generated using X-raymutagenesis.

Nuclear genome

The small size of its genome, and the fact that it is diploid, makes *Arabidopsis thaliana* useful for genetic mapping and sequencing - with about 135 mega base pairs and five chromosomes, *A. thaliana* has one of the smallest genomes among plants. It was long thought to have the smallest genome of all flowering plants,[34] but that title is now considered to belong to plants in the genus *Genlisea*, order Lamiales, with *Genlisea tuberosa*, a carnivorous plant, showing a genome size of approximately 61 Mbp. It was the first plant genome to be sequenced, completed in 2000 by the Arabidopsis Genome Initiative. The most up-to-date version of the *A. thaliana*genome is maintained by the Arabidopsis Information Resource (TAIR). Much work has been done to assign functions to its 27,000 genes and the 35,000 proteins they encode. Post-genomic research, such as metabolomics, has also provided useful insights to the metabolism of this species and how environmental perturbations can affect metabolic processes.

Chloroplast genome

The plastome of *Arabidopsis thaliana* is a 154,478 base pair long DNA molecule,[31] a size typically encountered in most flowering plants. It comprises 136 genes coding for small subunit ribosomal proteins (*rps*, in yellow: see figure), large subunit ribosomal proteins (*rpl*, orange), hypothetical chloroplast open reading frame proteins (*ycf*, lemon), proteins involved in photosynthetic reactions (green) or in other functions (red), ribosomal RNAs (*rrn*, blue), and transfer RNAs (*trn*, black),

Mitochondrial genome

The mitochondrial genome of *Arabidopsis thaliana* is 367,808 base pairs long and contains 57 genes. There are many repeated regions in the *Arabidopsis*mitochondrial genome. The largest repeats recombine regularly and isomerize the genome. Like most plant mitochondrial genomes, the *Arabidopsis* mitochondrial genome exists as a complex arrangement of overlapping branched and linear molecules *in vivo*.

Genetics

Genetic transformation of *A. thaliana* is routine, utilizing *Agrobacterium tumefaciens* to transfer DNA into the plant genome. The current protocol, termed "floral dip", involves simply dipping flowers into a solution containing *Agrobacterium* carrying a plasmid of interest and a detergent. This method avoids the need for tissue culture or plant regeneration. The *A. thaliana* gene knockout collections are a unique resource for plant biology made possible by the availability of high-throughput transformation and funding for genomics resources. The site of T-DNA insertions has been determined for over 300,000 independent transgenic lines, with the information and seeds accessible through online T-DNA databases. Through these collections, insertional mutants are available for most genes in *A. thaliana*.

Non-Mendelian inheritance controversy

In 2005, scientists at Purdue University proposed that *A. thaliana* possessed an alternative to previously known mechanisms of DNA repair, producing an unusual pattern of inheritance. However, the phenomenon observed (reversion of mutant copies of the *HOTHEAD* gene to a wild-type state) was later suggested to be an artifact because the mutants show increased outcrossing due to organ fusion.

Plant–pathogen interactions

It is important to understand how plants achieve resistance to protect the world's food production, as well as the agriculture industry. Many model systems have been developed to better understand interactions between plants and bacterial, fungal, oomycete, viral, and nematode pathogens. *Arabidopsis thaliana* has been a powerful tool for the study of the subdicipline of plant pathology, that is, the interaction between plants and disease-causing pathogens.

Pathogen type	Example in *Arabidopsis thaliana*
Bacteria	*Pseudomonas syringae*, *Xanthomonas campestris*
Fungi	*Colletotrichum destructivum*, *Botrytis cinerea*, *Golovinomyces orontii*
Oomycete	*Hyaloperonospora arabidopsidis*
Viral	Cauliflower mosaic virus (CaMV), tomato mosaic virus (TMV)
Nematode	*Meloidogyne incognita*, *Heterodera schachtii*

Evolutionary aspect of plant-pathogen resistance

Plants are affected by multiple pathogens throughout their lifetime. In response to the presence of pathogens, plants have evolved receptors on the cell surface to detect and respond to pathogens. *Arabidopsis Thaliana* is a model organism used to determine specific defense mechanisms of plant-pathogen resistance. These plants have special receptors on their cell surfaces that allow for detection of pathogens and initiate mechanisms to inhibit pathogen growth.

Self-pollination

A. thaliana is a predominantly self-pollinating plant with an outcrossing rate estimated at less than 0.3%. An analysis of the genome-wide pattern of linkage disequilibrium suggested that

self-pollination evolved roughly a million years ago or more. Meioses that lead to self-pollination are unlikely to produce significant beneficial genetic variability. However, these meioses can provide the adaptive benefit of recombinational repair of DNA damages during formation of germ cells at each generation. Such a benefit may have been sufficient to allow the long-term persistence of meioses even when followed by self-fertilization. A physical mechanism for self-pollination in *A. thaliana* is through pre-anthesis autogamy, such that fertilisation takes place largely before flower opening.

Advance Research

Exposing *A. thaliana* to *Agrobacterium tumifaciens*provides a means of efficient transformation vector making *A. thaliana* a versatile model organism for use in the biology laboratory. *A. thaliana* is widely used in the fields of plant science, genetics and evolution and has helped further our understanding of germination and aspects of plant growth that are important in commercial crops.[1,2] In recent years *A. thaliana* has even become a model organism for the study of the biochemical and molecular processes involved in human diseases.

Other research:

Ongoing research on *Arabidopsis thaliana* is being performed on the International Space Station by the European Space Agency. The goals are to study the growth and reproduction of plants from seed to seed in microgravity. 'Plant on a chip' devices in which *A. thaliana* tissues can be cultured in semi in-vitro conditions have been described. Use of these devices may aid our understanding of pollen tube guidance and the mechanism of sexual reproduction in *A. thaliana.*

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Prepared by Dr. P. Thirunavukkarasu, Assistant Professor, Dept. of Microbiology, KAHE

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W5. https://www.arabidopsis.org/portals/education/aboutarabidopsis.jsp
W6. https://andor.oxinst.com/learning/view/article/advantages-of-using-arabidopsis-thaliana-as-a-model-organism

POSSIBLE QUESTION

2marks

1. Write short notes on evolution
2. Define model organism
3. Write the function of trasfection
4. What is the role of ribosome
5. Write note on genetic engineering
6. Define cloning
7. Write short notes on vector?
8. Give short notes on mutation.
9. Comment on classical model organism ?
10. Write short notes on functions of Flagella.

8 marks

1. Explain the model organism and the genetic approach of E. coli (OR)
2. Explain the model organism and the genetic approach of Neurospora crassa
3 Describe the genetic analysis of Yeast (Saccharomyces cervisiae) (OR)
4. Why is Arabidopsis thaliana widely used a model organism?
5.. Detail of Mutation study in Caenorhabditis elecans (C. elecans) (OR)
6.Why is Drosophila melanogaster a good model organism?

KARPAGAM ACADEMY OF HIGHER EDUCATION

CLASS: III B. Sc MICROBIOLOGY **COURSE NAME: INHERITANCE BIOLOGY**

COURSE CODE: 17MBU504B **UNIT: 1** **BATCH-2017-2020**

Sno	Question	Opt 1	Opt 2	Opt 3	Opt 4	Answer
1	Which of the following is not a direct conclusion that can be drawn from Mendel's Experiment?	Only one parental trait is expressed	Two copies of each trait is inherited in sexually reproducing organism	For recessive trait to be expressed, both copies should be identical	Natural selection can alter frequency of an inherited trait.	Natural selection can alter frequency of an inherited trait.
2	Mendel's experimental material was	pisum sativum	Oryza sativa	Vigna sinensis	Arabidopsis thaliana	pisum sativum Oryza sativa
3	Which one is a possible progeny in F2 generation of pure bred tall plant with round seed and short plant with wrinkled seeds?	Tall plant with round seeds	Tall plant with wrinkled seeds	Short plant with round seed	All of the above	All of the above
4	Natural place where the organism or communities live is known as	Niche	Habit	Habitat	Biome	Habitat
5	With whom you can associate theory of evolution?	Charles Darwin	Mendel	Stanley miller	Harold Urey	Charles Darwin
6	Which of the following is called as Drosophila of the plant kingdom	Neurospora	E. coli	Pisum sativa	Arabidopsis thaliana	Arabidopsis thaliana
7	Homologous organ have	Same structure, same function	Different structure, different function	Same structure, different function	Different structure, same function	Same structure, different function
8	The organism used to study DNA replication	Neurospora crassa	Drosophila melanogaster	Escherichia coli	Bacillus subtilis	Escherichia coli
9	Mendel crossed a type breeding round seeded plant with	Oval seeded plant	Circular seeded plant	Wrinkled seed plant	Elongated seeded plant	Wrinkled seed plant
10	Why are copy numbers important in a cloning experiment?	Maximum expression	Ease of manipulation	Cost efficiency	Availability of stock	Maximum expression

11	Incomplete dominance was first described in	Mirabilis jalapa	Arabidopsis thaliana	Pisum sativum	Triticum aestivum	Mirabilis jalapa
12	In drosophila (fruit flies), eye colour is sex-linked and red eye colour is dominant to white eye colour. Which of the following are not possible in a cross between a red-eyed male and a heterozygous female?	Red-eyed male	White-eyed male	Carrier female	Homozygous white-eyed female	Homozygous white-eyed female
13	Mutation was discovered by Hugo de vries in	Pisum sativum	Triticum seclae	Oenothera lamarckiana	Mirabilis jalapa	Oenothera lamarckiana
14	The model organism widely used for developmental and toxicological studies	Neurospora crassa	Drosophila melanogaster	Danio rerio	Bacillus sublitis	Bacillus sublitis
15	Which of the following factors could lead to variations in the offspring of asexually reproducing organisms?	Crossing over	Fertilization	Mutations	Independent assortment	Mutations
16	Temin and Baltimore discovered reverse transcriptase in	retro virus	T2 phages	Roux’s sarcoma virus	herpes virus	Roux’s sarcoma virus
17	The concept of pure line put forward by johannsen was based on his experiments	Pisum sativum	Phaseolous vulgaris	Vigna sinensis	Arabidopsis thaliana	Phaseolous vulgaris
18	Incomplete dominance was first described in	Mirabilis jalapa	Arabidopsis thaliana	Pisum sativum	Tricum aestivum	Pisum sativum
19	The mitotic crossing over was reported in the fungus	Aspergillus niger	Penicillium notatum	Aspergillus nidulans	Sacharomyces cervisae	Aspergillus nidulans
20	Tetrad analysis confirmed the occurrence of crossing over during tetrad stage. This was first reported in	Neurospora	E. coli	Pisum sativum	Arabidopsis thaliana	Neurospora

21	The model organism widely used for developmental and toxicological studies	Neurospora crassa	Drosophila melanogaster	Danio rerio	Bacillus subtils	Danio rerio
22	Creighton and McClintock provided cytological evidence for crossing over based on experiments in	Maize	Rice	Pea	Arabidopsis	Maize
23	Sex determination in plants was extensively investigated in	Pisum sativum	Phaseolus vulgaris	Melandrium	Arabidopsis thaliana	Melandrium
24	The most widely used model for studying developmental biology and neurobiology	Escherichia coli	Saccharopmyces cervisae	Caenorhabditis elegans	Neurospora crassa	Caenorhabditis elegans
25	Which organism has the highest number of vectors?	Yeast	Mammalian cells	E.coli	Fungi	E.coli
26	Why is Arabidopsis thalania widely used as model organism?	Rapid life cycle	Requires little space	Genome has been sequenced	All of the above	All of the above
27	Divergent evolution of a single group of organisms in a new environment is called --------?	Adaptive radiation	Uniformitaranism	Catastrophism	Convergent evolution	Adaptive radiation
28	Darwin judged the fitness of an individual by	Ability to defend itself	Strategy to obtain food	Number of offspring	Dominance over other individuals	Number of offspring
29	Introduction of DNA molecules into the recipient organism is termed as _____	Transformation	Translation	Transduction	Transcription	Transformation
30	According to Darwin, Evolution is --------	A slow, gradual and continuous process	A sudden but discontinuous process	A slow and discontinuous process	A slow, sudden and discontinuous	A slow, gradual and continuous process
31	Which of the following sentences is correct about microspheres?	Don't have all properties of like	Composed of many protein molecules	Bud to form smaller microspheres	All of these are correct	All of these are correct

32	Which of the statements hold true for conjugation?	Conjugation is the natural process of transferring DNA from one species to another	It is the artificial process in case the cells are not able to take them up naturally	The plasmids are transferred from one cell to another by physical contact	The plasmids are transferred from one cell to another by chemical means	It is the artificial process in case the cells are not able to take them up naturally
33	Evolution of different species in an given area starting from appoint and spreading to other geographical area is know as	Migration	Divergent evolution	Divergent evolution	National selection	Divergent evolution
34	Transformation carried out using a particle gun is known as biolistic transformation. It falls under which category of transformation?	Physical	Chemical	Electroporation	Natural	Physical
35	When two species of different generalogy come to resemble each other as a result adaptation, the phenomenon is termed	Microevolution	Divergent evolution	Convergent evolution	Co-evolution	Convergent evolution
36	Organic compounds first evolved in earth required for origin of life were	Proteins and Amino acids	Proteins and Nucleic acids	Urea and Amino acids	Urea and Nucleic acids	Proteins and Nucleic acids
37	Which of the following instrument is used for recovery of yeast cells?	Fermenter	Centrifuge	Filter press	Mash storage	Filter press
38	Select the correct statement from the following:	Fitness is the end result of the ability to adapt and gets selected by nature	Darwinian variations are small and directionless	Mutations are random and directional	All mammals except whales and camels have seven cervical vertebrae	Fitness is the end result of the ability to adapt and gets selected by nature

39	Which statement is incorrect?	Alkaptonuria is due to a recessive gene	Gene controls in the metabolism	In eukaryotes DNA synthesis is faster than prokaryotes	Homogentistic acid is excreted in the urine in alkaptonuric patients	In eukaryotes DNA synthesis is faster than prokaryotes
40	Diversification in plant life appeared	Due to abrupt mutations	Suddenly on earth	By seed dispersal	Due to long periods of evolutionary changes	Due to long periods of evolutionary changes
41	Segregation of alleles can occur at anaphase I or at Anaphase II of meiosis. With reference to this statement, which one of the following organism is an ideal model system for identifying stage of allelic segregation at meiosis?	Neurospora crassa	Saccharomyces cervisiae	Drosophila melanogaster	Psium sativum	Neurospora crassa
42	Which one of the following sequences was proposed by Darwin and Wallace for organic evolution?	Overproduction, variations, constancy of population size, natural selection	Variations, constancy of population size, overproduction, natural selection	Overproduction, constancy of population size, variations, natural selection	Variations, natural selection, overproduction, constancy of population size	Overproduction, constancy of population size, variations, natural selection
43	Hybrid dysgenesis is Drosophila is caused by p-elements. Which one of the following crosses between different cytotypes will lead to dysgenesis?	M-cytotype ♀ X M-cytotype ♂	M-cytotype ♀ X P-cytotype ♂	P-cytotype ♀ X M-cytotype ♂	P-cytotype ♀ X P-cytotype ♂	M-cytotype ♀ X P-cytotype ♂
44	Name an Organelle which serves as a primary packaging area for molecules that will be distributed throughout the cell?	Mitochondria	Plastids	Golgi apparatus	Vacuole	Golgi apparatus

45	What generalization can be applied to the pole plasm of Drosophila, the P-granules of C. elegans, the yolk-free vegetal cytoplasm of Xenopus, and the localized mRNA for vasa in zebrafish?	All mark the posterior end of the antero-posterior axis	All are present at fertilization in the vegetal pole of the egg	All are determinants that specify the dorso-ventral axis of the fertilized egg	All mark the special region of cytoplasm, the germplasm that is involved in specification of germ cells	All mark the special region of cytoplasm, the germplasm that is involved in specification of germ cells
46	Name an organism which contains single chromosome and cell division occurs through fission or budding?	Eukaryotes	Prokaryotes	Bacteria	Primitive organism	Prokaryotes
47	Which among the following sentence is not correct about the organelles?	They are found in all Eukaryotic cells	They are found in multicellular organisms	They coordinate to produce the cell	They are small sized and mostly internal	They are found in multicellular organisms
48	Which of the following is not a characteristic of 'r' selected species	Produce large number of progenies	Reproduce quickly	Low survival rate of progenies	Parental care	Parental care
49	The mitotic crossing over was reported in the fungus	Aspergillus niger	Penicillum notatum	Aspergillus nidulans	Sacharomyces cervisease	Aspergillus nidulans
50	On which medium are yeast plasmids transformed cells plated?	Luria Broth	Agar	Minimal	Nutrient	Minimal
51	Any features of an organism or part which enable it to exist under conditions of its habitat is known as	Adaptive variation	Adjustment	Acclimatization	Adaptation	Adaptation
52	What are the signals, inside the host that surround the gene?	Amino acids	Nucleotides	Proteins	Bacterium	Nucleotides
53	Which of the following is not an important signal for the E.coli genes?	Promoter	Terminator	Inducer	Ribosome binding site	Inducer

54	A tem-loop structure in an E.coli cell is formed by _____	Gene	Terminator	Inducer	Promoter	Terminator
55	The initiation codon of the gene is located _____ of the ribosome binding site.	Upstream	Downstream	Away	Inside	Downstream
56	The 'TATA Box' in animals contains one more _____ as compared to that present in E. coli	Adenosine	Cytosine	Thymine	Guanine	Adenosine
57	What could be a possible reason for non-expression of a foreign gene in an E. coli host?	Recognition of expression signals	Non-recognition of expression signals	Indefinite size	inefficient ligation	Non-recognition of expression signals
58	Cloning vectors that can be used for recombinant protein production are called _____	Expression vectors	Hybrid vectors	Hosts	Advanced vectors	Expression vectors
59	E. coli glutathione-S-transferase protein can be purified by adsorption onto _____	Charcoal	Sucrose beads	Agarose beads	Glucose beads	Agarose beads
60	What is a disadvantage of fusion systems?	Property alteration	Reduced amount	Cost inefficiency	Host range	Property alteration

Unit II

Law of Dominance (the "Third Law")

Mendel's Law of Dominance states that recessive alleles will always be masked by dominant alleles. Therefore, a cross between a homozygous dominant and a homozygous recessive will always express the dominant phenotype, while still having a heterozygous genotype. The Law of Dominance can be explained easily with the help of a mono hybrid cross experiment:- In a cross between two organisms pure for any pair (or pairs) of contrasting traits (characters), the character that appears in the F1 generation is called "dominant" and the one which is suppressed (not expressed) is called "recessive." Each character is controlled by a pair of dissimilar factors. Only one of the characters expresses. The one which expresses in the F1 generation is called Dominant. However, the law of dominance is not universally applicable.

What Is Mendel's Law of Segregation?

Mendel formulated the law of segregation as a result of performing monohybrid cross experiments on plants. The specific traits that were being studied exhibited complete dominance. In complete dominance, one phenotype is dominant, and the other is recessive. Not all types of genetic inheritance, however, show total dominance.

The principles that govern heredity were discovered by a monk named Gregor Mendel in the 1860s. One of these principles, now called Mendel's Law of Segregation, states that allele pairs separate or segregate during gamete formation, and randomly unite at fertilization.

There are four main concepts related to this principle. They are as follows:

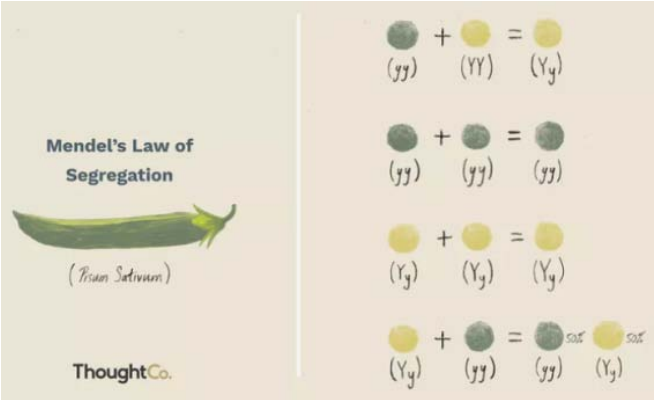
- A gene can exist in more than one form or allele.
- Organisms inherit two alleles for each trait.
- When sex cells are produced (by meiosis), allele pairs separate leaving each cell with a single allele for each trait.
- When the two alleles of a pair are different, one is dominant, and the other is recessive.
-

For example, the gene for seed color in pea plants exists in two forms. There is one form or allele for yellow seed color (Y) and another for green seed color (y). In this example, the allele for yellow seed color is dominant, and the allele for green seed color is recessive. When the alleles of a pair are different (heterozygous), the dominant allele trait is expressed, and the recessive allele trait is masked. Seeds with the genotype of (YY) or (Yy) are yellow, while seeds that are (yy) are green.

In incomplete dominance, neither allele is completely dominant over the other. In this type of intermediate inheritance, the resulting offspring exhibit a phenotype that is a mixture of both parent phenotypes. Incomplete dominance is seen in snapdragon plants. Pollination between a plant with red flowers and a plant with white flowers produces a plant with pink flowers.

In co-dominance relationships, both alleles for a trait are fully expressed. Co-dominance is exhibited in tulips. Pollination that occurs between red and white tulip plants can result in a plant

with flowers that are both red and white. Some people get confused about the differences between incomplete dominance and co-dominance.



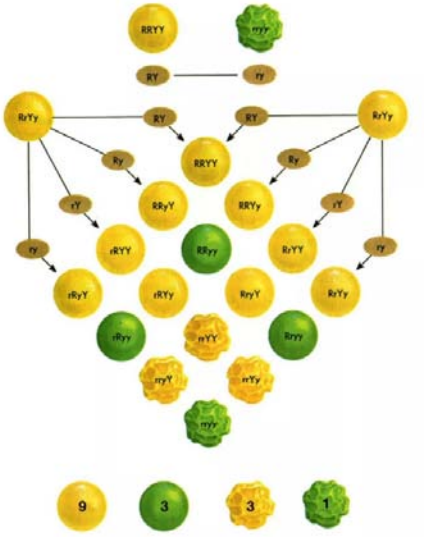
Mendel's Independent Assortment Experiment

Mendel performed dihybrid crosses in plants that were true-breeding for two traits. For example, a plant that had round seeds and yellow seed color was cross-pollinated with a plant that had wrinkled seeds and green seed color.

In this cross, the traits for round seed shape (RR) and yellow seed color (YY) are dominant. Wrinkled seed shape (rr) and green seed color (yy) are recessive.

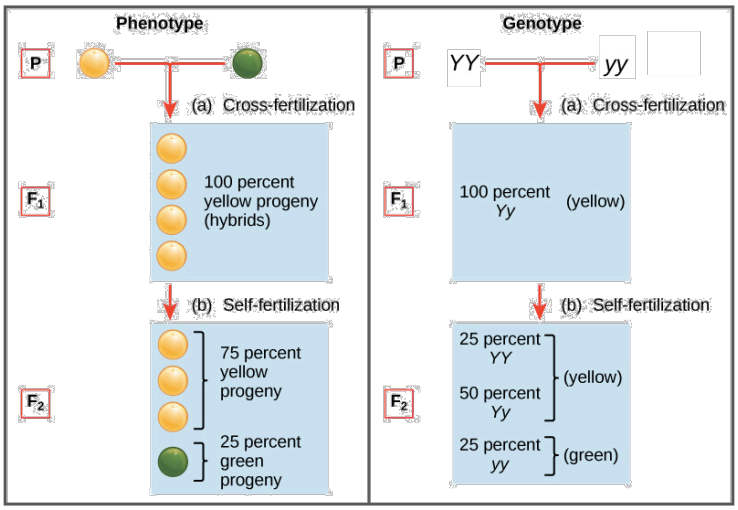
The resulting offspring (or F1 generation) were all heterozygous for round seed shape and yellow seeds (RrYy). This means that the dominant traits of round seed shape and yellow color completely masked the recessive traits in the F1 generation.

Discovering the Law of Independent Assortment



The F2 Generation: After observing the results of the dihybrid cross, Mendel allowed all of the F1 plants to self-pollinate. He referred to these offspring as the F2 generation.
Mendel noticed a 9:3:3:1 ratio in the phenotypes. About 9/16 of the F2 plants had round, yellow seeds; 3/16 had round, green seeds; 3/16 had wrinkled, yellow seeds; and 1/16 had wrinkled, green seeds.
Mendel's Law of Independent Assortment: Mendel performed similar experiments focusing on several other traits such as pod color and seed shape; pod color and seed color; and flower position and stem length. He noticed the same ratios in each case.
From these experiments, Mendel formulated what is now known as Mendel's law of independent assortment. This law states that allele pairs separate independently during the formation of gametes. Therefore, traits are transmitted to offspring independently of one another.

Mendel's model of inheritance
Based on his results (including that magic 3:13:13, colon, 1 ratio), Mendel came up with a model for the inheritance of individual characteristics, such as flower color.
In Mendel's model, parents pass along “heritable factors," which we now call genes, that determine the traits of the offspring. Each individual has two copies of a given gene, such as the gene for seed color (*Y* gene) shown below. If these copies represent different versions, or alleles, of the gene, one allele-the dominant one-may hide the other allele-the recessive one. For seed color, the dominant yellow allele *Y* hides the recessive green allele *y*.



A graphic with 2 columns, the first with the heading “Phenotype” and the second with the heading “Genotype.” In the phenotype column, one yellow pea plant cross-fertilizes with one green pea plant. The first generation of offspring is 100 percent yellow pea plants. After self-fertilization of these yellow pea offspring, 75 percent of the second generation offspring have yellow peas and 25 percent have green peas. The genotype column shows the first generation

offspring as 100 percent Yy, and the second generation as 25 percent YY, 50 percent Yy, and 25 percent yy.

The set of alleles carried by an organism is known as its genotype. Genotype determines phenotype, an organism's observable features. When an organism has two copies of the same allele (say, *YY* or *yy*), it is said to be homozygousfor that gene. If, instead, it has two different copies (like *Yy*), we can say it is heterozygous. Phenotype can also be affected by the environment in many real-life cases, though this did not have an impact on Mendel's work.

1900: Rediscovery of Mendel's Work:

DeVries, Correns and Tschermak independently rediscover Mendel's work. Three botanists - Hugo DeVries, Carl Correns and Erich von Tschermak - independently rediscovered Mendel's work in the same year, a generation after Mendel published his papers. They helped expand awareness of the Mendelian laws of inheritance in the scientific world.

The three Europeans, unknown to each other, were working on different plant hybrids when they each worked out the laws of inheritance. When they reviewed the literature before publishing their own results, they were startled to find Mendel's old papers spelling out those laws in detail. Each man announced Mendel's discoveries and his own work as confirmation of them.

By 1900, cells and chromosomes were sufficiently understood to give Mendel's abstract ideas a physical context.

After exploring various animal and plant systems, Mendel conducted studies of 34 different strains of peas and selected 22 kinds for further experiments. He chose to study traits that were distinct and discontinuous and exhibited clear patterns of dominance and recessiveness. The "law of segregation," also known as Mendel's first law, refers to Mendel's proof that recessive traits reappear in predictable patterns. Crosses of peas that differed in one trait produced the now-famous 3:1 ratios. Complex studies that followed the variations of two or three traits led to the patterns of recombination now known as Mendel's second law, or the "law of independent assortment."

Mendel discussed his results at a meeting of the Brno Society for Natural History in March 1865 and published his paper "Research on Plant Hybrids" in the 1866 issue of the Society's *Proceedings.* He also sent reprints of his article to prominent scientists but received little attention and virtually no understanding.

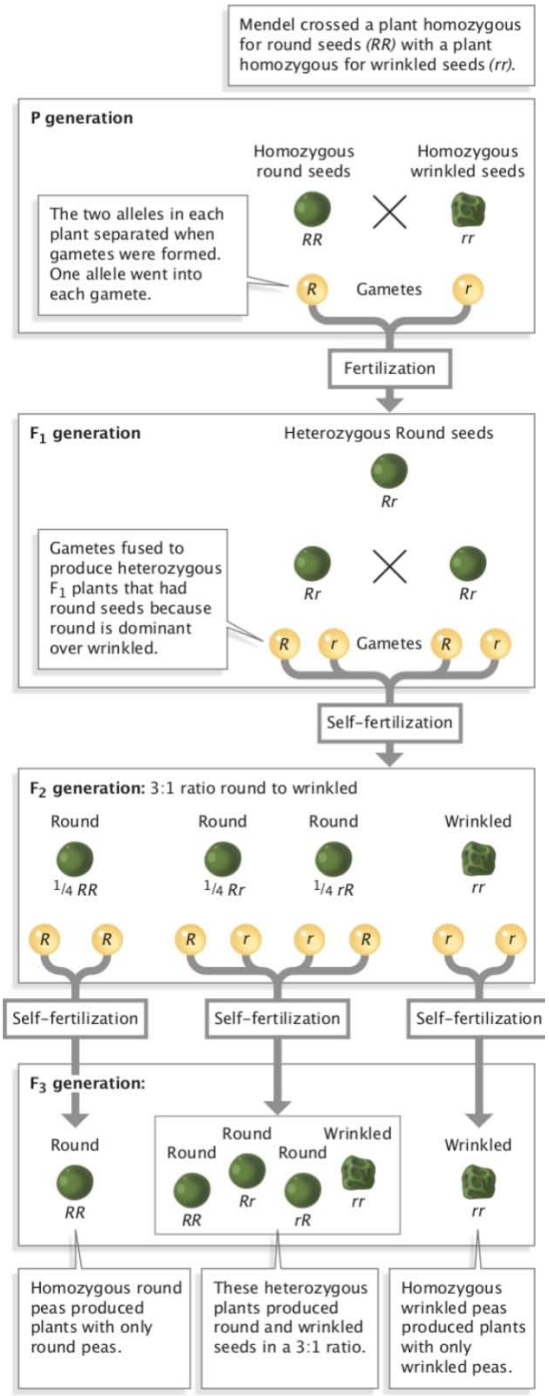
Contemporaries tended to dismiss Mendel's "numbers and ratios" as merely empirical and devoid of a respectable theoretical framework. Sir Ronald A. Fisher (1890-1962), however, argued that the experimental design reported in Mendel's classic paper was so elegant that the experiments had to have been a confirmation, or demonstration, of a theory Mendel had previously formulated. Furthermore, Fisher claimed that Mendel's ratios are closer to the theoretical expectation than sampling theory would predict and he insisted that such results could not be

obtained without an "absolute miracle of chance." Although Mendel was discouraged by the lack of response from the scientific community, he remained convinced of the fundamental value and universality of his work.

Mendel and Alleles

As mentioned, Mendel's data did not support the ideas about trait blending that were popular among the biologists of his time. As there were never any semi-wrinkled seeds or greenish-yellow seeds, for example, in the F_2 generation, Mendel concluded that blending should not be the expected outcome of parental trait combinations. Mendel instead hypothesized that each parent contributes some particulate matter to the offspring. He called this heritable substance "elementen." (Remember, in 1865, Mendel did not know about DNA or genes.) Indeed, for each of the traits he examined, Mendel focused on how the elementen that determined that trait was distributed among progeny. We now know that a single gene controls seed form, while another controls color, and so on, and that elementen is actually the assembly of physical genes located on chromosomes. Multiple forms of those genes, known as alleles, represent the different traits. For example, one allele results in round seeds, and another allele specifies wrinkled seeds.

One of the most impressive things about Mendel's thinking lies in the notation that he used to represent his data. Mendel's notation of a capital and a lowercase letter (*Aa*) for the hybrid genotype actually represented what we now know as the two alleles of one gene: *A* and *a*. Moreover, as previously mentioned, in all cases, Mendel saw approximately a 3:1 ratio of one phenotype to another. When one parent carried all the dominant traits (*AA*), the F_1 hybrids were "indistinguishable" from that parent. However, even though these F_1 plants had the same phenotype as the dominant P_1 parents, they possessed a hybrid genotype (*Aa*) that carried the potential to look like the recessive P_1 parent (*aa*). After observing this potential to express a trait without showing the phenotype, Mendel put forth his second principle of inheritance: the principle of segregation. According to this principle, the "particles" (or alleles as we now know them) that determine traits are separated into gametes during meiosis, and meiosis produces equal numbers of egg or sperm cells that contain each allele.



Chromosomal Theory of Inheritance

The speculation that chromosomes might be the key to understanding heredity led several scientists to examine Mendel's publications and re-evaluate his model in terms of the behavior of

chromosomes during mitosis and meiosis. In 1902, Theodor Boveri observed that proper embryonic development of sea urchins does not occur unless chromosomes are present. That same year, Walter Sutton observed the separation of chromosomes into daughter cells during meiosis. Together, these observations led to the development of the Chromosomal Theory of Inheritance, which identified chromosomes as the genetic material responsible for Mendelian inheritance.

Sutton and Boveri: (a) Walter Sutton and (b) Theodor Boveri are credited with developing the Chromosomal Theory of Inheritance, which states that chromosomes carry the unit of heredity (genes).

The Chromosomal Theory of Inheritance was consistent with Mendel's laws and was supported by the following observations:

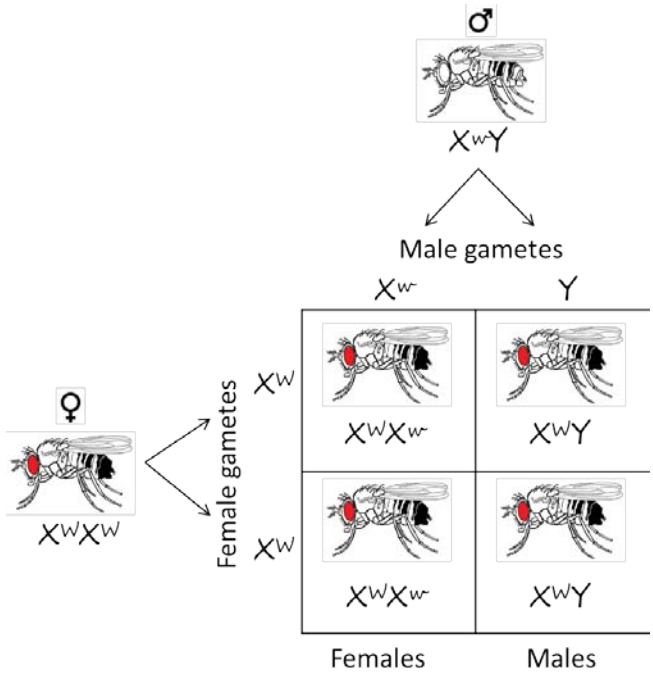
- During meiosis, homologous chromosome pairs migrate as discrete structures that are independent of other chromosome pairs.
- The sorting of chromosomes from each homologous pair into pre-gametes appears to be random.
- Each parent synthesizes gametes that contain only half of their chromosomal complement.
- Even though male and female gametes (sperm and egg) differ in size and morphology, they have the same number of chromosomes, suggesting equal genetic contributions from each parent.
- The gametic chromosomes combine during fertilization to produce offspring with the same chromosome number as their parents.

Despite compelling correlations between the behavior of chromosomes during meiosis and Mendel's abstract laws, the Chromosomal Theory of Inheritance was proposed long before there was any direct evidence that traits were carried on chromosomes. Critics pointed out that individuals had far more independently segregating traits than they had chromosomes. It was only after several years of carrying out crosses with the fruit fly, *Drosophila melanogaster*, that Thomas Hunt Morgan provided experimental evidence to support the Chromosomal Theory of Inheritance.

In 1910, Thomas Hunt Morgan started his work with *Drosophila melanogaster*, a fruit fly. He chose fruit flies because they can be cultured easily, are present in large numbers, have a short generation time, and have only four pair of chromosomes that can be easily identified under the microscope. They have three pair of autosomes and a pair of sex chromosomes. At that time, he already knew that X and Y have to do with gender. He used normal flies with red eyes and mutated flies with white eyes and cross bred them. In flies, the wild type eye color is red (XW) and is dominant to white eye color (Xw). He was able to conclude that the gene for eye color was on the X chromosome. This trait was thus determined to be X-linked and was the first X-linked trait to be identified. Males are said to be hemizygous, in that they have only one allele for any X-linked characteristic.

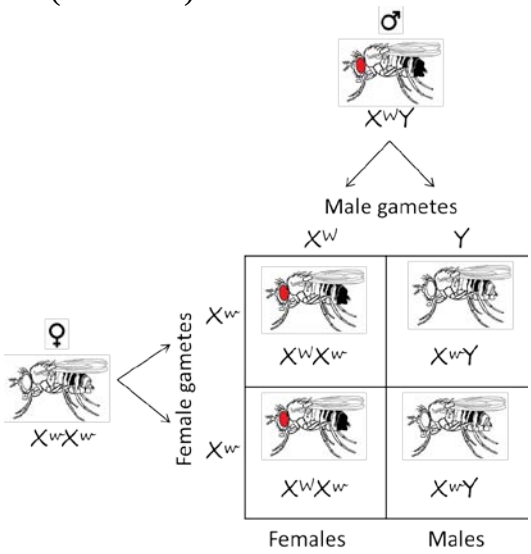
Eye Color in Fruit Flies: In Drosophila, the gene for eye color is located on the X chromosome. Red eye color is wild type and is dominant to white eye color.

n *Drosophila*, normal flies have red eyes. Red eye color is dominant. Morgan discovered a recessive mutation (allele) that caused white eyes. When Morgan mated a red eyed female to a white eyed male, all the progeny had red eyes. This result makes perfect sense with a dominant/recessive inheritance pattern, and here is the Punnett square demonstrating that (x^*w* = recessive white eye mutant allele; x^*W* = dominant red eye wild-type allele):



But Morgan got a surprising result when he made the reciprocal cross, mating white eyed females to red eyed males. Instead of all red eyed progeny, he saw that all the females had red eyes and all the males had white eyes. This result seemed to violate Mendel's principle of independent assortment, because two different traits (gender and eye color) seemed to be linked. The only way to explain these results was if the gene that caused eye color was located

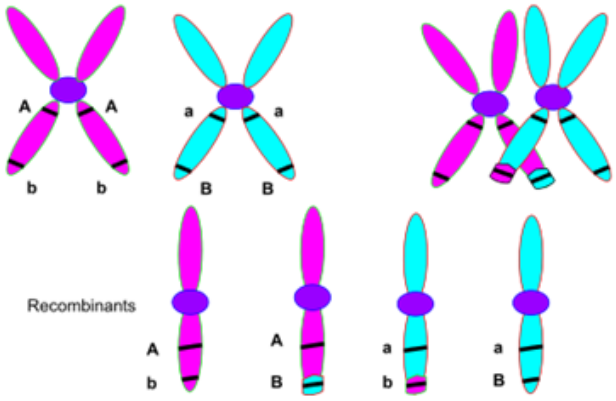
on (linked to) the X chromosome. Here is the Punnett square demonstrating this cross:



Linkage

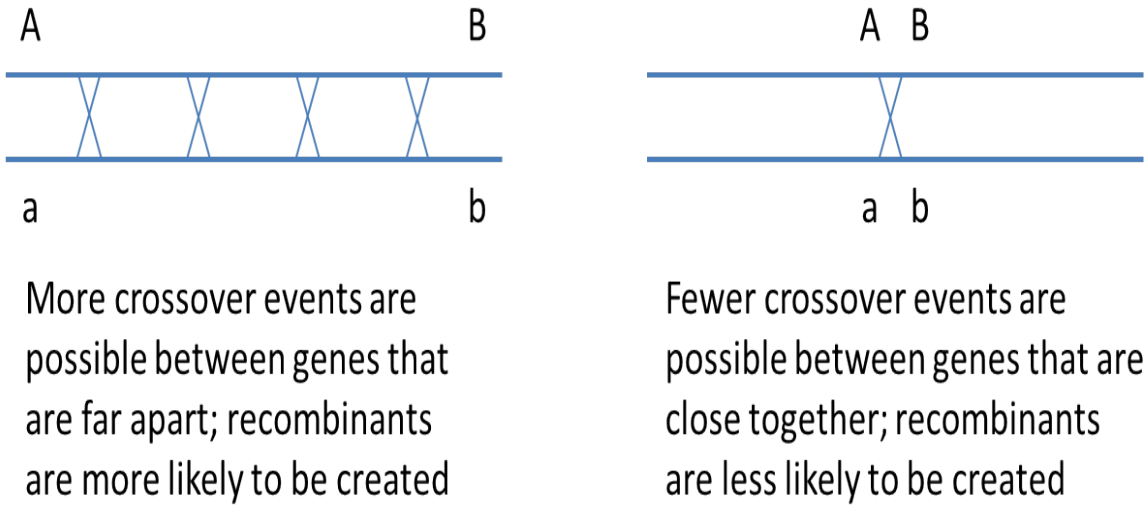
Linkage is inheritance of traits in a pattern that violates Mendel's principle of independent assortment, the idea that alleles for different traits are segregated into gametes independently. Sex-linkage is a special type of linkage, where traits are linked to sex chromosomes. Genetic linkage occurs when the genes controlling two different traits are located *near* each other on the same chromosome. The basic idea is that if two genes are on the same chromosome, and you inherit the *whole* chromosome, then you have to inherit those two genes (and whatever alleles they have) together.

However, this is biology so there is a caveat: the phenomenon of crossing over helps to shuffle the alleles for genes located on the same chromosome. A crossover event between the locations of two genes on a chromosome results in genetic recombination, or new combinations of alleles on a chromosome.



Crossing over between genes A and B results in recombinant chromosomes with new allele combinations a, b and A, B, in addition to the original parental combinations A, b and a, B. Image from Wikimedia by user Abbyprovenzano, with CC-BY-SA-3.0 license.

Crossing over occurs during meiotic prophase I, when the homologous chromosomes align and synapse, and results in physically swapping genetic material (DNA) between non-sister chromatids of the paired homologous chromosomes. Because crossing over occurs randomly along the chromosome, the closer two genes are physically located to each other on a chromosome, the less likely that a crossover will occur between them. Conversely, the farther apart two genes are located from each other along the chromosome, the more likely they are to be swapped with the alleles on the homologous chromosome. The image below illustrates this idea:



It may be surprising to realize that two genes on the same chromosome will assort independently (like genes located on separate chromosomes) if they are far enough apart that a crossover almost always occurs between them, producing 50% recombinants (because crossing over involves only two of the 4 chromatids in a synapsed pair of homologous chromosomes, the maximum recombination frequency is 50%).

The video below walks through linkage as a violation of independent assortment and explains how crossing over breaks linkage. Note this video uses an incomplete definition of linkage: linkage occurs when two genes are *located close together on the same chromosome* and thus *tend to be inherited together*. It is not sufficient for genes to be on the same chromosome to be linked; they also have to be close enough together that crossing over between them is a relatively rare event.

Allele

An allele is a variant form of a given gene. Sometimes, different alleles can result in different observable phenotypic traits, such as different pigmentation. A notable example of this trait of

color variation is Gregor Mendel'sdiscovery that the white and purple flower colors in pea plants were the result of "pure line" traits which could be used as a control for future experiments. However, most genetic variations result in little or no observable variation.

Most multicellular organisms have two sets of chromosomes; that is, they are diploid. In this case, the chromosomes can be paired: each pair is made up of two chromosomes of the same type, known as homologous chromosomes. If both alleles at a gene (or locus) on the homologous chromosomes are the same, they and the organism are homozygous with respect to that gene (or locus). If the alleles are different, they and the organism are heterozygouswith respect to that gene.

Alleles that lead to dominant or recessive

n many cases, genotypic interactions between the two alleles at a locus can be described as dominant or recessive, according to which of the two homozygous phenotypes the heterozygote most resembles. Where the heterozygote is indistinguishable from one of the homozygotes, the allele expressed is the one that leads to the "dominant" phenotype,[6] and the other allele is said to be "recessive". The degree and pattern of dominance varies among loci. This type of interaction was first formally described by Gregor Mendel. However, many traits defy this simple categorization and the phenotypes are modeled by co-dominance and polygenic inheritance.

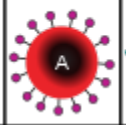
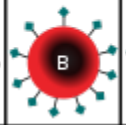
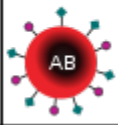
The term "wild type" allele is sometimes used to describe an allele that is thought to contribute to the typical phenotypic character as seen in "wild" populations of organisms, such as fruit flies (*Drosophila melanogaster*). Such a "wild type" allele was historically regarded as leading to a dominant (overpowering - always expressed), common, and normal phenotype, in contrast to "mutant" alleles that lead to recessive, rare, and frequently deleterious phenotypes. It was formerly thought that most individuals were homozygous for the "wild type" allele at most gene loci, and that any alternative "mutant" allele was found in homozygous form in a small minority of "affected" individuals, often as genetic diseases, and more frequently in heterozygous form in "carriers" for the mutant allele. It is now appreciated that most or all gene loci are highly polymorphic, with multiple alleles, whose frequencies vary from population to population, and that a great deal of genetic variation is hidden in the form of alleles that do not produce obvious phenotypic differences.

Multiple allele

A population or species of organisms typically includes multiple alleles at each locus among various individuals. Allelic variation at a locus is measurable as the number of alleles (polymorphism) present, or the proportion of heterozygotes in the population. A null allele is a gene variant that lacks the gene's normal function because it either is not expressed, or the expressed protein is inactive.

For example, at the gene locus for the ABO blood typecarbohydrate antigens in humans,[7] classical genetics recognizes three alleles, I^A, I^B, and i, which determine compatibility of blood transfusions. Any individual has one of six possible genotypes(I^AI^A, I^Ai, I^BI^B, I^Bi, I^AI^B,

and ii) which produce one of four possible phenotypes: "Type A" (produced by I^AI^A homozygous and I^Ai heterozygous genotypes), "Type B" (produced by I^BI^Bhomozygous and I^Bi heterozygous genotypes), "Type AB" produced by I^AI^B heterozygous genotype, and "Type O" produced by ii homozygous genotype. (It is now known that each of the A, B, and O alleles is actually a class of multiple alleles with different DNA sequences that produce proteins with identical properties: more than 70 alleles are known at the ABO locus.[8] Hence an individual with "Type A" blood may be an AO heterozygote, an AA homozygote, or an AA heterozygote with two different "A" alleles.)

	Group A	Group B	Group AB	Group O
Red blood cell type				
Antibodies in plasma	 Anti-B	 Anti-A	None	 Anti-A and Anti-B
Antigens in red blood cell	 A antigen	 B antigen	 A and B antigens	None

Complementation test

In genetics, complementation occurs when two strains of an organism with different homozygous recessive mutationsthat produce the same mutant phenotype (for example, a change in wing structure in flies) produce offspring with the wild-type phenotype when mated or crossed. Complementation will occur only if the mutations are in different genes. In this case, each strain's genome supplies the wild-type allele to "complement" the mutated allele of the other strain's genome. Since the mutations are recessive, the offspring will display the wild-type phenotype. A complementation test (sometimes called a "cis-trans" test) can be used to test whether the mutations in two strains are in different genes. Complementation will not occur if the mutations are in the same gene. The convenience and essence of this test is that the mutations that produce a phenotype can be assigned to different genes without the exact knowledge of what the gene product is doing on a molecular level. The complementation test was developed by American geneticistEdward B. Lewis.

If the combination of two genomes containing different recessive mutations yields a mutant phenotype, then there are three possibilities:

1. Mutations occur in the same gene.
2. One mutation affects the expression of the other.
3. One mutation may result in an inhibitory product.

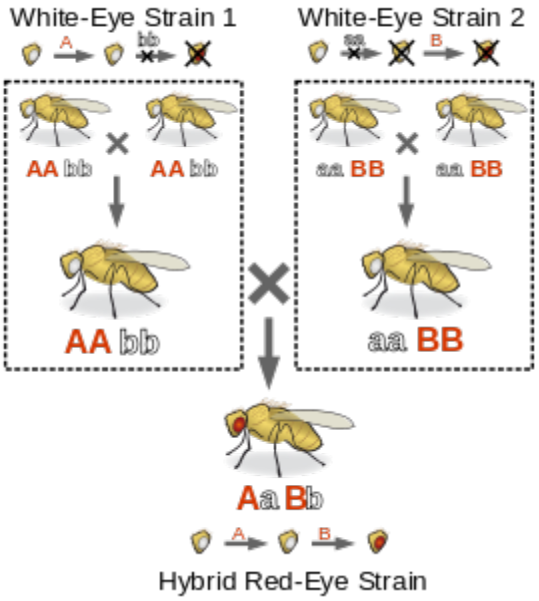
Example of a simple complementation test

For a simple example of a complementation test, suppose a geneticist is interested in studying two strains of white-eyed flies of the species Drosophila melanogaster, more commonly known

as the common fruit fly. In this species, wild type flies have red eyes and eye color is known to be related to two genes, A and B. Each one of these genes has two alleles, a dominant one that codes for a working protein (*A* and *B* respectively) and a recessive one that codes for a malfunctioning protein (*a* and *b*respectively). Since both proteins are necessary for the synthesis of red pigmentation in the eyes, if a given fly is homozygous for either *a* or *b*, it will have white eyes.

Knowing this, the geneticist may perform a complementation test on two separately obtained strains of pure-breeding white-eyed flies. The test is performed by crossing two flies, one from each strain. If the resulting progeny have red eyes, the two strains are said to complement; if the progeny have white eyes, they do not.

If the strains complement, we imagine that one strain must have a genotype aa BB and the other AA bb, which when crossed yield the genotype AaBb. In other words, each strain is homozygous for a different deficiency that produces the same phenotype. If the strains do not complement, they both must have genotypes aa BB, AA bb, or aa bb. In other words, they are both homozygous for the same deficiency, which obviously will produce the same phenotype.



Complementation test, also called cis-trans test, in genetics, test for determining whether two mutations associated with a specific phenotype represent two different forms of the same gene (alleles) or are variations of two different genes. The complementation test is relevant for recessive traits (traits normally not present in the phenotype due to masking by a dominant allele). In instances when two parent organisms each carry two mutant genes in a homozygous

recessive state, causing the recessive trait to be expressed, the complementation test can determine whether the recessive trait will be expressed in the next generation.

When two mutations occur in different genes, they are said to be complementary, because the heterozygote condition rescues the function otherwise lost in the homozygous recessive state. Hence, the term *complementation test* is used to describe the process to test for gene function in recessive allelism. The alternative name *cis-trans test* describes the two central components of the test. The terms *cis* and *trans* refer to the relationship of the two mutations, with *cis* used to describe mutations occurring on the same chromosome and *trans* used to describe mutations occurring on different chromosomes. The cis portion of the complementation test essentially acts as a control and involves creating heterozygotes (one mutated chromosome and one wild-type, or normal, chromosome) such that one parent bears both mutations. In the cis test, a functional protein is always produced regardless of whether both mutations are on the same gene or on different genes. The trans test involves creating heterozygotes with different mutations from different parents. In this case a functional protein is produced only if the mutations are on different genes.

One, or more than one gene?

As explained earlier in this chapter, mutant screening is one of the beginning steps geneticists use to investigate biological processes. When geneticists obtain two independently derived mutants (either from natural populations or during a mutant screen) with similar phenotypes, an immediate question is whether or not the mutant phenotype is due to a loss of function in the same gene, or are they mutant in different genes that both affect the same phenotype (e.g., in the same pathway). That is, are they allelic mutations, or non-allelic mutations, respectively? This question can be resolved using complementation tests, which bring together, or combine, the two mutations under consideration into the same organism to assess the combined phenotype.

4.6.2 - A hypothetical example of purple flowers

The easiest way to understand a complementation test is by example (Fig.4.9). The pigment in a purple flower could depend on a biochemical pathway much like the biochemical pathways leading to the production of arginine in Neurospora (review in Chapter 1). A plant that lacks the function of gene A (genotype *aa*) would produce mutant, white flowers that looked just like the flowers of a plant that lacked the function of gene B (genotype *bb*). (The genetics of two loci are discussed more in the following chapters.) Both A and B are enzymes in the same pathway that leads from a colorless compound#1, thorough colorless compound#2, to the purple pigment. Blocks at either step will result in a mutant white, not wild type purple, flower.

Figure 4.9: In this simplified biochemical pathway, two enzymes encoded by two different genes modify chemical compounds in two sequential reactions to produce a purple pigment. Loss of either of the enzymes disrupts the pathway and no pigment is produced. (Original-Deyholos-CC:AN)

Strains with mutations in gene A can be represented as the genotype *aa*, while strains with mutations in gene B can be represented as *bb*. Given that there are two genes here, A and B, then

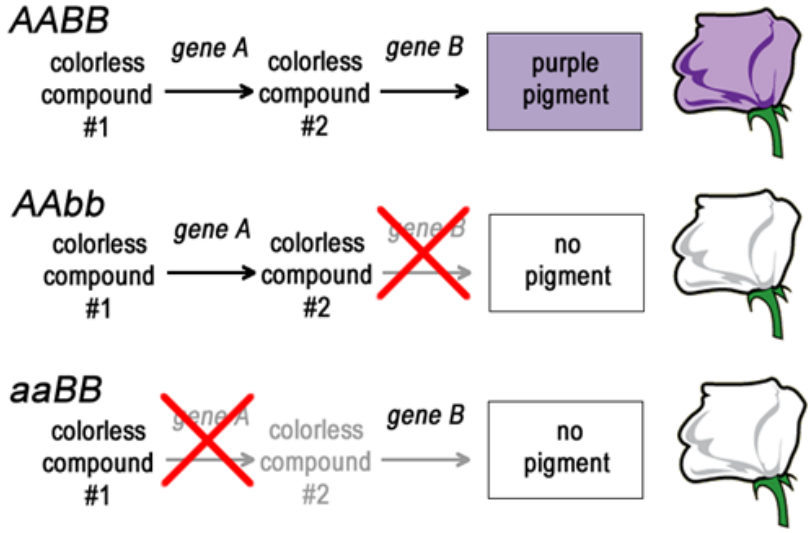
each of these mutant strains can be more completely represented as *aaBB* and *AAbb* . (LEARNING NOTE: Student often forget that genotypes usually only show mutant loci, however, one must remember all the other genes are assumed to be wild type.)

If these two strains are crossed together the resulting progeny will all be *AaBb*. They will have both a wild type, functional A gene and B gene and will thus have a pigmented, purple flower, a wild type phenotype. This is an example of complementation. Together, each strain provides what the other is lacking (*AaBb*). The mutations are in different genes and are thus called non-allelic mutations.

Now, if we are presented with a third pure-breeding, independently derived white-flower mutant strain, we won't initially know if it is mutant in gene A or gene B (or possibly some other gene altogether). We can use complementation testing to determine which gene is mutated. To perform a complementation test, two homozygous individuals with similar mutant phenotypes are crossed (Figure 4.10).

If the F1 progeny all have the same mutant phenotype (Case 1 - Figure 4.10A), then we infer that the same gene is mutated in each parent. These mutations would then be called allelic mutations - in the same gene locus. These mutations FAIL to COMPLEMENT one another (still mutant). These could be either the exact same mutant alleles, or different mutations in the same gene (allelic).

Conversely, if the F1 progeny all appear to be wild-type (Case 2 - Figure 4.10B), then each of the parents most likely carries a mutation in a different gene. These mutations would then be called non-allelic mutations - in a different gene locus. These mutations do COMPLEMENT one another.



Note: For mutations to be used in complementation tests they are (1) usually true-breeding (homozygous at the mutant locus), and (2) must be recessive mutations. Dominant mutation CANNOT be used in complementation tests. Also, remember, some mutant strains may have more than one gene locus mutated and thus would fail to complement mutants from more than one other locus (or group).

Complementation Groups = groups of allelic mutations.

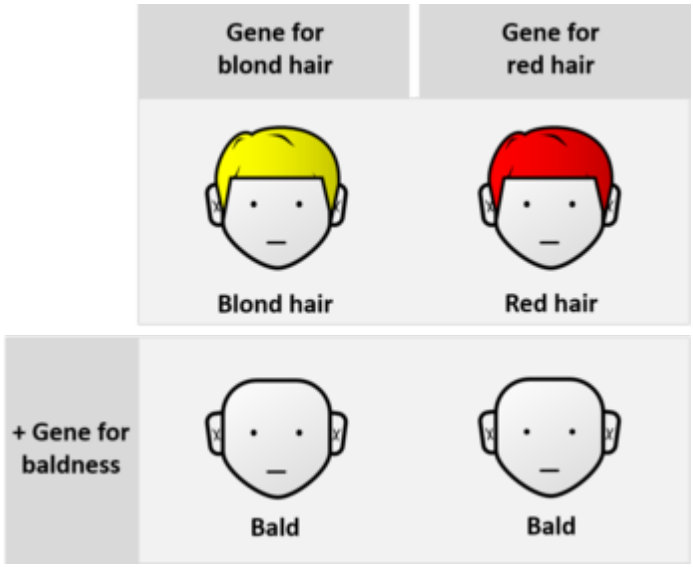
So, with the third mutant strain above, we could assign it to be allelic with either gene A or gene B, or some other locus, should it complement both gene A and gene B mutations. If we have a fourth, fifth, sixth, etc. (e.g. they came from different natural populations or from independently mutagenized individuals) white flower strains, then we could begin to group the allelic mutations into what are called complementation groups. These are groups of mutations that FAIL TO COMPLEMENT one another (a group of NON-complementing mutations).

A "group" can consist of as few as one mutation and as many as all the mutants under study. Each group represents a set of mutations in the same gene (allelic). The number of complementation groups represents the number of genes that are represented in the total collection of mutations. It all depends on how many mutations you have in that gene. For example, the *white* gene in Drosophila has >300 different mutations described in the literature. If you were to obtain and cross all these mutations to themselves you would find they all belonged to the same complementation group. Each complementation group represents a gene.

If, however, you obtained a different mutation, *vestigial* for example, and crossed it to a *white* mutation, the double heterozygote would result in red eyes and normal wings (wild type for both characters) so the two would complement and represent two different complementation groups: (1) *white*, (2) *vestigial*. The same would be true for the other eye-colour mutations mentioned in Section 4.5.4 above. For example, if you crossed a *scarlet* mutant to a *white* mutant, the double heterozygote would have wild type red eyes.

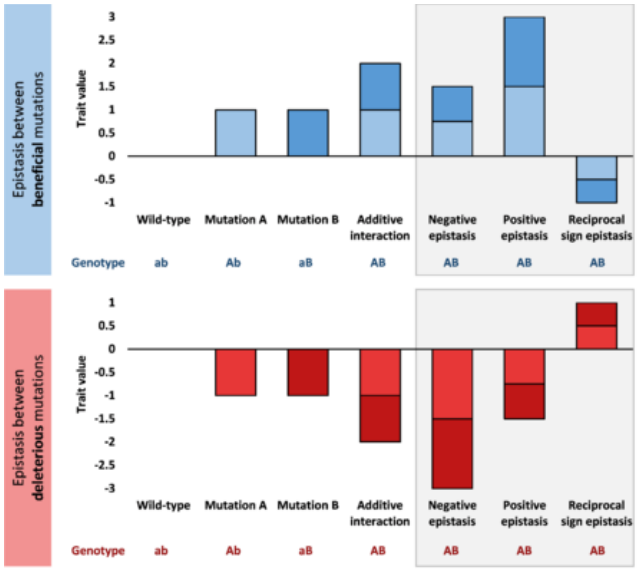
Epistasis

Epistasis is the phenomenon where the effect of one gene (locus) is dependent on the presence of one or more 'modifier genes', i.e. the genetic background.[1]Originally the term meant that the phenotypic effect of one gene is masked by a different gene (locus).[2] Thus, epistatic mutations have different effects in combination than individually. It was originally a concept from geneticsbut is now used in biochemistry, computational biologyand evolutionary biology. It arises due to interactions, either between genes, or within them, leading to non-linear effects. Epistasis has a large influence on the shape of evolutionary landscapes, which leads to profound consequences for evolution and evolvability of phenotypic traits.



Classification

terminology about epistasis can vary between scientific fields. Geneticistsoften refer to wild type and mutant alleleswhere the mutation is implicitly deleterious and may talk in terms of genetic enhancement, synthetic lethalityand genetic suppressors. Conversely, a biochemist may more frequently focus on beneficial mutations and so explicitly state the effect of a mutation and use terms such as reciprocal sign epistasis and compensatory mutation.[14]Additionally, there are differences when looking at epistasis within a single gene (biochemistry) and epistasis within a haploid or diploid genome (genetics). In general, epistasis is used to denote the departure from 'independence' of the effects of different genetic loci. Confusion often arises due to the varied interpretation of 'independence' among different branches of biology.[15] The classifications below attempt to cover the various terms and how they relate to one another.



Additivity[edit]

Two mutations are considered to be purely additive if the effect of the double mutation is the sum of the effects of the single mutations. This occurs when genes do not interact with each other, for example by acting through different metabolic pathways. Simple, additive traits were studied early on in the history of genetics, however they are relatively rare, with most genes exhibiting at least some level of epistatic interaction.

Magnitude epistasis

When the double mutation has a fitter phenotype than expected from the effects of the two single mutations, it is referred to as positive epistasis. Positive epistasis between beneficial mutations generates greater improvements in function than expected. Positive epistasis between deleterious mutations protects against the negative effects to cause a less severe fitness drop.

Conversely, when two mutations together lead to a less fit phenotype than expected from their effects when alone, it is called negative epistasis. Negative epistasis between beneficial mutations causes smaller than expected fitness improvements, whereas negative epistasis between deleterious mutations causes greater-than-additive fitness drops.

Independently, when the effect on fitness of two mutations is more radical than expected from their effects when alone, it is referred to as synergistic epistasis. The opposite situation, when the fitness difference of the double mutant from the wild type is smaller than expected from the effects of the two single mutations, it is called antagonistic epistasis.[13] Therefore, for deleterious mutations, negative epistasis is also synergistic, while positive epistasis is antagonistic; conversely, for advantageous mutations, positive epistasis is synergistic, while negative epistasis is antagonistic.

The term genetic enhancement is sometimes used when a double (deleterious) mutant has a more severe phenotype than the additive effects of the single mutants. Strong positive epistasis is

sometimes referred to by creationists as irreducible complexity (although most examples are misidentified).

Sign epistasis

Sign epistasis occurs when one mutation has the opposite effect when in the presence of another mutation. This occurs when a mutation that is deleterious on its own can enhance the effect of a particular beneficial mutation.For example, a large and complex brain is a waste of energy without a range of sense organs, but sense organs are made more useful by a large and complex brain that can better process the information.

At its most extreme, reciprocal sign epistasis[21] occurs when two deleterious genes are beneficial when together. For example, producing a toxin alone can kill a bacterium, and producing a toxin exporter alone can waste energy, but producing both can improve fitness by killing competing organisms.

Reciprocal sign epistasis also leads to genetic suppression whereby two deleterious mutations are less harmful together than either one on its own, i.e. one compensates for the other. This term can also apply sign epistasis where the double mutant has a phenotype intermediate between those of the single mutants, in which case the more severe single mutant phenotype is suppressed by the other mutation or genetic condition. For example, in a diploid organism, a hypomorphic (or partial loss-of-function) mutant phenotype can be suppressed by knocking out one copy of a gene that acts oppositely in the same pathway. In this case, the second gene is described as a "dominant suppressor" of the hypomorphic mutant; "dominant" because the effect is seen when one wild-type copy of the suppressor gene is present (i.e. even in a heterozygote). For most genes, the phenotype of the heterozygous suppressor mutation by itself would be wild type (because most genes are not haplo-insufficient), so that the double mutant (suppressed) phenotype is intermediate between those of the single mutants.

In non reciprocal sign epistasis, fitness of the mutant lies in the middle of that of the extreme effects seen in reciprocal sign epistasis.

When two mutations are viable alone but lethal in combination, it is called Synthetic lethality or unlinked non-complementation.

Haploid organisms

In a haploid organism with genotypes (at two loci) *ab*, *Ab*, *aB* or *AB*, we can think of different forms of epistasis as affecting the magnitude of a phenotype upon mutation individually (Ab and aB) or in combination (AB).

Interaction type	ab	Ab	aB	AB	
No epistasis (additive)	0	1	1	2	$AB = Ab + aB + ab$
Positive (synergistic) epistasis	0	1	1	3	$AB > Ab + aB + ab$
Negative (antagonistic) epistasis	0	1	1	1	$AB < Ab + aB + ab$
Sign epistasis	0	1	-1	2	*AB* has opposite sign to *Ab* or *aB*
Reciprocal sign epistasis	0	-1	-1	2	*AB* has opposite sign to Ab and *aB*

Diploid organisms[edit]

Epistasis in diploid organisms is further complicated by the presence of two copies of each gene. Epistasis can occur between loci, but additionally, interactions can occur between the two copies of each locus in heterozygotes. For a two locus, two allele system, there are eight independent types of gene interaction.[23]

Additive A locus

	aa	aA	AA
bb	1	0	–1
bB	1	0	–1
BB	1	0	–1

Additive B locus

	aa	aA	AA
bb	1	1	1
bB	0	0	0
BB	–1	–1	–1

Dominance A locus

	aa	aA	AA
bb	–1	1	–1
bB	–1	1	–1
BB	–1	1	–1

Dominance B locus

	aa	aA	AA
bb	–1	–1	–1
bB	1	1	1
BB	–1	–1	–1

Additive by Additive Epistasis

	aa	aA	AA
bb	1	0	–1
bB	0	0	0
BB	–1	0	1

Additive by Dominance Epistasis

	aa	aA	AA
bb	1	0	–1
bB	–1	0	1
BB	1	0	–1

Dominance by Additive Epistasis

	aa	aA	AA
bb	1	–1	1
bB	0	0	0
BB	–1	1	–1

Dominance by Dominance Epistasis

	aa	aA	AA
bb	–1	1	–1
bB	1	–1	1
BB	–1	1	–1

Other Types of Epistatic Interactions

Today, scientists know that Mendel's predictions about inheritance depended on the genes he chose to study. Specifically, Mendel carefully selected seven unlinked genes that affected seven different traits. However, unlike the phenotypes that Mendel considered, the majority of phenotypes are affected by more than one gene. Indeed, most of the characteristics of organisms are much more complex than the characteristics that Mendel studied, and epistasis is one source of this complexity. Epistasis can occur in a variety of different ways and result in a variety of different phenotypic ratios, as illustrated in Table 4. Beyond epistasis, gene-environment interactions further increase the variety of phenotypes we see around us each day.

Examples of Digenic Epistatic Ratios

Ratio	Description	Name(s) of Relationship (Used by Some Authors)
9:3:3 :1	Complete dominance at both gene pairs; new phenotypes result from interaction between dominant alleles, as well as from interaction between both homozygous recessives	Not named because the ratio looks like independent assortment
9:4:3	Complete dominance at both gene pairs; however, when one gene is homozygous	Recessive epistasis

	recessive, it hides the phenotype of the other gene	
9:7	Complete dominance at both gene pairs; however, when either gene is homozygous recessive, it hides the effect of the other gene	Duplicate recessive epistasis
12:3:1	Complete dominance at both gene pairs; however, when one gene is dominant, it hides the phenotype of the other gene	Dominant epistasis
15:1	Complete dominance at both gene pairs; however, when either gene is dominant, it hides the effects of the other gene	Duplicate dominant epistasis
13:3	Complete dominance at both gene pairs; however, when either gene is dominant, it hides the effects of the other gene	Dominant and recessive epistasis
9:6:1	Complete dominance at both gene pairs; however, when either gene is dominant, it hides the effects of the other gene	Duplicate interaction
7:6:3	Complete dominance at one gene pair and partial dominance at the other; when homozygous recessive, the first gene is epistatic to the second gene	No name
3:6:3:4	Complete dominance at one gene pair and partial dominanceat the other; when homozygous recessive, either gene hides the effects of the other gene; when both genes are homozygous recessive, the second gene hides the effects of the first	No name
11:5	Complete dominance for both gene pairs only if both kinds of dominant alleles are present; otherwise, the recessive phenotype appears	No name

henotype Variability: Penetrance and Expressivity

Dominance relationships between alleles for a given trait can impact phenotypic ratios, but interactions between different genes can also impact phenotype. Such traits that result from the interaction among multiple genes and their environment are called complex traits. So, given a specific trait, how can we tell whether it is complex? One way to recognize a complex trait is through inconsistent inheritance patterns in successive generations. For example, a dominant trait might skip an entire generation yet be expressed in the subsequent generation. How is this possible? The answer to this question lies in the concepts of penetrance and expressivity.

Penetrance

When studying the relationships between genotype and phenotype, it is important to examine the statistical occurrence of phenotypes in a group of known genotypes. In other words, given a group of known genotypes for one trait, how many identical genotypes show the related phenotype? You might be surprised to learn that, for some traits, the phenotype might not occur as often as the genotype. For example, say everyone in population W carries the same allele combinations for a certain trait, yet only 85% of the population actually shows the phenotype expected from those allele combinations. The proportion of genotypes that actually show expected phenotypes is called penetrance. Thus, in the preceding example, the penetrance is 85%. This value is calculated from looking at populations whose genotypes we know.

In fact, large population studies are necessary for measuring penetrance, and studies of penetrance help us predict how likely it is that a trait will be evident in those who carry the underlying alleles. In general, when we know that the genotype is present but the phenotype is not observable, the trait shows incomplete penetrance. Basically, anything that shows less than 100% penetrance is an example of incomplete penetrance. Therefore, although the penetrance of a trait is a statistically calculated value based on the appearance of a phenotype among known genotypes, incomplete penetrance is simply a qualitative description about a group of known genotypes.

A specific example of incomplete penetrance is the human bone diseaseosteogenesis imperfecta (OI). The majority of people with this disease have a dominant mutation in one of the two genes that produce type 1 collagen, *COL1A1* or *COL1A2*. Collagen is a tissue that strengthens bones and muscles and multiple body tissues. People with OI have weak bones, bluish color in the whites of their eyes, and a variety of afflictions that cause weakness in their joints and teeth. However, this disease doesn't affect everyone who has *COLIA1* and *COLIA2* mutations in the same way. In fact, some people can carry the mutation but have no symptoms. Thus, families can unknowingly transmit the mutation from one generation to the next through someone who carries the mutation but does not express the OI phenotype.

Incomplete penetrance examples such as OI demonstrate that even monogenic diseases do not have predictable expression patterns in a population. Is there a way to explain this unpredictability? Let's think about it. If two people have the same dominant mutation in *COL1A1*, why might only one of them actually display OI symptoms? Could it have to do with other genes

that rescue the bad effect of a mutated collagen gene? Could it be that those who have OI simply express more mutated collagen than the person who is unaffected? To consider the possible explanations for incomplete penetrance, we have to remember how many steps there are between gene transcription and protein expression.

Note that the expression of other genes, such as transcriptional or translational regulators, can influence the final effect of a gene product. Anything that interferes with the pathway from transcription to protein activation is known as an epigenetic factor. Indeed, there are multiple points at which another gene product can intervene in the stages prior to the production of a protein. Interference at these stages might stop production entirely, create an altered form of the protein that might never be active, or do any number of other things that renders the gene silent. So, the final stage of an active protein reflects many different processes that lead to the amino acid sequence and ultimate protein shape, all of which can be interfered with by other genes. Furthermore, some genes can up- or downregulate rates of transcription, which changes the total amount of protein produced. Thus, genes that affect the final form and expression amount of another gene can be influential in the formation of the phenotype derived from the regulated gene (Figure 1).

So, if so many different possible modification points for a gene product exist, how can we narrow down the question of what causes incomplete penetrance? Interestingly, some scientists have actually tried to do this by observing how the genetic mutations that cause OI affect mice. These investigators inserted a mutated form of *COL1A1* into mice and bred them so that they all contained this mutation. The mice were affected in similar ways to those with human OI: Many had severe bone weakness and multiple bone fractures, even at birth. In fact, when the researchers examined the mouse bones closely, they found that 70% of mice with the mutated *COL1A1* gene showed evidence of OI (bone fractures); however, the remaining 30% appeared completely normal. In these mice with no OI phenotype, there was the same amount of *COL1A1* expression as in those mice that did show the phenotype. Furthermore, the investigators used a purebred strain of mice that had little variability in their genomes to begin with. This means that the genetic context in which *COL1A1* was expressed did not vary among the mice studied. Yet, despite the fact that all the mice had extremely similar genomes and all of them expressed the same amount of *COL1A1*, 30% of them did not show any OI phenotype. These results continue to be perplexing.

Expressivity

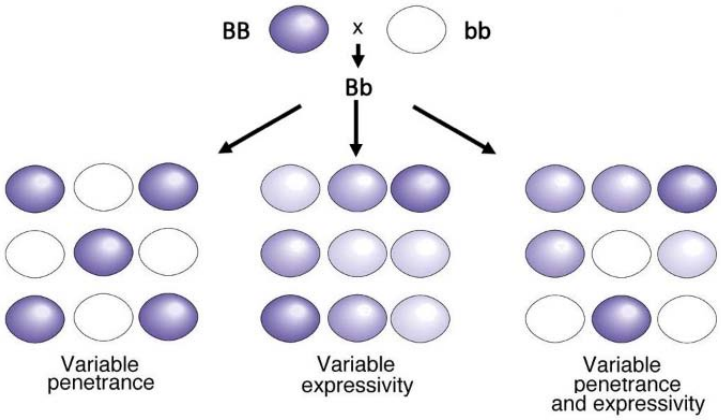
Individuals with the same genotype can also show different degrees of the same phenotype. Expressivity is the degree to which trait expression differs among individuals. Unlike penetrance, expressivity describes individual variability, not statistical variability among a population of genotypes. For example, the features of Marfan syndrome vary widely; some people have only mild symptoms, such as being tall and thin with long, slender fingers, whereas others also experience life-threatening complications involving the heart and blood vessels. Although the features of Marfan syndrome are highly variable, all people with this disorder have a dominant mutation in the gene coding for fibrillin 1, *FBN1*. However, it turns out that the position of the

mutation in the *FBN1* gene is correlated with the severity of the Marfan phenotype. Researchers found that a mutation in one *FBN1* position is prevalent in families with severe symptoms, whereas a mutation in another position is prevalent in families with less severe symptoms. These findings are an encouraging clue as to how specific defects in the fibrillin 1 protein can account for the variable expressivity in Marfan syndrome (Li *et al.*, 2008).

Another example of expressivity at work is the occurrence of extra toes, or polydactyly, in cats. The presence of extra toes on a cat's paw is a phenotype that emerges in groups of cats who have interbred for generations. In fact, there are several well-known groups of these cats, such as those on Key West Island (known as "Hemingway's cats"), as well as those in breeding clusters in the eastern U.S. and shores of the British Isles (Figure 2). The first to report on this phenomenon was C. H. Danforth, who studied the inheritance of polydactyly among 55 generations of cats. He observed that the polydactyly phenotype showed "good penetrance, but variable expression" because the gene always causes extra toes on the paw, but the number of extra toes varies widely from cat to cat (Danforth, 1947). Through his breeding studies, Danforth found that although a dominant allele underlies the cause of polydactyly, the degree of polydactyly depends on the condition of adjacent layered tissues in the developing limb; that is, the expression of genes in tissues surrounding tissue that will become the toe determines the degree of polydactyly (Willier, 1974).

Penetrance *versus* Expressivity

Egg colour of the endangered Hawai'ian *Oo'Aa* bird is controlled by a single locus, *BLU*, where the B allele is dominant to the b allele. As part of the recovery strategy, a pure-breeding blue-egg bird (BB) from one island is crossed with a pure-breeding white-egg bird (bb) from another island. Because all the offspring are Bb heterozygotes, they are all expected to show a uniform, blue phenotype like that of the BB parent. However, if penetrance and / or expressivity vary, three patterns of variation that differ from expectation are possible.



Penetrance *versus* Expressivity

If penetrance varies [left], the Bb genotype sometimes does not *penetrate through to the phenotype*: some Bb eggs are blue just like those of their BB parents, others are white like those of their bb parents, despite presence of the B allele. "*Lack of penetrance*" is sometimes used to explain individuals whose phenotypes do not reflect their inferred genotypes, e.g., a dominant trait that appears to "*skip*" a generation in a pedigree

If expressivity varies [middle], the Bb genotype will not be *expressed uniformly in the phenotype*: all eggs are blue, but the exact shade of blue *varies among individuals with the same genotype*. Variable expressivity is frequently attributable to environmental factors or variation at gene loci elsewhere in the genome.

If expressivity *and* penetrance both vary [right], there may be a continuous gradient of phenotypes between white and blue eggs. Note that *lack of penetrance can be considered as an extreme from of expressivity*, in which the range of expression includes non-expression.

POSSIBLE QUESTION

2marks

1. Define dominance
2. Define model organism and mendels law
3. short notes of segregation
4. What is the role of alleles
5. Write note on multiple allale
6. Define chromosome
7. Write short notes chromosome inheritance?
8. Give short notes on mutation.
9. Define recessiveness?
10. Write short notes co-dominations.

8 marks

1. describe the mendel's law
2. Explain the mendel's law - dominance

3 Describe the chromosome theory of inheritance

4. Extension of mendel's hypothesis?

5.. Detail of incomplete dominance and co-dominance

6. explain mendel's independent assortment?

KARPAGAM ACADEMY OF HIGHER EDUCATION

CLASS: III B. Sc MICROBIOLOGY **COURSE NAME: INHERITANCE BIOLOGY**

COURSE CODE: 17MBU504B **UNIT: 2** **BATCH-2017-2020**

Sno	Question	Opt 1	Opt 2	Opt 3	Opt 4	Answer
1	Which of the following relationship was not studies by Mendel?	Flower colour and seed colour	Height and seed colour	Flower colour and shape of pollen grain		Flower colour and shape of pollen grain
2	Choose the odd one out – Green pod, Yellow seed, Purple flower, Terminal flower	Green pod	Yellow seed	Purple flower	Terminal flower	Terminal flower
3	Which of the following two traits is characteristic of a single gene?	Seed colour and shape	Flower colour and position	Colour of flower and seed coat	Height and colour of seed	Colour of flower and seed coat
4	Which of Mendel's law is against the theory of Blending inheritance?	Law of segregation	Law of dominance	Law of recessive	Law of independent assortment	Law of segregation
5	Considering the concept of Multiple alleles, one organism can have _____ alleles	One	Two	Three	Four	Two
6	It is confirmed that phenotype of short pea plant height will be expressed only when_____	Both the parents are tall	One parent is tall and other short	The seeds are generated by selling	Both parents are short	Both parents are short
7	Mendel did not give _____	Concept of genes	Concept of inheritance	Concept of dominance	Concept of chromosomes	Concept of chromosomes
8	An allele is	Another word for a gene	A homozygous genotype	A heterozygous genotype	One of several possible forms of a gene	One of several possible forms of a gene
9	When the genotype consists of a dominant and a recessive allele, the phenotype will be like _____ allele	The dominant	The recessive	Neither	nill	The dominant

10	The idea that for any particular trait, the pair of alleles of each parent separate and only one allele from each parent passes to an offspring is Mendel's principle of:	Independent assortment	Hybridization	Segregation	dominant	Segregation
11	The tendency of offspring to differ from parents is called	variation	Heredity	inheritance	resemblance	variation
12	The physical expression or appearance of a character is called as	genotype	phenotype	ecotype	morphology	phenotype
13	The alternate forms of a gene is called	recessive character	dominant character	alleles	alternative gene	alleles
14	If different alleles are present in the same genotype then it is called	Homozygous	Heterozygous	diallelic	polyalllelic	Heterozygous
15	The number of types of gametes produced by a heterozygous individual is	1	2	3	many	2
16	The idea that different pairs of alleles are passed to offspring independently is mendel's principle of	unit inheritance	segregation	independent assortment	independent	independent assortment
17	Two linked genes a and b show 20% recombination, the individuals of a dihybrid cross between ++/+ + x ab/ab shall show gametes	++ 80 : ab : 20	++ 50 : ab : 50	++ 40 : ab 40 : + a 10 : + b : 10	++ 30 : ab 30 : + a 20 : + b : 20	++ 40 : ab 40 : + a 10 : + b : 10
18	A normal green male Maize is crossed with albino female. The progeny is albino because	trait for a albinism is dominant	the albinos have biochemical to destroy plastids derived from green male	plastids are inherited from female parent	green plastids of male mus. have mutated	plastids are inherited from female parent
19	tt mates with Tt. What will be characteristic of offspring?	75% recessive	50% recessive	25% recessive	All dominant	50% recessive

20	In a genetic cross having recessive epistasis, F2 phenotypic ratio would be	9:06:01	15:01	9:03:04	12:03:01	9:03:04
21	A dihybrid condition is	segregation	dominance	independent assortment	polygenic inheritance	polygenic inheritance
22	Multiple alleles control inheritance of	henylketonuria	colour blindness	sickle cell anaemia	blood groups	blood groups
23	Segregation of Mendelian factors (no linkage, no crossing over) occurs during	anaphase I	anaphase II	diplotene	metaphase I	anaphase I
24	A gene pair hides the effect of another. The phenomenon is	epitasis	dominance	mutation	none of these	epitasis
25	An allele is dominant if it is expressed in	both homozygous and heterozygous states	second generation	heterozygous combination	homozygous combination	both homozygous and heterozygous states
26	A polygenic inheritance in human beings is	skin colour	phenylketonuria	colour blindness	sickle cell anaemia	skin colour
27	Two dominant nonallelic genes are 50 map units apart. The linkage is	cis type	trans type	complete	absent/incomplete	absent/incomplete
28	Which of the following is suitable for experiment on linkage?	aaBB x aaBB	AABB x aabb	AaBb x AaBb	AAbb x AaBB	AABB x aabb
29	When two genetic loci produce identical phenotypes in cis and trans position, they are considered to be	multiple alleles	the parts of same gene	pseudoalleles	different genes	pseudoalleles
30	The polygenic genes show	different karyotypes	different genotypes	different phenotypes	none of these	different phenotypes
31	Crossing over in diploid organism is responsible for	segregation of alleles	recombination of linked alleles	dominance of genes	linkage between genes	recombination of linked alleles

32	If Mendel had studied the seven traits using a plant with 12 chromosomes instead of 14, in what way would his interpretation have been different?	he would not have discovered the law of independent assortment	he would have discovered sex linkage	he could have mapped the chromosome	he would have discovered blending or incomplete dominance	he would not have discovered the law of independent assortment
33	Due to the cross between TTRrxttrr the resultant progenies show what percent of tall, red flowered plants	50%	75%	25%	100%	50%
34	Ratio of complementary genes is	9:03:04	12:03:01	9 : 3 : 3 : 4	9:07	9:07
35	A gene is said to be dominant if	it expresses its effect only in homozygous state	it expresses its effect only in heterozygous condition	it expresses its effect both in homozygous and heterozygous condition	it never expresses its effect in any condition	it expresses its effect both in homozygous and heterozygous condition
36	There are three genes a, b, c. Percentage of crossing over between a and b is 20%, b and c is 28% and a and c is 8%. What is the sequence of genes on chromosome?	b, a, c	a, b, c	a, c, b	none of these	b, a, c
37	Two crosses between the same pair of genotypes or phenotypes in which the sources of the gametes are reversed in one cross, is known as	test cross	reciprocal cross	dihybrid cross	reverse cross	variation
38	One of the parents of a cross has a mutation in its mitochondria. In that cross, that parent is taken as a male. During segregation of F_2 progenies that mutation is found in	one-third of the progenies	none of the progenies	all the progenies	fifty percent of the progenies	none of the progenies

39	A nutritionally wild type organism, which does not required any additional growth supplement is known as	phenotype	holotype	autotroph	prototroph	prototroph
40	Phenotype of an organism is the result of	genotype and environment interactions	mutations and linkages	cytoplasmic effects and nutrition	environmental changes and sexual dimorphism	genotype and environment interactions
41	Test cross involves	crossing between two genotypes with dominant trait	) crossing between two genotypes with recessive trait	crossing between two F, hybrids	crossing the F, hybrid with a double recessive genotype	crossing the F, hybrid with a double recessive genotype
42	A common test to find the genotype of a hybrid is by	crossing of one F_2 progeny with female parent	studying the sexual behaviour of F. progenies	crossing of one F, progeny with male parent	crossing of one F_2 progeny with male parent	crossing of one F, progeny with male parent
43	On which of the following chromosomes are sex-linked traits carried?	18	13	Y	X	X
44	Which of the following chromosomes, if trisomic, cause failure of survival of development?	X	21	11	18	18
45	Which term represents a pair of contrasting characters?	Heterozygous	Homozygous	Codominant genes	Allelomorphs	Allelomorphs
46	The chromosomal theory of inheritance was proposed by ___	Mendel	Watson and Crick	Darwin	Sutton and Boveri	Sutton and Boveri
47	If there is a non-disjunction in the X chromosome, the progeny being XXY, what will be the constitution of the chromosome(s) in the gamete?	X and Y	X and XY	XX and Y	XXY with no separation	X and XY

48	You observe a genetic trait which is a common occurrence in the male of a particular pedigree, this is possibly a _____	X linked	Y linked	X linked recessive	Y linked dominant	Y linked
49	If the genes are located in a chromosome as A—B—C—D—E—O—-T. Which of the gene pairs will have least probability of being inherited together?	C and D	A and T	A and B	O and T	A and T
50	If a gamete has 16 chromosomes, what will be the number of chromatids before anaphase 1?	8	16	32	64	64
51	Which of the following can result from non-disjunction?	XY and XO	YY and XY	X and Y	XY and XXY	XY and XO
52	Which of the following processes may separate linked genes during meiosis?	genomic restricting	phenotypic plasticity	sexual differentiation	chiasma or crossover	chiasma or crossover
53	chiasma or crossover	0.5	1	1.5	2	1
54	Exchange of genes or alleles from one population of species to another	Gene flow	Penetrance	expresivity	co-dominance	Gene flow
55	Incomplete dominance is also termed as	Partial dominance	half dominace	co-dominance	multiple allele	Partial dominance
56	X shaped structure	Chiasma	gene	DNA	RNA	chiasma
57	Which one of the following is not the case of epistasis?	Fur colour in mouse	Fruit colour in summer squash	Fruit shape in summer squash	Coat colour in Labrador	Fruit shape in summer squash
58	In case of two gene interaction, the gene which is masking the expression of another is called_____ and the gene whose expression is masked is called_____	Dominant, recessive	Recessive, dominant	Epistatic, hypostatic	Hypostatic, Epistatic	Epistatic, hypostatic

59	Epistasis is the interaction between _____ genes	2	4	8	16	2
60	What is psudoallele?	Allele with similar function	Allele with similar structure	Alleles with similar function and structure	Alleles with similar function and different structure	Alleles with similar function and different structure

Unit-III
Sylabus

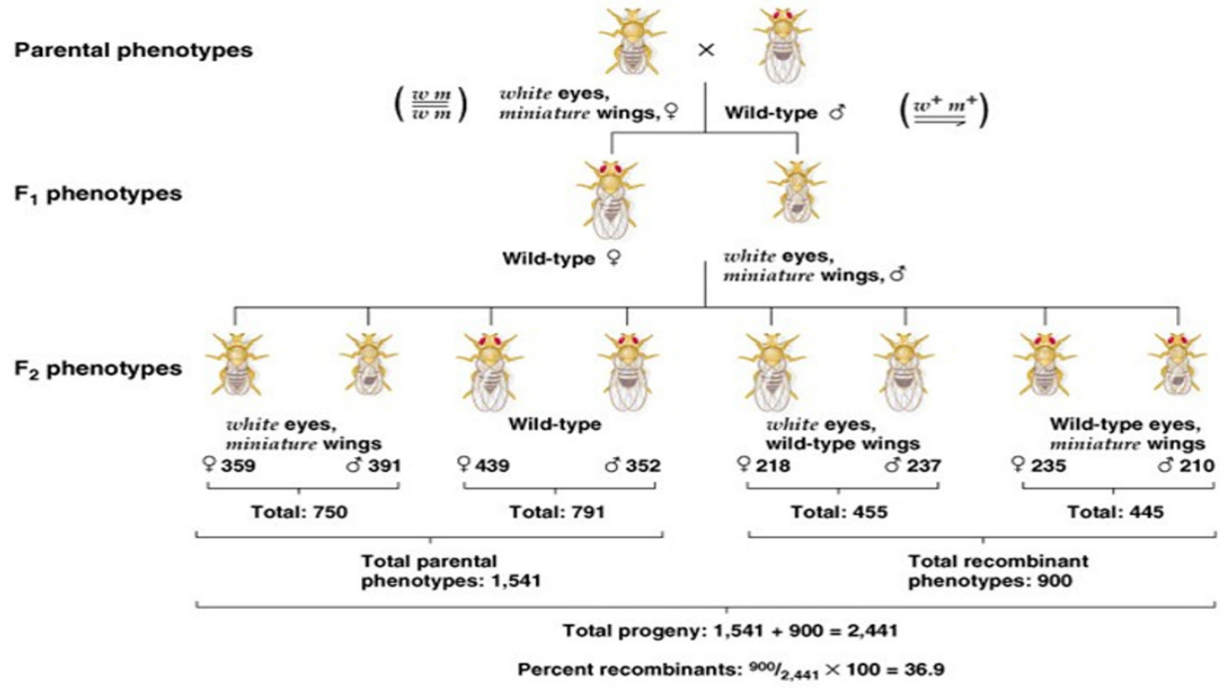
Linkage and recombination of genes, Cytological basis of crossing over, Crossing over at fourth strand stage, Molecular mechanisms of crossing over, mapping homologous and non homologous recombination,including transpositions,site-specific recombination.

Linkage and recombination of genes:

Linkage and recombination are phenomena that describe the inheritance of genes. A linkage is a phenomenon where two or more linked genes are always inherited together in the same combination for more than two generations. The recombination frequency of the test cross progeny is always lower than 50%. Therefore, if any two genes are completely linked, their recombination frequency is almost 0%. The phenomenon of linkage was studied by the scientist T.H. Morgan using the common fruit fly or *Drosophila melanogaster.*

Morgan's Experiment

Fig. 14.1, Morgan's experimental cross of white-eyes and miniature wings.



Morgan picked *Drosophila melanogaster* as his subject for the following reasons:

- He noticed a white-eyed male drosophila instead of the regular red eyes.
- It was small in size
- They have a short lifespan and so many generations can be studied in a short time frame.
- They have a high rate of reproduction

He crossed a purebred white eyed male with purebred red-eyed female. As expected following Mendel's laws, the F1 progeny were born with red eyes. When F1 generation was crossed among each other, the ratio of red-eyed to white eyed progeny were 3:1. However, he noticed that there was no white- eyed female in the F2 generation.

To understand further, he performed a cross between a heterozygous red-eyed female with a white-eyed male. This gave a ratio of 1:1:1:1 in the progeny(1 white eyed female, 1 red eyed female, 1 white eyed male and 1 red eyed male). This made Morgan think about the linkage between the traits and sex chromosomes. He performed many more crosses and determined that the gene responsible for the eye color was situated on the X chromosome.

Types of Linkage

Linkages are primarily of two types: Complete and incomplete

- **Complete Linkage:** When the combination of characters appears together in more than two generations in a regular manner, it is called as a complete linkage. Due to this complete linkage, only two types of gametes are formed. Example: Drosophila melanogaster
- **Incomplete Linkage:** When there is an incomplete linkage, new gene combinations are formed in the progeny or offsprings. This occurs due to the formation of a chiasma or crossing over between the linked genes.

Linkage Significance

- Due to the linkage between genes, desired characters cannot be brought together by breeders. This would be possible only if the genes would sort independently.
- The characters that are linked remain so as there is no chance of recombination of the linked genes.

Sex- chromosome Linked Diseases in Humans

Diseases like haemophilia, color blindness, male pattern of baldness are sex-linked diseases. Where color blindness and haemophilia are X- linked diseases, male pattern of baldness is a Y-linked one. This indicates that the X-linked diseases will express themselves in a male whereas the female is always a carrier until both the genes are recessive in the female. Male pattern of baldness being a Y-linked trait expresses itself only in the males while females are never affected by it.

Cytological basis of crossing over

Discussion in preceding sections of this section is based on the study of progeny in BC_1 generation or the testcross progeny. In such progenies, lack of independent assortment demonstrated linkage and presence of recombinants showed crossing over. It was concluded that crossing over should be the result of exchange of chromosome segments. However, since homologous chromosomes normally exchange reciprocal segments, resulting chromosomes will exhibit no morphological differences. Therefore, except the visible chiasmata, there is no other cytological observation which will substantiate that actual exchange of chromosome segments really takes place. However, it is not necessary that chiasmata should be associated with exchange of chromosome segments. Therefore, to demonstrate that crossing over is associated with actual exchange of chromosome segments, special experiments were devised by G. Stern in *Drosophila* and by **H.S. Creighton** and **B. McCHntock** in corn. These experiments were reported in 1931 and had utilized chromosomes, whose morphology was altered due to chromosomal aberrations in order to make it identifiable from its homologue. Another experiment was conducted by M. Meselson and J. Weigle in lambda *(λ)* phage, demonstrating exchange of DNA segments.

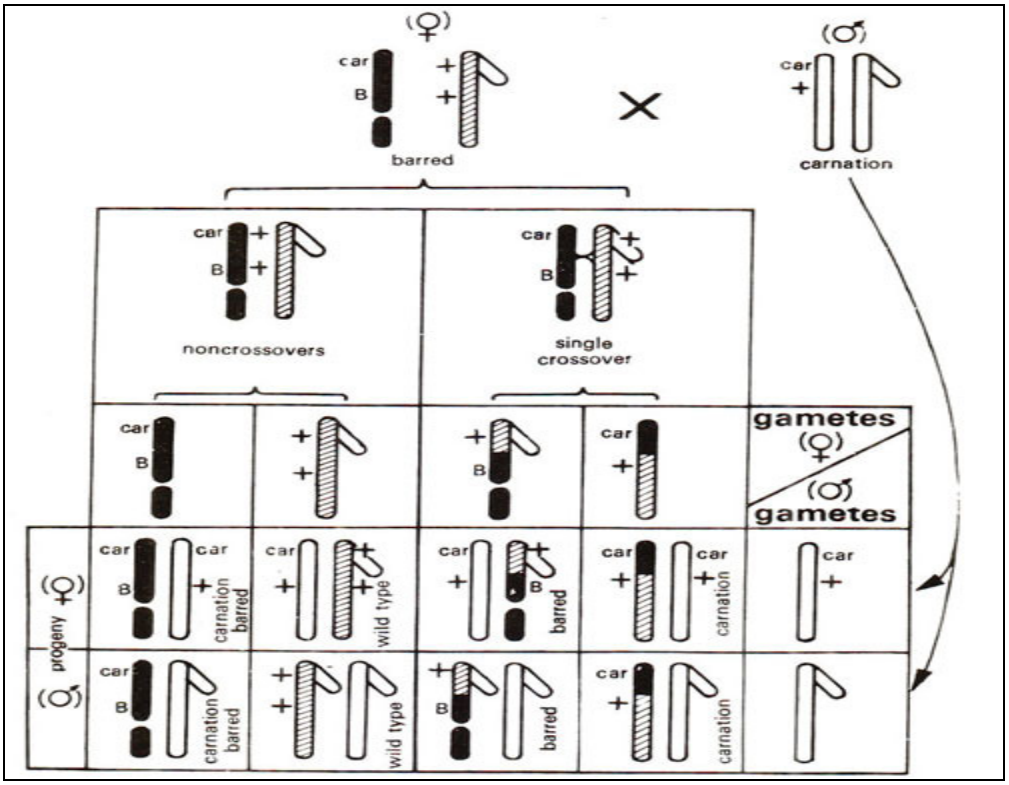


Fig.10.16.Stern's experiment to deomonstrate cytological crossing over

Stern's experiment in *Drosophila:*

Drosophila (fruitfly) stocks carrying translocations were utilised by **C. Stern** in order to produce a female *Drosophila* having a part of Y-chromosome attached to one of the two X-chromosomes. The **other** X-chromosome of this female fly was also marked (identifiable due to distinct morphology) and consisted of two approximately equal fragments, each carrying its centromere. These two X-chromosomes in the female fly could be distinguished not only from each other, but also from normal X-chromosome under the microscope.

In the above female fly, one of the two fragments of an X-chromosome carried mutant alleles for *carnation* eye *(car* is recessive showing light eye colour) and *barred* eye *(B* is dominant showing narrower eyes). The other X-chromosome, having a part of Y attached, carried normal alleles of these two genes, so that the female heterozygote for both these genes *(car B*/+ +) had barred eyes (but normal eye colour, since *car* is recessive to +). Such females were crossed with male flies having recessive alleles for both these genes *(car,* +). In such a situation, this makes a simple testcross. If no crossing over takes place

between the two genes in question, two types of gametes i.e., *car B* and ++ will be produced from the female flies. Crossing over will give two additional types ot gametes i.e., *car* + and + *B* (Figure 10.16). Due to fertilization of two types of non-crossover and the other two types of crossover gametes by male gametes carrying X-chromosome (*car* +), four kinds of female flies will be produced. Another four kinds of male flies will be produced due to fertilization by Y carrying male gametes (Fig. 10.16).

The flies which are classified as crossovers on the basis of phenotype i.e., carnation (with normal eye shape) and barred (with normal eye colour) were studied cytologically. It was found that carnation flies did not have any fragmented X-chromosome, but rather had normal X-chromosome. On the other hand, barred flies had a fragmented X-chromosome with a segment of Y-chromosome attached to one of the two fragments of X-chromosome. Such cytological observations suggested that genetic crossing over was accompanied with an actual exchange of chromosome segments.

The Molecular Mechanism of Crossing-Over

There are two important theories :

1. Copy choice theory and

2. Breakage and reunion theory to explain the mechanism of crossing over.

These are briefly presented below:

i. Copy Choice Theory:

This theory was proposed by Belling. This theory states that the entire recombinant section or part arises from the newly synthesised section. The non-sister chromatids when come in close contact they copy some section of each other resulting in recombination. According to this theory, physical exchange of preformed chromatids does not take place.

The non-sister chromatids when come together during pairing, copy part of each other. Thus, recombinant chromosome or chromatids have some alleles of one chromatids and some of other. The information may be copied by one strand or both the strands. When only one strand copies, non-reciprocal recombinant is produced.

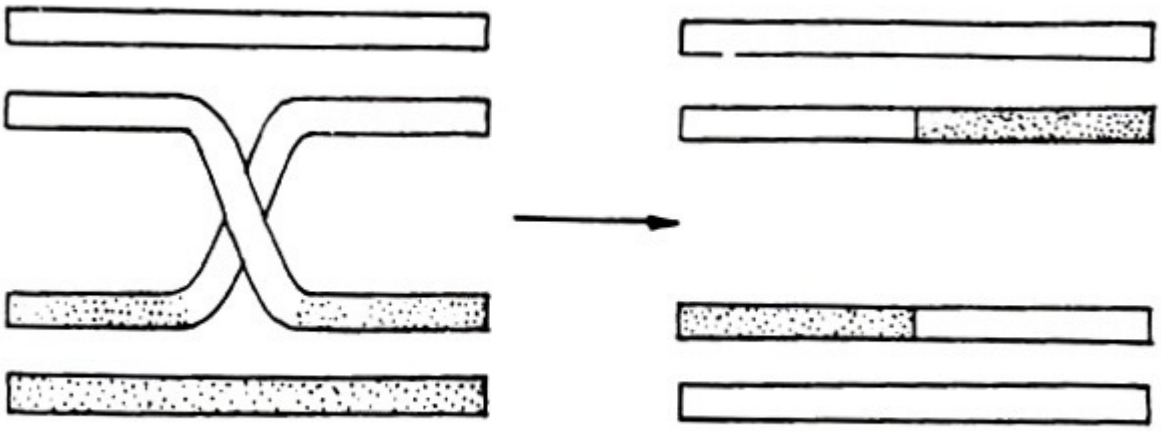


Fig. 9.1. Crossing over according to copy choice theory.

If copy process involves both strands of chromosomes, reciprocal recombinants are produced. Assume, there are two chromosomes, viz., AB and ab. When their chromatids come in close contact they copy each other and result in Ab and aB re-combinations besides parental combinations (Fig. 9.1).

This theory has two objections:

1. According to this theory breakage and reunion does not occur, while it has been observed cytological.

2. Generally crossing over takes place after DNA replication but here it takes place at the same time.

ii. Breakage and Reunion Theory:

This theory states that crossing over takes place due to breakage and reunion of non-sister chromatids. The two segments of parental chromosomes which are present in recombinants arise from physical breaks in the parental chromosomes with subsequent exchange of broken segments (Fig. 9.2).

The breakage results due to mechanical strains that result from the separation of paired homologous chromosomes and chromatids in each chromosome during pachytene stage. The broken ends of non-sister chromatids unite to produce chiasmata resulting in crossing over.

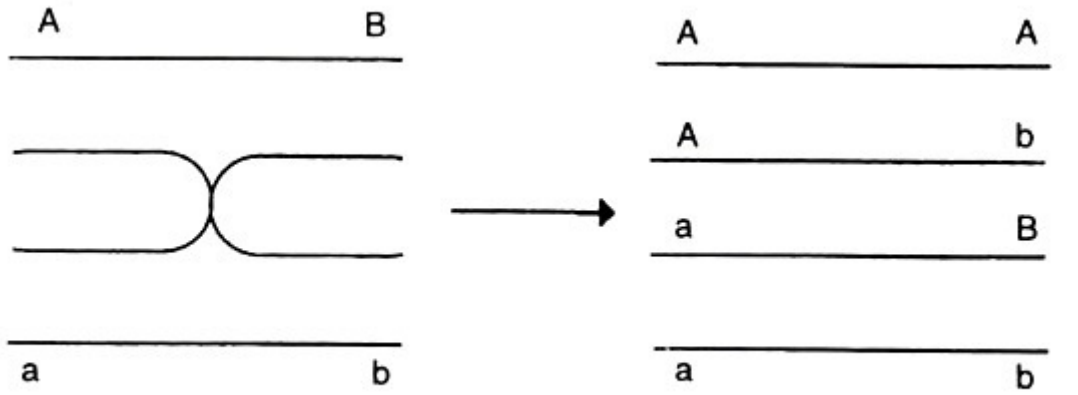


Fig. 9.2. Crossing over according to breakage and reunion theory.

Crossing over at four strand stage:

In the last section, evidences for actual exchange of chromosome segments leading to crossing over were presented. One would, however, like to know whether exchange of segments takes place between entire chromosomes or between chromatids at four-strand stage. There is enough evidence which suggests that crossing over takes place at pachytene stage after the chromosomes have already duplicated giving rise to four strands, two strands belonging to each paired chromosome. The theoretical consequences of two

Strand and four strand crossing over are given in Figure 10.19. While two strand crossing over would lead to four recombinants, four strand crossing over will give two parental combinations and two recombinants among four gametes produced from a mother cell. By using attached X-chromosomes in *Drosophila* and also by studying linear order in which recombinants and parental combinations are found in an ascus of fungus *Neurospora,* it could be proved that crossing over takes place at four strand stage rather than at two strand stage.

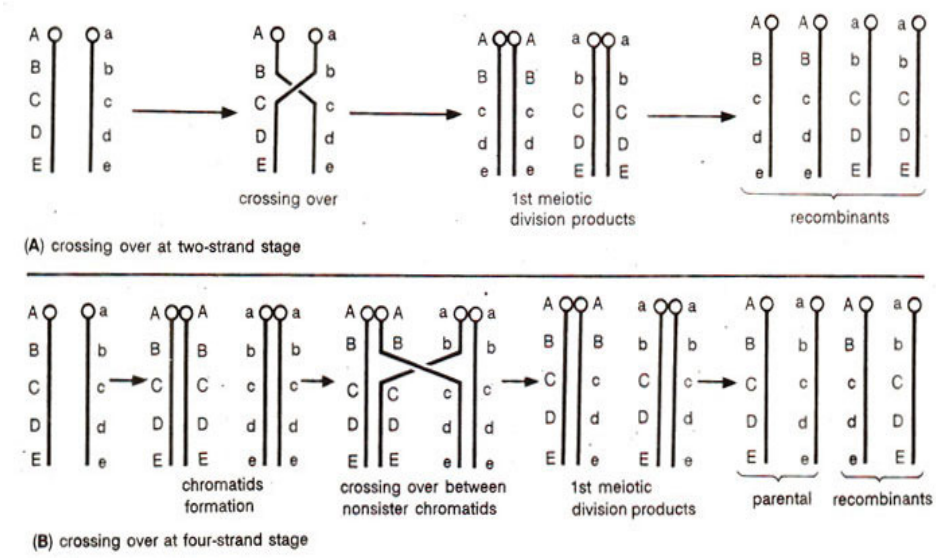


Fig.10.19. Difference in consequences between crossing over at the two strand and four strand stage (Redrawn from strickberger's "Genetics").

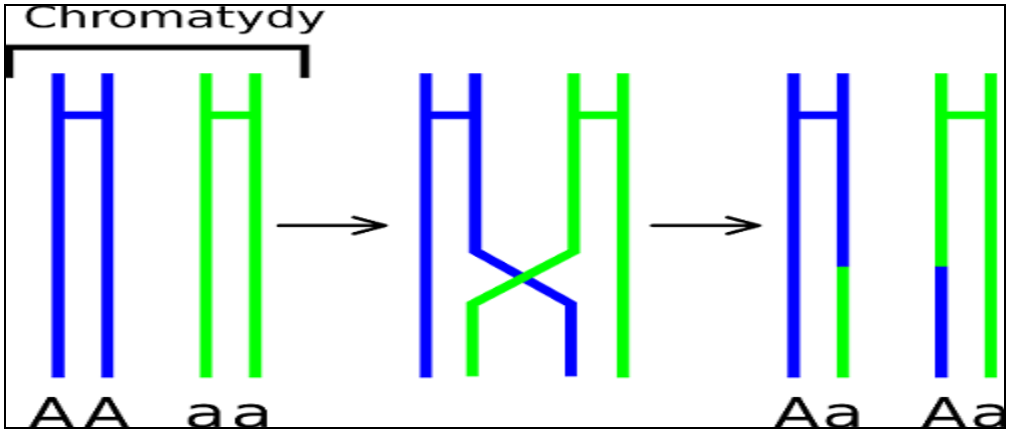
Genetic Recombination Definition:

Genetic recombination occurs when genetic material is exchanged between two different *chromosomes* or between different regions within the same chromosome. We can observe it in both *eukaryotes* (like animals and plants) and *prokaryotes* (like archaea and bacteria). Keep in mind that in most cases, in order for an exchange to occur, the sequences containing the swapped regions have to be *homologous*, or similar, to some degree.

The process occurs naturally and can also be carried out in the lab. Recombination increases the genetic diversity in sexually reproducing organisms and can allow an organism to function in new ways.

Examples of Genetic Recombination

Genetic recombination occurs naturally in *meiosis*. Meiosis is the process of cell division that occurs in eukaryotes, such as humans and other mammals, to produce offspring. In this case, it involves *crossing-over*. What happens is that two chromosomes, one from each parent, pair up with each other. Next, a segment from one crosses over, or overlaps, a segment of the other. This allows for the swapping of some of their material, as you can see in the illustration below. What we end up with is a new combination of genes that didn't exist before and is not identical to either parent's genetic information. Note that recombination is also observed in *mitosis*, but it doesn't occur as often in mitosis as it does in meiosis.



Natural Self-Healing

The cell also can also undergo recombinational repair, for example, if it notices that there is a harmful break in the DNA: the kind of break that occurs in both strands. What we observe is an exchange between the broken DNA and a homologous region of DNA that will fill the gaps. There are also other ways that recombination is used to repair DNA.

Functions of Genetic Recombination:

We've already covered some the consequences of genetic recombination, but in this section we will discuss *Recombinant DNA Technology*. This is a relatively new technology that is allowing scientists to change genes and organisms by manipulating DNA. What makes this so important is the fact that it has improved our understanding of diseases and, consequently, has expanded our ways of fighting them.
As you might expect, DNA segments are joined together in this Technology. For example, a gene can be cut out from a human and introduced into the DNA of a bacterium. The bacterium will then be able to produce human protein that is otherwise only made by humans. The same thing is done in gene therapy. Let's assume a person is born without a particular essential gene, and is suffering from an illness due to the absence of that gene. Scientists can now introduce the missing gene into that person's *genome* by using a virus that infects humans. First, they join the needed gene with the virus's DNA and then they expose the person to that virus. Since all viruses blend their DNA with their host's DNA, the gene that is added by the scientists ends up being part of the person's genome.

Types of Genetic Recombination:

Scientists have observed the following types of recombination in nature:

Homologous (general) recombination: As the name implies, this type occurs between DNA molecules of similar sequences. Our cells carry out general recombination during meiosis.

Nonhomologous (illegitimate) recombination: Again, the name is self-explanatory. This type occurs between DNA molecules that are not necessarily similar. Often, there will be a degree of similarity between the sequences, but it's not as obvious as it would be in homologous recombinations.
Site-specific recombination: This is observed between particular, very short, sequences, usually containing similarities.

Mitotic recombination: This doesn't actually happen during mitosis, but during *interphase*, which is the resting phase between mitotic divisions. The process is similar to that in meiotic recombination, and has its possible advantages, but it's usually harmful and can result in tumors. This type of recombination is increased when cells are exposed to radiation.

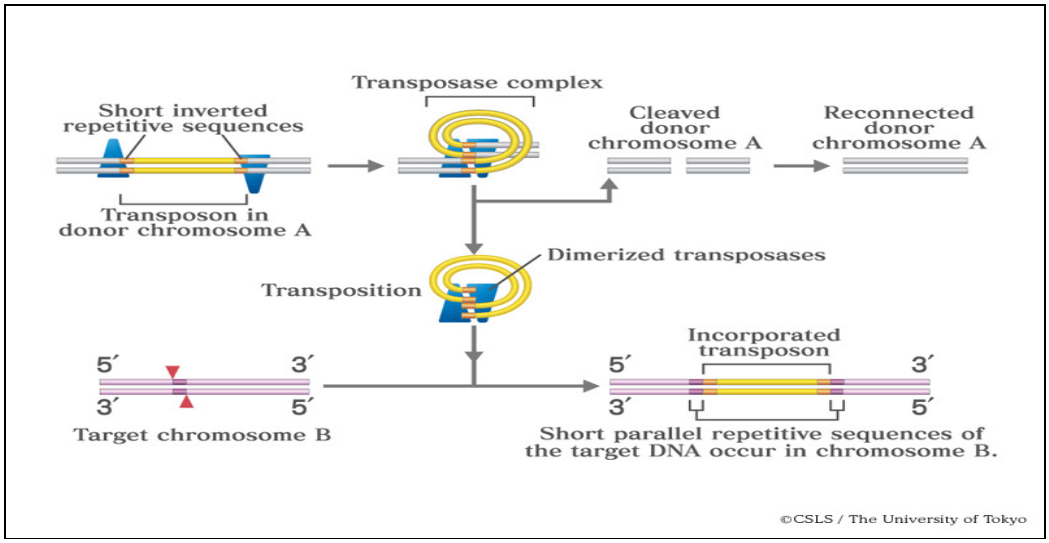
Prokaryotic cells can undergo recombination through one of these three processes:

Conjugation is where genes are donated from one organism to another after they have been in contact. At any point, the contact is lost and the genes that were donated to the recipient replace their equivalents in its chromosome. What the offspring ends up having is a mix of traits from different strains of bacteria.

Transformation: This is where the organism acquires new genes by taking up naked DNA from its surroundings. The source of the free DNA is another bacterium that has died, and therefore its DNA was released to the environment.
Transduction is gene transfer that is mediated by viruses. Viruses called *bacteriophages* attack bacteria and carry the genes from one bacterium to another.

Site-Specific Recombination:

In general recombination, DNA rearrangements occur between DNA segments that are very similar in sequence. Although these rearrangements can result in the exchange of alleles between chromosomes, the order of the genes on the interacting chromosomes typically remains the same. A second type of recombination, called site-specific recombination, can alter gene order and also add new information to the genome. Site-specific recombination moves specialized nucleotide sequences, called *mobile genetic elements,* between nonhomologous sites within a genome. The movement can occur between two different positions in a single chromosome, as well as between two different chromosomes.
Mobile genetic elements range in size from a few hundred to tens of thousands of nucleotide pairs, and they have been identified in virtually all cells that have been examined. Some of these elements are viruses in which site-specific recombination is used to move their genomes into and out of the chromosomes of their host cell. A virus can package its nucleic acid into viral particles that can move from one cell to another through the extracellular environment. Many other mobile elements can move only within a single cell (and its descendents), lacking any intrinsic ability to leave the cell in which they reside.



The relics of site-specific recombination events can constitute a considerable fraction of a genome. The abundant repeated DNA sequences found in many vertebrate chromosomes are mostly derived from mobile genetic elements; in fact, these sequences account for more than 45% of the human genome . Over time, the nucleotide sequences of these elements have been altered by random mutation. As a result, only a few of the many copies of these elements in our DNA are still active and capable of movement.

In addition to moving themselves, all types of mobile genetic elements occasionally move or rearrange neighboring DNA sequences of the host cell genome. These movements can cause deletions of adjacent nucleotide sequences, for example, or can carry these sequences to another site. In this way, site-specific recombination, like general recombination, produces many of the genetic variants upon which evolution depends. The translocation of mobile genetic elements gives rise to spontaneous mutations in a large range of organisms including humans; in some, such as the fruit fly *Drosophila*, these elements are known to produce most of the mutations observed. Over time, site-specific recombination has thereby been responsible for a large fraction of the important evolutionary changes in genome.

Three of the many types of mobile genetic elements found in bacteria. Each of these DNA elements contains a gene that encodes a *transposase*, an enzyme that conducts at least some of the DNA breakage and joining reactions needed for the element to move.

Site-specific recombination can proceed via either of two distinct mechanisms, each of which requires specialized recombination enzymes and specific DNA sites.

(1) **Transpositional site-specific recombination** usually involves breakage reactions at the ends of the mobile DNA segments embedded in chromosomes and the attachment of those ends at one of many different nonhomologous target DNA sites. It does not involve the formation of heteroduplex DNA.

(2) **Conservative site-specific recombination** involves the production of a very short heteroduplex joint, and it therefore requires a short DNA sequence that is the same on both donor and recipient DNA molecules. We first discuss transpositional site-specific recombination *(transposition* for short), returning to conservative site-specific recombination at the end of the chapter.

Transpositional Site-specific Recombination Can Insert Mobile Genetic Elements into Any DNA Sequence:

Transposons, also called transposable elements, are mobile genetic elements that generally have only modest target site selectivity and can thus insert themselves into many different DNA sites. In transposition, a specific enzyme, usually encoded by the transposon and called a *transposase,* acts on a specific DNA sequence at each end of the transposon—first disconnecting it from the flanking DNA and then inserting it into a new target DNA site. There is no requirement for homology between the ends of the element and the insertion site.

Most transposons move only very rarely (once in 10^5 cell generations for many elements in bacteria), and for this reason it is often difficult to distinguish them from nonmobile parts of the chromosome. In most cases, it is not known what suddenly triggers their movement

.

On the basis of their structure and transposition mechanisms, transposons can be grouped into three large classes , each of which is discussed in detail in subsequent sections. Those in the first two of these classes use virtually identical DNA breakage and DNA joining reactions to translocate. However, for the *DNA-only transposons,* the mobile element exists as DNA throughout its life cycle: the translocating DNA segment is directly cut out of the donor DNA and joined to the target site by a transposase. In contrast, *retroviral-like retrotransposons* move by a less direct mechanism. An RNA polymerase first transcribes the DNA sequence of the mobile element into RNA. The enzyme reverse transcriptase then transcribes this RNA molecule back into DNA using the RNA as a template, and it is this DNA copy that is finally inserted into a new site in the genome. For historical reasons, the transposase-like enzyme that catalyzes this insertion reaction is called an *integrase* rather than a transposase.. However, the mechanism involved for these *nonretroviral retrotransposons* is distinct from that just described in that the RNA molecule is directly involved in the transposition reaction.

Three Major Classes of Transposable Elements.

DNA-only Transposons Move By DNA Breakage and Joining Mechanisms

Many DNA-only transposons move from a donor site to a target site by cut-and-paste transposition, using the mechanism outlined in Figure 5-70. Each subunit of a transposase recognizes the same specific DNA sequence at an end of the element; the joining together of these two subunits to form a dimeric transposase creates a DNA loop that brings the two ends of the element together. The

transposase then introduces cuts at both ends of this DNA loop to expose the element termini and remove the element completely from its original chromosome (Figure 5-71). To complete the reaction, the transposase catalyses a direct attack of the element's two DNA termini on a target DNA molecule, breaking two phosphodiester bonds in the target molecule as it joins the element and target DNAs together.

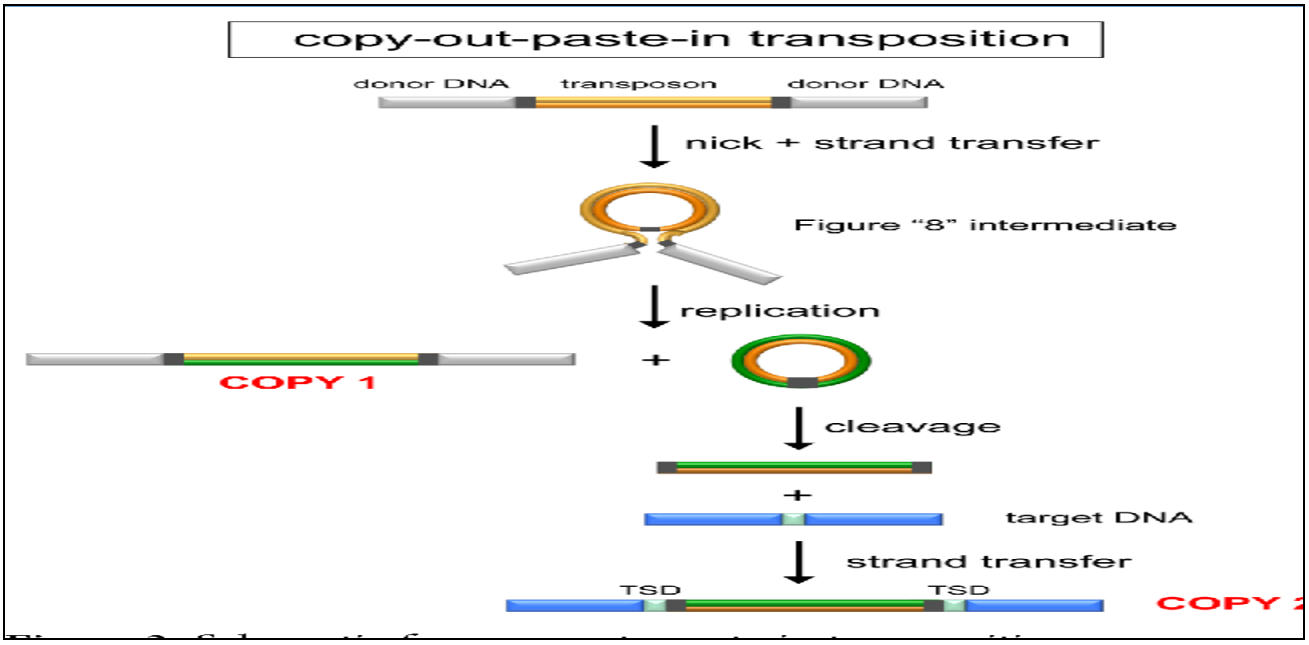


Figure 5-70

Cut-and-paste transposition. DNA-only transposons can be recognized in chromosomes by the "inverted repeat DNA sequences" *(red)* at their ends. Experiments show that these sequences, which can be as short as 20 nucleotides, are all that

The structure of the central intermediate formed by a cut-and-paste transposase. (A) Schematic view of the overall structure. (B) The detailed structure of a transposase holding the two DNA ends, whose 3′-OH groups are poised to attack a target.

Because the breaks made in the two target DNA strands are staggered *(red arrowheads* in Figure 5-70), two short, single-stranded gaps are initially formed in the product DNA molecule, one at each end of the inserted transposon. These gaps are filled-in by a host cell DNA polymerase and DNA ligase to complete the recombination process, producing a short duplication of the adjacent target DNA sequence. These flanking direct repeat sequences, whose length is different for different transposons, serve as convenient markers of a prior transpositional site-specific recombination event.

When a cut-and-paste DNA-only transposon is excised from the donor chromosome, a double-strand break is created in the vacated chromosome. This break can be perfectly "healed" by a homologous end-joining reaction. Alternatively, the break can be resealed by a nonhomologous end-joining reaction; in this case, the DNA sequence that flanked the transposon is often altered, producing a mutation at the chromosomal site from which the transposon was excise.

Some DNA-only transposons move using a variation of the cut-and-paste mechanism called *replicative transposition*. In this case, the transposon DNA is replicated and a copy is inserted at a new chromosomal site, leaving the original chromosome intact. Although the mechanism used is more complex, it is closely related to the cut-and-paste mechanism just described; indeed, some transposons can move by either pathway.

Replicative transposition. In the course of replicative transposition, the DNA sequence of the transposon is copied by DNA replication. The end products are a DNA molecule that is identical to the original donor and a target DNA molecule that has a transposon.

Transposition: Meaning and Mechanism:

Meaning of Transposition:

The phenomenon of moving genetic segments from one location to the other in a genome is known as transposition. There are two types of transposition, replicative and conservative transposition.
The replicative transposition involves the events of both replication and recombination processes generating the two daughter copies of the original transposable elements, one remaining at the parental site and the other at the target site.

Mechanism of Transposition:

The bacterial transposon Tn3 has been extensively studied. Analysis of DNA sequences and its junction with target DNA provides some clue to the mechanism of transposition.
Movement of transposons occurs only when the enzyme transposase recognises and cleaves at either 5′ or 3′ of both ends of transposon, and catalyses at either 5 or 3′ of both ends of transposon and catalyses a staggered cut at the target site (Figs. 8.30 and 8.34A). Depending on transposon, a duplication of 3-12 bases of target DNA occurs at the site where insertion is to be done. One copy remains at each end of the transposon sequence.

After attachment of both ends of transposon to the target site, two replication forks are immediately formed (Fig. 8.34 B-C). From this stage there starts two path for carrying out onward processes. The first model is the replication path where the transposon replicates and the replicated DNA sealed to flanking sequences generating a co-integrate (D).

Co-integrate is resolved by the genetic exchange between the two copies of transposon resulting in a simple insertion and regeneration of donor replicon (E). This model explains the transposition of only TnA family but not explain completely for IS elements of Mu.

The second model (F-G) is the non-replicative path that generates simple insertions without formation of co-integrate. At the prime termini in the target DNA, repair synthesis occurs. The displaced single strand that attaches the transposon to the donor replicon is broken. This forms a simple insertion (G). It is likely that both the pathways can be used but the frequency of simple insertion and co-integrate formation varies.

Thus, for transposition the two enzymes, transposase and resolvase coded by tnpA and tnpR respectively are required. Transposase recognises the ends of transposon and connects them to the target site. Resolvase provides a site-specific recombination function.

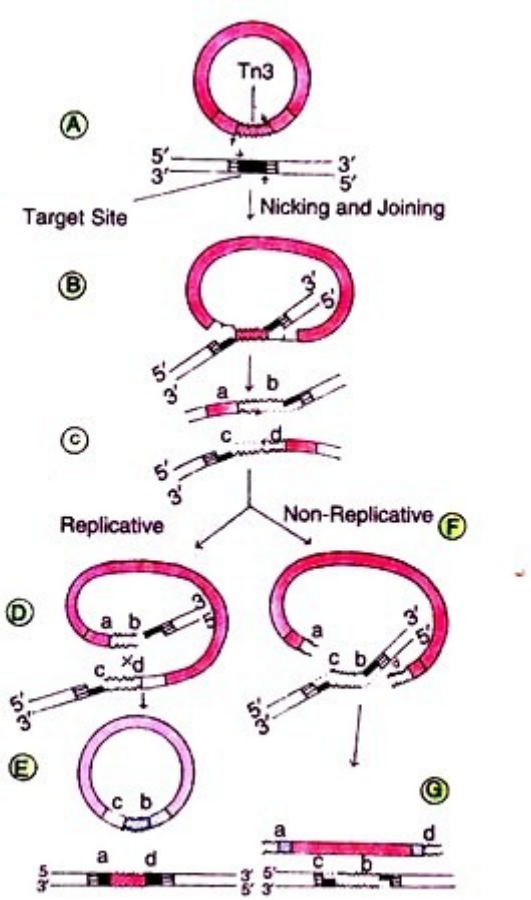


Fig. 8.34 : A model to explain the transposition mechanism of transposon Tn3.

Genetics of Transposition:

The genes of transposase and resolvase i.e. tnpA and tnpR are identified by recessive mutations. The above enzymes accomplish the two stages of TnA mediated transposition. Like IS type elements the transposition stage involves the ends of the elements. A unique feature of TnA family is that a specific internal site is required for resolution.

The mutants of tnpA cannot transpose because the enzyme transposase will not be encoded. However, transposase recognises the ends of elements and binds to 25 bp long sequence located within 38 bp of the inverted terminal repeat. Transposase also makes the staggered 5 bp breaks in target DNA where transposon is to be inserted.

Questions:

Long answers questions:

1. Explain Linkage and Recombination of genes.
2. Cytology basis of cross over
3. Molecular mechanisms of cross over
4. Crossing over at fourth strand stage
5. Homologous and nonhomologous recombination.
6. Site –specific recombination
7. Transposition.

Short answer questions:

1. What is recombination of gene
2. What is cross over
3. What is jumbing genes
4. What is genetic mapping.

KARPAGAM ACADEMY OF HIGHER EDUCATION

CLASS: III M. Sc MICROBIOLOGY **UNIT: 3** **COURSE NAME: INHERITANCE BIOLOGY**
COURSE CODE: 17MBU504B **BATCH-2017-2020**

Sno	Question	Opt 1	Opt 2	Opt 3	Opt 4	Answer
1	Linkage _____ as the distance between two genes _____	Decreases, decreases	Unaffected, Decreases	Decreases, Increases	Increases, Increases	Decreases, Increases
2	In Drosophila males there is complete linkage	The genes are very closely located	Coupling theory	No synapsis	Unknown reason	No synapsis
3	Linkage results in _____	Formation of more Dominant phenotype	Formation of more wild phenotype	Formation of more parental phenotype	Formation of more recombinant phenotype	Formation of more parental phenotype
4	If you suddenly observe linkage between two genes that are present in two chromosomes, this can be due to _____	Coupling	Translocation	Inversion	Non-homologous end joining	Translocation
5	Accurate mapping of genes can be done using _____	Two point mapping	Three point mapping	Single gene mapping	None of the mentioned	Three point mapping
6	Recombination occurs in _____	Single strand stage	Two strand stage	Three strand stage	Four stand stage	Four stand stage
7	Double crossovers can involve two, three or four strands at a time	0%	50%	70%	90%	50%
8	You cross a p+/v+ p+/v+ male drosophila to a p-/v- p-/v- and obtain the F1 hybrid	p+/v+ p-/v- only	p+/v+ p-/v- and p-/v- p-/v-	p+/v+ p-/v- and p-/v- p-/v- also p+/v- p-/v- and p-/v- p-/v-	p+/v+ p-/v- and p-/v- p-/v- also p-/v+ p-/v- and p-/v- p-/v-	p+/v+ p-/v- and p-/v- p-/v-
9	In animals cytological study of recombination was done by_____	Barbara McClintok	Stern	Creigton	Mandel	Stern
10	Two basic rules of probability to solve problems in genetics include	addition	multiplication	both A and B	division	both A and B

11	The tendency of two or more than two genes to stay together during inheritance is called _____	Genetics	Gene interaction	Crossing over	Linkage	Linkage
12	Which of the following statement is NOT true regarding linkage group?	Group of physically linked genes	Represent a haploid number of chromosomes	Shown by linkage map	Linkage groups are not correlated with each other	Linkage groups are not correlated with each other
13	The linkage maps are constructed by using recombination frequencies between genes	yes	no	some time	non of this	yes
14	What is the unit of linkage map?	Morgan	Centi-morgan	Centimeter	Angstrom	Centi-morgan
15	What is the maximum percentage of recombination frequency between two genes?	75%	100%	50%	25%	100%
16	Name the phenomenon which can break the occurrence of linkage?	Crossing over	Linkage	Reconstruction	Breakage	Crossing over
17	Failure in which of the following phenomenon would result in linkage?	Law of dominance	Law of segregation	Law of independent assortment	Law of separation	Law of independent assortment
18	Name the organism whose first genetic map was made?	Rat	Arabidopsis	Fly	Drosophila	Drosophila
19	Name the sites of DNA, which have a high probability of crossing over?	Cold spots	Hot spots	Covalent bond	Hydrophobic bond	Hot spots
20	The only people who likely would be genetically identical are _____ twins	monozygotic	dizygotic	monozygotic and dizygotic	none of this	monozygotic

21	T he inheritance of new combinations of alleles in children results from:	puberty	recombination	genetic linkage	genetic flow	recombination
22	Linked genes are:	located on different chromosomes of the same size and shape	located on the same chromosome	rarely inherited together	located on other then chromosome	located on different chromosomes of the same size and shape
23	Crossing-over of parts of chromosomes:	as no effect on genetic linkage	usually decreases the number of genetic combinations in a population	can increase the number of genetic combinations in a population	the genetic linkage depends on the factors	can increase the number of genetic combinations in a population
24	Crossing-over resulting in the inheritance of altered chromosomes by children occurs:	during mitosis	during meiosis	both of the above	non of this	during meiosis
25	Mendel did not recognize the linkage phenomenon in his experiments because [CMC Vellore 1993]	There were many chromosomes to handle	Characters he studied were located on different chromosomes	He did not have powerful microscope	He studied only pure plants	Characters he studied were located on different chromosomes
26	Crossing Over occurs when the homologous chromosomes contain	One chromatid	Two chromatid	Four chromatid	Eight chromatid	Four chromatid
27	The genes located on the same Chromosome that are inherited together are known as	Complementary genes	Supplementary genes	Mutant genes	Linked genes	Linked genes
28	Linkage usually gets broken due to	Mutation	Cross over	Epistasis	Variation	Cross over
29	The tendency of two different	Coupling	Repulsion	Linkage	Crossing over	Repulsion

	genes to remain apart if they come from two different parents is					
30	The phenomenon in which genes are present on the same chromosomes is:	Cross over	Segregation	Linkage	assortment	Linkage
31	The linked gene does not follow:	Cross over	Segregation	Linkage	assortment	assortment
32	The linkage groups in man are:	46	23	22	24	23
33	The linkage group of sickle cell anemia, leukemia and albinism is present on chromosome:	10	11	12	13	11
34	The gene linkage minimize the chances of:	Cross over	Segregation	recombination	assortment	recombination
35	Gene A and B are linked gene	AB	ab	Ab	ab	AB
36	There is 30% recombination frequency between two genes. The distance between them in unit map is:	15	30	60	80	30
37	There are 80% parental and 20% recombinant in a cross	10%	20%	40%	80%	20%
38	Due to linkage in maize, the number of colourless shrunken seeds produced are	4032	4035	149	152	4035
39	Bar is a gene often used in recombination study. Which of the following is true for the Bar gene?	It is normally present in two copies	Three copies of bar are called ultra bar	Heterozygous bar females have a less severe effect than homozygous bar female	Homozygous bar are of common occurrence	Three copies of bar are called ultra bar
40	Consider that recombination occurs in 2 strand stage of meiosis. If a Drosophila is	The recombination will make them	It will produce ultra bar phenotype	It will be heterozygous	No exchange	It will be heterozygous

	heterozygous for the bar locus what will be the result of recombination?	homozygous				
41	If two genes are unlinked the recombination frequency will be?	25%	50%	75%	100%	50%
42	How many rounds of replication in BrdU will be needed to visualize Harlequin chromosome?	Single	Two	Three	Four	Two
43	Is two crossovers occur between same two strands, this will result in_____	All recombinant strands	Three recombinant strands with different loci exchanged	Exchange of middle portion between two strands	Exchange of ends	Exchange of middle portion between two strands
44	Double cross over involving _____ strands result in 100% recombinant strands	1	2	3	4	4
45	If a recombination event of three points crossing produces 6 DCO, 142 SCO and 352 NCO. What will be the percentage cross over between the terminal genes.	10%	20.80%	14.80%	30.80%	30.80%
46	If single cross over frequency between two genes r and q and q and s in 3 point mapping is 0.6 and 0.2 respectively. What will be the expected double cross over frequency?	0.012	0.01	0.022	0.024	0.022
47	an experiment you calculate	Coincidence	Interference	Penitence	Expressivity	Interference

	the expected DCO frequency to be 0.022 but in reality you observe that only 0.012 recombination frequency. What is the phenomenon resulting in this?					
48	Which of the following will result in parental phenotype?	DCO in between two genes considering four strands	Even number of DCO between two genes	Odd number of DCO between two genes	Single cross over at 4 strand stage between two genes	Even number of DCO between two genes
49	What will be the nature of curve with map distances plotted in X axis and percentage recombination in Y axis?	Parallel to X axis	Increasing in a straight line	Parabolic	Exponential	Exponential
50	Homologous DNA recombination in prokaryotes take place for_____	Increasing variability	Repair	Incorporation of gene	Taking up a plasmid from media	Repair
51	If an organism has 8 chromosomes in diploid condition, what will be the number of chromosomes after telophase of meiosis 1?	2	4	8	16	8
52	If there are 2 strands of chromosomes that can pair with a single strand, and they are both paired to the same strand, their junction is called_____	Chimera	Chi	Double binding	Branch point	Branch point
53	Holliday intermediate could be mistaken for _____	Hetero chromatin	Circular plasmid	Linear extracellular	Broken chromosome	Circular plasmid

	under microscope			chromosome		
54	How many Rec A are present in one turn around the single stranded chromosome?	5.2	9	2.3	6.2	6.2
55	Rec A doesn't_____	Line up the homologous chromosome with the one it surrounds	Perform spooling	Cleaves at recombination site	Help in branch migration	Cleaves at recombination site
56	The Ruv A of the resolvosome complex binds at_____	On each chromosome on either side of branch point	At the branch point	After exchange	At the terminals	At the branch point
57	In case of chicken foot Holliday intermediate, the template strand for synthesis across lesion is_____	The parent strand aligned along strand with lesion	The parent strand aligned against lesion strand	The daughter strand with lesion	The daughter strand without lesion	The daughter strand without lesion
58	Recombination occurs in _____	Leptotene	Zygotene	Pachytene	Diplotene	Diplotene
59	Gene mapping provides useful information about chance of	inheritance of disorders	inheritance of genes	inheritance of recessive gene	inheritance of dominant gene	inheritance of disorders
60	Methods used to identify locus of gene and distances between genes are called as	gene localization	gene linkage	gene pool	gene mapping	gene mapping

UNIT: IV
Syllabus

Rules of extra nuclear inheritance,Organelle heredity-Chloroplast mutation in *Chlamydomonas,* mitochondrial mutation in *Saccharomyces*, Menternal effects-Shell coiling in *Limnaea peregre* infection heredity-Kappa partical in *Paramecium*. Pedigree analysis, lod scorefor linkage testing, karyotypes, genetic disorders. Polygenic ingeritance, heritability and its measurements, QTL mapping.

Extranuclear Inheritance :

Extranuclear inheritance or cytoplasmic inheritance is the transmission of genes that occur outside the nucleus. It is found in most eukaryotes and is commonly known to occur in cytoplasmic organelles such as mitochondria and chloroplasts or from cellular parasites like viruses or bacteria.

Organelle Heredity:

Mitochondria are organelles which function to transform energy as a result of cellular respiration. Chloroplasts are organelles which function to produce sugars via photosynthesis in plants and algae. The genes located in mitochondria and chloroplasts are very important for proper cellular function, yet the genomes replicate independently of the DNA located in the nucleus, which is typically arranged in chromosomes that only replicate one time preceding cellular division. The extranuclear genomes of mitochondria and chloroplasts however replicate independently of cell division. They replicate in response to a cell's increasing energy needs which adjust during that cell's lifespan. Since they replicate independently, genomic recombination of these genomes is rarely found in offspring, contrary to nuclear genomes in which recombination is common. Mitochondrial diseases are inherited from the mother, not from the father: mitochondria with their mitochondrial DNA from the mother's egg cell are incorporated into the zygote and passed to daughter cells, whereas those from the sperm are not.

Parasites:

Extranuclear transmission of viral genomes and symbiotic bacteria is also possible. An example of viral genome transmission is perinatal transmission. This occurs from mother to fetus during the perinatal period, which begins before birth and ends about 1 month after birth. During this time viral material may be passed from mother to child in the bloodstream or breastmilk. This is of particular concern with mothers carrying HIV or Hepatitis C viruses.[2][3] Symbiotic cytoplasmic bacteria are also inherited in organisms such as insects and protists.

Types:

Three general types of extranuclear inheritance exist.

- Vegetative segregation results from random replication and partitioning of cytoplasmic organelles. It occurs with chloroplasts and mitochondria during mitotic cell divisions and results in daughter cells that contain a random sample of the parent cell's organelles. An example of vegetative segregation is with mitochondria of asexually replicating yeast cells.
- Uniparental inheritance occurs in extranuclear genes when only one parent contributes organellar DNA to the offspring. A classic example of uniparental gene transmission is the maternal inheritance of human mitochondria. The mother's mitochondria are transmitted to the offspring at fertilization via the egg. The father's mitochondrial genes are not transmitted to the offspring via the sperm. Very rare cases which require further investigation have been reported of paternal mitochondrial inheritance in humans, in which the father's mitochondrial genome is found in offspring.[6] Chloroplast genes can also inherit uniparentally during sexual reproduction. They are historically thought to inherit maternally, but paternal inheritance in many species is increasingly being identified. The mechanisms of uniparental inheritance from species to species differ greatly and are quite complicated. For instance, chloroplasts have been found to exhibit maternal, paternal and biparental modes even within the same species.
- Biparental inheritance occurs in extranuclear genes when both parents contribute organellar DNA to the offspring. It may be less common than uniparental extranuclear inheritance, and usually occurs in a permissible species only a fraction of the time. An example of biparental mitochondrial inheritance is in the yeast *Saccharomyces cerevisiae*. When two haploid cells of opposite mating type fuse they can both contribute mitochondria to the resulting diploid offspring.

Mutant Mitochondria:

Poky is a mutant of the fungus Neurospora crassa that has extranuclear inheritance. Poky is characterized by slow growth, a defect in mitochondrial ribosome assembly and deficiencies in several cytochromes. The studies of poky mutants were among the first to establish an extranuclear mitochondrial basis for inheritance of a particular genotype. It was initially found, using genetic crosses, that poky is maternally inherited. Subsequently, the primary defect in the poky mutants was determined to be a deletion in the mitochondrial DNA sequence encoding the small subunit of mitochondrial ribosomal RNA

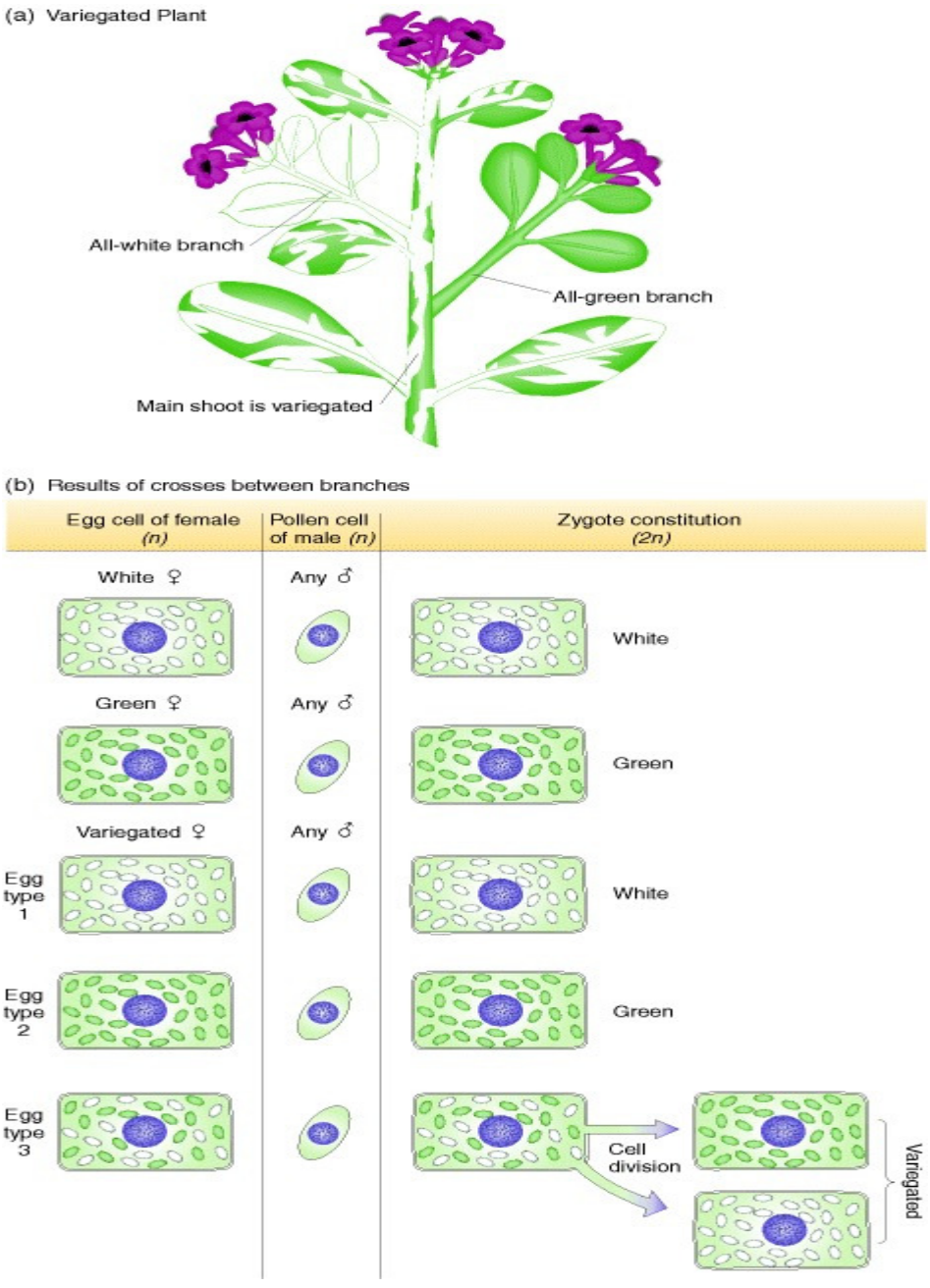
Inheritance of Organelle Genes:

Mitochondria and chloroplasts are specialized organelles located in the cytoplasm. They contain a defined subset of the total cell genome .These genes show their own special mode of inheritance. In a cross, both parents contribute equally to the nuclear genome of the zygote. However, the cytoplasmic contribution of the male and the female parent is generally unequal; the egg contributes the bulk of the cytoplasm and the sperm essentially none. Because organelles reside in the cytoplasm, the organelle genes generally show strictly maternal inheritance. In other words, essentially none of the organelle DNA in the zygote is from the male parent. A simple example is seen in the inheritance of the *Neurospora* slow-growing mutant poky, which is caused by a defect in one of the mitochondrial genes. *Neurospora* can be crossed in such a way that one parent acts as the maternal and the other the paternal parent. In the cross of a poky female with a normal male, the progeny are all poky (FIG1), the precise inheritance pattern expected from a mitochondrial gene.

Maps of yeast and human mtDNAs. Each map is shown as two concentric circles corresponding to the two strands of the DNA helix. Note that the mutants used in yeast mtDNA analysis are shown opposite their corresponding structural genes. Green = exons and

Explanation of the different results from reciprocal crosses of poky and normal *Neurospora.* The parent contributing most of the cytoplasm of the progeny cells is called *female.* Brown shading represents cytoplasm with the poky determinants. The nuclear.

Figure 4-30 on page 120 demonstrates maternal inheritance in the four-o'clock plant. The color of the chloroplasts in this plant determines the color of the various branches. Variegated branches are mosaics of all-green and all-white cells. Flowers can come from green, white, or variegated branches, but when crossed, it is the egg cell that determines branch color in the resulting plant. For example, if the egg cell comes from a flower on the white branch, regardless of the origin of the pollen, the resulting plant will have white branches, thus showing maternal inheritance. The variegated zygotes (bottom of Figure 4-30) are cytoplasmic mixtures of two chloroplast types, and, interestingly, these two types undergo cytoplasmic segregation during cell division, yielding the distinct green and white sectors that cause the variegation in the branches.


(a) Variegated Plant
All-white branch
All-green branch
Main shoot is variegated
(b) Results of crosses between branches
Egg cell of female (n)
Pollen cell of male (n)
Zygote constitution (2n)
White ♀
Any ♂
White
Green ♀
Any ♂
Green
Variegated ♀
Any ♂
Egg type 1
White
Egg type 2
Green
Egg type 3
Cell division
Variegated

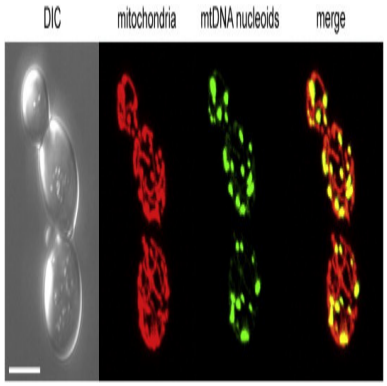


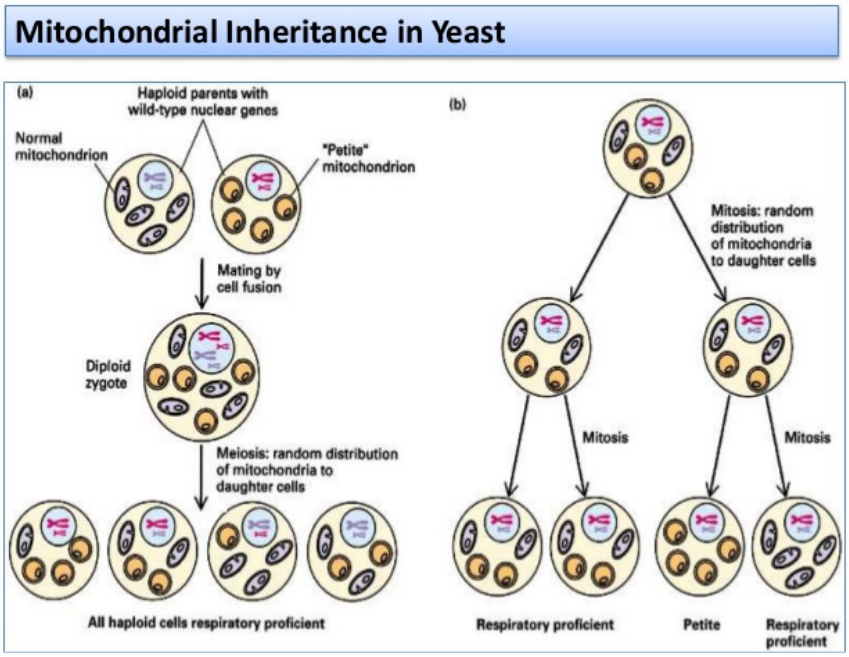
Figure 4-30

Leaf variegation in *Mirabilis jalapa,* the four-o'clock plant. (a) Flowers may form on any branch (varie-gated, green, or white), and these flowers may be used in crosses. (b) In crosses between flowers on different-colored branches, color of the zygote and resulting plant is deter-mined by maternal inheritance. The first two crosses shown here exhibit strict maternal inheritance. If the maternal branch is variegated, three types of zygotes can result, depending on whether the egg cell contains only white, only green, or both green and white chloroplasts. Maternal inheritance still applies in all three types, but in the variegated zygotes, a process of cytoplasmic segregation during subsequent cell divisions produces a mosaic of all-green and all-white cells, hence, a variegated plant.

Mitochondrial Mutation in Yeast:

The yeast *Saccharomyces cerevisiae* can mutate to the respiratory-incompetent petite colony form. The mutation is probably caused by damage to, or loss of, the yeast's mitochondrial DNA, for petite mutants often lack mitochondrial DNA, possess it in abnormal amounts or with abnormal buoyant density. Some of the agents, such as acrifiavine or ethidium bromide, which induce the petite mutation interfere with mitochondrial DNA synthesis whereas ethidium bromide also causes or permits degradation of *Saccharomyces cerevisiae* mitochondrial DNA. We have observed that nalidixate (50 µg/ml.), an inhibitor of DNA synthesis, can prevent or delay petite mutation induced by ethidium bromide[4]. A similar effect has been observed by Hollenberg and Borst using a higher nalidixate concentration

The mitochondrial genome is packaged into protein–DNA complexes. These structures are called nucleoids by analogy to DNA-organizing structures in bacteria, even though mtDNA packaging proteins probably are of eukaryotic origin . *S. cerevisiae* has about 10–40 nucleoids per cell which are anchored to the mitochondrial inner membrane and evenly spaced along the mitochondrial reticulum (Fig. 1). Each nucleoid contains several mtDNA copies . The major DNA-binding protein of yeast nucleoids is the non-histone high mobility group protein Abf2 . Abf2 plays a major role in packaging of mtDNA, protects it against nuclease attack and chemical damage, and binds and stabilizes recombination intermediates . Additional nucleoid components are the proteins required for DNA replication, transcription, repair, and recombination . Other proteins that were found in nucleoids include the mitochondrial chaperonin Hsp60, which was proposed to be required for nucleoid division , the citric acid cycle enzyme aconitase, which was suggested to couple mtDNA maintenance with cell metabolism , and various other heat shock proteins, metabolic enzymes, and proteins of unknown function.



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Surprisingly little is known about the cellular mechanisms of mtDNA segregation in yeast cells. During its sexual life cycle two haploid yeast cells of opposite mating type fuse to form a diploid zygote. If the parental cells contribute different mitochondrial genomes the zygote contains a mixture of mtDNAs with different genotypes, a state termed heteroplasmy. However, within few cell divisions the mtDNAs unmix, and cells become homoplasmic . Genetic evidence suggests that only a small fraction of the

mtDNA pool is transferred from the zygote to the bud, and that the position of the bud determines which parental cell contributes its mtDNA. Cells that bud from the mid-point of the zygote inherit mtDNA from both parents, whereas those that bud from either end preferentially inherit mtDNA from only one parent . Furthermore, examination of fluorescently labeled nucleoids in zygotes indicated that nucleoids are anchored within the organelle and remain localized in distinct parts of the cell .

Thus, it is thought that diffusion of mtDNA within the organelle is limited. Instead, it is actively transported into the bud by a yet poorly characterized nucleoid segregation apparatus . Presumably, similar mtDNA segregation mechanisms are active in zygotes and vegetatively growing cells.

S. cerevisiae has been used extensively to study the molecular mechanisms of organelle inheritance.During mitotic growth yeast cells multiply by asymmetric cell division, a process termed budding. At the beginning of each cell cycle cells become polarized and select a site for bud emergence. Growth is initially restricted to the bud tip and then switches to even expansion over the entire bud surface. As the bud reaches the size of the mother cell, growth is directed to the bud neck, and a septum is formed that separates the daughter cell from its mother. Correct organelle partitioning is achieved by active and directed transport of organelles to the growing bud concomitant with retention of a portion of the organelles in the mother cell . Actin cables that consist of bundles of actin filaments provide the tracks for directed transport processes during cell growth. These cables are assembled by formins, conserved proteins that are located at the bud tip or bud neck and associate with the plus ends of actin filaments. Thus, polarized actin cables initially extend from the growing bud deep into the mother cell. When the bud grows larger formins are relocated from the bud tip to the bud neck and assemble cables that emanate from the bud neck and extend into the mother and daughter .

Immediately after bud emergence mitochondria enter the bud to ensure inheritance of the organelle . Mounting evidence suggests that bud-directed mitochondrial movement along actin cables is driven by myosin motor proteins.

Chloroplast mutation in clamydomonas:

The single chloroplast of the alga *Chlamydomonas reinhardtii* contains at least 100 copies of the chloroplast chromosome. It is not known how the chloroplast (or cell) becomes homoplasmic for a mutation that arises in one of these copies. Under suitable selection conditions, clones with chloroplast mutations for streptomycin resistance induced by methyl methanesulfonate can be recovered with direct plating after mutagenesis. Using an adaptation of the LURIA-DELBRÜCK fluctuation test, mutagenized cultures grown on nonselective liquid medium for seven to nine doublings show negligible proliferation of cells capable of forming such mutant colonies. In contrast, cells among the same cultures with reduced

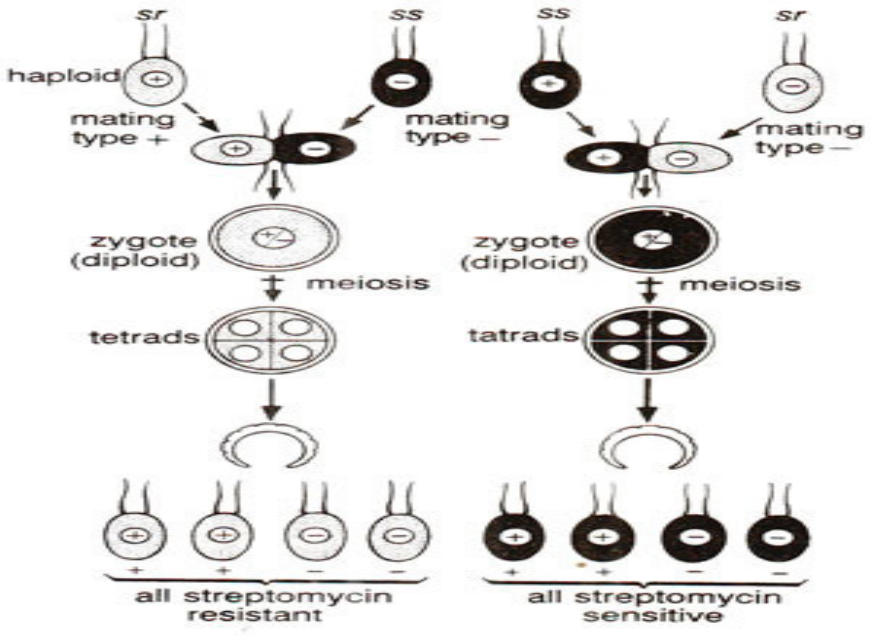
nuclear mutations conferring streptomycin resistance reveal considerable clonal propagation prior to plating on selection medium. Reconstruction growth-rate experiments show no reduced growth of cells with chloroplast mutations relative to either wild-type cells or to those with nuclear mutations.

All eukaryotic cells so far examined have multiple copies of their chloroplast A and/or mitochondrial chromosomes. Despite this fact, cell lines homoplasmic for a chloroplast or mitochondrial mutation can appear among the mitotic descendants of at least some cells that initially contained single mutations in only one of these copies. An important step toward understanding how homoplasmic lines originate is to establish the pattern(s) by which an induced mutant allele is transmitted to daughter cells during vegetative division. If there is good reason to believe that the mutant allele, or the cells containing it, are not at a significant replicative disadvantage under the conditions of growth employed, we can ask if this allele initially segregates in a random or nonrandom fashion. With random segregation, copies of the mutant allele would sometimes go to the same daughter cell and sometimes to both daughter cells; with nonrandom segregation, one or the other pattern would prevail for the first several divisiom following induction of the mutation. The haploid unicellular alga Chlamydomonas reinhardtii is well suited for investigating the induction and vegetative transmisson of chloroplast mutations. It possesses only a single chloroplast, so that complications associated with multiple organelles can be avoided. Also, non-Mendelian mutations for streptomycin resistance in this alga provide a convenient chloroplast genetic marker. All such mutations, so far mapped, are localized in one of four loci on a single nonMendelian linkage group , and there is substantial evidence that this linkage group resides in the chloroplast .

Chloroplast mutations for streptomycin resistance in this alga confer moderate to high-level resistance to streptomycin on solid medium and are thus phenotypically distinct from Mendelian (nuclear) streptomycin-resistant mutants, which confer only low-level resistance to this antibiotic. The correlation between high-level resistance (at least 500 pg/ml streptomycin sulfate) and inheritance pattern was originally described by SAGER (1954) and has since been confirmed with numerous streptomycin-resistant mutations that have either arisen spontaneously or were induced with the alkylating mutagens nitrosoguanidine (MNNG) or methyl methanesulfonate (MMS). In addition, certain chloroplast streptomycin-resistant mutants have been recovered after MNNG mutagenesis that are reported to be sensitive to high levels of antibiotic .

However, using screening conditions similar to those employed in this study, we have reexamined one of these mutants and routinely detect slight but positive growth on 500 pg/ml of antibiotic, whereas nuclear streptomycin-resistant mutants on the same plates always score as sensitive . In the present study, the mutations resistant to low and high levels of streptomycin are designated str-50 and str-500, respectively. Chloroplast mutants for streptomycin resistance induced with MNNG or MMS can be recovered on low levels of streptomycin (50 to 100 pg/ml) with plating directly after mutagenesis,

but these mutants cannot normally be recovered on the concentration of streptomycin (500 pg/ml) to which they are ultimately resistant. The apparent linear relationship between MNNG dose and the recovery of both nuclear and chloroplast mutants on low levels of antibiotic suggests that one mutational event is sufficient for their detection under such selection conditions . In this study, the transmission of chloroplast (str-500) , and nuclear (str-50) -coded, streptomycin-resistant mutations during the first several cell divisions following their induction with MMS. Mutagenesis was performed on wild-type haploid cells harvested from cultures synchronized by growth under alternating 12-hr light, 12-hr dark periods. At the cell-cycle stage employed (near the onset of light), cells had just completed division and contain about 100 copies of the chloroplast chromosome per cell. This estimate is based on the average cellular content of chloroplast DNA in such cells being about 2.2 X 10-14g and on the molecular weight of individual chloroplast DNA molecules being about 1.3 x lo8 daltons. The transmission of chloroplast and nuclear mutations during vegetative cell division was followed by an adaptation of the classical fluctuation test . Starting cell concentrations and culture numbers were employed to insure that several cultures received one cell with an induced chloroplast or nuclear streptomycin-resistance mutation, but that no cultures were likely to receive more than one. The results show little evidence for the proliferation of cells, preceding action of the antibiotic, that are capable of forming chloroplast mutant colonies on low-level streptomycin agar medium. In contrast, within many of the same culture tubes, there was a marked proliferation of cells capable of forming nuclear mutant colonies.



[G-) FIGURE 1 : Proposed segregation of chloroplast mutations during vegetative cell division of C. reinhardtii. Wild-type chromosomes are represented by white circles and mutant chromosomes by black circles. The single chloroplast of C. reinhardtii has 60 to 100 chromosomes, SO that 6 to 7 divisions would be required before the segregation of a cell homoplasmic for a chloroplast mutation. 1954; RYAN, FRIED and SCHWARTZ 1954). With such a model, segregation of the mutant allele to more than one daughter cell would usually be delayed until cells become homoplasmic, or nearly so, for this mutation. If all mutant and wild-type alleles replicate once with each chloroplast (or cell) doubling and if the partition of chloroplast chromosomes is numerically equal, then the length of this delay in cell doublings (N) would be related to the average number of chromosomes per chloroplast

Snail shell coiling and maternal effects:

The embryo is formed when a female gamete unites with a male gamete. In the vast majority of species, the female gamete is physically larger than the male gamete and provides the cytoplasm for the developing embryo. Within this cytoplasm are factors that were released by the nuclear genes of the female. Those factors may have specific effects upon the developing embryo. The female cytoplasm also contributes the mitochondria for all species as well as the chloroplast for plant species. These two organelles contain DNA and control certain traits in the offspring. Those phenotypes that are controlled by nuclear factors found in the cytoplasm of the female are said to express a maternal effect. Those phenotypes controlled by organelle genes exhibit maternal inheritance.

The classic phenotype which exhibits maternal effects is coiling direction of snail shells. The coiling phenotype that is seen in the offspring is controlled by the genotype of the mother. The following crosses were made between pure line snails, and the following results were seen. By convention, the female is always given first.

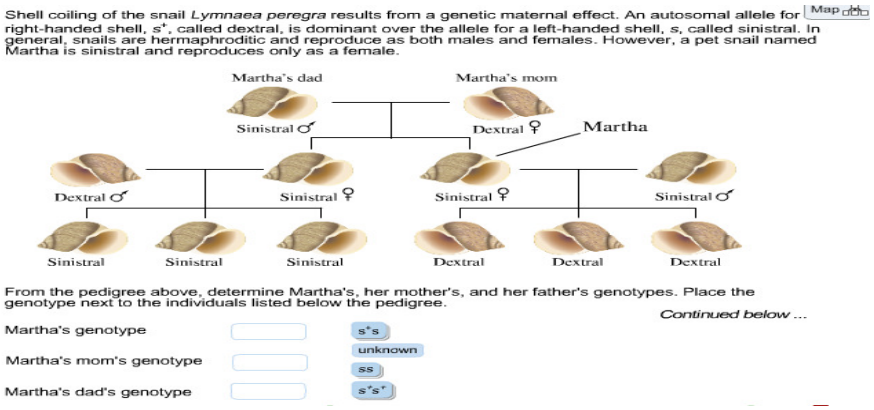
	Cross 1	Cross 2
Parents	Right coil x Left coil	Left coil x Right coil
F1	All right coil	All left coil
F2	All right coil	All right coil
F3	3 right coil : 1 left coil	3 right coil : 1 left coil

These results at first glance appear to be at odds with Mendel's laws. First, the F1 phenotype is not the same for both crosses. With other experiments, the results of reciprocal crosses (complementary crosses were the phenotypes of female and male are reversed in the initial parental cross) were equivalent, but with this experiment it appears that the female controls the phenotype. Yet, the F2 appears to contradict this hypothesis because the left- and right-coiled F1 individuals produced all right progeny. Furthermore, the 3:1 Mendelian ratio is not seen in the F2, but rather appears in the F3 generation.

How can this result be explained? First, let's look for results that are familar. The F3 ratio of 3 right:1 left for both crosses suggests that right-coiled shells are dominant to left-coiled shells. If this is the case, then we can assign the following genotypes to the pure lines:

- Right-coiled shell: *s+s+*
- Left-coiled shell: *ss*

The next observation is that the phenotype of the F1 generation is always that of the female parent. One hypothesis would suggest that the genotype of the female controls the genotype of its offspring. Can these result be confirmed in the subsequent generations? If the genotypes we assigned to the parents are correct, then the genotype of F1 individuals from each cross are s+s (from s+s+ x ss and ss x s+s+). If the female genotype does control the phenotype of its offspring, then we would predict that all the F2 snails would have right coils. This is the exact result that is seen. But what would the genotypes of the F2 snails be? If we intermate snails with the genotype s+s the genotypic ratio should be 3 *s+_* to 1 ss. These genotypes would not be expressed as a phenotype until the F3 generation. These are the results that were obtained. A general conclusion from all traits that express a maternal effect is that the normal Mendelian ratios are expressed one generation than expected.



Kappa Particles in Paramecium:

One of the most striking and spectacular cases of cytoplasmic inheritance occurs in paramecium aurelia. In 1938, T.M. Sonneborn reported that some strains contain kappa particles in the cytoplasm and are known as "Killers ". Kappa particles are about 2 μ x in diameter and contain DNA and protein.
Individuals not possessing Kappa particles are sensitive and are killed by a poison 'paramecin' which is secreted by Killer individuals. The secretion paramecin is harmless to the killers. The different killer strains have different means of killing their victims.

Most of them do not kill their mates. But there are some strains that instead of killing from a distance by secretion, kill their mates through close contact. The killer character has a nuclear as well as cytoplasmic basis.

The existence and increase of Kappa particles is determined by the presence of a nuclear dominant gene K. The animals that are homozygous for recessive 'k' are sensitive to killing and they cannot themselves become killers. Animals that are homozygous for dominant K or heterozygous in normal cytoplasm are potential killers.

They are actual killers when their cytoplasms contain kappa particles which in turn produce the lethal poison. In animals of genotype KK or Kk, kappa particles are transmitted from cell to cell; once they have been lost from a cell, they do not again develop by themselves.

The individuals with genotype kk may also contain Kappa particles of some sort in the cytoplasm, although this state is unstable and eventually the particles disappear.

Paramecium generally reproduces by conjugation method, a system of parasexual reproduction (Fig. 18.6) and autogamy (Fig. 18.6). When a killer strain of paramecium aurelia with genotype KK conjugates with sensitive strain having genotype kk, the ex-conjugants are all heterozygous (Kk).

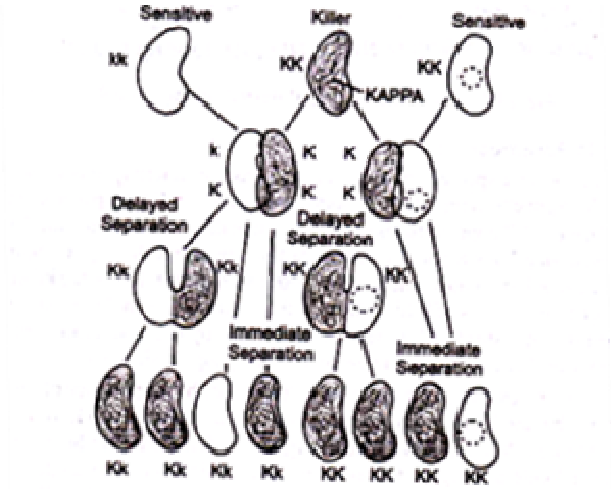


Fig. 18.6 Inheritance of Kappa particle in *Paramecium*.

The genotype Kk of hetrozygous ex-conjugants suggests that they should be identical and killers. But, this is not always the case and Kk hetrozygotes are equally divided into killers and sensitive (Fig. 18.6). If the conjugation is accomplished in a short duration normally no exchange of cytoplasm takes place between the killers and sensitive individuals.

When autogamy takes place in hetrozygotes 8 nuclei are formed after meiosis and mitosis divisions and then 7 of the 8 haploid nuclei degenerate and the remaining nucleus undergoes mitosis and the two identical nuclei so formed fuse to form a homozygous diploid. Thus all the sensitive hetrozygotes produce only sensitive offspring and the killer hetrozygotes produce only killer offspring.

Since a heterozygote Kk after autogamy does not produce sensitive and killer types, this pattern of inheritance is Non-Mendelian which confirms cytoplasmic basis of killer trait. The inheritance of Kappa was at first considered a good example of cytoplasmic inheritance.

These particles are not true cell organelles like the plastids or mitochondria. Closer studies, however, have shown that kappa particles are infectious and resemble bacterium caedobacter taeniospiralis.

Their transmission in cytoplasm from cell to cell is, therefore, more correctly compared with the transmission of parasitic micro-organisms. The toxic substance produced by killer paramecia is diffusible

in liquid medium. This is evident from the fact that when the killers were allowed to remain in a fluid medium for a time and were then replaced by sensitive individuals, the latter were killed.

The toxic substance had no effect on the killer strain. The fact that kappa particles can be maintained only in the animals with gene K is no rigid argument against the interpretations. Individuals with genotype KK will be sensitive if there are no Kappa particles in the cytoplasm.

When such sensitive cells are placed in concentrated suspension of disintegrated killer animals, some of them acquire kappa from the suspension and are changed to killers. Kappa is subject to mutation and if killer Paramecia is exposed to high temperature.

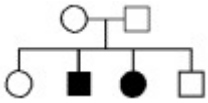
Pedigre Analysis:

Pedigree Analysis is a tabular representation of a family history by taking a particular disease or character into consideration.

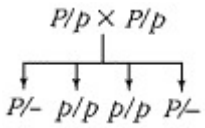
In humans, controlled crosses cannot be made, so geneticists must resort to scrutinizing family records in the hope that informative matings have been made that can be used to deduce dominance and distinguish autosomal from X-linked inheritance. The investigator traces the history of some variant phenotype back through the history of the family and draws up a family tree, or pedigree. The clues in the pedigree have to be interpreted differently depending on whether one of the contrasting phenotypes is a rare disorder or whether both phenotypes of a pair are common morphs of a polymorphism. The genetic disorders of human beings can be dominant or recessive phenotypes and can be either autosomal or X-linked

Autosomal Recessive Disorders

The unusual phenotype of a recessive disorder is determined by homozygosity for a recessive allele, and the unaffected phenotype is determined by the corresponding dominant allele. In Chapter 3 we saw that phenylketonuria (PKU) is a recessive phenotype. PKU is determined by an allele that we can call *p*, and the normal condition by *P*. Therefore, sufferers of this disease are of genotype *p/p*, and unaffected people are either *P/P* or *P/p*. What patterns in a pedigree would reveal such an inheritance? Two key points are that generally the disease appears in the progeny of unaffected parents and that the affected progeny include both males and females equally. When we know that both male and female phenotypic proportions are equal, we can assume that we are dealing with autosomal inheritance, not X-linked inheritance. The following typical pedigree illustrates the key point that affected children are born to unaffected parents:



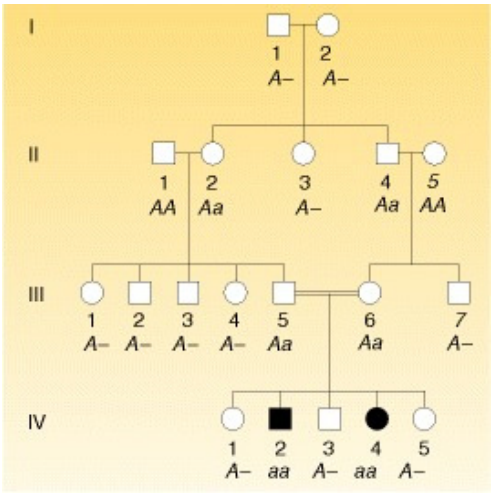
From this pattern we can immediately deduce autosomal inheritance, with the recessive allele responsible for the exceptional phenotype (indicated by shading). Furthermore, we can deduce that the parents must both be heterozygotes, *P/p*. (Both must have a *p* allele because each contributed one to each affected child, and both must have a *P* allele because the people are phenotypically normal.) We can identify the genotypes of the children (in the order shown) as *P/–*, *p/p*, *p/p*, and *P/–*. Hence, the pedigree can be rewritten



Notice another interesting feature of pedigree analysis: even though Mendelian rules are at work, Mendelian ratios are rarely observed in single families because the sample sizes are too small. In the above example, we see a 1:1 phenotypic ratio in the progeny of what is clearly a monohybrid cross, in which we might expect a 3:1 ratio. If the couple were to have, say, 20 children, the ratio would undoubtedly be something like 15 unaffected children and 5 with PKU (the expected monohybrid 3:1 ratio), but in a sample of four any ratio is possible and all ratios are commonly found.

In the case of a rare recessive allele, in the population most of these alleles will be found in heterozygotes, not in homozygotes. The reason is a matter of probability: to conceive a recessive homozygote, both parents must have had the *p* allele, but to conceive a heterozygote all that is necessary is one parent with the allele. The formation of an affected individual usually depends on the chance union of unrelated heterozygotes, and for this reason the pedigrees of autosomal recessives look rather bare, generally with only siblings of one cross affected.

Inbreeding (mating between relatives) increases the chance that a mating will be between two heterozygotes. An example of a cousin marriage is shown in Figure 4-18. Individuals III-5 and III-6 are first cousins and produce two children. You can see from the figure that an ancestor who is a heterozygote may produce many descendants who are also heterozygotes. Matings between relatives thus run a higher risk of producing abnormal homozygous recessives than do matings between nonrelatives. It is for this reason that first cousin marriages are responsible for a large portion of recessive diseases in human populations.



Pedigree of a rare recessive phenotype determined by a recessive allele*a*. Gene symbols normally are not included in pedigree charts, but genotypes are inserted here for reference. Note that individuals II-1 andII-5 marry into the family; they are assumed to be normal because the heritable condition under scrutiny is rare. Note also that it is not possible to be certain of the genotype in some individuals with normal phenotype; such individuals are indicated by A–

Albinism is another rare condition that is inherited in a Mendelian manner as an autosomal recessive phenotype in many animals, including humans. The striking "white" phenotype is caused by a defect in an enzyme that synthesizes melanin, the pigment responsible for most black and brown coloration of animals. In humans, such coloration is most evident in hair, skin, and retina, and its absence in albinos (who have the homozygous recessive genotype *a/a*) leads to white hair, white skin, and eye pupils that are pink because of the unmasking of the red hemoglobin pigment in blood vessels in the retina.

In pedigree analysis, the main clues for identifying an autosomal dominant disorder are that the phenotype tends to appear in every generation of the pedigree and that affected fathers and mothers transmit the phenotype to both sons and daughters. Again, the representation of both sexes among the affected offspring argues against X-linked inheritance. The phenotype appears in every generation because generally the abnormal allele carried by an individual must have come from a parent in the previous generation. (Abnormal alleles can arise de novo by mutation. This is relatively rare, but must be kept in mind as a possibility.) A typical pedigree for a dominant disorder . Once again, notice that Mendelian ratios are not necessarily observed in families. As with recessive disorders, individuals bearing one copy of the rare allele (*A/a*) are much more common than those bearing two copies (*A/A*), so most affected people are heterozygotes, and virtually all matings involving dominant disorders are *A/a* × *a/a*. Therefore, when the progeny of such matings are totaled, a 1:1 ratio is expected of unaffected (*a/a*) to affected individuals (*A/a*).

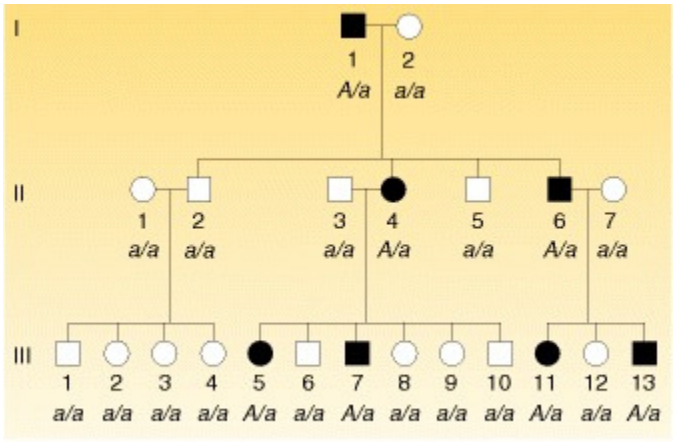


Figure 4-19

Pedigree of a dominant phenotype determined by a dominant allele *A*. In this pedigree, all the genotypes have been deduced.

Huntington's disease is an example of an autosomal dominant disorder. The phenotype is one of neural degeneration, leading to convulsions and premature death. However, it is a late-onset disease, the symptoms generally not appearing until after the person has begun to have children. Each child of a carrier of the abnormal allele stands a 50 percent chance of inheriting the allele and the associated disease. This tragic pattern has led to a drive to find ways of identifying people who carry the abnormal allele before they experience the onset of the disease. The discovery of the molecular nature of the mutant allele, and of neutral DNA mutations that act as "markers" close to the affected allele on the chromosome, has revolutionized this sort of diagnosis.

MESSAGE

Pedigrees of autosomal dominant disorders show affected males and females in each generation and also show affected men and women transmitting the condition to equal proportions of their sons and daughters.

LOD score for Linkage testing:

The LOD score (logarithm (base 10) of odds), developed by Newton Morton, is a statistical test often used for linkage analysis in human, animal, and plant populations. The LOD score compares the likelihood of obtaining the test data if the two loci are indeed linked, to the likelihood of observing the same data purely by chance. Positive LOD scores favour the presence of linkage, whereas negative LOD scores indicate that linkage is less likely. Computerised LOD score analysis is a simple way to analyse complex family pedigrees in order to determine the linkage between Mendelian traits (or between a trait and a marker, or two markers).

The method is described in greater detail by Strachan and Read. Briefly, it works as follows:

1. Establish a pedigree
2. Make a number of estimates of recombination frequency
3. Calculate a LOD score for each estimate
4. The estimate with the highest LOD score will be considered the best estimate

The LOD score is calculated as follows:

LOD=Z=$\log_{10}$ Probability of birth sequence with a given lnkage value=$\log_{10}$ $(1-\theta)^{NR}\times\theta^{R}$

Probability of birth sequence with no linkage $(0.5^{(NR+R)})$

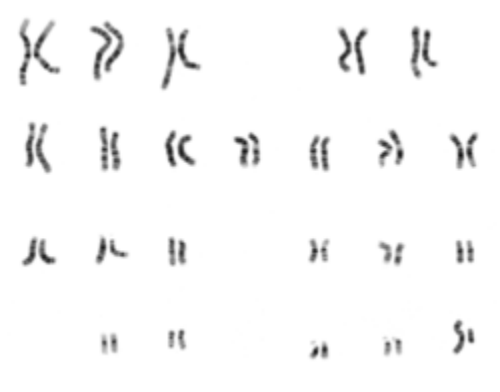
NR denotes the number of non-recombinant offspring, and R denotes the number of recombinant offspring. The reason 0.5 is used in the denominator is that any alleles that are completely unlinked (e.g. alleles on separate chromosomes) have a 50% chance of recombination, due to independent assortment. 'θ' is the recombinant fraction, i.e. the fraction of births in which recombination has happened between the studied genetic marker and the putative gene associated with the disease. Thus, it is equal to R / (NR + R)

By convention, a LOD score greater than 3.0 is considered evidence for linkage, as it indicates 1000 to 1 odds that the linkage being observed did not occur by chance. On the other hand, a LOD score less than -2.0 is considered evidence to exclude linkage. Although it is very unlikely that a LOD score of 3 would be obtained from a single pedigree, the mathematical properties of the test allow data from a number of pedigrees to be combined by summing their LOD scores. A LOD score of 3 translates to a *p*-value of approximately 0.05,[9] and no multiple testing correction (e.g. Bonferroni correction) is required.

Karyotype

Karyotyping is the process by which cytogeneticists take photographs of chromosomes in order to determine the chromosome complement of an individual, including the number of chromosomes and any abnormalies. The term is also used for the complete set of chromosomes in a species or in an individual organism and for a test that detects this complement or measures the number.

Karyotypes describe the chromosome count of an organism and what these chromosomes look like under a light microscope. Attention is paid to their length, the position of the centromeres, banding pattern, any differences between the sex chromosomes, and any other physical characteristics. The preparation and study of karyotypes is part of cytogenetics.



Karyogram of human male using Giemsa staining

The study of whole sets of chromosomes is sometimes known as *karyology*. The chromosomes are depicted (by rearranging a photomicrograph) in a standard format known as a *karyogram* or *idiogram*: in pairs, ordered by size and position of centromere for chromosomes of the same size.

The basic number of chromosomes in the somatic cells of an individual or a species is called the *somatic number* and is designated *2n*. In the germ-line (the sex cells) the chromosome number is *n* (humans: n = 23). Thus, in humans 2n = 46.

So, in normal diploid organisms, autosomal chromosomes are present in two copies. There may, or may not, be sex chromosomes. Polyploid cells have multiple copies of chromosomes and haploid cells have single copies.

The study of karyotypes is important for cell biology and genetics, and the results may be used in evolutionary biology (*karyosystematics*) and medicine. Karyotypes can be used for many purposes; such as to study chromosomal aberrations, cellular function, taxonomic relationships, and to gather information about past evolutionary events.

Observations On Karyotypes

Staining

The study of karyotypes is made possible by staining. Usually, a suitable dye, such as Giemsa,[19] is applied after cells have been arrested during cell division by a solution of colchicine usually in metaphase or prometaphase when most condensed. In order for the Giemsa stain to adhere correctly, all chromosomal proteins must be digested and removed. For humans, white blood cells are used most frequently because they are easily induced to divide and grow in tissue culture. Sometimes observations may be made on non-dividing (interphase) cells. The sex of an unborn fetus can be determined by observation of interphase cells (see amniotic centesis and Barr body).

Observations

Six different characteristics of karyotypes are usually observed and compared:

1. Differences in absolute sizes of chromosomes. Chromosomes can vary in absolute size by as much as twenty-fold between genera of the same family. For example, the legumes *Lotus tenuis* and *Vicia faba* each have six pairs of chromosomes, yet *V. faba* chromosomes are many times larger. These differences probably reflect different amounts of DNA duplication.
2. Differences in the position of centromeres. These differences probably came about through translocations.
3. Differences in relative size of chromosomes. These differences probably arose from segmental interchange of unequal lengths.
4. Differences in basic number of chromosomes. These differences could have resulted from successive unequal translocations which removed all the essential genetic material from a chromosome, permitting its loss without penalty to the organism (the dislocation hypothesis) or through fusion. Humans have one pair fewer chromosomes than the great apes. Human chromosome 2 appears to have resulted from the fusion of two ancestral chromosomes, and many of the genes of those two original chromosomes have been translocated to other chromosomes.
5. Differences in number and position of satellites. Satellites are small bodies attached to a chromosome by a thin thread.
6. Differences in degree and distribution of heterochromatic regions. Heterochromatin stains darker than euchromatin. Heterochromatin is packed tighter. Heterochromatin consists mainly of genetically inactive and repetitive DNA sequences as well as containing a larger amount of Adenine-Thymine pairs. Euchromatin is usually under active transcription and stains much lighter as it has less affinity for the giemsa stain Euchromatin regions contain larger amounts of Guanine-Cytosine pairs. The staining technique using giemsa staining is called G banding and therefore produces the typical "G-Bands".

A full account of a karyotype may therefore include the number, type, shape and banding of the chromosomes, as well as other cytogenetic information.

Variation is often found:

1. between the sexes,
2. between the germ-line and soma (between gametes and the rest of the body),
3. between members of a population (chromosome polymorphism),
4. in geographic specialization, and
5. in mosaics or otherwise abnormal individuals.

Human karyotype

human karyotype (male)

The normal human karyotypes contain 22 pairs of autosomal chromosomes and one pair of sex chromosomes (allosomes). Normal karyotypes for females contain two X chromosomes and are denoted 46,XX; males have both an X and a Y chromosome denoted 46,XY. Any variation from the standard karyotype may lead to developmental abnormalities.

Autosomal dominant

Only one mutated copy of the gene will be necessary for a person to be affected by an autosomal dominant disorder. Each affected person usually has one affected parent. The chance a child will inherit the mutated gene is 50%. Autosomal dominant conditions sometimes have reduced penetrance, which means although only one mutated copy is needed, not all individuals who inherit that mutation go on to develop the disease. Examples of this type of disorder are Huntington's disease, neurofibromatosis type 1, neurofibromatosis type 2, Marfan syndrome, hereditary nonpolyposis colorectal cancer, hereditary multiple exostoses (a highly penetrant autosomal dominant disorder), Tuberous sclerosis, Von Willebrand disease, and acute intermittent porphyria. Birth defects are also called congenital anomalies.

Diversity and evolution of Karyotypes

Although the replication and transcription of DNA is highly standardized in eukaryotes, the same cannot be said for their karyotypes, which are highly variable. There is variation between species in chromosome number, and in detailed organization, despite their construction from the same macromolecules. This variation provides the basis for a range of studies in evolutionary cytology.In some cases there is even significant variation within species.

Genetic disorder

A genetic disorder is a genetic problem caused by one or more abnormalities formed in the genome. Most genetic disorders are quite rare and affect one person in every several thousands or millions. The earliest known genetic condition in a hominid was in the fossil species *Paranthropus robustus,* with over a third of individuals displaying Amelogenesis imperfecta.

Genetic disorders may be hereditary or non-hereditary, meaning that they are passed down from the parents' genes. However, in some genetic disorders, defects may be caused by new mutations or changes to the DNA. In such cases, the defect will only be passed down if it occurs in the germline. Genetic disorders can be monogenic, multifactoral, or chromosomal.

Single-Gene

A single-gene (or monogenic) disorder is the result of a single mutated gene. Over 6000 human diseases are caused by single-gene defects.[9] Single-gene disorders can be passed on to subsequent generations in

several ways. Genomic imprinting and uniparental disomy, however, may affect inheritance patterns. The divisions between recessive and dominant types are not "hard and fast", although the divisions between autosomal and X-linked types are (since the latter types are distinguished purely based on the chromosomal location of the gene). For example, achondroplasia is typically considered as a dominant disorder, but children with two genes for achondroplasia have a severe skeletal disorder of which achondroplasics could be viewed as carriers. Sickle-cell anemia is also considered as a recessive condition, but heterozygous carriers have increased resistance to malaria in early childhood, which could be described as a related dominant condition.

Autosomal recessive

Two copies of the gene must be mutated for a person to be affected by an autosomal recessive disorder. An affected person usually has unaffected parents who each carry a single copy of the mutated gene and are referred to as "carriers". Each parent with a defective gene normally do not have symptoms. Two unaffected people who each carry one copy of the mutated gene have a 25% risk with each pregnancy of having a child affected by the disorder. Examples of this type of disorder are Albinism, Medium-chain acyl-CoA dehydrogenase deficiency, cystic fibrosis, sickle-cell disease, Tay–Sachs disease, Niemann-Pick disease, spinal muscular atrophy, and Roberts syndrome. Certain other phenotypes, such as wet versus dry earwax, are also determined in an autosomal recessive fashion.

X-linked dominant

X-linked dominant disorders are caused by mutations in genes on the X chromosome. Only a few disorders have this inheritance pattern, with a prime example being X-linked hypophosphatemic rickets. Males and females are both affected in these disorders, with males typically being more severely affected than females. Some X-linked dominant conditions, such as Rett syndrome, incontinentia pigmenti type 2, and Aicardi syndrome, are usually fatal in males either *in utero* or shortly after birth, and are therefore predominantly seen in females. Exceptions to this finding are extremely rare cases in which boys with Klinefelter syndrome (47,XXY) also inherit an X-linked dominant condition and exhibit symptoms more similar to those of a female in terms of disease severity. The chance of passing on an X-linked dominant disorder differs between men and women. The sons of a man with an X-linked dominant disorder will all be unaffected (since they receive their father's Y chromosome), and his daughters will all inherit the condition. A woman with an X-linked dominant disorder has a 50% chance of having an affected fetus with each pregnancy, although in cases such as incontinentia pigmenti, only female offspring are generally viable.

X-linked recessive

X-linked recessive conditions are also caused by mutations in genes on the X chromosome. Males are more frequently affected than females, and the chance of passing on the disorder differs between men and women. The sons of a man with an X-linked recessive disorder will not be affected, and his daughters will carry one copy of the mutated gene. A woman who is a carrier of an X-linked recessive disorder (X^RX^r)

has a 50% chance of having sons who are affected and a 50% chance of having daughters who carry one copy of the mutated gene and are therefore carriers. X-linked recessive conditions include the serious diseases hemophilia A, Duchenne muscular dystrophy, and Lesch-Nyhan syndrome, as well as common and less serious conditions such as male pattern baldness and red-green color blindness. X-linked recessive conditions can sometimes manifest in females due to skewed X-inactivation or monosomy X (Turner syndrome).

Mutifactorial Disorder:

Genetic disorders may also be complex, multifactorial, or polygenic, meaning they are likely associated with the effects of multiple genes in combination with lifestyles and environmental factors. Multifactorial disorders include heart disease and diabetes. Although complex disorders often cluster in families, they do not have a clear-cut pattern of inheritance. This makes it difficult to determine a person's risk of inheriting or passing on these disorders. Complex disorders are also difficult to study and treat, because the specific factors that cause most of these disorders have not yet been identified. Studies which aim to identify the cause of complex disorders can use several methodological approaches to determine genotype-phenotype associations. One method, the genotype-first approach, starts by identifying genetic variants within patients and then determining the associated clinical manifestations. This is opposed to the more traditional phenotype-first approach, and may identify causal factors that have previously been obscured by clinical heterogeneity, penetrance, and expressivity.

On a pedigree, polygenic diseases do tend to "run in families", but the inheritance does not fit simple patterns as with Mendelian diseases. But this does not mean that the genes cannot eventually be located and studied. There is also a strong environmental component to many of them (e.g., blood pressure).

Chromosomal Disorder:

A chromosomal disorder is a missing, extra, or irregular portional of chromosomal DNA. It can be from an atypical number of chromosome or a structural abnormality in one or more chromosome. An example of these disorder is Trisomy 21 (Down syndrome), in which there is an extra copy of chromosome 21.

Heritability and its measurements:

Amount of phenotypic (observable) variation in a population that is attributable to individual genetic differences. Heritability, in a general sense, is the ratio of variation due to differences between genotypes to the total phenotypic variation for a character or trait in a population. The concept typically is applied in behaviour genetics and quantitative genetics, where heritability estimates are calculated by using either correlation and regression methods or analysis of variance (ANOVA) methods.

Heritability is expressed as $H^2 = Vg/Vp$, where H is the heritability estimate, Vg the variation in genotype, and Vp the variation in phenotype. Heritability estimates range in value from 0 to 1. If $H = 1$, then all variation in a population is due to differences or variation between genotypes (i.e., there is no environmentally caused variation). If $H = 0$, there is no genetic variation; in this case all variation in the population comes from differences in the environments experienced by individuals.

Heritability is commonly used in twin studies in the field of behaviour genetics. The methodology is based on the fact that identical twins (monozygotic, or one-egg twins) share 100 percent of their genes in common and nonidentical, or fraternal, twins (dizygotic, or two-egg twins) are similar to other siblings (i.e., brothers and sisters) in that they share 50 percent of their genes in common. The correlation between identical twins is expected to be equal to 1.0 and that of fraternal twins to be 0.50. In the field of quantitative genetics, the concept of heritability is used to partition observable phenotypic variation between individuals into genetic and environmental components.

There are several drawbacks to the use of heritability estimates. First, heritability is not a measurement of how sensitive a character or trait might be to a change in environment. For example, a trait may have complete heritability ($H = 1$) yet be altered drastically by environmental change. This can be seen in certain genetic disorders of metabolism, such as phenylketonuria and Wilson disease, where heritability of phenotypic outcomes equals 1.0 but effective treatment is possible through dietary interventions. A second problem with heritability estimates is that they measure variation only within populations. In other words, a heritability estimate cannot be used to determine the causes of differences between populations, nor can it be used to determine the extent to which an individual's phenotype is determined by genes versus environment.

Quantitative Trait Locus

A quantitative trait locus (QTL) is a locus (section of DNA) which correlates with variation of a quantitative trait in the phenotype of a population of organisms.[1] QTLs are mapped by identifying which molecular markers (such as SNPs or AFLPs) correlate with an observed trait. This is often an early step in identifying and sequencing the actual genes that cause the trait variation.

For organisms whose genomes are known, one might now try to exclude genes in the identified region whose function is known with some certainty not to be connected with the trait in question. If the genome is not available, it may be an option to sequence the identified region and determine the putative functions of genes by their similarity to genes with known function, usually in other genomes. This can be done using BLAST, an online tool that allows users to enter a primary sequence and search for similar sequences within the BLAST database of genes from various organisms. It is often not the actual gene underlying the phenotypic trait, but rather a region of DNA that is closely linked with the gene.

Another interest of statistical geneticists using QTL mapping is to determine the complexity of the genetic architecture underlying a phenotypic trait. For example, they may be interested in knowing whether a phenotype is shaped by many independent loci, or by a few loci, and do those loci interact. This can provide information on how the phenotype may be evolving.

In a recent development, classical QTL analyses were combined with gene expression profiling i.e. by DNA microarrays. Such expression QTLs (eQTLs) describe cis- and trans-controlling elements for the expression of often disease-associated genes.[17] Observed epistatic effects have been found beneficial to identify the gene responsible by a cross-validation of genes within the interacting loci with metabolic pathway- and scientific literature databases.

Analysis of variance

The simplest method for QTL mapping is analysis of variance (ANOVA, sometimes called "marker regression") at the marker loci. In this method, in a backcross, one may calculate a t-statistic to compare the averages of the two marker genotype groups. For other types of crosses (such as the intercross), where there are more than two possible genotypes, one uses a more general form of ANOVA, which provides a so-called F-statistic. The ANOVA approach for QTL mapping has three important weaknesses. First, we do not receive separate estimates of QTL location and QTL effect. QTL location is indicated only by looking at which markers give the greatest differences between genotype group averages, and the apparent QTL effect at a marker will be smaller than the true QTL effect as a result of recombination between the marker and the QTL. Second, we must discard individuals whose genotypes are missing at the marker. Third, when the markers are widely spaced, the QTL may be quite far from all markers, and so the power for QTL detection will decrease.

Interval mapping

Lander and Botstein developed interval mapping, which overcomes the three disadvantages of analysis of variance at marker loci.[18] Interval mapping is currently the most popular approach for QTL mapping in experimental crosses. The method makes use of a genetic map of the typed markers, and, like analysis of variance, assumes the presence of a single QTL. In interval mapping, each locus is considered one at a time and the logarithm of the odds ratio (LOD score) is calculated for the model that the given locus is a true QTL. The odds ratio is related to the Pearson correlation coefficient between the phenotype and the marker genotype for each individual in the experimental cross

The term ‘interval mapping’ is used for estimating the position of a QTL within two markers (often indicated as ‘marker-bracket’). Interval mapping is originally based on the maximum likelihood but there are also very good approximations possible with simple regression.

The principle for QTL mapping is: 1) The Likelihood can be calculated for a given set of parameters (particularly QTL effect and QTL position) given the observed data on phenotypes and marker genotypes. 2) The estimates for the parameters are those where the likelihood are highest. 3) A significance threshold can be established by permutation testing.

Question:

Long answer question:

1. Explain Orgenelle heredity
2. Chloroplast mutation in *Chamydomonas*
3. Mitochondrial mutation in *saccharomyces*.
4. Explain Meternal effect with example.
5. Account on kappa particles in *Paramecium*.
6. Pedigree Analysis.

Short answer question:

1. What is Pedigree
2. LOD score for linkage
3. Karyotypes
4. Polygenic inheritance
5. Qlt mapping.

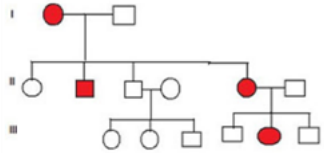
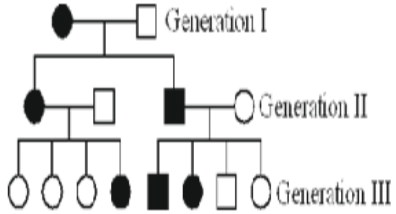
KARPAGAM ACADEMY OF HIGHER EDUCATION

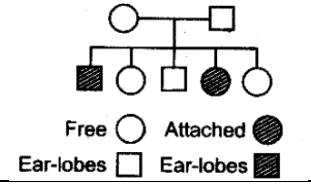
CLASS: III M. Sc MICROBIOLOGY **UNIT: 4** **COURSE NAME: INHERITANCE BIOLOGY**
COURSE CODE: 17MBU504B **BATCH-2017-2020**

Sno	Question	Opt 1	Opt 2	Opt 3	Opt 4	Answer
1	Chlamyodomonas genome is _____ rich	AT	GC	Only A	Only C	GC
2	Transformation of Chlamydomonas is most efficient in which method?	Lithium acetate method	Electroporation	Protoplast based method	Both electroporation and protoplast based method	Protoplast based method
3	OEE1 gene encodes a component of _____	photosystem I	photosystem II	both photosystem I and II	which neither belongs to photosystem I nor II	photosystem I
4	Homologue of yeast ARG4 in Chlamydomonas is _____	ARG1	ARG2	ARG5	ARG7	ARG7
5	cw15 is a mutant strain, it _____ and thus called as _____	lacks cell wall, natural protoplast	lacks cell wall, artificial protoplast	has cell wall, artificial protoplast	has cell wall, natural protoplast	lacks cell wall, natural protoplast
6	Damage and errors in DNA cause_____	Mutation	DNA repair	Translation	Transcription	Mutation
7	Mark the INCORRECT statement about mutation?	Mutation is predestined	Major source of evaluation	Usually deleterious and recessive	It is a reversible process	Mutation is predestined
8	Which of the following is NOT a type of reverse mutation?	Back mutation	Intergenic suppressor mutation	non-Intragenic suppressor mutation	Missense mutation	Missense mutation
9	Which of the following is NOT true for loss of function mutation?	Usually recessive	Most common mutation	Increases the activity of the gene	Null allelic mutation	Increases the activity of the gene
10	Name the term given to the type of mutation which depends on the conditions of the	Forward mutation	Reverse mutation	Conditional lethal mutation	Gain of function mutation	Conditional lethal mutation

	environment?					
11	the type of mutation in which the cause of mutation is not known?	Spontaneous mutation	Suppressor mutation	Nonsense mutation	Mis-sense mutation	Spontaneous mutation
12	Addition or deletion of bases causes which kind of mutation?	Transversion	Frameshift mutation	Transition	Transcription	Frameshift mutation
13	Which of the following chemical mutagen affects only replicating DNA?	Acridine dye	Alkylating agent	Deaminating agent	Base analog	Base analog
14	If the mitochondira were bloked at the site of NADH oxidation and were treated with succinate as substrate, what would the P: O ratio is?	Zero	One less the normally produced by succinate	same as that normally produced by succinate	One more than normally produced by succinate	same as that normally produced by succinate
15	If the oxidative phosphorylation was uncoupled in the mitochondria, what would one exprect?	A decreased concentration of ADP in the mitochondria	Increased inorganic phosphate in the mitochondria	A decreased oxidative rate	A decreased production of heat	Increased inorganic phosphate in the mitochondria
16	The prosthetic froup of NADH dehydrogenase	FMN	NADH	FAD	NADPH	FMN
17	How many human mitochondrial proteins are encoded in the mitochondrial genome and synthesized within mitochondria?	11	12	13	14	13
18	How many mitochondrial proteins are encoded in nuclear genes and imported into mitochondria after their synthesis?	600	700	800	900	900
19	Mitochondrial DNA is a	Simple, single stranded linear DNA molecule	Simple, single stranded circular DNA molecule	Simple, double stranded linear DNA molecule	Simple, double stranded circular DNA molecule	Simple, double stranded circular DNA molecule
20	Oxysomes or F0 – F1 particles occur on	Inner mitochondrial	Chloroplast surface	Mitochondrial surface	Thylakoids	Inner mitochondrial

		membrane				membrane
21	ore than what proportion of mitochondrial proteins are coded by nuclear DNA?	95%	50%	10%	40%	95%
22	The size of human mitochondrial DNA is	16kb	200kb	2500kb	100kb	16kb
23	The size of plant mitochondrial DNA is	16kb	200-2500kb	100- 2550kb	100-2500kb	200-2500kb
24	Typically how many copies of DNA is/are there in each mitochondrion?	1	11	10	12	10
25	Mitochondrial DNA is one of the best marker tools for population biologists and evolutionary biologists because	Absence of genetic recombination in mt-DNA	Mitochondrial genes are specific to mt-DNA	It can be easily isolated	It undergoes spontaneous mutation	Absence of genetic recombination in mt-DNA
26	The mechanism of action of cyanide, a mitochondrial toxin, is by inhibiting	ATP synthase	Succinate dehydrogenase	Cytochrome c oxidase	NADH dehydrogenase	Cytochrome c oxidase
27	Which one of the following is true about C3 plants?	First stable product is phosphoglyceric acid	Photosynthetically more efficient	More efficient in CO2 fixation than C4 plants	None	First stable product is phosphoglyceric acid
28	Which of the following is the distinguishable feature of cyclic photophosphorylation?	Phosphorylation only takes place	Phosphorylation and photolysis take place	Photolysis of water is taking place	None	Phosphorylation only takes place
29	The light reaction of photosynthesis takes place in	Inner membrane of chloroplast	Outer membrane of chloroplast	Stroma	Matrix	Inner membrane of chloroplast
30	How many kinds of mutation are found in DNA which includes mutation of only one base?	1	2	3	4	2
31	What is the overall rate at which new mutations arise spontaneously	≈ 10-8 – 10-12	≈ 10-7 – 10-9	≈ 10-6 – 10-11	≈ 10-5 – 10-10	≈ 10-6 – 10-11

	at any given site on the chromosome per round of replication?					
32	What is the dinucleotide sequence of microsatellites?	CA	AT	CC	GC	CA
33	How many steps are required to attain mismatch repair?	1	3	2	4	2
34	The nicking of DNA is followed by the adherence of a helicase known as _____	Uvr D	Uvr A	Uvr B	Uvr C	Uvr D
35	Kappa particles indicate	nuclear inheritance	cytoplasmic inheritance	mutation	nucleo-cytoplasmic inheritance	cytoplasmic inheritance
36	Who discovered kappa particles in paramecium?	T. Sonneborn	A. William john	W. Albert Born	C. John	T. Sonneborn
37	 In the above pedigree, find out of the following four	Autosomal Dominant	Autosomal recessive	X-linked dominant	X-linked recessive	Autosomal Dominant
38	A pedigree is shown below for a disease that is autosomal dominant. The genetic made up of the first generation is 	AA, Aa	Aa, aa	Aa, AA Aa, Aa		Aa, aa

39	Given below is a pedigree chart of a family with five children. It shows the inheritance of attached earlobes as opposed to the free ones. Which one of the following conclusions drawn is correct? 	The parents are homozygous recessive	The trait is Y-linked	The parents are homozygous dominant	The parents are heterozygous	The parents are heterozygous
40	Which, if any, of the following statements is true?	The heritability of a disease can vary from one human population to another, but remains fairly constant within any individual population	The risk ratio in complex diseases is high compared to in monogenic disorders	In complex diseases the concordance in phenotype between monozygotic twins is higher than between dizygotic twins	Disorders in which genetic factors have a large role always have a significantly higher concordance in phenotype between monozygotic twins and between dizygotic twins than do disorders where genetic factors play a less significant role	In complex diseases the concordance in phenotype between monozygotic twins is higher than between dizygotic twins
41	With regard to affected sib pair (ASP) analysis which, if any, of the following statements is true.	ASP analysis is a type of parametric	It is highly convenient because samples	It is less suited to studying complex disease where the	A lod score of 3 is highly significant evidence for	It is less suited to studying complex disease where the

		linkage analysis that is popularly used to study complex diseases.	are required from the affected sibs only and samples from just 100 affected sib pairs are usually enough to obtain decent results.	relative risk of disease is low.	linkage in ASP analysis.	relative risk of disease is low
42	Regarding two-point linkage analysis, which, if any, of the following statements is true?	A lod score of 3 means that the likelihood of the data, given that the two loci are linked, is 1000 times greater than is the likelihood of the data, if the two loci are unlinked	A lod score of 3 is highly significant evidence for linkage	A lod score of -2 is highly significant evidence against linkage	A lod score of 3 is 100,000 times more convincing evidence of linkage than a lod score of -2	A lod score of 3 means that the likelihood of the data, given that the two loci are linked, is 1000 times greater than is the likelihood of the data, if the two loci are unlinked & A lod score of 3 is 100,000 times more convincing evidence of linkage than a lod score of -2
43	Which of the following is NOT a DNA marker?	RAPD	Hormone	RFLP	AFLP	Hormone
44	OD scores are used to predict __	Crossover frequency	gene sequence	Gene linkage	the number of chromosomes in a	Gene linkage

					genome	
45	Linkage _____ as the distance between two genes _____	Decreases, decreases	Unaffected, Decreases	Decreases, Increases	Increases, Increases	Decreases, Increases
46	Linkage results in _____	Formation of more Dominant phenotype	Formation of more Wild phenotype	Formation of more parental phenotype	Formation of more recombinant phenotype	Formation of more parental phenotype
47	If you suddenly observe linkage between two genes that are present in two chromosomes, this can be due to _____	Coupling	Translocation	Inversion	Non-homologous end joining	Translocation
48	Accurate mapping of genes can be done using _____	Two point mapping	Three point mapping	Single gene mapping	None of the mentioned	Three point mapping
49	What event during meiosis produces trisomies and monosomies?	independent assortment of chromosomes	allele segregationc	non disjunction	recombination	non disjunction
50	Which one of the following individuals will be expected to be phenotypically normal?	a woman with 45 chromosomes, including a Robertsonian translocation between chromosome 14 and 21	a man with 46 chromosomes, including a Robertsonian translocation between chromosome 14 and 21	a woman with the karyotype 47, XX, + 18	a man with a deletion of a band on chromosome 5	a woman with 45 chromosomes, including a Robertsonian translocation between chromosome 14 and 21
51	What would be the % reduction in fertility in an individual who is heterozygous for a reciprocal translocation?	25%	33%	50%	67%	67%
52	What is polyploidy?	a chromosome which has replicated many times, without	an extra set of chromosomes	a chromosomal inversion that includes the centromere	extra copies of a gene on a chromosome	an extra set of chromosomes

		mitosis occurring				
53	Which of the following cytogenetic techniques would be the most likely to identify a microdeletion?	G banding	R banding	Fluorescence in situ hybridization	inversion analysis	Fluorescence in situ hybridization
54	Which of the following processes is the most likely to lead to production of a mosaic?	nondisjunction during meiosis	nondisjunction during mitosis	interference during crossing over	polyspermy	nondisjunction during mitosis
55	In which of the following individuals will there be the most problems in producing viable gametes during meiosis?	an allotetraploid with 40 chromosomes	an allotetraploid with 20 chromosomes	an autotriploid with 30 chromosomes	an autotetraploid with 40 chromosomes	an autotriploid with 30 chromosomes
56	What is believed to be the main mechanism producing duplication of chromosome segments?	Robertsonian translocations	reciprocal translocations	unequal allele segregation	unequal crossing over	unequal crossing over
57	Which karyotype correctly describes an inverted duplication?	46, XY, inv(3) (q11q21)	46, XY, inv(3) (q21q11)	46, XY, dup(3) (q21q11)	46, XY, dup(3) (q11q21)	46, XY, dup(3) (q21q11)
58	A child expresses a rare autosomal recessive disease. Only one parent is a carrier. Which of the following best explains expression of this disease?	monosomy	uniparental disomy	trisomy	somatic mosaicism	trisomy
59	Name the mapping technique used to determine the position of restriction sites in a DNA molecule	Genetic map	Restriction mapping	Biochemical markers	DNA markers	Restriction mapping
60	Out of the following, which technique detect single nucleotide polymorphism?	RFLP	AFLP	SSLP	SNP	SNP

Unit V:
Sylabus

Structural organization of chromosomes-centromere, telomeres and repitive DNA, Packaging of DNA molecules into chromosomes, concept of Euchromatin and Hetrochromatin, Normal and abnormal karyotypes of human chromosomes, Chromosome banding, Giant chromosome, Polytene and Lampbrush chromosomes, Variations in chromosome structure: deletion, inversion, translocation, Variations in chromosome numbers and structural abnormalities: Klinefelter syndrome, Turner syndrome, Down syndrome.

Structural Organization of chromosomes:

Centromere, structure in a chromosome that holds together the two chromatids (the daughter strands of a replicated chromosome). The centromere is the point of attachment of the kinetochore, a structure to which the microtubules of the mitotic spindle become anchored. The spindle is the structure that pulls the chromatids to opposite ends of the cell during the cell division processes of mitosis and meiosis. Once separated, each chromatid becomes a chromosome. Thus, when the cell divides, both daughter cells have complete sets of chromosomes.

The **centromere** is the specialized DNA sequence of a chromosome that links a pair of sister chromatids (a dyad). During mitosis, spindle fibers attach to the centromere via the kinetochore. Centromeres were first thought to be genetic loci that direct the behavior of chromosomes.

The physical role of the centromere is to act as the site of assembly of the kinetochores – a highly complex multiprotein structure that is responsible for the actual events of chromosome segregation – i.e. binding microtubules and signalling to the cell cycle machinery when all chromosomes have adopted correct attachments to the spindle, so that it is safe for cell division to proceed to completion and for cells to enter anaphase.

There are, broadly speaking, two types of centromeres. "Point centromeres" bind to specific proteins that recognize particular DNA sequences with high efficiency. Any piece of DNA with the point centromere DNA sequence on it will typically form a centromere if present in the appropriate species. The best characterised point centromeres are those of the budding yeast, *Saccharomyces cerevisiae*. "Regional centromeres" is the term coined to describe most centromeres, which typically form on regions of preferred DNA sequence, but which can form on other DNA sequences as well. The signal for formation of a regional centromere appears to be epigenetic. Most organisms, ranging from the fission yeast *Schizosaccharomyces pombe* to humans, have regional centromeres.

Positions

Each chromosome has two arms, labeled *p* (the shorter of the two) and *q* (the longer). Many remember that the short arm 'p' is named for the French word "petit" meaning 'small', although this explanation was shown to be apocryphal. They can be connected in either metacentric, submetacentric, acrocentric or telocentric manner

Metacentric

These are X-shaped chromosomes, with the centromere in the middle so that the two arms of the chromosomes are almost equal.

A chromosome is metacentric if its two arms are roughly equal in length. In a normal human karyotype, five chromosomes are considered metacentric: chromosomes 1, 3, 16, 19, and 20. In some cases, a metacentric chromosome is formed by balanced translocation: the fusion of two acrocentric chromosomes to form one metacentric chromosome.

Submetacentric

If arms' lengths are unequal, the chromosome is said to be submetacentric. Their shape is L shape.[11]

Acrocentric

If the p (short) arm is so short that it is hard to observe, but still present, then the chromosome is acrocentric (the "acro-" in acrocentric refers to the Greek word for "peak"). The human genome includes five acrocentric chromosomes: 13, 14, 15, 21, 22.The Y chromosome is also acrocentric

In an acrocentric chromosome the p arm contains genetic material including repeated sequences such as nucleolar organizing regions, and can be translocated without significant harm, as in a balanced Robertsonian translocation. The domestic horse genome includes one metacentric chromosome that is homologous to two acrocentric chromosomes in the conspecific but undomesticated Przewalski's horse. This may reflect either fixation of a balanced Robertsonian translocation in domestic horses or, conversely, fixation of the fission of one metacentric chromosome into two acrocentric chromosomes in Przewalski's horses. A similar situation exists between the human and great ape genomes; in this case, because more species are extant, it is apparent that the evolutionary sequence is a reduction of two acrocentric chromosomes in the great apes to one metacentric chromosome in humans (see Karyotype#Aneuploidy).[11]

Strikingly, harmful translocations in disease context, especially unbalanced translocations in blood cancers, more frequently involve acrocentric chromosomes than non-acrocentric chromosomes. Although the cause is not known, this probably relates to the physical location of acrocentric chromosomes within the nucleus. Acrocentric chromosomes are usually located in and around the nucleolus, so in the center of the nucleus, where chromosomes tend to be less densely packed than chromosomes in the nuclear periphery.Consistently, chromosomal regions that are less densely packed are also more prone to chromosomal translocations in cancers.

Telocentric

A telocentric chromosome's centromere is located at the terminal end of the chromosome. A telocentric chromosome has therefore only one arm. Telomeres may extend from both ends of the chromosome, their shape is similar to letter "i" during anaphase. For example, the standard house mouse karyotype has only telocentric chromosomes. Humans do not possess telocentric chromosomes.

Subtelocentric

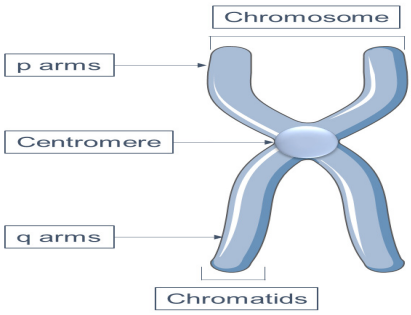
If the chromosome's centromere is located closer to its end than to its center, it may be described as subtelocentric.

Holocentric

With **holocentric** chromosomes, the entire length of the chromosome acts as the centromere. Examples of this type of centromere can be found scattered throughout the plant and animal kingdoms, with the most well-known example being the nematode *Caenorhabditis elegans*.

Acentric

If a chromosome lacks a centromere, it is said acentric. The macronucleus of ciliates for example contains hundreds of acentric chromosomes. Chromosome-breaking events can also generate acentric chromosomes or acentric fragments.

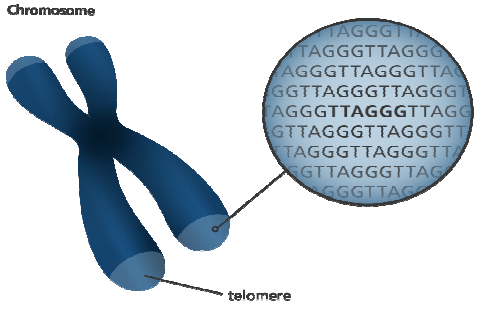


Telomeres

Thess are distinctive structures found at the ends of our chromosomes. They consist of the same short DNA sequence repeated over and over again.

- Telomeres are sections of DNA[?] found at the ends of each of our chromosomes[?].
- They consist of the same sequence of bases [?]repeated over and over.

- In humans the telomere sequence is TTAGGG.
- This sequence is usually repeated about 3,000 times and can reach up to 15,000 base pairs[?] in length.



Telomeres serve three major purposes:

- They help to organise each of our 46 chromosomes in the nucleus[?] (control centre) of our cells[?].
- They protect the ends of our chromosomes by forming a cap, much like the plastic tip on shoelaces. If the telomeres were not there, our chromosomes may end up sticking to other chromosomes.
- They allow the chromosome to be replicated properly during cell division[?]:
- Every time a cell[?] carries out DNA replication[?] the chromosomes are shortened by about 25-200 bases (A, C, G, or T) per replication.
- However, because the ends are protected by telomeres, the only part of the chromosome that is lost, is the telomere, and the DNA is left undamaged.

- Without telomeres, important DNA would be lost every time a cell divides (usually about 50 to 70 times).

- This would eventually lead to the loss of entire genes?.

What happens to telomeres as we age?

- Each time a cell divides, 25-200 bases are lost from the ends of the telomeres on each chromosome.
- Two main factors contribute to telomere shortening during cell division?:
    - The "end replication problem" during DNA replication: Accounts for the loss of about 20 base pairs? per cell division.
    - Oxidative stress: Accounts for the loss of between 50-100 base pairs per cell division. The amount of oxidative stress in the body is thought to be affected by lifestyle factors such as diet, smoking and stress.
- When the telomere becomes too short, the chromosome reaches a 'critical length' and can no longer be replicated.
- This 'critical length' triggers the cell to die by a process called apoptosis?, also known as programmed cell death.

How is telomere length maintained?

- Telomerase? is an enzyme? that adds the TTAGGG telomere sequence to the ends of chromosomes.
- Telomerase is only found in very low concentrations in our somatic cells?. Because these cells do not regularly use telomerase they age leading to a reduction in normal function.
- The result of ageing cells, is an ageing body.

- Telomerase is found in high levels in germline? cells (egg and sperm) and stem cells. In these cells telomere length is maintained after DNA replication and the cells do not show signs of ageing.
- Telomerase is also found in high levels in cancer? cells. This enables cancer cells to be immortal and continue replicating themselves. If telomerase activity was switched off in cancer cells, their telomeres would shorten until they reached a 'critical length'. This would, prevent the cancer cells from dividing uncontrollably to form tumours.
- The action of telomerase allows cells to keep multiplying and avoid ageing.

Use of telomeres in medicine

- Research on telomeres and the role of telomerase could uncover valuable information to combat ageing and fight cancer.
- The medical relevance of telomeres is uncertain.
- Human cells cultured in the lab have been observed to stop dividing when telomerase is inactivated, because the length of telomeres is not maintained after cell division.
- The cells then enter a state of inactivity called senescence. However, once telomerase is reactivated, the cells are able to continue dividing.
- If telomerase can be used to help human cells live forever, it may also be possible to mass produce cells for transplantation. These cells could help to treat a range of conditions, from severe burns to diabetes?.

Telomeres and ageing

- Mice models lacking the enzyme telomerase were found to show signs of premature ageing.
- However, it is not certain whether telomere shortening is responsible for ageing in humans or whether it is just a sign of ageing, like grey hair.
- There are several indications that telomere length is a good predictor of lifespan.

- Newborn babies tend to have telomeres ranging in length from around 8,000 to 13,000 base pairs. It has been observed that this number tends to decline by around 20-40 base pairs each year. So, by the time someone is 40 years old they could have lost up to 1,600 base pairs from their telomeres.
- However, looking at the bigger picture, the overall shortening of our telomeres is not significant, even in very old people.
- Cells that divide rapidly, such as germ cells? and stem cells?, are among the few cell types in our bodies containing active telomerase.
- This means that in these cells telomere length is maintained or even lengthened over time.
- However, there are a number of other factors that have an effect on the length of our telomeres that all need to be considered, such as smoking and obesity.

Telomeres and cancer

- Telomeres and telomerase present a number of potential targets for the design of new cancer therapies.
- Cancer cells contain active telomerase to enable them to become 'immortal' and continue dividing uncontrolled.
- Cancer is a disease characterised by the rapid and uncontrolled division of cells.
- Without telomerase activity, these cells would become inactive, stop dividing and eventually die.
- Drugs that inhibit telomerase activity, or kill telomerase-producing cells, may potentially stop and kill cancer cells in their tracks.
- However, blocking telomerase activity could affect cells where telomerase activity is important, such as sperm, eggs, platelets and immune cells.
- Disrupting telomerase in these cell types could affect fertility, wound healing and the ability to fight infections.
- However, telomerase activity in somatic cells is very low. These cells would therefore be largely unaffected by anti-telomerase therapy.

- Scientists hope this would result in fewer side effects for the patient, compared to current cancer therapies.
- Telomere biology is incredibly important in human cancer and scientists are working hard to understand the best way to exploit their knowledge of it to advance the treatment of cancer.

Repetitive DNA:

DNA sequences that are repeated in the genome. These sequences do not code for protein. One class termed highly repetitive DNA consists of short sequences, 5-100 nucleotides, repeated thousands of times in a single stretch and includes satellite DNA. Another class termed moderately repetitive DNA consists of longer sequences, about 150-300 nucleotides, dispersed evenly throughout the genome, and includes what are called Alu sequences and transposons.

Functions

Debates regarding the potential functions of these elements have been long standing. Controversial references to 'junk' or 'selfish' DNA were put forward early on, implying that repetitive DNA segments are remainders from past evolution or autonomous self-replicating sequences hacking the cell machinery to proliferate. Originally discovered by Barbara McClintock, dispersed repeats have been increasingly recognized as a potential source of genetic variation and regulation. Together with these regulatory roles, a structural role of repeated DNA in shaping the 3D folding of genomes has also been proposed.This hypothesis is only supported by a limited set of experimental evidence. For instance in human, mouse and fly, several classes of repetitive elements present a high tendency for co-localization within the nuclear space, suggesting that DNA repeats positions can be used by the cell as a genome folding map.

Tandem repeats in human disease

Tandem repeat sequences, particularly trinucleotide repeats, underlie several human disease conditions. Trinucleotide repeats may expand in the germline over successive generations leading to increasingly severe manifestations of the disease. The disease conditions in which expansion occurs include Huntington's disease, fragile X syndrome, several spinocerebellar ataxias, myotonic dystrophy and Friedrich ataxia. Trinucleotide repeat expansions may occur through strand slippage during DNA replication or during DNA repair synthesis.

major categories of **repeated sequence** or **repeats**:

Tandem repeats: copies which lie adjacent to each other, either directly or inverted

Satellite DNA - typically found in centromeres and heterochromatin

- Minisatellite - repeat units from about 10 to 60 base pairs, found in many places in the genome, including the centromeres
- Microsatellite - repeat units of less than 10 base pairs; this includes telomeres, which typically have 6 to 8 base pair repeat units
- Interspersed repeats (aka. interspersed nuclear elements)
- Transposable elements
- DNA transposons
- retrotransposons
- LTR-retrotransposons (HERVs)
- non LTR-retrotransposons
- SINEs (**S**hort **I**nterspersed **N**uclear **E**lements)
- LINEs (**L**ong **I**nterspersed **N**uclear **E**lements)

In primates, the majority of LINEs are LINE-1 and the majority of SINEs are Alu's. SVAs are hominoid specific.

In prokaryotes, CRISPR are arrays of alternating repeats and spacers.

DNA in Chromosomes

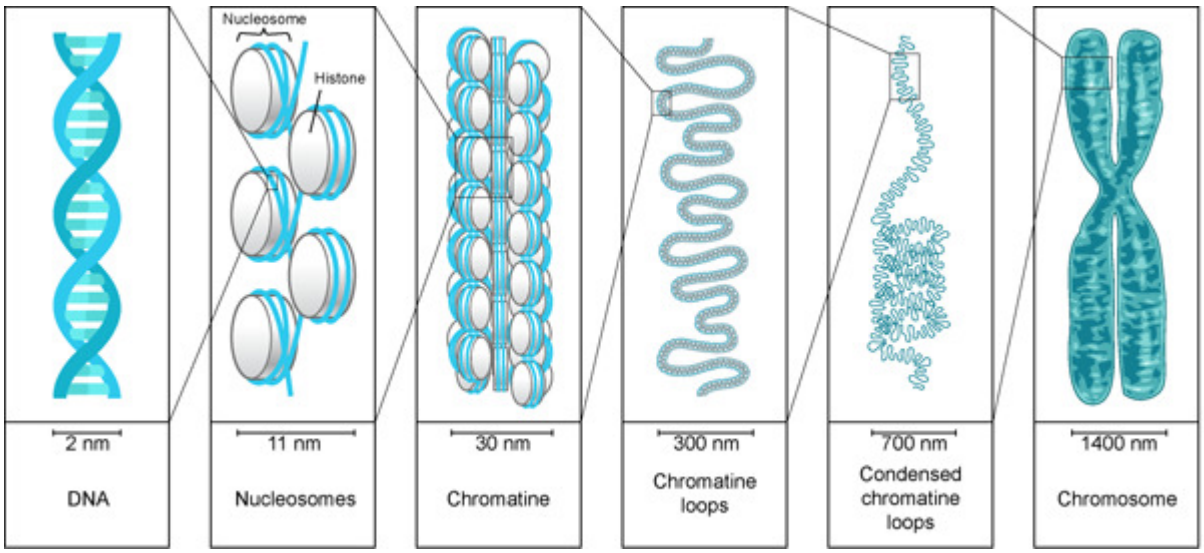
Chromosomes are made up of long pieces of double-stranded DNA twisted and condensed into a compact package. If left uncondensed, the strands of DNA would be about two meters each, far too long to fit inside your cells. A person's entire DNA is separated into 22 matched pairs of chromosomes, plus two sex chromosomes, for a total of 46. Along the length of the DNA, some of the regions code for proteins, while others do not. The protein-coding sections are your genes, so each chromosome is home to hundreds or thousands of genes.

Packaging Chromosomes

Specialized proteins bind to the DNA and help fold it properly so that it condenses into the tight configuration required to make chromosomes without getting tangled. The condensed DNA must also be configured so that enzymes can reach each part of it for repair, transcription, and translation. The basic DNA double helix is wound around histone proteins, and these DNA-protein complexes then fold into structures called nucleosomes. A strand of nucleosomes winds into a fiber called chromatin, which is about 30 nanometers in diameter and visible in an electron microscope. A chromosome is made up of tightly packed chromatin strands.

Packed Like Sardines

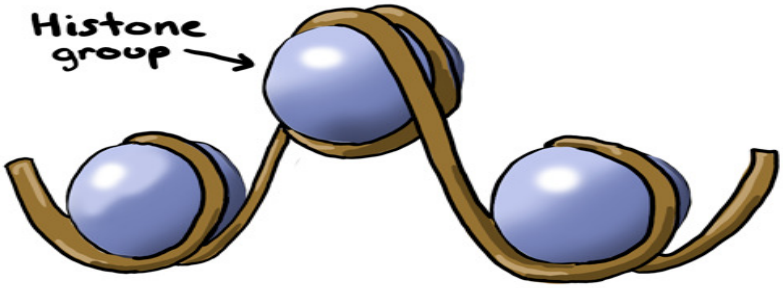
The double helix of DNA is highly negatively charged due to all the negatively charged phosphates in the backbone. All that negative charge must be counterbalanced by a positive charge, and the cell makes proteins called **histones** that bind DNA and aid in DNA's packaging. Histones are positively charged proteins that wrap up DNA through interactions between their positive charges and the negative charges of DNA. Double-stranded DNA loops around 8 histones twice, forming the **nucleosome**, which is the building block of **chromatin packaging**.



DNA can be further packaged by forming coils of nucleosomes, called **chromatin fibers**. These fibers are condensed into chromosomes during **mitosis**, or the process of **cell division**. However, packaging of **chromatin** into **chromosomes** that we are most familiar with occurs only during a few stages of mitosis. Most of the time, DNA is loosely packaged.

Histones: DNA Tupperware™

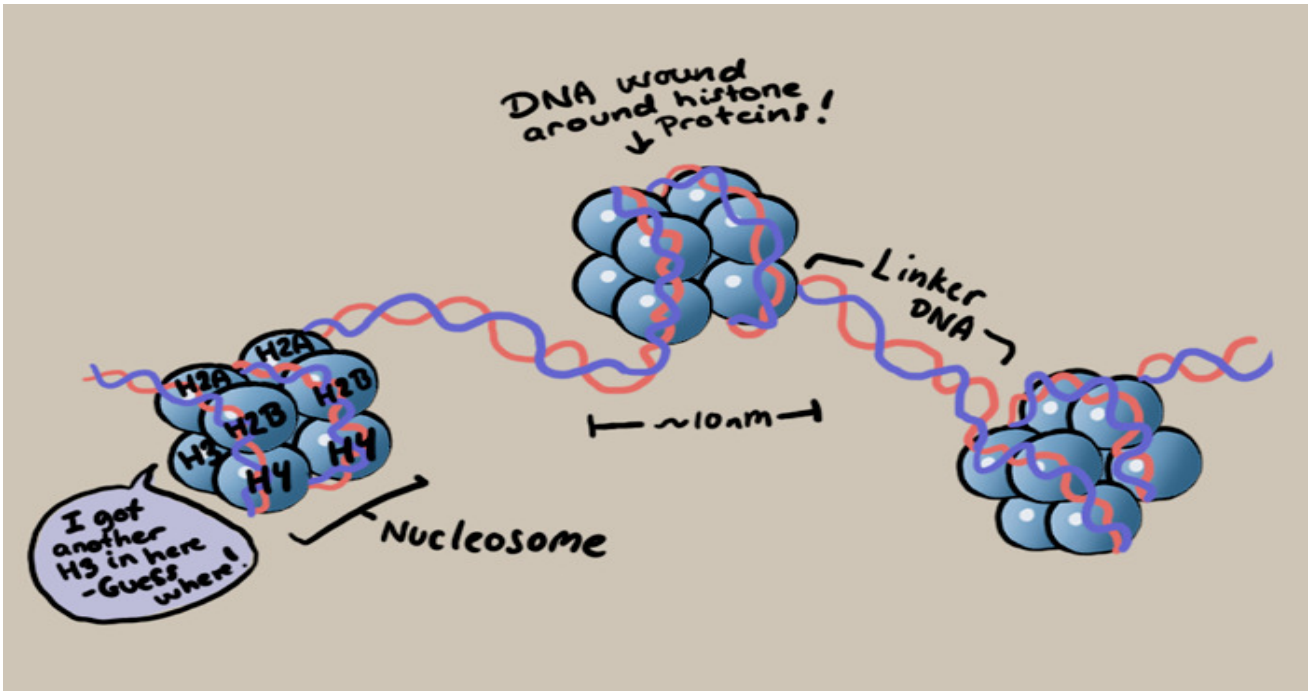
Histones are positively charged proteins that facilitate the packing of DNA into condensed **chromatin fibers**. They are basically the Tupperware™ of DNA packaging, and they come in many kitchen-friendly colors. Histones have many arginine and lysine amino acids that easily bind to the negatively charged DNA, based on Paula Abdul's principle that **opposites attract**. Just kidding on that last part. DNA is highly negatively charged because of the phosphate group of each nucleotide is negatively charged.



Histones are divided into two groups:

- **Corehistones**
- **Linkerhistones**

Core histones are H2A, H2B, H3, and H4, where two H3/H4 dimers (H3 and H4 hooked together) and two H2A/H2B dimers (these two hooked together) form the octamer (all eight of these guys together). **Linker** histone H1 basically locks the DNA in place onto the **nucleosome** and can be removed for **transcription** while linker histone H5 is a variant of H1 predominantly used in birds.



Is that confusing? Well, it gets worse. H1, H2A, H2B, H3, H4, and H5 are all names that define **families** of proteins. Individual histone proteins are specific for certain types of DNA or certain cell types. Just as H5 is the avian version of H1, there are individual histone proteins that package certain regions of DNA, or package DNA in specific **tissue types**. Just like you would not put a giant pot of chili in small Tupperware containers (or maybe you would…we try not to judge, but seriously?), specific histones are important for specific parts of DNA.

One important aspect of histones is that they can be changed to alter how much packing the DNA is capable of. There are several modifications that affect how well DNA is packaged. The three major types of modifications can be seen in the following table.

Modification	Modification Structure (R = chemical functional group)	Charge	Effect
Methylation	R-CH_3	Neutral	Increases packing
Acetylation	R-$COCH_3$	Negative	Decreases packing

PhosphorylationR-PO NegativeDecreases packing

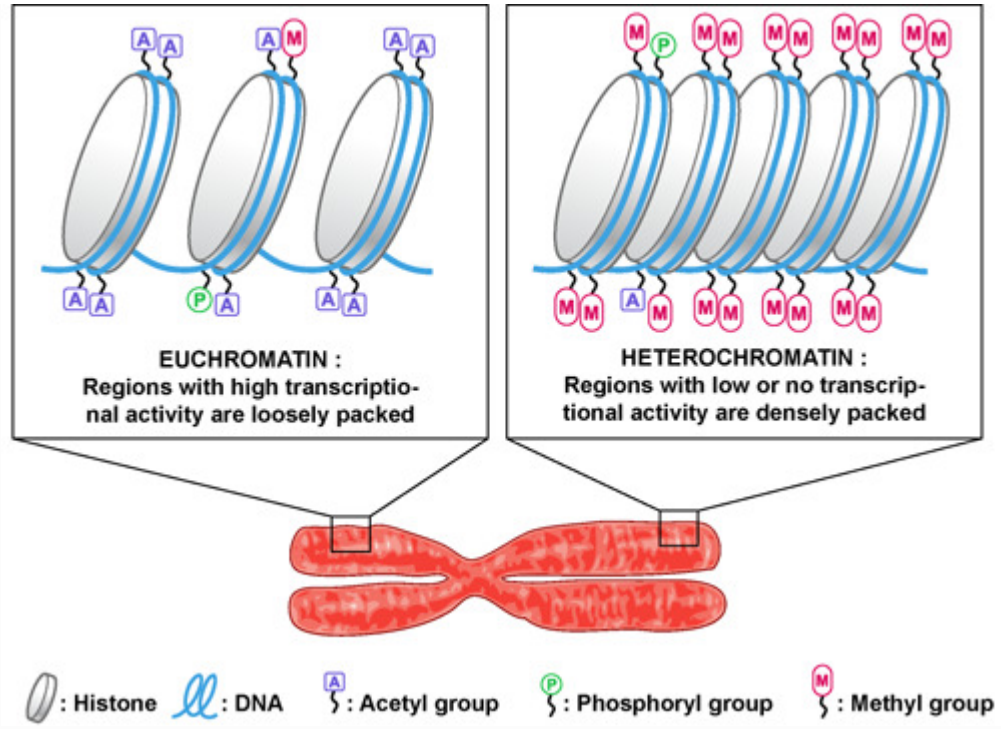
Normally, histones are positively charged molecules, and the addition of methyl groups (**methylation**) makes them more **hydrophobic** (water-hating). Hydrophobic molecules tend to stick together, and increasing **histone methylation will** cause the histones to pack even more tightly than usual.

Acetylation (adding an acetyl group) and **phosphorylation** (adding a phosphate group) make the histones more negatively charged because acetyl and phosphoryl groups are negative. They are "glass is half empty" molecules. By making histones more negatively charged, their grip on DNA will be much looser because DNA is also negatively charged. Similar charges (negative and negative) repel one another.

Lockup: DNA Edition

One of the perks of packaging DNA is that you can separate it into things you use a lot and things you do not. Unless you are a maniacal hoarder, every fall, you put away your summer clothes for things more winter-appropriate. In the same way, certain parts of DNA are only important for certain times. However, some things you need year-round, like shoes, so there is no point in putting those things away. The cell does the same thing with DNA.

Regions that are necessary for making proteins and are important for the cell are loosely packed and called **euchromatin**. By having a loose packing of DNA in euchromatin, proteins involved in **transcription** can easily get in and make RNA (see Genes to Proteins section for more detail). On the other hand, some regions of DNA you do not need except for special occasions, like that velvet suit you have that you never wear. These regions are called **heterochromatin** and are tightly packed through DNA as well as through good ol' **histone methylation**.

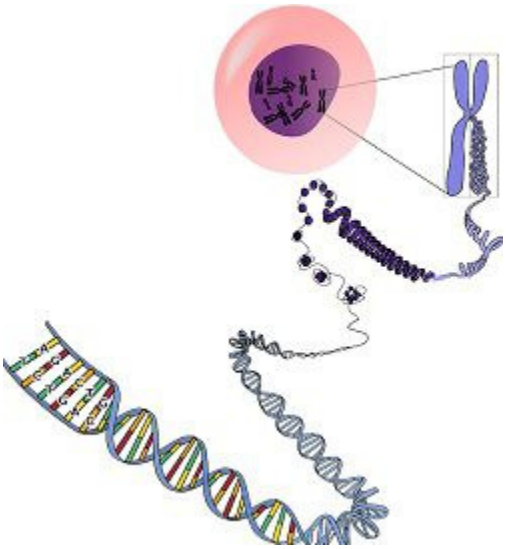


Enzymes that add **acetyl groups** to histones are called **histone acetyltransferases (HATs)** while those that remove acetyl groups are called **histone deacetylases (HDACs)**. Enzymes that add methyl groups are called **histone methyltransferases (HMTs)**. Activity of these enzymes affects whether or not regions of DNA are tightly packed, and unable to **transcribe**, or are loosely packed and therefore, highly transcribed.

Histone methylation is a tricky concept, though, because usually, **histone methylation** goes along with methylation of cytosines in DNA, called **DNA methylation**. Together, these processes create regions of DNA that cannot be transcribed. However, sometimes, methylation of positively charged amino acids in histones promotes **transcriptional activation**, but only when DNA is not methylated. The methylation of DNA and modifications of histones that affect **transcription** are the focus of study called **epigenetics**.

When the cell is undergoing the process of **mitosis**, **chromatin packing** is important, and this packing is done by packing DNA into condensed **chromatin fibers** to the point where they are the recognized **chromosomes** that we know and love…or "really like," if you are unprepared to make that kind of commitment. These chromosomes divide into **daughter cells**, and after mitosis is complete, the DNA is unpacked so **transcription** can occur again. Therefore, we can think of mitosis like a big DNA moving day. The packing starts with HDACs and HMTs tightening the packaging, and once mitosis is completed, HATs and **phosphoryltransferases (HPTs)** reduce the packaging.

Heterochromatin and Euchromatin:



The major difference between heterochromatin and euchromatin is that **heterochromatin** is such part of the chromosomes, which is a firmly packed form and are **genetically inactive**, while **euchromatin** is an uncoiled (loosely) packed form of chromatin and are **genetically active**.

When the non-dividing cells of the nucleus were observed under the light microscope, it exhibited the two regions, on the ground of concentration or intensity of staining. The **dark stained** areas are said as heterochromatin and **light stained** areas are said as euchromatin.

Around **90%** of the total human genome is euchromatin. They are the parts of chromatin and participate in the protection of DNA in the genome present inside the nucleus. **Emil Heitz** in the year 1928, coined the term Heterochromatin and Euchromatin.

By focussing on the few more points, we will be able to understand the difference between both types of chromatin. Given below is the comparison chart along with the brief description of them.

Content: Heterochromatin Vs Euchromatin

1. Comparison Chart
2. Definition
3. Key Differences
4. Conclusion

Comparison Chart

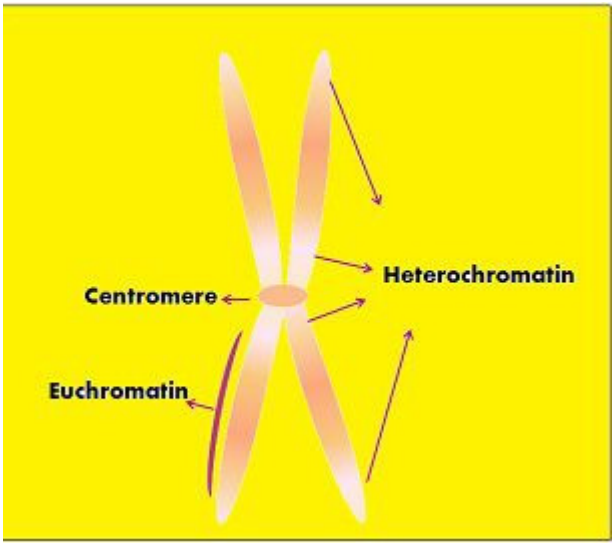
BASIS FOR COMPARISON	HETEROCHROMATIN	EUCHROMATIN
Meaning	The tightly packed form of DNA in the chromosome is called as heterochromatin.	The loosely packed form of DNA in the chromosome is called as euchromatin.
DNA density	High DNA density.	Low DNA density.
Kind of stain	Stained dark.	Lightly stained.
Where they are present	These are found at the periphery of the nucleus in eukaryotic cells only.	These are found in the inner body of the nucleus of prokaryotic as well as in eukaryotic cells.
Transcriptional activity	They show little or no transcriptional activity.	They actively participate in the process of transcription.
Other features	They are compactly coiled.	They are loosely coiled.
	They are late replicative.	They are early replicative.
	Regions of heterochromatin are sticky.	Regions of euchromatin are non-sticky.
	Genetically inactive.	Genetically active.
	Phenotype remains unchanged of	Variation may be seen, due

BASIS FOR COMPARISON	HETEROCHROMATIN	EUCHROMATIN
	an organism.	to the affect in DNA during the genetic process.
	It permits the gene expression regulation and also maintains the structural integrity of the cell.	It results in genetic variations and permits the genetic transcription.

Definition of Heterochromatin

The area of the chromosomes which are **intensely stained** with DNA-specific strains and are relatively condensed is known as **heterochromatin**. They are the **tightly packed** form of DNA in the nucleus.

The organization of heterochromatin is so highly compact in the way that these are inaccessible to the protein which is engaged in gene expression. Even the chromosomal crossing over is not possible due to the above reason. Resulting them to be transcriptionally as well as genetically inactive.



Heterochromatin is of two types: Facultative heterochromatin and constitutive heterochromatin. The genes which get silenced through the process of **Histone methylation or siRNA** through **RNAi** are called

as **facultative heterochromatin**. Hence they contain inactive genes and is not a permanent character of every nucleus of the cells.

While the **repetitive and structurally functional genes** like telomeres or centromeres are called as **Constitutive heterochromatin**. These are the continuing nature of the cell's nucleus and contains no gene in the genome. This structure is retainable during the interphase of the cell.

The **main function** of the heterochromatin is to protect the DNA from the endonuclease damage; it is due to its compact nature. It also prevents the DNA regions to get accessed to proteins during gene expression.

Definition of Euchromatin

That part of chromosomes, which are **rich in gene** concentrations and are loosely packed form of chromatin is called as **euchromatin**. They are active during transcription.

Euchromatin covers the maximum part of the dynamic genome to the inner of the nucleus and is said that euchromatin contains about **90% of the entire human genome**.

To allow the transcription, some parts of the genome containing active genes are loosely packed. The wrapping of DNA is so loose that DNA can become readily available. The structure of euchromatin resembles the nucleosomes, which consist of histones proteins having around 147 base pairs of DNA wrapped around them.

Euchromatin actively participates in transcription from DNA to RNA. The **gene regulating mechanism** is the process of transforming euchromatin into heterochromatin or vice versa.

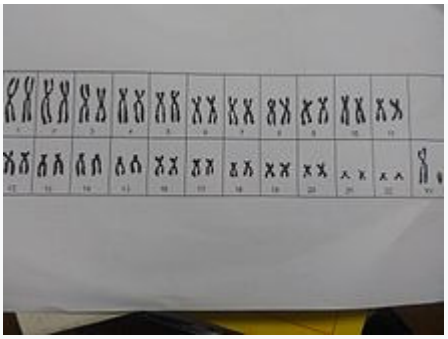
The active genes present in euchromatin gets transcribed to make mRNA whereby further encoding the functional proteins is the **main function** of euchromatin. Hence they are considered as genetically and transcriptionally active. **Housekeeping** genes are one of the forms of euchromatin.

Conclusion

From the above information regarding chromatin – their structure and types. We can say that only Euchromatin is vigorously involved in the transcription process although heterochromatin and its types do not play such significant role.

Constitutive heterochromatin contains the satellite DNA, and it surrounds the centromere, and facultative heterochromatin is disbanded. So apparently it can be said that the eukaryotic cells and their inner structure are relatively complex.

Human karyotype[edit]



human karyotype (male)

The normal human karyotypes contain 22 pairs of autosomal chromosomes and one pair of sex chromosomes (allosomes). Normal karyotypes for females contain two X chromosomes and are denoted 46,XX; males have both an X and a Y chromosome denoted 46,XY. Any variation from the standard karyotype may lead to developmental abnormalities.

Diversity and Evoution of Karyotype:

Although the replication and transcription of DNA is highly standardized in eukaryotes, the same cannot be said for their karyotypes, which are highly variable. There is variation between species in chromosome number, and in detailed organization, despite their construction from the same macromolecules. This variation provides the basis for a range of studies in evolutionary cytology.

In some cases there is even significant variation within species. In a review, Godfrey and Masters conclude:

In our view, it is unlikely that one process or the other can independently account for the wide range of karyotype structures that are observed ... But, used in conjunction with other phylogenetic data, karyotypic fissioning may help to explain dramatic differences in diploid numbers between closely related species, which were previously inexplicable.[23]

Although much is known about karyotypes at the descriptive level, and it is clear that changes in karyotype organization has had effects on the evolutionary course of many species, it is quite unclear what the general significance might be.

We have a very poor understanding of the causes of karyotype evolution, despite many careful investigations ... the general significance of karyotype evolution is obscure.

Changes during development

Instead of the usual gene repression, some organisms go in for large-scale elimination of heterochromatin, or other kinds of visible adjustment to the karyotype.

- Chromosome elimination. In some species, as in many sciarid flies, entire chromosomes are eliminated during development.
- Chromatin diminution (founding father: Theodor Boveri). In this process, found in some copepods and roundworms such as *Ascaris suum*, portions of the chromosomes are cast away in particular cells. This process is a carefully organised genome rearrangement where new telomeres are constructed and certain heterochromatin regions are lost. In *A. suum*, all the somatic cell precursors undergo chromatin diminution.
- X-inactivation. The inactivation of one X chromosome takes place during the early development of mammals (see Barr body and dosage compensation). In placental mammals, the inactivation is random as between the two Xs; thus the mammalian female is a mosaic in respect of her X chromosomes. In marsupials it is always the paternal X which is inactivated. In human females some 15% of somatic cells escape inactivation,[and the number of genes affected on the inactivated X chromosome varies between cells: in fibroblast cells up about 25% of genes on the Barr body escape inactivation.[30]

Number of chromosomes in a set

A spectacular example of variability between closely related species is the muntjac, which was investigated by Kurt Benirschke and his colleague Doris Wurster. The diploid number of the Chinese muntjac, *Muntiacus reevesi*, was found to be 46, all telocentric. When they looked at the karyotype of the closely related Indian muntjac, *Muntiacus muntjak*, they were astonished to find it had female = 6, male = 7 chromosomes.

They simply could not believe what they saw ... They kept quiet for two or three years because they thought something was wrong with their tissue culture ... But when they obtained a couple more specimens they confirmed

The number of chromosomes in the karyotype between (relatively) unrelated species is hugely variable. The low record is held by the nematode *Parascaris univalens*, where the haploid n = 1; and an ant: *Myrmecia pilosula*.[32] The high record would be somewhere amongst the ferns, with the adder's tongue fern *Ophioglossum* ahead with an average of 1262 chromosomes. Top score for animals might be the shortnose sturgeon *Acipenser brevirostrum* at 372 chromosomes. The existence of supernumerary or B chromosomes means that chromosome number can vary even within one interbreeding population; and aneuploids are another example, though in this case they would not be regarded as normal members of the population.

Fundamental number

The fundamental number, *FN*, of a karyotype is the number of visible major chromosomal arms per set of chromosomes Thus, FN ≤ 2 x 2n, the difference depending on the number of chromosomes considered single-armed (acrocentric or telocentric) present. Humans have FN = 82, due to the presence of five acrocentric chromosome pairs: 13, 14, 15, 21, and 22 (the human Y chromosome is also acrocentric). The fundamental autosomal number or autosomal fundamental number, *FN* or *AN*, of a karyotype is the number of visible major chromosomal arms per set of autosomes (non-sex-linked chromosomes).

Ploidy

Ploidy is the number of complete sets of chromosomes in a cell.

- Polyploidy, where there are more than two sets of homologous chromosomes in the cells, occurs mainly in plants. It has been of major significance in plant evolution according to Stebbins The proportion of flowering plants which are polyploid was estimated by Stebbins to be 30–35%, but in grasses the average is much higher, about 70%.Polyploidy in lower plants (ferns, horsetails and psilotales) is also common, and some species of ferns have reached levels of polyploidy far in excess of the highest levels known in flowering plants.
- Polyploidy in animals is much less common, but it has been significant in some groups.
- Polyploid series in related species which consist entirely of multiples of a single basic number are known as euploid.
- Haplo-diploidy, where one sex is diploid, and the other haploid. It is a common arrangement in the Hymenoptera, and in some other groups.
- Endopolyploidy occurs when in adult differentiated tissues the cells have ceased to divide by mitosis, but the nuclei contain more than the original somatic number of chromosomes. In the *endocycle* (endomitosis or endoreduplication) chromosomes in a 'resting' nucleus undergo reduplication, the daughter chromosomes separating from each other inside an *intact* nuclear membrane.
  In many instances, endopolyploid nuclei contain tens of thousands of chromosomes (which cannot be exactly counted). The cells do not always contain exact multiples (powers of two), which is why the simple definition 'an increase in the number of chromosome sets caused by replication without cell division' is not quite accurate.
  This process (especially studied in insects and some higher plants such as maize) may be a developmental strategy for increasing the productivity of tissues which are highly active in biosynthesis.
  The phenomenon occurs sporadically throughout the eukaryote kingdom from protozoa to humans; it is diverse and complex, and serves differentiation and morphogenesis in many ways.
- See palaeopolyploidy for the investigation of ancient karyotype duplications.

Aneuploidy[edit]

Aneuploidy is the condition in which the chromosome number in the cells is not the typical number for the species. This would give rise to a chromosome abnormality such as an extra chromosome or one or more chromosomes lost. Abnormalities in chromosome number usually cause a defect in development. Down syndrome and Turner syndrome are examples of this.

Aneuploidy may also occur within a group of closely related species. Classic examples in plants are the genus *Crepis*, where the gametic (= haploid) numbers form the series x = 3, 4, 5, 6, and 7; and *Crocus*, where every number from x = 3 to x = 15 is represented by at least one species. Evidence of various kinds shows that trends of evolution have gone in different directions in different groups.[50] Closer to home, the great apes have 24x2 chromosomes whereas humans have 23x2. Human chromosome 2 was formed by a merger of ancestral chromosomes, reducing the number.

Chromosomal polymorphism

Some species are polymorphic for different chromosome structural forms. The structural variation may be associated with different numbers of chromosomes in different individuals, which occurs in the ladybird beetle *Chilocorus stigma*, some mantids of the genus *Ameles*,the European shrew *Sorex araneus*.There is some evidence from the case of the mollusc *Thais lapillus* (the dog whelk) on the Brittany coast, that the two chromosome morphs are adapted to different habitats.

Species trees

The detailed study of chromosome banding in insects with polytene chromosomes can reveal relationships between closely related species: the classic example is the study of chromosome banding in Hawaiian drosophilids by Hampton L. Carson.

In about 6,500 sq mi (17,000 km^2), the Hawaiian Islands have the most diverse collection of drosophilid flies in the world, living from rainforests to subalpine meadows. These roughly 800 Hawaiian drosophilid species are usually assigned to two genera, *Drosophila* and *Scaptomyza*, in the family Drosophilidae.

The polytene banding of the 'picture wing' group, the best-studied group of Hawaiian drosophilids, enabled Carson to work out the evolutionary tree long before genome analysis was practicable. In a sense, gene arrangements are visible in the banding patterns of each chromosome. Chromosome rearrangements, especially inversions, make it possible to see which species are closely related.

The results are clear. The inversions, when plotted in tree form (and independent of all other information), show a clear "flow" of species from older to newer islands. There are also cases of colonization back to older islands, and skipping of islands, but these are much less frequent. Using K-Ar dating, the present islands date from 0.4 million years ago (mya) (Mauna Kea) to 10mya (Necker). The oldest member of the Hawaiian archipelago still above the sea is Kure Atoll, which can be dated to 30 mya. The archipelago itself (produced by the Pacific plate moving over a hot spot) has existed for far

longer, at least into the Cretaceous. Previous islands now beneath the sea (guyots) form the Emperor Seamount Chain.

All of the native *Drosophila* and *Scaptomyza* species in Hawai'i have apparently descended from a single ancestral species that colonized the islands, probably 20 million years ago. The subsequent adaptive radiation was spurred by a lack of competition and a wide variety of niches. Although it would be possible for a single gravid female to colonise an island, it is more likely to have been a group from the same species

Using Karyograms to Detect Chromosomal Abnormalities

Today, G-banded karyograms are routinely used to diagnose a wide range of chromosomal abnormalities in individuals. Although the resolution of chromosomal changes detectable by karyotyping is typically a few megabases, this can be sufficient to diagnose certain categories of abnormalities. For example, aneuploidy, which is often caused by the absence or addition of a chromosome, is simple to detect by karyotype analysis. Cytogeneticists can also frequently detect much more subtle deletions or insertions as deviations from normal banding patterns. Likewise, translocations are often readily apparent on karyotypes.

When regional changes in chromosomes are observed on karyotypes, researchers often are interested in identifying candidate genes within the critical interval whose misexpression may cause symptoms in patients. This search process has been greatly facilitated by the completion of the Human Genome Project, which has correlated cytogenetic bands with DNA sequence information. Consequently, investigators are now able to apply a range of molecular cytogenetic techniques to achieve even higher resolution of genomic changes. Fluorescence *in situ* hybridization (FISH) and comparative genomic hybridization (CGH) are examples of two approaches that can potentially identify abnormalities at the level of individual genes.

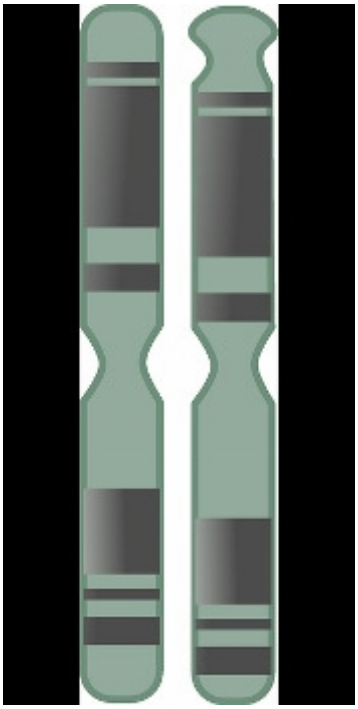
Molecular cytogenetics is a dynamic discipline, and new diagnostic methods continue to be developed. As these new technologies are implemented in the clinic, we can expect that cytogeneticists will be able to make the leap from karyotype to gene with increasing efficiency.

What is Chromosome Banding

You may talk about your genes from time to time - 'Oh, I have the gene for that.' But how do you see your genes? A gene is a functional unit of DNA, and your DNA is organized onto chromosomes. **Chromosome banding** is a little like tie-dying your chromosomes.

A **chromosome** is a unit of tightly-packed DNA. DNA has to wrap tightly around itself, because you have quite a lot of it. In fact, if you unrolled all the DNA in a single one of your cells, it would be about three meters long. Humans have 46 chromosomes - 23 from Mom and 23 from Dad.

In **chromosome banding**, we treat chromosomes with chemicals to stain them and learn about a chromosome by how it stains. There are several different types of stains we can use.



Banded chromosomes

There are several types of **chromosome banding**. Here, we will list a few of the most common types.

- **G-banding** uses a stain called Giemsa stain. G-banding gives you a series of light and dark stripes along the length of the chromosome. We will discuss G-banding in the most detail, because you will likely see G-banding if you take a genetics class.
- **Q-banding** uses a stain called quinacrine. Q-banding yields a fluorescent pattern. It is similar in pattern to G-banding, but glows yellow.
- **C-banding** only stains the centromeres. Centromeres are little constricted portions of chromosomes. That's where sister chromatids (two copies of the same chromosome) will attach to each other when the cell is getting ready to divide.
- **R-banding** is the opposite of C-banding. R-banding stains non-centromeric regions.

Giemsa Stain

G-banding is useful because the patterns of stripes on the chromosomes are unique enough that you should be able to confidently identify each chromosome.

Giemsa staining was named after the German scientist **Gustav Giemsa**, who worked in the early part of the 20th century. Giemsa's immediate goal was to find a stain that would work on *Plasmodium*, the parasite that causes malaria. Giemsa stain, however, was quickly found to have many uses. Dr. Giemsa lamented the fact that he would be known for his staining procedure rather than for his work on tropical diseases.

Giemsa stain is a mixture of a stain called methylene blue and one called azure, which form a type of stain called an eosin compound. Researchers will typically wash a sample in Giemsa stain for around seven minutes. You would typically stain chromosomes during the early parts of the cell cycle (prophase or metaphase), because the chromosomes are partially but not fully condensed.

Karyotypes

A **karyotype** is a profile of a person's chromosomes, organized by size. Scientists will use a karyotype to identify any abnormalities that may lead to a genetic disorder. For instance, people who have Down syndrome carry an extra copy of Chromosome 21. Having an extra chromosome makes it hard for cells to properly regulate how much protein to make. Down syndrome is a developmental disorder that is characterized by intellectual disability and distinctive facial features such as a flat face, abnormal ears, large tongue, and upward-slanting eyes. People with Down syndrome are prone to medical complications including respiratory problems, heart defects, hearing loss, and leukemia.

Kinds of Chromosomes: Lampbrush, Polytene :

I] Lampbrush chromosomes:

These are the largest known chromosomes found in the yolk rich oocytic nuclei of certain vertebrates such as fishes, amphibians, reptiles and birds.

They can be seen with naked eye and are characterized by fine lateral loops, arising from the chromomeres, during first prophase (diplotene) of meiosis.

These loops give it a brush-like appearance; that is why these are called lampbrush chromosomes first discovered by Flemming in 1882 and were described in shark oocytes by Ruckert (1892). Lampbrush chromosomes of certain urodele oocytes may reach upto 5900µ in length.

It consists of longitudinal axis formed by a single DNA molecule along which several hundred bead-like chromomeres are distributed in a linear fashion. From each chromomere there emerge two symmetrical lateral loops (one for each chromatid), which are able to expand or contract in response to various environmental conditions.

About 5 to 10% of the DNA is in the lateral loops. Loop formation reduces the mass of the corresponding chromomeres, implying a spinning out of chromomere material into the lateral strands. The centromeres also have the appearance of elongate Feulgen-positive chromomeres but they characteristically lack lateral loops.

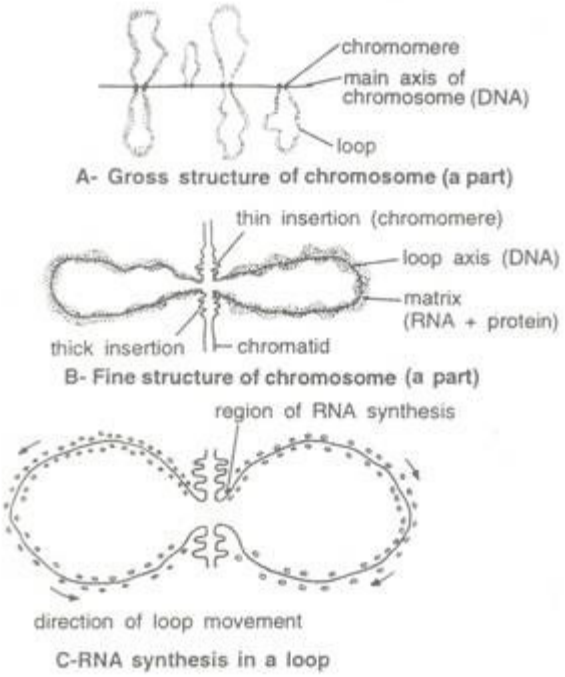


Fig. 11. Lampbrush chromosome.

Lampbrush chromosomes can be dissected in (toto) from oocyte nucleus. Individual chromosomes are liable to stretching. With extreme stretching, chromomeres begin to separate transversely into two halves, so that the paired loops form double stranded bridges. The axis between chromomeres is also double, which can be seen in certain special regions where two elements separate longitudinally and bear single loops (Callan, 1955).

These experiments indicate that each chromomere possesses four quadrants separated by both a transverse and a longitudinal line of division (Fig. C). Callan (1963) regards it as that the entire chromatid pair is made up of two continuous strands, which lie parallel to one another in the interchromomere

regions, are tightly folded in the chromomeres, and separate as single, unfolded fibres in the loops. Each of the two fibres would correspond to one conventional metaphase chromatid.

There is fundamental similarity in the organization of amphibian lmpbrush chromosomes and dipteran giant polytene chromosomes: in both cases, very long single fibres correspond to single chromatids and are partly but not completely extended. The substructure of the salivary chromosome 'puffs' also bear some similarity to that of the lampbrush lateral loops.

Lateral loops are formed of DNA, in chromomeres regions DNA is tightly folded and transcriptionally inactive. In lateral loops RNA synthesis is intense. Each loop in turn has an axis formed by a single DNA molecule, which is coated by a matrix of nascent RNA and proteins. The matrix is asymmetrical, being thicker at one end of the loop. RNA synthesis starts at the thinner end and progresses toward the thicker end.

Functions of Lampbrush chromosomes,

(a) Synthesis of RNA:

Functions of lampbrush chromosomes involve synthesis of RNA and protein by their loops. RNA is synthesized only at the thin insertion and then carried around the loops to the thick insertion. There it may be either destroyed or released into nucleus.

(b) Formation of yolk material:

There are some probabilities that lampbrush chromosomes help in the formation of certain amount of yolk material for the egg.

[II] Polytene chromosomes:

These are also giant chromosomes but relatively smaller than lampbrush chromosomes, found in the larvae of certain dipterans. Such banded chromosomes occur in the larval salivary glands, midgut epithelium, and rectum and Malpighian tubules of various genera (Drosophila, Sciara, Rhynchosciara, and Chironomus). In these larvae the salivary glands contain salivary cells so large in size that they can easily be seen with the lens power of a dissecting microscope.

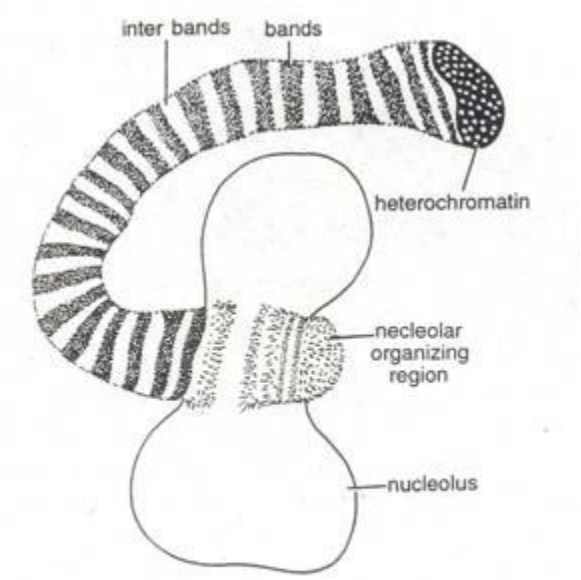


Fig. 12. Structure of a polytene chromosome of *Cecidomyia serotinae* showing nucleolar part.

Nuclei of these cells are much larger than those of ordinary cells being generally about 25μ in diameter, and chromosomes in nuclei are so large that they are 50 to 200 times as large as chromosomes in other body cells of the organism.

Ultrastructure of giant polytene (poly=many, tene=strands) chromosomes:

It was first investigated by Beermann and Bahr (1954), who observed numerous fine fibrils in the Balbiani rings of Chironomus and estimated that each chromosome contains 1000 to 2000 separate strands (corresponding to the degree of ploidy).

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Later Gay (1956) observed strands 200 to 500 A in diameter in sectioned Drosophila salivary chromosomes. The individual fibres in band and interband regions are similar in appearance, but the

fibres in the bands exhibit a considerable degree of metaphase-like folding and are much more tightly packed.

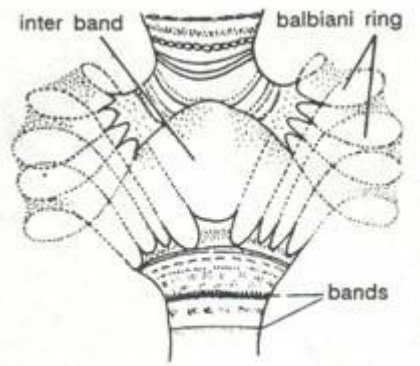


Fig. 13. Balbiani ring of a polytene chromosome.

Polytene chromosomes get their name from the fact that they are formed by many parallel chromatids, often more than a thousand strands, which do not separate from one another following duplication. Along each chromatid strand some regions of chromatin are tightly coiled and other regions are less coiled, with the result that polytene chromosomes appear to consist of light and dark bands when observed under a microscope.

During larval development, specific areas on polytene chromosomes become uncoiled, forming localized regions called 'pufs'. Puffs represent regions of active RNA synthesis (transcription). In the puff individual fibres remain continuous across the puff and they become extended as short lateral loops (Bahr, 1954). DNA is concentrated almost entirely in the bands. Protein and RNA is also found in puffs. Puffing is due to the uncoiling of chromosome fibres which are usually closely folded or coiled in the dense band regions. These fibres then project in the form of loops.

Structural Variations in Chromosomes :

The following point highlight the five main types of structural variation in chromosomes. The types are: 1. Deletion or Deficiency 2. Duplications 3. Translocations 4. Inversions .

Type # 1. Deletion or Deficiency:

A deficiency means deletion of a small portion of a chromosome resulting in loss of one or more genes. A deficiency originates from breakage occurring at random in both chromatids of a chromosome (called chromosome break), or only in one chromatid (chromatid break).

The breakage may be caused by various agents such as radiation, chemicals, drugs or viruses at any time during the cell cycle, either in somatic or in germ cells. Depending upon its location, a deletion may be terminal when a single break occurs near the end of the chromosome; or interstitial when two breaks occur in a middle portion of the chromosome

Each break produces two raw ends which may behave in one of following three ways:

(a) There might be reunion of the broken ends called restitution so that the original chromosome structure is restored;

(b) The broken ends may not unite giving rise to a chromosomal segment without a centromere which is eventually lost during cell division;

(c) If two single breaks occur in two different chromosomes in a cell, the deleted segment of one chromosome may unite with the raw broken end on the other chromosome; this is called exchange union.

Fate of a Deleted Fragment:

If the fragment does not have a centromere (acentric), then at metaphase it will not be able to get attached to spindle fibres and move towards a pole with other centric chromosomes. It will remain at the centre of the cell and will not be included within any of the two daughter nuclei. It will be free in the cytoplasm and will eventually be lost (Fig. 12.1). In this way, the cell will lose one or more genes contained in the deleted fragment.

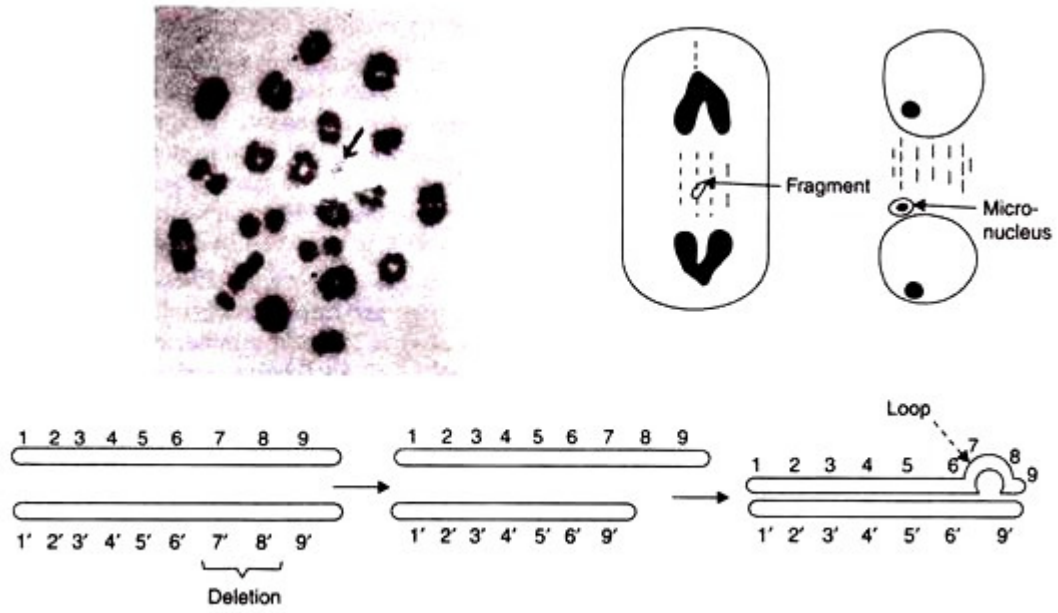


Fig. 12.1 Acentric chromosome fragment (arrow) at diakinesis.

A diploid cell has a homologue of the chromosome which has lost a segment. The corresponding segment of the intact homologue will have alleles of the genes that the cell has lost. Such a cell is said to be heterozygous for a deficiency. A very small deficiency in the heterozygous state is viable, but if homozygous it is lethal. When a deletion is large it is lethal even in the heterozygous state.

If a deletion occurs in cells of the germ line, then 50% of the gametes formed will have a deleted chromosome and 50% gametes would be normal. This would result in half the offspring with phenotypic abnormalities related to the genes carried on a small deleted fragment.

If the deficiency occurs in a developing embryo, some cells would have normal chromosomes and other cells would have the deficiency. This could produce a mosaic individual with two different phenotypes.

Detection of Deficiency:

The occurrence of a deficiency can sometimes be inferred from the results of a genetic cross when a rare recessive phenotype unexpectedly appears in the progeny. Consider a cross between two

parents DD and dd where D controls the dominant expression of a trait, and d is the recessive allele. The F1 is expected to show the dominant trait and have the genotype Dd.

If on the contrary, some F1 individuals show the recessive phenotype, one explanation could be sought in a deletion of the chromosomal segment bearing gene D. Since other interpretations are also possible, it is best to confirm the occurrence of deficiency from a cytological study of the chromosomes as described below.

Deficiencies are best observed in preparations of homologously paired chromosomes at meiotic prophase either in large sized plant chromosomes or in polytene chromosomes. Normally during pachytene homologous chromosomes are intimately synapsed throughout their length.

If one of the homologues is deficient over a small length, the corresponding portion of the second homologue has nothing to pair with. It therefore, forms a loop (Fig. 12.1), which is clearly visible in cytological preparations and is clear-cut proof that deficiency has occurred.

Type # 2. Duplications:

A duplication involves attachment of a chromosomal fragment resulting in addition of one or more genes to a chromosome. Whenever there is a duplication in a chromosome, there is a corresponding deletion in another chromosome.

Following types of duplications are known (Fig. 12.3: the diagrams are self-explanatory):

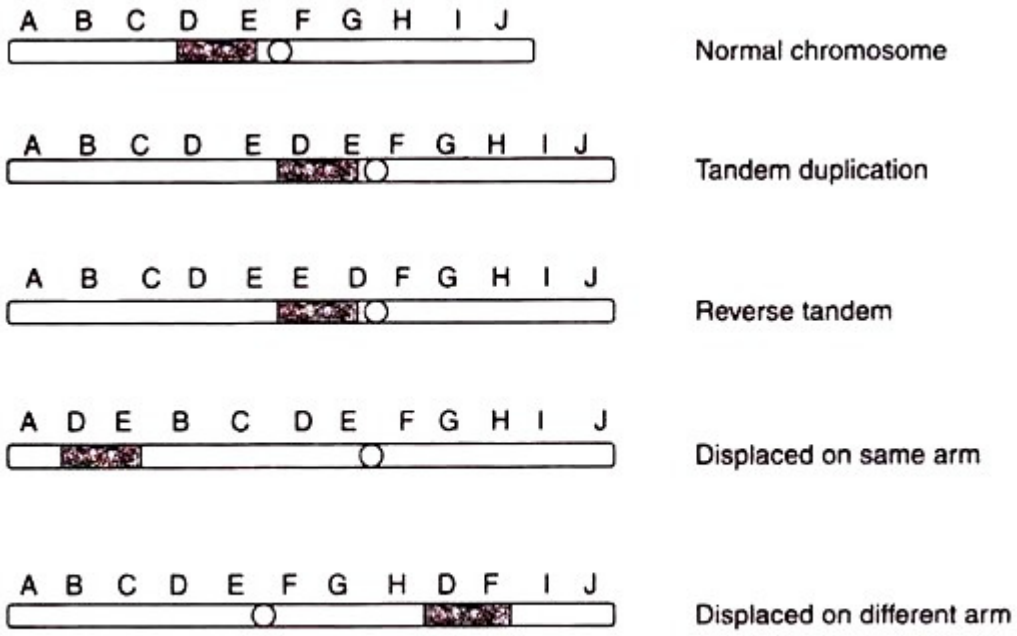


Fig. 12.3 Diagrams showing different types of duplications.

The phenotypic effect produced by a duplication is illustrated by the attached-X females in Drosophila. Consider such flies which are homozygous for some recessive sex-linked traits. It is found that when a fly receives a fragment of an X chromosome carrying the wild type allele from its male parent, then only the dominant phenotype is expressed.

The recessive alleles of the same gene although present in the homozygous condition, are not able to express themselves. Evidently the presence of a single dominant allele in a duplication is enough to produce the wild type phenotype.

The origin of duplications can be traced to unequal crossing over during meiosis. Normally homologous chromosomes are paired in a perfect manner so that identical loci lie exactly opposite each other.

The mechanism ensures that after crossing over between non-sister chromatids, equal exchange products are formed. If paired chromosomes are misaligned, it is not possible for exchange to take place between exactly opposite locations on two chromatids.

Instead, exchange occurs between adjacent points on two chromatids so that one resulting chromatid will have a duplication, the other a deletion. Such an exchange is called unequal crossing over. A gamete that receives a chromosome with a duplication will be diploid for some genes. When it fertilises a normal gamete, the zygote will have three sets of those genes that are present in the duplicated segment.

Bar eyes is a dominant X-linked trait in Drosophila females which provides a range of interesting phenotypes resulting from duplication. In a homozygous wild type female there is a large oval compound eye (non-bar) with about 779 facets.

The Bar trait reduces the eye to a vertical bar with very few facets. Bridges analysed the salivary gland chromosomes of Drosophila and found that the Bar gene (B) was present on a region designated 16A of the X chromosome.

When the band in the 16A region is present in duplicate in one X chromosome of the female (i.e. heterozygous for the duplication B/X), it results in an elongated Bar-shaped eye, smaller than the wild type (+/+) due to the presence of only 358 facets.

When a female is homozygous for the duplication (B/B), the Bar-shaped eye is further reduced in size and has 68 facets. If there is unequal crossing over in a female homozygous for Bar (B/B), it results in one chromatid where the 16A region (Bar locus) is present in triplicate, and the second chromatid with only one Bar locus.

Such a heterozygous triplicate condition produces a phenotype known as ultra-bar (B^u) with only 45 facets. If the triplicate condition becomes homozygous (B^U/B^U), the result is a very small eye with only 25 facets (Fig. 12.4). Unequal crossing over is also responsible for a rare human haemoglobin known as haptoglobin.

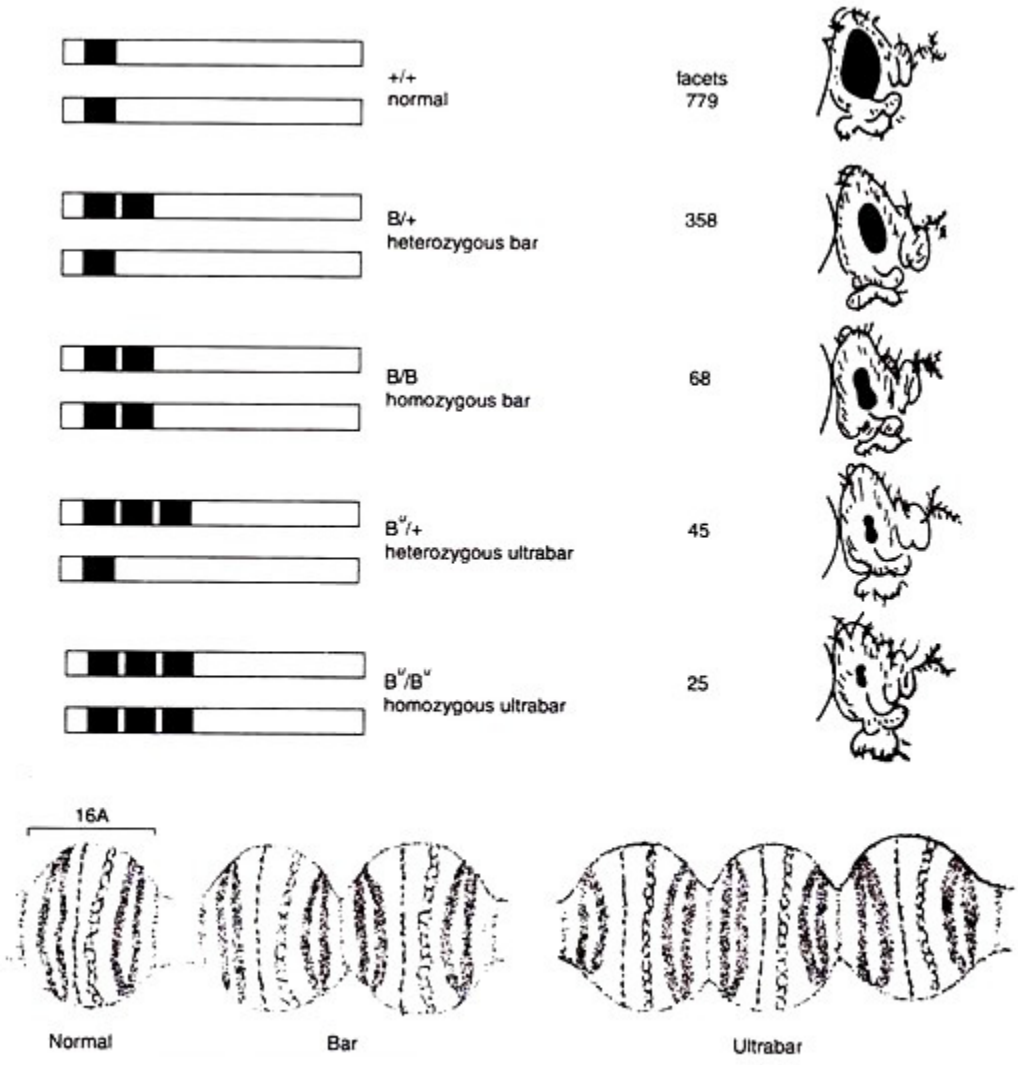


Fig. 12.4 Diagrams showing correlation between duplication of region 16A and inheritance of bar eye trait in *Drosophila*. Below is enlargement of 16A region of the chromosome.

The Bar locus in Drosophila provides an explanation for position effect. According to this phenomenon the expression of a gene becomes altered when the position of the gene is physically changed. Cytologically, a duplication is identified by the same method as deficiency, since in the heterozygous condition the extra fragment forms a loop in one of the two homologues.

Type # 3. Translocations:

Sometimes a segment of a chromosome becomes detached and unites with another non-homologous chromosome. Such an inter-chromosomal rearrangement is called translocation.

The rearrangements are of following types (Fig. 12.5):

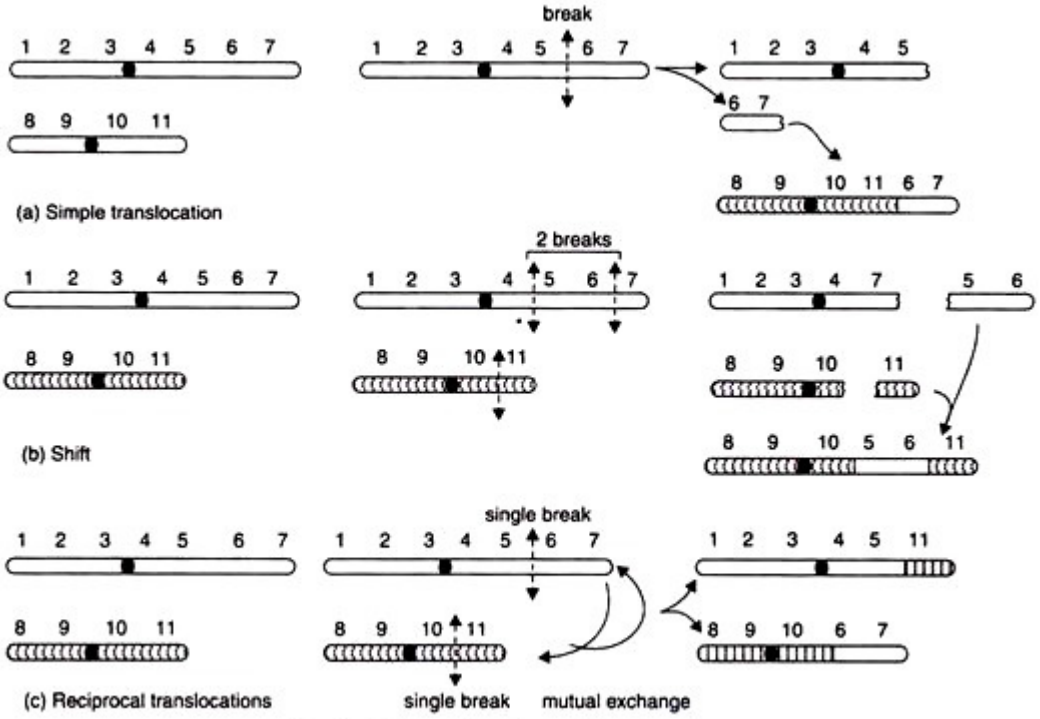


Fig. 12.5 The various types of translocations.

a. Simple Translocation:

A single break occurs in a chromosome, and the broken fragment becomes attached to the end of another chromosome. However, due to the presence of "non-sticky" telomeres at the unbroken ends of a chromosome, such a terminal attachment of a segment does not take place.

b. Shifts:

In this type three breaks are involved. Two breaks occur in a chromosome to produce an interstitial fragment. This fragment becomes inserted into one of the arms of another non-homologous chromosome in which a single break has produced two "sticky" ends.

c. Reciprocal Translocations:

These are the most frequent and extensively studied translocations. A single break occurs in each of the two non-homologous chromosomes followed by a mutual exchange of the broken fragments. This results in two new chromosomes each having one segment of the other chromosome.

d. Multiple Translocations:

Sometimes more than two pairs of non-homologous chromosomes may be involved in a translocation as observed Drosophila and Oenothera. In 1930 Stern studied a multiple translocation system in Drosophila in which a segment of the Y chromosome became attached to the X chromosome. At the same time a reciprocal translocation occurred between the X and chromosome IV. This resulted in a female with 9 chromosomes instead of 8.

e. Half Translocations:

When the nucleus containing two broken chromosomes is small, the broken ends are not widely separated in space and have better chance of undergoing reciprocal exchange. This is true for the small compact nucleus in the head of a sperm.

Type # 4. Inversions:

Inversions result when there are two breaks in a chromosome and the detached segment becomes reinserted in the reversed order. They are classified into two types depending upon the inclusion or absence of the centromere within the inverted segment.

Thus when both breaks occur in one arm of the chromosome it leads to a paracentric inversion; when a break occurs in each of the two arms, the centromere is included in the detached segment and leads to a pericentric inversion.

CHRO.MOSOME	
CHRO.SOMOME	Paracentric inversion
CHOM.OROSOME	Pericentric inversion

Meiosis is normal in inversion homozygotes. In heterozygotes pairing between homologous chromosomes is affected in the region of the inverted segment. Consequently, there is a suppression of recombination and fertility is impaired.

Genetic disorders:

Klinefelter syndrome

Klinefelter syndrome (KS) is a condition that occurs in males when they have an extra X chromosome. Some males with KS have no obvious signs or symptoms while others may have varying degrees of cognitive, social, behavioral, and learning difficulties. Adults with Klinefelter syndrome may also have primary hypogonadism (decreased testosterone production), small and/or undescendent testes (cryptorchidism), enlarged breast tissue (gynecomastia), tall stature, and/or inability to have biological children (infertility), as well as an abnormal opening of the penis (hypospadias), and an small penis (micropenis). KS is not inherited, but usually occurs as a random event during the formation of reproductive cells (eggs and sperm) that results in the presence of one extra copy of the X chromosome in each cell (47,XXY). KS treatment is based on the signs and symptoms present in each person.[1][2][3] Life expectancy is usually normal and many people with KS have normal life. There is a very small risk of developing breast cancer and other conditions such as a chronic inflammatory disease called systemic lupus erythematosus.[3]

In some cases, there is more than one X chromosome in each cell (for example, 48,XXXY or 49,XXXXY). These conditions, which are often called "variants of Klinefelter" syndrome usually have more serious problems (intellectual disability, skeletal problems, and poor coordination) than classic Klinefelter syndrome (47,XXY).[3]

Last updated: 2/14/2018

Symptoms

Listen

The signs and symptoms of Klinefelter syndrome (KS) vary among affected people. Some men with KS have no symptoms of the condition or are only mildy affected. In these cases, they may not even know that they are affected by KS. When present, symptoms may include:[1][2][3]

- Small, firm testicles
- Delayed or incomplete puberty with lack of secondary sexual characteristics resulting in sparse facial, body, or sexual hair a high-pitched voice and body fat distribution resulting in a rounder, lower half of the body, with more fat deposited in the hips, buttocks and thigh instead of around the chest and abdomen
- Breast growth (gynecomastia)
- Reduced facial and body hair
- Infertility
- Tall stature
- Abnormal body proportions (long legs, short trunk, shoulder equal to hip size)
- Learning disablity
- Speech delay
- Crypthochirdism
- Opening (meatus) of the urethra (the tube that carries urine and sperm through the penis to the outside) on the underside of the penis (hypospadias) instead of the tip of the head of the penis
- Social, psychologic and behavioral problems
- Whether or not a male with KS has visible symptoms depends on many factors, including how much testosterone his body makes, if he is mosaic (with both XY and XXY cells), and his age when the condition is diagnosed and treated.[1] Some people have a slightly increased risk of developing breast cancer, a rare extragonadal germ cell tumor, lung disease, varicose veins and osteoporosis as well as some autoimmune disorders such as systemic lupus erythematosus, rheumatoid arthritis and Sjogren's syndrome.[2][4]

  Some people with features of Klinefelter syndrome have more than one extra X chromosome in each cell (such as 48,XXXY or 49,XXXXY). In these cases, known as "variants of Klinefelter syndrome", the signs and symptoms can be more severe and may include:[1][2][4]

- Intellectual disability
- Distinctive facial features
- Skeletal abnormalities
- Poor coordination

- Severe speech difficulties
- Behavioral problems
- Heart defects
- Teeth problems.

CauseKlinefelter syndrome usually occurs as a random event during the formation of reproductive cells (eggs and sperm). An error in cell division called nondisjunction results in a reproductive cell with an abnormal number of chromosomes. For example, an egg or sperm cell may gain one or more extra copies of the X chromosome as a result of nondisjunction. If one of these atypical reproductive cells contributes to the genetic makeup of a child, the child will have one or more extra X chromosomes in each of the body's cells.[2]

Most often, Klinefelter syndrome is caused by a single extra copy of the X chromosome, resulting in a total of 47 chromosomes per cell. Males normally have one X chromosome and one Y chromosome in each cell (46, XY), while females have two X chromosomes (46, XX). People with Klinefelter syndrome usually have two X chromosomes and one Y chromosome (47, XXY). Some people with Klinefelter syndrome have the extra X chromosome in only some of their cells; these people are said to have mosaic Klinefelter syndrome.[2]

It is estimated that about half of the time, the cell division error occurs during development of the sperm, while the remainder are due to errors in egg development. Women who have pregnancies after age 35 have a slightly increased chance of having offspring with this syndrome.[5]

The features of Klinefelter syndrome are due to the extra copies of genes on the extra X chromosome, which can alter male sexual development.

some people with features of Klinefelter syndrome have conditions known as "variants of Klinefelter syndrome" where there is more than one extra sex chromosome in each cell (48,XXXY, 48,XXYY and 49,XXXXY).[5]
Last updated: 2/14/2018

Inheritance:

klinefelter syndrome is not inherited, but usually occurs as a random event during the formation of reproductive cells (eggs and sperm). An error in cell division called nondisjunction can result in reproductive cells with an abnormal number of chromosomes. For example, an egg or sperm cell may gain one or more extra copies of the X chromosome as a result of nondisjunction. If one of these reproductive cells contributes to the genetic makeup of a child, the child will have one or several extra X chromosomes in each of the body's cells.

Turner syndrome:

Turner syndrome, a condition that affects only females, results when one of the X chromosomes (sex chromosomes) is missing or partially missing. Turner syndrome can cause a variety of medical and developmental problems, including short height, failure of the ovaries to develop and heart defects.

Turner syndrome may be diagnosed before birth (prenatally), during infancy or in early childhood. Occasionally, in females with mild signs and symptoms of Turner syndrome, the diagnosis is delayed until the teen or young adult years.

Girls and women with Turner syndrome need ongoing medical care from a variety of specialists. Regular checkups and appropriate care can help most girls and women lead healthy, independent lives.

Symptoms

Signs and symptoms of Turner syndrome may vary among girls and women with the disorder. For some girls, the presence of Turner syndrome may not be readily apparent, but in other girls, a number of physical features and poor growth are apparent early. Signs and symptoms can be subtle, developing slowly over time, or significant, such as heart defects.

Before birth

Turner syndrome may be suspected prenatally based on prenatal cell-free DNA screening — a method to screen for certain chromosomal abnormalities in a developing baby using a blood sample from the mother — or prenatal ultrasound. Prenatal ultrasound of a baby with Turner syndrome may show:

- Large fluid collection on the back of the neck or other abnormal fluid collections (edema)
- Heart abnormalities
- Abnormal kidneys

At birth or during infancy

Signs of Turner syndrome at birth or during infancy may include:

- Wide or weblike neck
- Low-set ears
- Broad chest with widely spaced nipples
- High, narrow roof of the mouth (palate)
- Arms that turn outward at the elbows
- Fingernails and toenails that are narrow and turned upward
- Swelling of the hands and feet, especially at birth
- Slightly smaller than average height at birth
- Slowed growth
- Cardiac defects
- Low hairline at the back of the head
- Receding or small lower jaw
- Short fingers and toes

In childhood, teens and adulthood

The most common signs in almost all girls, teenagers and young women with Turner syndrome are short stature and ovarian insufficiency due to ovarian failure that may have occurred by birth or gradually during childhood, the teen years or young adulthood. Signs and symptoms of these include:

- Slowed growth
- No growth spurts at expected times in childhood
- Adult height significantly less than might be expected for a female member of the family
- Failure to begin sexual changes expected during puberty
- Sexual development that "stalls" during teenage years
- Early end to menstrual cycles not due to pregnancy
- For most women with Turner syndrome, inability to conceive a child without fertility treatment.
- Causes

Most people are born with two sex chromosomes. Boys inherit the X chromosome from their mothers and the Y chromosome from their fathers. Girls inherit one X chromosome from each parent. In girls who have Turner syndrome, one copy of the X chromosome is missing, partially missing or altered.

The genetic alterations of Turner syndrome may be one of the following:

- **Monosomy.** The complete absence of an X chromosome generally occurs because of an error in the father's sperm or in the mother's egg. This results in every cell in the body having only one X chromosome.
- **Mosaicism.** In some cases, an error occurs in cell division during early stages of fetal development. This results in some cells in the body having two complete copies of the X chromosome. Other cells have only one copy of the X chromosome.
- **X chromosome abnormalities.** Abnormal or missing parts of one of the X chromosomes can occur. Cells have one complete and one altered copy. This error can occur in the sperm or egg with all cells having one complete and one altered copy. Or the error can occur in cell division in early fetal development so that only some cells contain the abnormal or missing parts of one of the X chromosomes (mosaicism).

- **Y chromosome material.** In a small percentage of Turner syndrome cases, some cells have one copy of the X chromosome and other cells have one copy of the X chromosome and some Y chromosome material. These individuals develop biologically as female, but the presence of Y chromosome material increases the risk of developing a type of cancer called gonadoblastoma.

Effect of the chromosomal errors

The missing or altered X chromosome of Turner syndrome causes errors during fetal development and other developmental problems after birth — for example, short stature, ovarian insufficiency and heart defects. Physical characteristics and health complications that arise from the chromosomal error vary greatly.

Risk factors

The loss or alteration of the X chromosome occurs randomly. Sometimes, it's because of a problem with the sperm or the egg, and other times, the loss or alteration of the X chromosome happens early in fetal development.

Family history doesn't seem to be a risk factor, so it's unlikely that parents of one child with Turner syndrome will have another child with the disorder.

Complications

Turner syndrome can affect the proper development of several body systems, but varies greatly among individuals with the syndrome. Complications that can occur include:

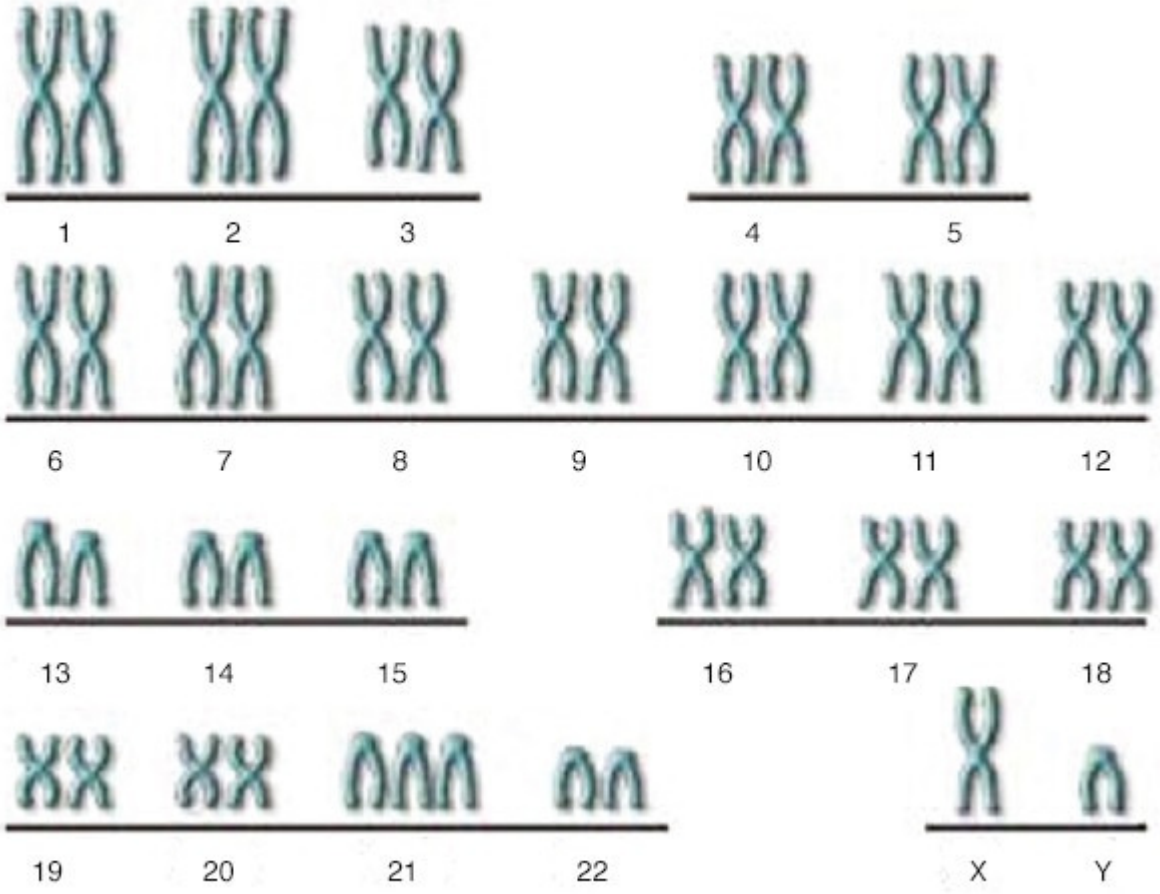
- **Heart problems.** Many infants with Turner syndrome are born with heart defects or even slight abnormalities in heart structure that increase their risk of serious complications. Heart defects often include problems with the aorta, the large blood vessel that branches off the heart and delivers oxygen-rich blood to the body.

- **High blood pressure.** Women with Turner syndrome have an increased risk of high blood pressure — a condition that increases the risk of developing diseases of the heart and blood vessels.
- **Hearing loss.** Hearing loss is common with Turner syndrome. In some cases, this is due to the gradual loss of nerve function. An increased risk of frequent middle ear infections can also result in hearing loss.
- **Vision problems.** Girls with Turner syndrome have an increased risk of weak muscle control of eye movements (strabismus), nearsightedness and other vision problems.
- **Kidney problems.** Girls with Turner syndrome may have some malformation of the kidneys. Although these abnormalities generally don't cause medical problems, they may increase the risk of high blood pressure and urinary tract infections.
- **Autoimmune disorders.** Girls and women with Turner syndrome have an increased risk of an underactive thyroid (hypothyroidism) due to the autoimmune disorder Hashimoto's thyroiditis. They also have an increased risk of diabetes. Some women with Turner syndrome have gluten intolerance (celiac disease) or inflammatory bowel disease.
- **Skeletal problems.** Problems with the growth and development of bones increase the risk of abnormal curvature of the spine (scoliosis) and forward rounding of the upper back (kyphosis). Women with Turner syndrome are also at increased risk of developing weak, brittle bones (osteoporosis).
- **Learning disabilities.** Girls and women with Turner syndrome usually have normal intelligence. However, there is increased risk of learning disabilities, particularly with learning that involves spatial concepts, math, memory and attention.
- **Mental health issues.** Girls and women with Turner syndrome may have difficulties functioning well in social situations and have an increased risk of attention-deficit/hyperactivity disorder (ADHD).
- **Infertility.** Most women with Turner syndrome are infertile. However, a very small number of women may become pregnant spontaneously, and some can become pregnant with fertility treatment.

- **Pregnancy complications.** Because women with Turner syndrome are at increased risk of complications during pregnancy, such as high blood pressure and aortic dissection, they should be evaluated by a cardiologist before pregnancy.

Down syndrome:

Overview



The genetic basis of Down syndrome

Down syndrome is a genetic disorder caused when abnormal cell division results in an extra full or partial copy of chromosome 21. This extra genetic material causes the developmental changes and physical features of Down syndrome.

Down syndrome varies in severity among individuals, causing lifelong intellectual disability and developmental delays. It's the most common genetic chromosomal disorder and cause of learning disabilities in children. It also commonly causes other medical abnormalities, including heart and gastrointestinal disorders.

Better understanding of Down syndrome and early interventions can greatly increase the quality of life for children and adults with this disorder and help them live fulfilling lives.

Symptoms

Each person with Down syndrome is an individual — intellectual and developmental problems may be mild, moderate or severe. Some people are healthy while others have significant health problems such as serious heart defects.

Children and adults with Down syndrome have distinct facial features. Though not all people with Down syndrome have the same features, some of the more common features include:

- Flattened face
- Small head
- Short neck
- Protruding tongue
- Upward slanting eye lids (palpebral fissures)
- Unusually shaped or small ears
- Poor muscle tone

- Broad, short hands with a single crease in the palm
- Relatively short fingers and small hands and feet
- Excessive flexibility
- Tiny white spots on the colored part (iris) of the eye called Brushfield's spots
- Short height

Infants with Down syndrome may be average size, but typically they grow slowly and remain shorter than other children the same age.

Intellectual disabilities

Most children with Down syndrome have mild to moderate cognitive impairment. Language is delayed, and both short and long-term memory is affected.

Causes

Human cells normally contain 23 pairs of chromosomes. One chromosome in each pair comes from your father, the other from your mother.

Down syndrome results when abnormal cell division involving chromosome 21 occurs. These cell division abnormalities result in an extra partial or full chromosome 21. This extra genetic material is responsible for the characteristic features and developmental problems of Down syndrome. Any one of three genetic variations can cause Down syndrome:

- **Trisomy 21.** About 95 percent of the time, Down syndrome is caused by trisomy 21 — the person has three copies of chromosome 21, instead of the usual two copies, in all cells. This is caused by abnormal cell division during the development of the sperm cell or the egg cell.
- **Mosaic Down syndrome.** In this rare form of Down syndrome, a person has only some cells with an extra copy of chromosome 21. This mosaic of normal and abnormal cells is caused by abnormal cell division after fertilization.

- **Translocation Down syndrome.** Down syndrome can also occur when a portion of chromosome 21 becomes attached (translocated) onto another chromosome, before or at conception. These children have the usual two copies of chromosome 21, but they also have additional genetic material from chromosome 21 attached to another chromosome.
- There are no known behavioral or environmental factors that cause Down syndrome.

Is it inherited?

Most of the time, Down syndrome isn't inherited. It's caused by a mistake in cell division during early development of the fetus.

Translocation Down syndrome can be passed from parent to child. However, only about 3 to 4 percent of children with Down syndrome have translocation and only some of them inherited it from one of their parents.

When balanced translocations are inherited, the mother or father has some rearranged genetic material from chromosome 21 on another chromosome, but no extra genetic material. This means he or she has no signs or symptoms of Down syndrome, but can pass an unbalanced translocation on to children, causing Down syndrome in the children.

Risk factors

Some parents have a greater risk of having a baby with Down syndrome. Risk factors include:

- **Advancing maternal age.** A woman's chances of giving birth to a child with Down syndrome increase with age because older eggs have a greater risk of improper chromosome division. A woman's risk of conceiving a child with Down syndrome increases after 35 years of age. However, most children with Down syndrome are born to women under age 35 because younger women have far more babies.
- **Being carriers of the genetic translocation for Down syndrome.** Both men and women can pass the genetic translocation for Down syndrome on to their children.

- **Having had one child with Down syndrome.** Parents who have one child with Down syndrome and parents who have a translocation themselves are at an increased risk of having another child with Down syndrome. A genetic counselor can help parents assess the risk of having a second child with Down syndrome.
- Complications

- People with Down syndrome can have a variety of complications, some of which become more prominent as they get older. These complications can include:

- **Heart defects.** About half the children with Down syndrome are born with some type of congenital heart defect. These heart problems can be life-threatening and may require surgery in early infancy.
- **Gastrointestinal (GI) defects.** GI abnormalities occur in some children with Down syndrome and may include abnormalities of the intestines, esophagus, trachea and anus. The risk of developing digestive problems, such as GI blockage, heartburn (gastroesophageal reflux) or celiac disease, may be increased.
- **Immune disorders.** Because of abnormalities in their immune systems, people with Down syndrome are at increased risk of developing autoimmune disorders, some forms of cancer, and infectious diseases, such as pneumonia.
- **Sleep apnea.** Because of soft tissue and skeletal changes that lead to the obstruction of their airways, children and adults with Down syndrome are at greater risk of obstructive sleep apnea.
- **Obesity.** People with Down syndrome have a greater tendency to be obese compared with the general population.
- **Spinal problems.** Some people with Down syndrome may have a misalignment of the top two vertebrae in the neck (atlantoaxial instability). This condition puts them at risk of serious injury to the spinal cord from overextension of the neck.
- **Leukemia.** Young children with Down syndrome have an increased risk of leukemia.

- **Dementia.** People with Down syndrome have a greatly increased risk of dementia — signs and symptoms may begin around age 50. Having Down syndrome also increases the risk of developing Alzheimer's disease.
- **Other problems.** Down syndrome may also be associated with other health conditions, including endocrine problems, dental problems, seizures, ear infections, and hearing and vision problems.

Questions:

Long answer questions:

1. Explain about centromeres and telomeres.
2. Packaging of DNA molecules into chromosome
3. Concept of Euchromatin and heterochromatin.
4. Chromosome banding.
5. Giant and lumpbrush chromosome.
6. Variation in chromosome structure.
7. Genetic disorders.

Short answer questions:

1. Centromeres
2. Euchromatin
3. Polytene chromosome
4. Inversion of chromosome
5. Down syndrome.

KARPAGAM ACADEMY OF HIGHER EDUCATION

CLASS: III M. Sc MICROBIOLOGY **COURSE NAME: INHERITANCE BIOLOGY**

COURSE CODE: 17MBU504B **BATCH-2017-2020**

UNIT: 5

Sno	Question	Opt 1	Opt 2	Opt 3	Opt 4	Answer
1	Chromosomes are made from protein and what other molecule?	ammonia	ATP	Carbon dioxide	DNA	DNA
2	Chromosomes are found inside what structure in the cell?	Membrane	Mitochondria	Nucleus	Centromere	Nucleus
3	How many pairs of chromosomes are in a human being?	26	44	89	54	26
4	What form does the chromosome take when the cell is not dividing? What form does the chromosome take when the cell is not dividing?	Wound up in tubes	Long and thin strand	Tubes shaped like an X	All of the above	Long and thin strand
5	When a cell is getting ready to divide, what are the longer arms of the chromosome called?	p arms	l arms	c arms	q arms	p arms
6	What is the centromere of a chromosome?	The part of the cell where the chromosome is located	The longest arm of the chromosome	The point where the tubes are pinched together before the split	All of the above	The point where the tubes are pinched together before the split
7	Which of the following is considered the basic unit of heredity?	Traits	Chromosomes	Genes	Lipids	Genes
8	What is the name for the sequence of a gene that determines a specific trait like brown eyes?	Allele	DNA	Centromere	RNA	Allele
9	What does the X/Y pair of chromosomes determine in humans?	What color of hair you have	How tall you will be	Whether you are a boy or a girl	What color of eyes you have	Whether you are a boy or a girl
10	The DNA threads which appear inside the nucleus at the time of	Spindle fibers	Centrioles	Asters	Chromosomes	Chromosomes

	cell division					
11	Which of the following is not a major class of chromatin proteins?	Histones	Topoisomerases	SMC proteins	Cohesins	Cohesins
12	Which of the following plays a substantial role in linking together sister chromatids immediately after replication?	Cohesins	Condensins	Histones	Topoisomerase	Cohesins
13	Which of the following are essential to the condensation of chromosomes as cells enter mitosis?	Cohesins	Condensins	Histones	Topoisomerases	Condensins
14	Chromatin is composed of	DNA	DNA and proteins	DNA, RNA and proteins	None	DNA, RNA and proteins
15	Which of the following histones bind to linker DNA?	H1	H2A	H2B	H3	H1
16	Which of the following has beads on a string structure?	Chromosomes	Chromatin	Nucleosomes	Heterochromatin	Nucleosomes
17	Which of the following histones shows more sequence similarity among eukaryotic species?	H1	H2A	H2B	H3	H4
18	The sister chromatids separate at	Prophase	Metaphase	Telophase	Anaphase	Anaphase
19	Cellular DNA is uncondensed throughout	Prophase	Interphase	Telophase	Anaphase	Interphase
20	Proteins responsible for compact packing and winding of chromosomal DNA are	histones	nonhistones	trypsin	Serein	histones
21	When DNA helix has normal number of base pairs per helical turn than it is in	coiled state	supercoiled state	normal state	elongated state	normal state
22	Tightly packed form of DNA is called	supercoiling	compressed state	Euchromatin	heterochromatin	heterochromatin

23	Changing twist from relaxed state requires adding energy and increases the	stress along the molecule	strain over the molecule	forces in the molecule	Collusion between the molecules	stress along the molecule
23	Changing twist from relaxed state requires adding energy and increases the	stress along the molecule	strain over the molecule	forces in the molecule	Collusion between the molecules	stress along the molecule
24	Chromosomal elements: The most precise modern definition of a gene is a segment of genetic material that:	codes for one polypeptide	codes for one polypeptide or RNA product	determines one phenotype	determines one trait	codes for one polypeptide or RNA product
25	Chromosomal elements: The DNA in a bacterial (prokaryotic	a single circular double-helical molecule	a single linear double-helical molecule	a single linear single-stranded molecule	multiple linear double-helical molecules	a single circular double-helical molecule
26	Chromosomal elements: Bacterial plasmids:	are always covalently joined to the bacterial chromosome	are composed of RNA	are never circular	are circular	are circular
27	Chromosomal elements: The DNA in a eukaryotic chromosome is best described as:	a single circular double-helical molecule	a single linear double-helical molecule	a single linear single-stranded molecule	multiple linear double-helical molecules	a single linear double-helical molecule
28	Chromosomal elements: Introns	encode unusual amino acids in proteins	are frequently present in prokaryotic genes but are rare in eukaryotic genes	are translated but not transcribed	are translated but not transcribed	are translated but not transcribed
29	Chromosomal elements: The chromosomal region that is the point of attachment of the mitotic spindle is the:	centromere	endomere	exon	intron	centromere
30	Exchange of paternal and maternal chromosome material	Crossing over	Bivalent formation	Dyad formation	Synapsis	Crossing over

	during cell division is					
31	DNA supercoiling: DNA in a closed-circular, double-stranded molecule with no net bending of the DNA axis on itself is:	a left-handed helix	a mixed right- and left-handed helix	relaxed	supercoiled	relaxed
32	DNA supercoiling: The linking number (Lk	breaking a strand, then rejoining it	breaking a strand, unwinding or rewinding the DNA, then rejoining it	breaking all hydrogen bonds in the DNA	supercoiling without the breaking of any phosphodiester bonds	breaking a strand, unwinding or rewinding the DNA, then rejoining it
33	DNA supercoiling: Topoisomerases can:	change the linking number (Lk) of a DNA molecule	change the number of base pairs in a DNA molecule	change the number of nucleotides in a DNA molecule	convert D isomers of nucleotides to L isomers	change the linking number (Lk) of a DNA molecule
34	The structure of chromosomes: Histones are _____ that are usually associated with _____	acidic proteins; DNA	acidic proteins; RNA	basic proteins; DNA	basic proteins; RNA	basic proteins; DNA
35	The structure of chromosomes: The fundamental repeating unit of organization in a eukaryotic chromosome is	the centrosome	the lysosome	the microsome	the nucleosome	the nucleosome
36	The structure of chromosomes: Nucleosomes:	are important features of chromosome organization in eukaryotes and bacteria	are composed of proteins rich in acidic amino acids, such as Asp and Glu	are composed of protein and RNA	bind DNA and alter its supercoiling	bind DNA and alter its supercoiling
37	The structure of chromosomes: Bacterial chromosomes:	are highly compacted into structures called	are seen in electron microscopy as “beads on a string”	are surrounded by a nuclear membrane	contain large numbers of nucleosomes	are highly compacted into structures called

		nucleoids				nucleoids
38	Heterochromatin is usually localized to periphery of the	cell membrane	cytoplasm	nucleus	cell wall	nucleus
39	Type of chromatin that participates in active transcription of DNA to mRNA products is	heterochromatin	Euchromatin	Centromere	Acrocentric chromosomes	Euchromatin
40	Percentage of human genome to be euchromatic is	0.72	0.52	0.92	0.5	0.92
41	A type of heterochromatin that is usually repetitive and forms structural functions such as centromeres or telomeres is	constitutive heterochromatin	facultative heterochromatin	both A and B	none of above	constitutive heterochromatin
42	Anti-codon describes triplet bases on	mRNA	rRNA	tRNA	DNA	tRNA
43	A series of compounds that transfer electrons from an electron donor to an electron acceptor which than transfers protons across a membrane is called	electron transport chain	proton transport chain	neutron transport chain	Exchange of protons	electron transport chain
44	During mitosis, spindle fibers attach to centromere via	kinetochore	spindle	microtubule	Chromosomes	kinetochore
45	Tendency of alleles that are located close together on chromosome to be inherited together during meiosis is	genetic linkage	genetic code	inheritance	gene expression	genetic linkage
46	In allosteric control activator that activates glycogen phosphorylase is	AMP	glucose 6 phosphate	ATP	ADP	AMP
47	5'-ATGC-3' will be complementary to	5'-GCAT-3'	5'-TACG-3'	3'-GCAT-5'	none of above	5'-TACG-3'
48	The likelihood of a child being	the mother's uterus	cells from the	the father's blood	together	the mother's

	born with a major genetic defect, such as mental retardation, can often be detected by sampling:	cells	embryo or fetus	cells		uterus cells
49	Which of the following can be detected now by examining a karyotype?	over 3,000 genetic defects	an unborn child's gender or sex	both of the above	over 2,000 genetic defects	an unborn child's gender or sex
50	If there is a family history of genetic disorders, knowing the gender of an unborn child can be important because:	male children are more likely to have autosomal defects show up in their phenotypes	female children are more likely to have autosomal defects show up in their phenotypes	male children are more likely to have X-linked traits show up in their phenotype	A and C	female children are more likely to have autosomal defects show up in their phenotypes
51	Most genetic disorders are due to:	Gross chromosomal abnormalities such as irregular shapes or numbers of chromosomes	the gender of an individual	neither of the above	Gross chromosomal abnormalities only	neither of the above
52	Which of the following statements is true regarding karyotype analysis?	It is rarely done on the cells of unborn children because it cannot detect most genetic disorders	It is now an important medical tool used in predicting the likelihood that an unborn child will be normal	It is not done any more because human pregnancy has only a small risk of birth defects	cells from the embryo or fetus	It is now an important medical tool used in predicting the likelihood that an unborn child will be normal
53	It is likely that as many as _____ newborn infants inherits a chromosomal abnormality	1 in 5	1 in 57	1 in 118	1 in 10000	1 in 118
54	There are two major categories of inherited chromosomal	mechanical errors during meiosis	mechanical errors during mitosis	mitosis and meiosis	neither of the above	mechanical errors during

	abnormalities: 1					meiosis
55	If a child had a karyotype that had 23 + 23 + 23 chromosomes or 23 + 24, it would be:	within the range of normal	an irregular number of chromosomes	a structural modification in the chromosomes	neither of the above	an irregular number of chromosomes
56	nherited chromosomal abnormalities usually result from	defective sperm or ova	a failure of the mother's uterus and placenta in carrying a fetus to full term	inadequate nutrition and medical care during early infancy	neither of the above	defective sperm or ova
57	When only some of an individual's cells have a chromosomal abnormality, it is referred to as _____	crossing-over	mosaicism	nondisjunction	junction	mosaicism
58	During meiosis I, the number of chromosomes is	Halved	Tripled	Doubled	Quadrupled	Halved
59	During which stage the chromosomes first become visible	Anaphase	Metaphase	Prophase	Telophase	Prophase
60	What are dominant selectable markers?	Drug-resistance genes	Inducing genes	Exogenous genes	Endogenous genes	Drug-resistance genes