COURSE CODE:	ABG 301
COURSE TITLE:	Principles of Genetics
NUMBER OF UNITS:	3 Units
COURSE DURATION:	Three hours per week

COURSE DETAILS:

Course Coordinator:	Dr. Martha N. Bemji
Email:	bemjimn@unaab.edu.ng
Office Location:	Department of Animal Breeding and Genetics
Other Lecturers:	Prof. D.K. Ojo, Dr. C.O. Alake, Dr. M.A. Adeleke

COURSE CONTENT:

History of genetics and livestock domestication, Mendelian genetics, Modifications to Mendelian inheritance/Epistasis, Chromosomes, DNA structure and expression, Pleiotropism, Additive genes, Penetrance and expressivity, Linkage and crossing over, Gene classification, Gene mapping.

COURSE REQUIREMENTS:

This is a compulsory course for all students in the Bachelor of Agriculture programme. In view of this, students are expected to participate in all the lectures and practical and must meet up with a minimum of 75% attendance to qualify for the final examination.

READING LIST:

1. A Student's Guide to Biotechnology: Words and Terms. Greenwood Press, 2002. Dynamic Timeline from Human Genome Project Website.

2. Genetics in Context [timeline]: http://www.esp.org (scroll down and choose Chronology).

3. Griffiths, A.J.F. et al. (2003). An Introduction to Genetic Analysis. 7th Edition. W.H. Freeman and Company, New York. pp 860.

4. Hall, Upper Saddle River, New Jersey 07458.

5. Hartl. D.L. and Jones, E.W. 2005.Genetics: Analysis of genes and genomes, 6th edition, Jones and Bartlett publishers, Inc. Pg. 854.

6. King, R.C. and Stansfield, W.D. 1997. A Dictionary of Genetics. 5th Edition. New York: Oxford University Press.

7. Klug, W.S. and Cummnings, M.R. (2000). Concepts of Genetics. Sixth Edition. Prentice.

8. Klung, W.S. and Cummings, M.R. 2000. Genetics, 6th edition, Prentice Hall, Inc. pg. 816.

9. Microsoft ® Encarta ® 2009. © 1993-2009 Microsoft Corporation. On-line.
10. Peters, J.A. (Ed). 1959. Classic Papers in Genetics. Englewood Cliffs: Prentice-Hall, Inc.

11. Stansfield, W.D. 1986. Schaum's outiline of theory and problems of genetics, 2nd edition, McGraw-Hill Book Company. Pg. 392.

12. Sturtevant, A.H. A History of Genetics: Chronology Appendix

13. Wikipedia, the free Encyclopedia 2005. http://en.wikipedia.org

LECTURE NOTES

Introduction

Genetics could be defined as science of heredity concerned with behaviour of **genes** passed from parents to offspring in the reproductive process. It is a branch of Biology concerned wit heredity and variation. It involves the study of cells, individuals, their offspring and the population within which organisms live.

Gene is the functional unit of heredity. (More recently, it is defined as a segment of linear or non-linear deoxyribonucleic acid (DNA) which encodes a polypeptide or protein).

Breeding deals with application of genetic principles for the improvement of economically important characteristics or traits.

Importance of Genetics
The modern science of genetics influences many aspects of daily life, from the food we eat to how we identify criminals or treat diseases (Encarta, 2006).

1. In **Agriculture**, some food crops (oranges, potatoes, wheat, and rice) have been genetically altered to withstand insect pests, resulting in a higher crop yield. Tomatoes and apples have been modified so that they resist discoloration or bruising.

Genetic makeup of cows has been modified to increase their milk production, and cattle raised for beef have been altered so that they grow faster.

2. In **Law**, genetic technologies have also helped **convict criminals**. DNA recovered from semen, blood, skin cells, or hair found at a crime scene can be analyzed in a laboratory and compared with the DNA of a suspect. An individual's DNA is as unique as a set of fingerprints, and a DNA match can be used in a courtroom as evidence connecting a person to a crime.

3. In **medicine**, scientists can genetically alter bacteria so that they mass-produce specific proteins, such as insulin used by people with diabetes mellitus or human growth hormone used by children who suffer from growth disorders.

Gene therapy is used in treating some devastating conditions, including some forms of cancer and cystic fibrosis. Genetically engineered vaccines are being tested for possible use against HIV.

1. History of Genetics and Livestock Domestication

1.1 History of Genetics

A summary of landmarks in the history of genetics as reported by M.Tevfik Dorak is shown below:

1859: C. Darwin published *The Origin of Species*

Darwin's five theories:

1. The organisms steadily evolve over time (evolution theory).

2. Different kinds of organisms descended from a common ancestor (common descent theory).

3. Species multiply over time (speciation theory)

4. Evolution takes place through the gradual change of populations (gradualism theory).

5. The mechanism of evolution is the competition among vast numbers of unique individuals for limited resources under selective pressures, which leads to differences in survival and reproduction (natural selection theory or survival the fittest).

1865: G. J. Mendel discovered the principles of heredity (particulate inheritance).

Mendel's work showed that:

1. Each parent contributes one factor of each trait shown in offspring.

2. The two members of each pair of factors segregate from each other during gamete formation.

3. Males and females contribute equally to the traits in their offspring.

4. The blending theory of inheritance was not correct.

5. Acquired traits are not inherited.

Mendel had referred to the genes as 'particles of inheritance'.

1866: E.H. Haeckel hypothesized that the nucleus of a cell transmits its hereditary information.

1882: A. Weismann noted the distinction between somatic and germ cells; He used the word ‘mitosis’ to describe cell division when chromosomes were observed by Walther Flemming in the nuclei of dividing salamander cells.

1887: A Weismann postulated the reduction of chromosome number in germ cells.

1892: A. Weismann's book *Das Keimplasma* (*The Germ Plasm*) emphasized meiosis as an exact mechanism of chromosome distribution.

1900: The Dutch botanist Hugo de Vries and two others discovered Mendel's principles; W. Bateson published its translation to English in the following year.

1902: W.S. Sutton and T. Boveri (studying sea urchins) independently proposed the chromosome theory of heredity that:
- Full set of chromosomes are needed for normal development.
- Individual chromosomes carry different hereditary determinants.
- Independent assortment of gene pairs occurs during meiosis.

1905: W. Bateson gave the name ***genetics*** (means 'to generate' in Greek) to this branch of science, and introduced the words ***allele*** (allelomorph), ***heterozygous*** (impure line) and ***homozygous*** (pure line); W. Bateson & R.C. Punnett worked out the principles of multigenic interaction (linkage) and heredity.

1908: G.H. Hardy and W. Weinberg independently formulated the Hardy-Weinberg principle of population genetics that gene and genotype frequencies remain constant from generation to generation in a large randomly mating population where the forces of migration, mutation and genetic drift and absent.

W. Johannsen used the words ***phenotype***, ***genotype*** and ***gene*** for the first time in his studies with beans.

1910: T. H. Morgan discovered the white-eye and its sex-linkage in Drosophila (the beginning of Drosophila genetics). (Received the Nobel prize in 1933);
J. Herrick described sickle cell anaemia.

1911: T.H. Morgan showed the first example of chromosomal linkage in the X chromosome of Drosophila (Nobel prize 1933);
E.B. Wilson showed that the gene for colour-blindness was on the X chromosome (first gene identified on a chromosome).

1912: T.H. Morgan showed that genetic recombination does not take place in males in Drosophila and also discovered the first sex-linked lethal gene (Nobel prize 1933).

1919: A Hungarian engineer, Karl Ereky, coined the term biotechnology (to mean production of beer, cheese, bread, etc with the help of living organisms).

1925: C.B. Bridges proposed the balanced chromosome determination of sex theory (relationship between the autosomes and sex chromosomes).
1941: G.W. Beadle & E.L. Tatum proposed the one gene - one enzyme (polypeptide) concept. (Tatum received the Nobel prize in 1958).

1944: O.T. Avery *et al.* described the DNA as the hereditary material.
1949: L. Pauling showed that a defect in the structure of haemoglobin causes sickle cell anaemia.
1950: E. Chargaff *et al* demonstrated for DNA that the numbers of adenine and thymine groups are always equal, so are the numbers of guanine and cytosine group.
B. McClintock discovered the transposable elements in maize (she received the Nobel prize in 1983).

Early 1950s: R. Franklin and M.H.F. Wilkins at King's College, London showed by X-ray crystallography that DNA exists as two strands wound together in a spiral or helical shape.

1953: On the basis of Chargaff's chemical data (1950; numbers of A and T, and C and G are the same in DNA), and Wilkins and Franklin's already available X-ray diffraction data,

J.D. Watson & F.H.C. Crick described the DNA's double helix structure by inference (They shared the Nobel prize in 1962).

1956: J.H. Tijo & A. Levan showed that diploid chromosome number for humans is 46.
Ochoa's laboratory discovered RNA polymerase and A. Kornberg's group DNA polymerase and synthesized nucleic acids *in vitro* (They received the Nobel prize in 1959)

1957: V.M. Ingram reports the amino acid sequence of HbS;

1959: J. Lejeune *et al.* showed that Down's syndrome is a chromosomal abnormality (trisomy of a small telocentric chromosome) as the first identification of the genetic basis of a disease;
P.A. Jacobs & J.A. Strong identified the chromosomal basis of Klinefelter's syndrome as XXY
1962: W. Arber noticed that E.coli extracts restricted viral replication with some enzymatic activity, hence the name restriction endonucleases. He later shared the 1978 Nobel prize with Smith and Nathan.

1981: Identification of the first cancer causing gene.
DNA analysis is developed for diagnosis of sickle cell trait.
2003: Complete sequence of human Y-chromosome is published (*Nature* 423:825-38)

1.2 Livestock domestication

Domesticated animals are those whose collective behavior, life cycle, or physiology has been altered as a result of their breeding and living conditions being under human control for multiple generations. Humans have brought these populations under their care for a wide range of reasons: for help with various types of work, to produce food or valuable commodities (such as wool, cotton, or silk), and to enjoy as pets (Wikipedia, 2005).

A great difference exists between a tamed animal and a domesticated animal. The term "domesticated" refers to an entire species or variety while the term "tame" can refer to just one individual within a species or variety.

Process of domestication
1. Mutations outside of human control make some members of a species more compatible to human cultivation or companionship.
2. Selective breeding is responsible for many of the collective changes associated with domestication.
. Natural selection probably played a role in the domestication of some species.

These categories are not mutually exclusive and it is likely that mutations, selective breeding, and natural selection have all played some role in the process of domestication throughout history.

It is speculated that a mutation made some wolves less suspicious of humans. This allowed these wolves to start following humans to scavenge for food in their garbage dumps. Presumably, a symbiotic relationship developed between humans and this population of wolves. The wolves benefited from human food scraps, and humans may have found that the wolves could warn them of approaching enemies, help with hunting, carry loads, provide warmth, or supplement their food supply. As this relationship

evolved, humans eventually began to raise the wolves and breed the types of dogs that we have today. Other theorists have pointed out that natural selection rather than a random mutation could also be used to explain this process. Wolves that were more comfortable eating food scraps near human settlements would have had an advantage over other wolves. They would have been more likely to survive and pass on their tolerance of humans to the next generation. Thus the process of domestication would have started naturally before any human intervention or selective breeding was involved.

Criteria for domestication of animals

According to physiologist Jared Diamond, animal species must meet six criteria in order to be considered for domestication:

1. ***Flexible diet***: Creatures that are willing to consume a wide variety of food sources and can live off less cumulative food from the food pyramid are less expensive to keep in captivity. Most carnivores can only be fed meat, which requires the expenditure of many herbivores.
2. ***Reasonably fast growth rate****:* Fast maturity rate compared to the human life span allows breeding intervention and makes the animal useful within an acceptable duration of caretaking. Large animals such as elephants require many years before they reach a useful size.
3. ***Ability to be bred in captivity***: Creatures that are reluctant to breed when kept in captivity do not produce useful offspring, and instead are limited to capture in their wild state. Creatures such as the panda and cheetah are difficult to breed in captivity.
4. ***Pleasant disposition***: Large creatures that are aggressive toward humans are dangerous to keep in captivity. The African buffalo has an unpredictable nature and is highly dangerous to humans.
5. ***Temperament*** which makes it unlikely to panic: A creature with a nervous disposition is difficult to keep in captivity as they will attempt to flee whenever they are startled. The gazelle is very flighty and it has a powerful leap that allows it to escape an enclosed pen.
6. ***Modifiable social hierarchy****:* Social creatures that recognize a hierarchy of dominance can be raised to recognize a human as its leader. A herding instinct aids in domesticating animals: tame one and others will follow, regardless of chiefdom.

Degrees of domestication

1. ***In the Wild***:

Species experience their full life cycles without deliberate human intervention.

2. ***Raised at zoos or botanical gardens****:*

Species are nurtured and sometimes bred under human control, but remain as a group essentially indistinguishable in appearance or behavior from their wild counterparts. (It should be noted that zoos and botanical gardens sometimes exhibit domesticated or feral animals and plants such as camels, dingoes, mustangs, and some orchids).

3. ***Raised commercially***:

Species are ranched or farmed in large numbers for food, commodities, or the pet trade, but as a group they are not substantially altered in appearance or behavior. Examples include the ostrich, deer, alligator, cricket, pearl oyster, and ball python. (These species are sometimes referred to as *partially domesticated*).

4. ***Domesticated***:
Species or varieties are bred and raised under human control for many generations and are substantially altered as a group in appearance or behavior. Examples include dogs, sheep, cattle, chickens, guinea pigs and laboratory mice.

History of domestication
The first domestic animal was probably the dog, possibly as early as 10000 BC in the Natufian culture of the Levant. However there is evidence of an association between humans and wolves going back 150000 years, and also some early evidence of beekeeping (in the form of rock paintings) dates to 13,000 BC. The next three - the goat, sheep and pig were domesticated around 8000 BC, all in western Asia. However, there is recent archaeological evidence from Cyprus of domestication of a type of cat by perhaps 7500 BC: this might make the cat second. The cow followed around 6000 BC. The horse was first domesticated (probably in northern Russia) around 4000 BC. Local equivalents and smaller species were domesticated from the 2500s BC. The processes of domestication and the distribution of domesticated species were both radically affected by the establishment of regular contact between the Eastern and Western Hemispheres following the voyages of Christopher Columbus. As indicated the Table below, the dates are possibly far from being accurate due to the lack of evidence and proof. It is estimated, however, that animals started to be domesticated approximately 9000 years ago (7000 B.C), and they were first domesticated for milk 2000 years after 5000 B.C.

Approximate dates and locations of first domestication

Species	**Date**	**Location**
Dog	10000 BC to 150000 BC	Asia
Sheep	8000 BC	Middle East
Goat	8000 BC	Middle East
Pig	8000 BC	China
Cow	6000 BC	Middle East
Horse	4000 BC	Ukraine
Donkey	4000 BC	Egypt
Water buffalo	4000 BC	China
Honeybee	4000 BC	Southern Asia
Chicken	3500 BC	Southeast Asia ?
Cat	3500 BC to 7500 BC	Egypt or Cyprus
Llama	3500 BC	Peru
Silkworm	3000 BC	China
Bactrian camel	2500 BC	Central Asia
Dromedary (Arabian camel)	2500 BC	Arabia
Turkey	100	Mexico
Guinea pig	900	Peru
Rabbit	1500	Europe
Fox	1800s	Europe
Mink	1800s	Europe
Hamster	1930s	United States
Deer	1970s	New Zealand

Source: Wikipedia (2005)

Limits of domestication

Domesticated species, when bred for tractability, companionship or ornamentation rather than for survival, can often fall prey to disease: several sub-species of cattle face extinction and many dogs with very respectable pedigrees appear prone to genetic problems. Cattle have given humanity various viral poxes, measles, and tuberculosis; Pigs gave influenza; and horses the rhinoviruses. Humans share over sixty diseases with dogs. Many parasites also have their origins in domestic animals.

2. Simple Mendelian inheritance

Gregor J. Mendel (1865) was the first scientist to discover the principles of heredity and deduce the laws which could explain the process of inheritance.

Mendel's work showed that:

1. There is existence of some factors now called **genes** which are responsible for the inheritance of traits or characteristics.
2. Genes occur in pairs: Alternative phenotypes of a character are determined by different forms of a single type of gene called **alleles**.
3. Each parent contributes one factor of each trait shown in offspring.
4. The two members of each pair of alleles segregate during gamete formation so that each gamete receives one of the alleles.
5. Genes are transmitted unchanged from generation to generation.

2.1 Monohybrid inheritance

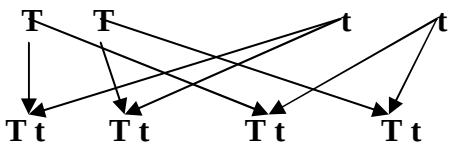
The simplest experiments Mendel performed involved only one pair of contrasting characteristics. In a monohybrid cross, he mated individuals from two parent strains, each of which exhibits one of the two contrasting forms of the character under study. The original parents in the genetic cross are called **P1** or **parental generation** and their offspring are the **F1** or **first filial generation**. If individuals of the F1 generation undergo self-fertilization or selfing (**interse mating**), their offspring are called **F2** or **second filial generation**.

The cross between true breeding pea plants with tall stems and dwarf stems represents Mendel's monohybrid crosses. *Tall* and *dwarf* represent contrasting forms of one character (stem height). When **true breeding** tall plants (**TT**) were crossed with dwarf (**tt**) plants, the resulting F1 generation consisted of only tall plants.

Parental phenotype: Tall Short

Parental genotype (2n): **T T** **X** **t t**

Gametes (n)



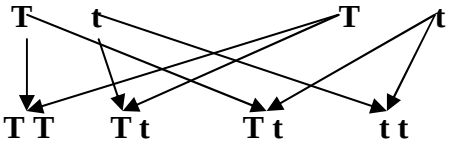
F1 Genotype (2n): **T t** **T t** **T t** **T t**

Phenotype: All Tall

When members of the F1 generation were selfed, Mendel observed that 787 of 1064 F2 plants were tall, while 227 of 1064 were dwarf – a ratio of approximately 2.8:1 or about 3:1. Three-fourths(3/4) appeared like F1 plants while one-fourth (1/4) exhibited the contrasting trait which has disappeared in the F1 generation, only to reappear in the F2.

P2 phenotype: Tall Tall
P2 genotype (2n): **T t** **X** **T t** (*Selfing*)

P2 gametes (n)



F2 Genotype (2n): **T T** **T t** **T t** **t t**

F2 Phenotype: 3 Tall 1 Dwarf (3/4 tall: ¼ dwarf)

(787/1064) (227/1064)

The crosses could be made either ways, that is, pollen from the tall plant pollinating dwarf plants or vice versa. These are called **reciprocal crosses**. To explain these results, Mendel proposed the existence of what he called particulate **unit factors** or genes for each trait which served as the basic unit of heredity and are passed unchanged from generation to generation.

Mendel's first law
It states that two members of a gene pair segregate from each other into the gametes, so that half of the gametes carry one member of the pair and the other half of the gametes carry the other member of the pair.

Modern genetic terminology
Genes are factors responsible for the inheritance of traits or characteristics.
Alleles are different forms of one type of gene, e.g **T** or **t**.
Phenotype of an individual is the physical expression of a trait or outward appearance.
Genotype is the genetic make up of an individual e.g TT, Tt or tt.
Homozygotes or pure lines are individuals having identical alleles (TT or tt).
Heterzygotes or hybrids are individuals with un-identical alleles (Tt).

Summary of seven pairs of contrasting traits and results of Mendel's monohybrid crosses using the garden pea (*Pisum sativum*)

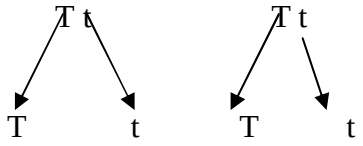
Character	Contrasting trait	F1 results	F2 results	F2 ratio
Stem	Tall/dwarf	All tall	287 Tall 277 Dwarf	2.81:1
Seeds	Round/wrinkled	All round	5474 Round 1850 Wrinkled	2.96:1
	Yellow/green	All yellow	6022 Yellow 2001 green	3.01:1
	Full/constricted	All full	882 Full 299 Constricted	2.95:1
Pods	Green/Yellow	All green	428 Green 152 Yellow	2.82:1
	Axial/Terminal	All Axial	651 Axial 207 Terminal	3.14:1
Flowers	Violet/White	All Violet	705 Violet 224 White	3.15:1

Punnett Square

A convenient method of predicting the relative ratios of the progeny in any cross is by constructing a **Punnett Square** named after R.C. Punnett, who first devised the approached. After the gametes are entered in rows and columns, we can predict the new generation by combining the male and female gametic information for each combination and entering the resulting genotypes in the boxes. This process represents all possible random fertilization events.

F1 cross : **T t** X **T t**
Tall *Tall*

Gametes formation by F1 parents:



Setting up Punnet square:

Male/Female	**T**	**T**
T	**TT** *Tall*	**Tt** *Tall*
T	**Tt** *Tall*	**Tt** *Dwarf*

	Genotype	**Phenotype**
	1 TT	¾ Tall
	2 Tt	
	1 tt	¼ Dwarf
Ratio:	1:2:1	3:1

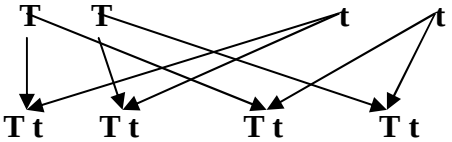
Test Cross: one character

The organism of a dominant phenotype but unknown genotype is crossed to a homozygous recessive individual (tester). Consider a test cross illustrated with a single character in the following cases:

1. *If the tall parent is homozygous,*

Parental phenotype: Homozygous tall Homozygous dwarf
Parental genotype (2n): **T T** **X** **t t**

Gametes (n)



F1 Genotype (2n): **T t** **T t** **T t** **T t**

Resulting phenotype: **All Tall**

2. *If the tall parent is heterozygous,*

***Assignment:** Similarly draw the crosses and clearly show the resulting phenotype if the tall parent is heterozygous.

Dominance-recessive
It is a result of interaction between alleles at a singe locus in which one allele completely suppresses or covers the expression of the alternative allele which is said to be **recessive**. **Dominance** is said to be complete when both the heterozygotes and dominant homozygotes cannot be distinguished phenotypically. That is, they have the same phenotypic value. E.g. Among breeds of poultry used for meat production, the gene for white skin (**WW**) is dominant to that for yellow skin (**ww**). F1 progeny have white skin but heterozygotes. *(Assignment: *Draw the crosses*).

2.2 Dihybrid inheritance

A dihybrid inheritance involves inheritance of 2 pairs of contrasting characteristics. It can be considered theoretically as consisting of 2 monohybrid crosses conducted separately.
E.g. Crosses between plants that are different with respect to 2 separate characters (pea shape and cotyledon colour). Pure breeding (dominant) homozygous plants having round and yellow peas (**RRYY**) were crossed with pure breeding recessive plants having wrinkled and green peas (**rryy**) to produce F1 generation seeds that were round and yellow (**RrYy**).

Round (**R**) is dominant to wrinkle (**r**), and
Yellow (**Y**) is dominant to green (**y**)

Parental phenotypes: Round-yellow X wrinkled-green
Parental genotypes (2n): **RRYY** X **rryy**
Gametes (n): **RY** **ry**
F1 Genotype (2n): **RrYy** (*Round-yellow*)

F1 heterozygote plants were self pollinated to produce F2 generation from four kinds of gametes.

F1 cross: **RrYy** X **RrYy**

Gametes (n) **RY** **Ry** **rY** **ry**

	R	r
Y	**RY**	**rY**
y	**Ry**	***ry***

Note: Segregation of alleles (**R, r, Y, y**) and their independent assortment (recombination) result to RY, Ry, rY and ry which are four possible arrangements of alleles in each of the male and female gametes.

Mendel's second law (Law of independent assortment)
The law states that gene pairs assort independently during gamete formation.

Male/Female	Sperms				
Eggs		RY	Ry	rY	ry
	RY	**RRYY** *Round-yellow*	**RRYy** *Round-yellow*	**RrYY** *Round-yellow*	**RrYy** *Round-yellow*
	Ry	**RRYy** *Round-yellow*	**RRyy** *Round-green*	**RrYy** *Round-yellow*	**Rryy** *Round-green*

	rY	**RrYY** *Round-yellow*	**RrYy** *Round-yellow*	**rrYY** *wrinkled-yellow*	**rrYy** *wrinkled-yellow*
	ry	**RrYy** *Round-yellow*	**Rryy** *Round-green*	**rrYy** *wrinkled-yellow*	**rryy** *Wrinkled-green*

F2 ratios:

Genotypic	**Phenotypic ratios**	**Actual plant counts**	**Ratios**
1/16 RRYY 2/16 RRYy 2/16 RrYY 4/16 RrYy	**16** Round-yellow (**R- Y-**)	315	9
1/16 RRyy 2/16 Rryy	**3/16** Round-green (**R- yy**)	108	3
1/16 rrYY 2/16 rrYy	**3/16** Wrinkled-yellow (**rr Y-**)	101	3
1/16 rryy	**1/16** wrinkled-green (**rryy**)	32	1

The proportion of each phenotype in the F2 generation approximated to a ratio of **9:3:3:1**, known as the **dihybrid ratio**. This applies to characteristics controlled by genes on different chromosomes, with alleles showing complete dominance in their interaction.

Law of product probability

It states that "If two events are independent, the probability that both events will occur simultaneously is the product of their separate probabilities".

The dihybrid ratio is also obtained by multiplying the expected monohybrid ratios for two gene pairs considered separately.

Ratios		**3**		**1**
	X	¼ RR	½ Rr	¼ rr
3	¼ YY ½ Yy	**9/16 R-Y-**		**3/16 rrY-**
1	¼ yy	**3/16 R-yy**		**1/16 rryy**

Summary:

No. of genes (**n**)	Gametes (**2^n**)	F2 genotypic ratio (**3^n**)	F2 phenotypic ratio **$(3:1)^n$**
1	$2^1 = 2$	1:2:1	$(3:1)^1 = 3:1$
2	$2^2 = 4$	1:2:2:4:1:2:1:2:1	$(3:1)^2 = 9:3:3:1$
3			

Example 2: In cattle, pollness (**P**) is dominant to horned (**p**), and black (**B**) is dominant to red (**b**). When homozygous polled-black bull (**PPBB**) is mated to homozygous horned-red

(**ppbb**) cow, the first filial generation was polled-black with genotype **PpBb** under complete dominance. The F2 generation was produced by mating the F1 generation among themselves (**interse** mating). 16 individuals in the F2 contained 9 different genotypes and 4 different phenotypes of ratio 9 polled-black: 3 polled-red: 3 horned-black: 1 horned-red.

*__Draw these crosses with the aid of a Punnet square__.

What is the probability that F2 genotype will be: (i) **PpBb** (ii) **P-bb** (iii) **ppB- ?**

Test cross: Two characters

It applies to individuals that express two dominant traits, but whose genotypes are unknown. E.g. The expression of a round-yellow phenotype may result from **RRYY, RRYy, RrYY or RrYy** genotypes. If an F2 round-yellow plant is crossed with a recessive wrinkled-green **(rryy)** plant which is the **tester,** analysis of the offspring will indicate the exact genotype of the round-yellow plant.

1. Test cross results of **RRYy** will be as follows:

F2 Parental phenotypes: Round-yellow Wrinkled-green

Genotypes (2n): **RRYy** X **rryy**

Gametes (n):

	R
Y	RY
y	Ry

ry

Offspring genotype:

	RY	**Ry**
ry	RrYy	Rryy

Phenotypic ratio: ½ **Round-yellow:** ½ **Round-green**

__*Assignment__

2. Similarly draw the test cross results of RRYY, RrYY and RrYy.

3. Modifications to mendelian inheritance

3.1 Incomplete dominance

The inheritance of a dominant and a recessive allele results in a blending of traits to produce intermediate characteristics, so that heterozygotes can be distinguished phenotypically from the dominant homozygotes. There are two types:

i. __Co-dominance__:

The phenotypic expression of the heterozygote is intermediate between the two homozygotes. For example, **in plants**: four-o'clock paint plants may have red, white, or pink flowers. Plants with red flowers have two copies of the dominant allele *R* for red flower color (*RR*). Plants with white flowers have two copies of the recessive allele *r* for white flower color (*rr*). Pink flowers result in plants with one copy of each allele (*Rr*), with each allele contributing to a blending of colors. *(*Draw the crosses*).

In poultry, blue Andalusian fowls results when pure breeding black (**BB**) and splashed white (**B^WB^W**) parental stock are crossed. All F1 heterozygotes (**BB^W**) are 'blue', while 50% of the F2 offspring have the F1 phenotype. *(*Draw the crosses*).

ii. <u>Over-dominance</u>: Phenotypic expression of the heterozygote exceeds that of either homozygotes. Example is found in white Wyandotte breed of poultry. The gene for Rose comb **R**, is dominant to the gene for single comb, **r**. Heterozygous males have normal fertility while homozygous dominant males have lowered fertility.

	RR (Rose comb)	**Rr** (Rose comb)	**rr** (Single comb)
Male:	*Lower fertility	Normal fertility	Normal fertility
Female:	Normal fertility	Normal fertility	Normal fertility

3.2 Multiple alleles

A single characteristic may appear in several different forms controlled by 3 or more alleles of which any two may occupy the same loci on the homologous chromosome. This is known as multiple allele (multiple allelomorph) and control such characteristic such as coat and eye colour in mice, and blood group.

<u>Inheritance of blood groups</u>: Blood group is controlled by an autosomal gene locus I, standing for Isohaemaglutinogen and there are 3 alleles representing the symbols **A, B, O**. A and B are equally dominant and O is recessive to both.

Human blood group genotypes:

<u>Genotypes</u>	<u>Blood group</u>
I^AI^A	A
I^AI^O	A
I^BI^B	B
I^BI^O	B
I^AI^B	AB
I^OI^O	O

Presence of single dominant allele results in the blood producing a substance called agglutinin which acts as an antibody. E.g. ***I^AI^O*** *produces Agglutinin **A**.*

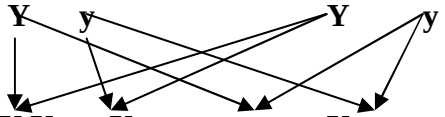
3.3 Lethal genes

A single gene may affect several characteristics including mortality. E.g. In chickens which are homozygous for an allele controlling feather structure called 'frizzled', several phenotypic effects results from the incomplete development of the feathers. These chicken lack adequate feather insulation and suffer from heat loss leading to high mortality rate. The effect of lethal gene is also clearly illustrated by the inheritance of fur, a condition known as agouti. Some mice have yellow fur. Crossbreeding yellow mice produces offspring in the ratio, **2 yellow: 1 agouti** (*Yellow is dominant to agouti and all yellow coat mice are heterozygous*). A ratio of 2:1 instead of the typical Mendelian ratio of 3:1 is explained by the fetal death of the dominant homozygous coat mice.

Let Y represent yellow fur (dominant)
y represents agouti (recessive)

Parental phenotype: Yellow fur Yellow fur
Parental genotype (2n): **Y y** **X** **Y y**

Gametes (n)



F1 Genotype (2n): ***Y Y** **Y y** **Y y** **y y**

Phenotype: **1** : 2 : 1
Yellow fur *Yellow fur* *Agouti*
(*Dies before birth)

*YY is a lethal genotype.

3.4 Gene Linkage

An exception to independent assortment of genes develops when genes appear near one another on the same chromosome. When genes occur on the same chromosome, they are inherited as a single unit and do not assort independently. Genes inherited in this way are said to be linked. For example, in fruit flies the genes affecting eye color and wing length are inherited together because they appear on the same chromosome. In many cases, genes on the same chromosome that are inherited together produce offspring with unexpected allele combinations from a process called crossing over during meiosis.

3.5 Sex-Linked Traits

Genes located on the sex chromosomes display different patterns of inheritance than genes located on other chromosomes. In human females, the sex chromosomes consist of two X chromosomes (**XX**), while males have an X chromosome and a shorter Y chromosome with fewer genes (**XY**). A male's X chromosome may contain a recessive allele associated with a genetic disorder, such as hemophilia or muscular dystrophy. In this case, males do not have a normal second copy of the gene on the Y chromosome to mask the effects of the recessive gene, and disease typically results. Red-green colour blindness in humans and baldness are also sex-linked traits.

3.6 Quantitative Inheritance

Mendel focused his studies on traits determined by a single pair of genes, and the resulting phenotype was easy to distinguish. A tall plant can be markedly different from a short one, and a green pea can easily be distinguished from a yellow one. Traits such as skin color differ from the ones Mendel studied because they are determined by more than one pair of genes. In this form of inheritance, known as quantitative inheritance, each pair of genes has only a slight effect on the trait, while the cumulative effect of all the genes determines the physical characteristics of the trait. At least four pairs of genes control human skin color. Multiple genes also control many traits important in agriculture, such as milk production in cows and ear length in corn.

3.7 Modification of dihybrid ratios (Epistasis)

The Mendelian dihybrid ratio (***9:3:3:1***) could be modified through non-allelic interaction, a phenomenon known as epistasis. Epistasis involves two or more genes which are not alleles. A gene or gene pair at one locus is said to be epistatic to a gene or gene pair at a second locus when the gene product of the first locus suppresses the expression of the second. In other words, an epistatic gene is one that covers up the phenotypic expression of a gene at a different locus. **Epistatic genes are sometimes called 'inhibiting genes'** because of their effect on other genes which are described as **hypostatic** (hypo=under), which cannot express themselves.

Note: Epistasis is analogous (similar) to dominance because in both phenomena, one gene covers the expression of another: at the *same locus in dominance* but at *different loci in epistasis*.

Types of epistasis

1. **Inhibitory or dominant epistasis**

The classical Mendelian phenotypic ratio (9:3:3:1) is modified to **12:3** (2 phenotypic classes). An example of inhibitory or dominant epistasis is found in *feather colour*

inheritance of two populations of poultry breeds. White feathered (I) is dominant to the recessive (i) and Coloured feathered (C) is dominant to the recessive (c).

*Matings between dominant White Leghorn (IICC) and recessive White Wyandotte (iicc) will give an F1 generation of white feathered birds (IiCc).

Parental phenotype: White Leghorn X White Wyandotte
Parental genotype (2n): **IICC** X **iicc**
Gamete (n): **IC** **ic**
F1 genotypes (2n): **IiCc**
Phenotype: All white feathered

Both parents and F1 generation are phenotypically white because the presence of dominant **I-** inhibits the expression of the coloured gene **C**. The dominant coloured gene can only be expressed in the presence of the recessive white gene as illustrated in 3/16 of F2 generation.

F1 phenotypes: All white feathered
F1 Genotypes (2n): **IiCc** X **IiCc**
Gametes (n):

	I	I
C	**IC**	**Ic**
C	**Ic**	**Ic**

Male/Female	Sperms				
Eggs		IC	Ic	iC	ic
	IC	IICC White	IICc White	IiCC White	IiCc White
	Ic	IICc White	IIcc White	IiCc White	Iicc White
	iC	IiCC White	IiCc White	**iiCC** **Coloured**	**iiCc** **Coloured**
	Ic	IiCc White	Iicc White	**iiCc** **Coloured**	iicc White

The resulting phenotypic ratio is 13 white: 3 coloured, instead of the classical 9:3:3:1.

2. **Recessive epistasis**
The modified ratio becomes **9:3:4** phenotypic classes. An example is found in the inheritance of coat colour in mice. The normal wild type coat colour is **agouti**, a grayish pattern formed by alternating bands of pigment on each hair. Agouti is dominant to black (non-agouti).
*A cross between **agouti (AABB)** and **Albino (aabb)** gives F1 which are all **AaBb** with agouti coat colour. F2 genotypes segregate in the same manner as the pea plant.

F2 Genotypic ratio	Phenotype	Final phenotypic ratio
9/16 A-B-	Agouti	9/16 Agouti
3/16 A-bb	Albino	
3/16 aaB-	Black	3/16 Black
1/16 aabb	Albino	4/16 Albino

Note: In the presence of **aa** genotype, all hairs remain black.
In the presence of **bb** genotype, no black pigment is produced and the mouse is albino. Therefore the **bb** genotype mask the expression of the **A** gene.

3. **Complementary epistasis**

The modified ratio becomes **9:7**. An example is found in the inheritance of flower colour in sweet peas. *All F1 heterozygotes from a cross between two strains of white flowered sweet peas are purple while the F2 phenotypes segregate into 9/16 purple: 7/16 white.

F2 Genotypic ratio	Final phenotypic ratio
9/16 P-W-	9/16 Puple
3/16 P-ww **3/16 ppW-** **1/16 ppww**	7/16 White

Note: The presence of at least one dominant allele of each gene pair is essential for the flower to be purple. i.e. Two genes at two loci which are in a dominant condition complement each other to produce a single phenotype. In the absence of either dominant genes, all other genotypes express themselves as one phenotypic class.

4. **Duplicate epistasis**

The expected 9:3:3:1 phenotypic ratio gets modified into two phenotypic classes of **15:1.** Two gene loci in a dominant condition or one gene locus in a dominant condition will give the same phenotypic expression. Such genes are known as **duplicate genes**. An example is found in the inheritance of the shape of seed capsule in Shepherd's purse. The F1 heterozygotes are all triangular in the shape of seed capsule while the F2 phenotypes segregate into 15/16 triangular: 1/16 Ovoid.

F2 Genotypic ratio	Final phenotypic ratio
9/16 T-O- **3/16 T-oo** **3/16 ttO-**	15/16 Triangular
1/16 ttoo	1/16 Ovoid

4.0 Chromosomes

Chromosome is a threadlike structure containing genetic information arranged in a linear sequence. Hence, chromosome serves as a carrier or vehicle for the transmission of genetic information from parents to their offspring. Since chromosomes contain and carry genetic information, the manner in which they are transmitted is exceedingly precise. In higher organisms, each somatic cell contains a set of chromosomes inherited from the maternal parent and a comparable set of chromosomes (homologous chromosomes or homologues) from the paternal parent.

Haploid and diploid cells

Species having 2 sets of chromosomes are referred to as **diploid** (2n). The sex cells or gametes contain half the number of chromosome sets found in somatic cells and are referred to as **haploid** cells (n). A genome is a set of chromosome corresponding to haploid set in a species. The great majority of animal species and about half the plant species are diploid with 2 sets of chromosomes per nucleus or cell. A few simple organisms have only one set or half (n) the number of chromosomes, e.g. gametes, alternation of generation in fern.

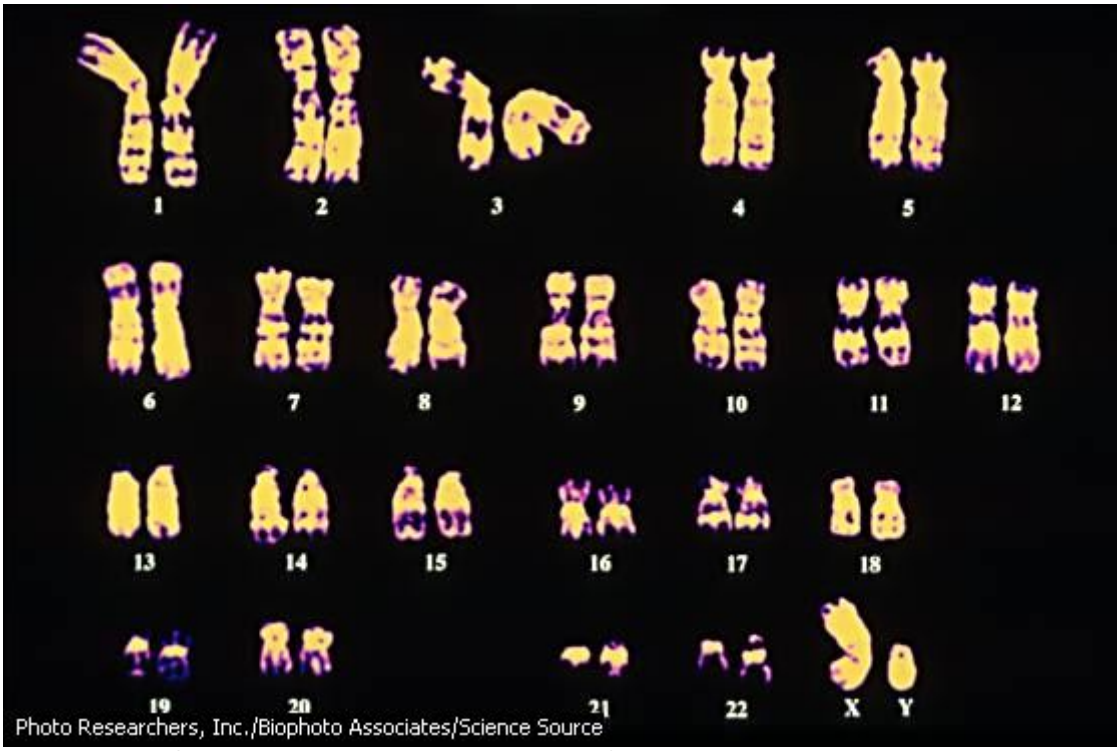
Every species have a characteristic chromosome number as illustrated in Table 1 and Figure 1. For example, haploid cells contain 23 chromosomes in human, 30 in cattle, 39 in chicken, 39 in dog, 6 in house fly, 3 in mosquito, 12 in rice, 21 in wheat e.t.c. Other organisms, especially many plant species, are sometimes characterized by more than two sets of chromosomes and are said to be polyploids. Chromosomal mutations (chromosomal aberrations) is one of the sources of genetic variation and include duplication, deletion or rearrangement of chromosome segments.

Table 1. A karyotype of eight common domestic animals

Common name	**Specific name**	**Haploid No. (n)**	**Diploid No. (2n)**	**No of Metacentrics**	**No of Telocentrics**	**X**	**Y**
Dog	Canis familiaris	39	78	0	38	M	A
Cat	*Felis catus*	19	38	16	2	M	M
Pig	*Sus scrofa*	19	38	12	6	M	M
Goat	*Capra hircus*	30	60	0	29	A	M
Sheep	*Ovis aries*	26	54	3	23	A	M
Cattle	*Bos Taurus*	30	60	0	29	M	M
Horse	*Uquus caballus*	32	64	13	18	M	A
Donkey	*Equus asinus*	31	62	24	6	M	A

Figure 1. Human Male Karyotype

This karyotype of a human male shows the 23 pairs of chromosomes that are typically present in human cells. The chromosome pairs labeled 1 through 22 are called autosomes, and have a similar appearance in males and females. The 23rd pair, shown on the bottom right, represents the sex chromosomes. Females have two identical-looking sex chromosomes that are both labeled X, whereas males have a single X chromosome and a smaller chromosome labeled Y.



Source: Microsoft ® Encarta ® 2006. © 1993-2005 Microsoft Corporation.

Structure of chromosome

The structure of chromosomes becomes visible only when cells are actually dividing during mitosis and meiosis with the aid of microscope. When cells are not dividing, the genetic material making up chromosomes unfolds and uncoils into a diffuse network within the nucleolus. The uncoiled genetic material, collectively, is called chromatin. Each chromosome contains a condensed or constricted region called the centromere, which establishes the general appearance of each chromosome as shown in Figure 2 below.

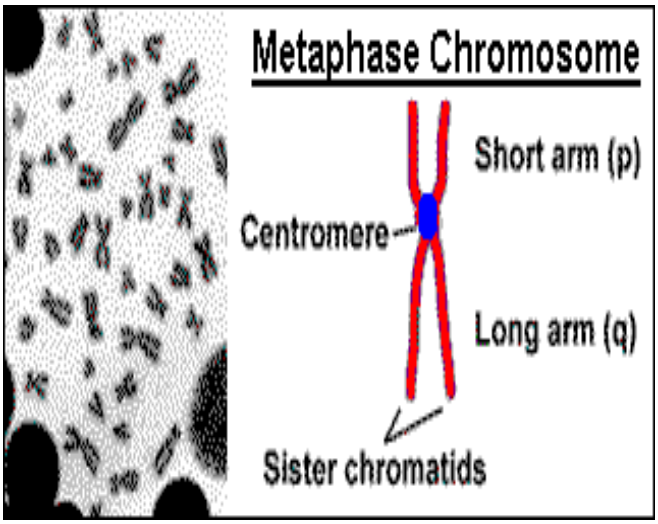


Figure 2. Structure of a chromosome

Each chromosome in the genome can usually be distinguished from all others by several criteria:

1. The relative lengths of chromosome
2. The position of a the centromere
3. The presence and position of enlarged areas called chromomeres
4. The presence of tiny terminal extensions of chromatin material called satellites

A chromosome with a median centromere (metacentric) will have arms approximately equal size. If a chromosome has its centromere between the middle and the end, it is designated as submetacentric, close to the end is called acrocentric and at the end is referred to as telocentric. Extending from either side of the centromere are the arms of the chromosome. Depending on the position of the centromere, different arm rations are produced. By convention, the arm above the centromere is named p arm while the arm below the centromere is labeled q arm. Each chromosome of the genome (with the exception of sex chromosomes) is numbered consecutively according to length, beginning with longest chromosome first (See Figure 3).

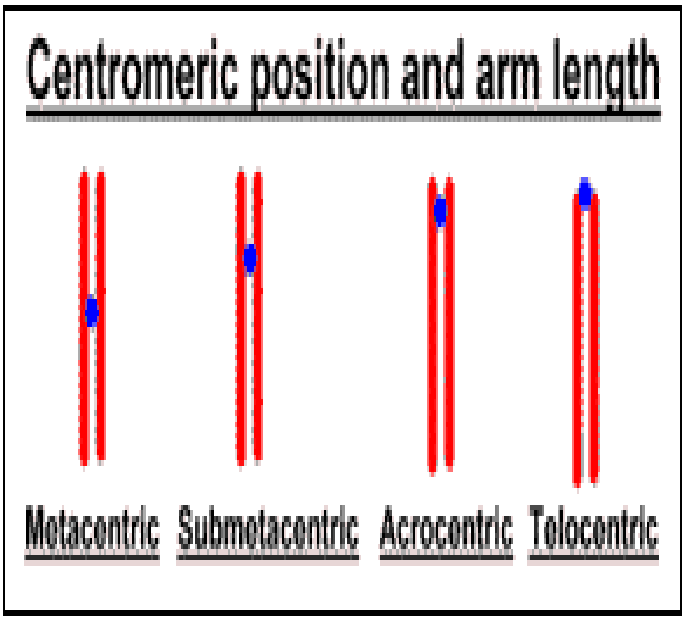


Figure 3. Classification of chromosomes based on the position of centromere

In the males of some species, including humans, sex is associated with a morphologically dissimilar (heteromorphic) pair of chromosomes called sex chromosomes. In many species, one of the pair is often not homologous in size, centromere placement arm ratio or genetic potential. Such a chromosome pair is often labeled X and Y particularly in human. But during meiosis, they behave as homologous though they are not strictly so. Genetic factors on the Y chromosome determine maleness. Females have two morphologically identical X chromosomes. The members of any other homologous pairs of chromosomes are morphologically indistinguishable, usually are visibly different from other pairs (non-homologous chromosomes). Homologous pairs of chromosomes have important genetic similarity. They contain identical gene sites along their lengths, each called a locus.

Therefore, they have identical genetic potential. All chromosomes exclusive of the sex chromosomes are called autosomes.

Self Assessment Exercise

i. *What are chromosomes and where are they found in an organism?*
ii. *How many chromosomes did you receive from your mother?*
iii. *How many autosomes are present in your gamete?*
iv. *How many sex chromosomes are in a man's spermatozoa?*
v. *How many autosomes are in body cells of a woman?*
vi. *If two chromosomes of a species are the same length and have similar centromere placements, yet are not homologous, what is different about them?*
vii. *What is the probability that in human that a sperm will be formed that contains all 23 chromosomes whose centromeres were derived from maternal homologues?*
viii. *How are chromosomes designated on the basis of centromere location?*

5.0 DNA structure and expression

The era of molecular genetics followed the discovery of DNA structure when fundamental unit of heredity was determined to be the DNA nucleotide and the gene was found to consist of an aggregate of nucleotides. The nucleic acid which serves as the carrier of genetic information in all organisms other than some viruses is called deoxyribonucleic acid (DNA). In 1953, James Watson and Francis Crick proposed the first essentially correct three-dimensional structure of the DNA molecule. In the Watson-Crick structure, DNA consists of two long chains of subunits, each twisted around the other to form a double stranded helix. The backbone of the helix is composed of two chains with alternating sugar (S)-phosphate (P) units. The sugar is a pentose (5-carbon) called deoxyribose, differing from its close relative called ribose by one oxygen atom in the 2' position. The phosphate group (PO_4) links adjacent sugars through a 3'-5' phosphodiester linkage; in one chain the linkages are polarized 3'-5', in the other chain they are in the reverse order 5'-3'.

The polarity or directionality is determined by the direction in which the nucleotides are pointing. The trunk end of the strand is called the 3' end of the strand, and the tail end is called the 5' end. In double-stranded DNA, the paired strands are oriented in opposite directions, the 5' end of one strand aligned with the 3' end of the other. The steps in the spiral staircase consist of two paired chemical constituents called bases classified into two groups, the purines and pyrimidines. Purines only pair with pyrimidines and vice versa, thus producing a symmetrical double helix. The base pairs are linked in such a manner that the number of bonds between them is always maximized. Therefore, adenine (A) pairs only with thymine (T) and guanine (G) only with cytosine (C). The pairing between A and T and between G and C is said to be complementary. A base plus its sugar is termed a nucleoside; a nucleoside plus its phosphate is called a nucleotide. Thus, the DNA molecule is a long polymer (i.e. a macromolecule composed of a number of similar or identical subunits, monomers, covalently bonded) of thousands of nucleotide pairs.

The sequence of nucleotides in the DNA determines the bio-chemical characteristics of cells and organisms. Information created out from the complex and diverse DNA codes is protein. Protein is a class of macromolecules that carries out most of the biochemical activities in the cell. Cells are largely made up of proteins. In a region of DNA that directs the synthesis of a protein, the genetic code for the protein is contained in only one strand and it is decoded in a linear order. A typical protein is made up of one or more polypeptide chains. Each polypeptide chain consists of a linear sequence of amino acids connected end to end. There are 20 essential amino acids coded for by only four bases with each word in the genetic code consisting of three adjacent bases called codons or triplets. DNA codes for protein not directly but indirectly through the processes of transcription and translation. The DNA to RNA to Protein is known as the central dogma of molecular genetics as shown in figure 4. The structure of RNA is similar to, but not identical with, that of DNA. There is a difference in sugar (RNA contains the sugar ribose instead of deoxyribose), RNA is usually single-stranded (not double stranded), and RNA contains the base uracil (U) instead of thymine (T), which is present in DNA. There are three types of RNA that are involved in the formation of proteins.

1. Messenger RNA (mRNA): this carries the genetic information from DNA and is used as a template for polypeptide synthesis.

2. Ribosomal RNA (rRNA): these are major constituents of the cellular particles called ribosomes on which polypeptide synthesis takes place.

3. Transfer RNA (tRNA): each of these carries a particular amino acid as well as a three-base recognition region that base-pairs with a group of three adjacent bases in the mRNA.

The characteristic of ‘storage’ may be viewed as genetic information that is present as a repository of all hereditary characteristics of an organism. However, that information may or may not be expressed. It is clear that, whereas most cells contain a complete complement of DNA, at any given point they express only a part of this genetic potential. Inherent in the concept of storage is the need for the genetic material to be able to encode the nearly infinite variety of gene products found among the countless forms of life present on our planet. The chemical language of the genetic material must be capable of this potential task as it stores information and as it is transmitted to progeny cells and organisms.

Expression of the stored information is the basis for the concept of information flow within the cell. The initial step of making an RNA strand from a DNA template is known as transcription, and the RNA molecule that is made is the transcript. Transcription is defined as the production of an RNA that is complementary in base sequence to a DNA strand. The second step is the synthesis of a polypeptide under the direction of an mRNA molecule is known as translation. Although the sequence of bases in the mRNA codes for the sequence of amino acids in a polypeptide, the molecules that actually do the translating are the Trna molecules. The mRNA molecule is translated in nonoverlaping groups of three bases called codons. For each codon in the mRNA that specifies an amino acid, there is one Trna molecule containing a complementary group of three adjacent bases that can pair with the codon. The correct amino acid is attached to one end of the tRNA, and when the tRNA comes into line, the amino acid to which it is attached becomes the most recent addition to the growing end of the polypeptide chain.

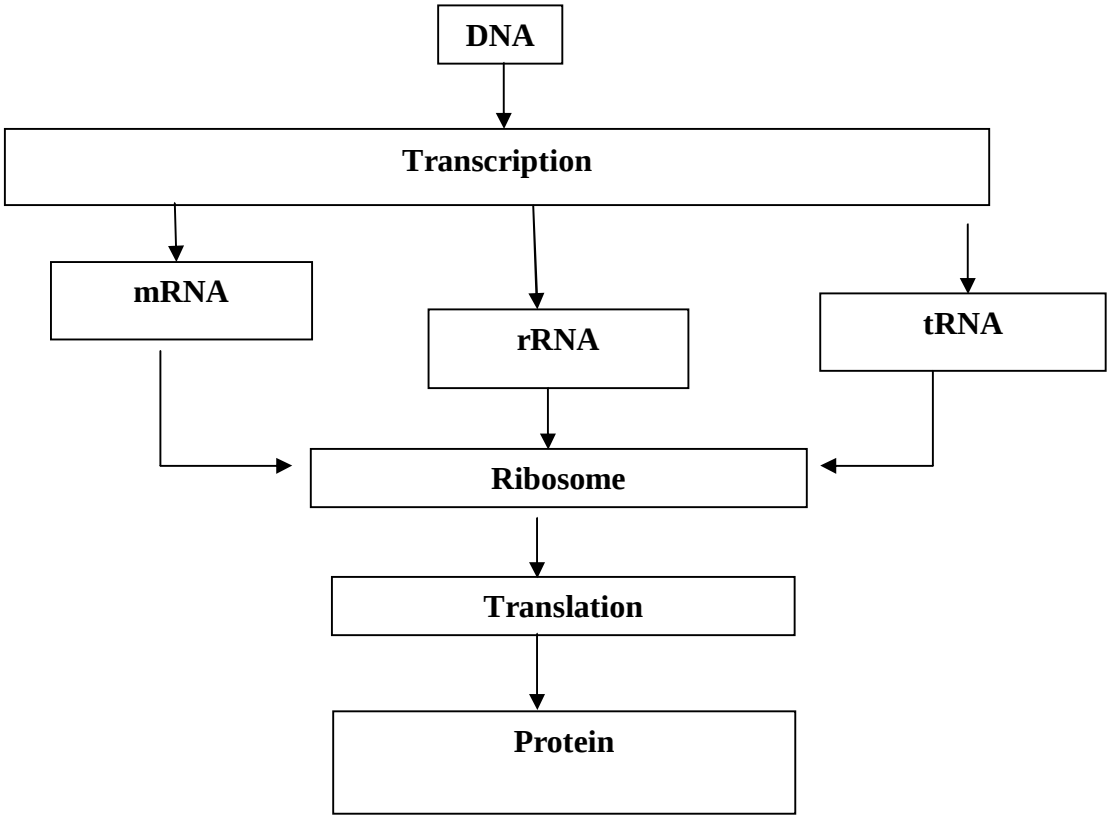


Figure 4. Central dogma of molecular genetics

Self Assessment Exercise

i. *Describe the various characteristics of the Watson-Crick double-helix model for DNA.*
ii. *With the aid of diagram, explain the central dogma of molecular genetics.*
iii. *List three main differences between DNA and RNA.*
iv. *Name the three types of RNA that are involved in protein synthesis and state the role each of the RNA performs.*

6.0 Pleiotopism

Although a change in a single enzyme usually disrupt a single biochemical pathway. If frequently has more than one effect in phenotype. Multiple effects are referred to as pleiotropy. It is the production by one particular mutant gene of apparently unrelated multiple effects at phenotypic level. Sometimes one that trait will be clearly evident (major effect) and other perhaps seemingly unrelated raminification (secondary effect).

In other cases, the number of unrelated changes may be considered as a syndrome. All the manifold phenotypic effect of the single gene is known as pleiotropic gene effects. For example, sickle cell anemia caused by a mutation in the gene for β chain of the haemoglobin molecule. In a homozygote, this mutation causes a sickling of red blood cells. The sickling of these cells has two major raminification. First, the liver destroys the sickle cells, causing anaemia. The phenotype effect of this anaemia includes physical weakness, slow development and hypertrophy of the bone marrow.

The second major effect of sickle cell anemia is that the sickle cells interfere with the capillary blood flow, clumping together and resulting in damage of every major organ. The individual can suffer heart failure, rheumatism and other effects. Hence a single mutation shows itself in many aspects of the phenotype.

7.0 Additive genes

Additive genes are more than one gene that genetically code for the same function. This function will usually have a wide range of possible phenotypes, such as plant yields, plant height, milk yield, egg size etc. because the wide range of genes and possible permutations of genetic coding allows for a wide range of results. The net effect is the sum of their individual allelic effects i.e. they show neither dominance nor epistatis.

Additive genetic variance is the net effect of the expression of additive genes, and thus the chief cause of the resemblance between relatives. It represents the main determinant of the response of a population to selection.

8.0 Penetrance and expressivity

Penetrance: This refers to the appearance in the phenotype of genetically determined traits. Unfortunately for geneticists not all genotypes 'penetrate' the phenotype. For example, a person could have a genotype that specifies vitamin D resistant rickets and yet not have ricket (a bone disease). The disease is caused by a sex linked dominant allele and is distinguished from normal D deficiency by its failure to respond to low level of vitamin D. It does however respond to very high levels of vitamin D and is thus treatable. In any case, in some family trees, affected children are born to unaffected parents. This would violate the rules of dominant inheritance because one of the parents must have had the allele yet did not express it. The fact that the parent actually had the allele is demonstrated by the occurrence of low level of phosphorus in the blood, a pleiotropic effect of the same allele. The low phosphorous aspect of the phenotype is always fully penetrate.

Thus, certain genotypes, often those of development traits are not always fully penetrant. Most genotypes however are fully penetrant. For example, no known cases exist of individuals homozygous for albinism who does not lack pigment i.e. fully penetrant. Vitamin D resistant rickets illustrates another case in which a phenotype that is not genetically determined mimics a phenotype that is. This phenocopy is the result of dietary deficiency or environmental trauma. A dietary deficiency of vitamin D for example produces rickets that is virtually indistinguishable from genetically controlled rickets.

Many development traits not only sometimes fail to penetrate but also show a variable pattern of expression, from very mild to very extreme when they do i.e. slight, intermediate or severe.

Expressivity also depends on the genotype and external environment e.g. in polydactylous individual there may be external toes and no extral or vice-verse.

9.0 Linkage and crossing over

Linkage

The law of independent assortment does not apply to all situations. On a given chromosome, there are set of genes that are physically linked to one another. During reproduction these linked genes tends to be transmitted as a unit instead of independently. This is referred to as linkage and these genes are said to be linked, although they may break during meiosis. Therefore the law of independent assortment does not always hold true. Independent assortment sometimes occur when the genes are located on the chromosome but are relatively far apart from one another making the occurrence of cross over between the two locations likely. Some points to consider are:

(1) The F_2 generation does not fit the predicted ratio of 1:1:1:1 that would be expected for dihybrid test cross. Thus the crossover violate rule of independent assortment
(2) Two phenotypes are in high frequency, have the same phenotypes as the original parents (P_1). These are called non-recombinants or parental
(3) Two phenotypes are in low frequencies and combine the phenotypes of the two original parents. These are called recombinants or non-parentals.

The simplest explanation is that these two loci lie close to each other on the same chromosome. They are linked on the same chromosome.

$$\% \text{ of recombination} = \frac{\text{number of recombinants}}{\text{Number of offspring}} \times 100$$

1% recombination = 1 map unit or centimorgan in honour of T. N Morgan, one of the first person to propose this linkage and first to win a noble price in genetics.
When two genes are linked, the linkage may be of two types in an individual heterozygous for both pairs:
(a) The two dominants may be linked on one member of the chromosome pair with the two recessives on the other. This arrangement is called Coupling or Cis configuration
(b) The dominant of one pair and the recessive of the other pair may be located on one chromosome of the pair, with the recessive of the first gene pair and the dominant of the second gene pair on the other chromosome. This arrangement is called Repulsion or Trans configuration.

Mechanism for recombinant gametes

Recombinant gametes which eventually form recombinant offsring result from crossing over in prophase 1. In zygotene, bivalents are formed via synaptomenal complex and the homologues are paired with one another called synapsis and the point of genetic exchange called chiasmata. By pachytene we can see the tetrads, and by diplootene, we can see the chiasmata where crossing over occurs.

Crossing over

During the entire prophase, crossing over takes place. When two chromatids came to lie in close proximity enzymes can break both chromatids strands and reattach them differently. Thus, although genes have a fixed position on a chromosome, alleles that stated out affected to a paternal centromere can end up attached to a maternal centromere. Crossing over can greatly increase the genetic variability in genetics by associating alleles that were not previously joined. Before crossing over takes place, densely staining nodules are visible. First, in the zygonema and lasting through pochynema. These are called

recombination nodules; they are correlated with crossing over and presumably represent the enzymatic machinery present on the chromosomes.

As the chromosome shorten and thicken further in diplonema, each anomose can be seen to be made of two sister chromatids. At about this time, the synaptonenial complex disintegrate in all but the area of chiasma (singular chiasmata), the X-shaped configuration marking the places of crossing over. Virtually all tetrads exhibit chiasmata, in cases in which no crossing over occurs, the tetrad tends to fall apart and segregate randomly. Thus, crossing over of only increase genetic diversity but also ensures the proper separation of homologous chromosomes. A meiosis-specific form of cohesion keeps sister chromatids together.

During the diplotene stage, chromosomes can again uncondense and become active. This is especially obvious in amphibians and birds, which produce a great amount of cytoplasmic nutrient for the future zygote. Recombination of the chromosomes takes place at the end of diplonema. When crossing over, we make the following three assumptions:

(1) It leads to recombination of linked genes in reproduction, which can be seen in the results of the crosses
(2) It takes place after chromosome have replicated (in the four strand stage). Each cross over event involve only two of the four chromatids
(3) It is a process that involves exchange of part of homologous chromosomes.

Chiasma frequency
A pair of synapsed chromosomes (bivalent) consists of four chromatids called a Tetrad. Every tetrad usually experiences at least one chiasma somewhere along its length. Generally speaking, the longer the chromosome the greater the length of chiasmata. The further apart two genes are located on the chromosome, the greater the opportunity of a chiasma to occur between them. The closer two genes are linked, the smaller the chance for a chiamata occurring between them. The percentage of crossover (recombinant gamete) formed by a given genotype is a direct refection of the frequency with which a chiasma form between the genes in question. Only when a crossover form between the gene loci under consideration will recombinants be detected. When a chiasma form between two gene loci, only half of the meiotic product will be of crossover type.
Note: Absolute linkage occur when chiasma is not formed between two gene loci while close or tight linkage occurs when two gene loci give very few recombinants. Therefore, chiasma frequency is twice the frequency of cross over product.

Chiasma % = 2(crossover %)

Crossover % = ½ (chiasma %)

10.0 Gene mapping

Linkage deals with the association of genes to each other and to specific chromosomes. Mapping deals with the sequence of genes on a chromosome and the distances between genes on the same chromosome. This is the basic information for a study of the structure and function of genes. In genetic mapping, there are two major aspects:
1. The determination of a linear order with which the genetic units are arranged with respect to one another i.e. the gene order.

2. The determination of a relative distances between the genetic units i.e. the gene distance. One unit of map distance is equivalent to 1% cross over e.g. If the genotype Ab/aB produces 8% each of a cross over gametes (AB and ab). Then the distance between A and B is estimated to be 16 map units, also if the map distance between the loci B and C is 12 units, then 12% of the gametes of genotype Bc/bc should be cross over types (i.e. 6% Bc and 6% bC.

Interference and coincidence

In many higher organisms, the formation of one chiasma actually reduces the probability of another chiasma forming in an adjacent region of the chromosome. This is due to the physical inability of the chromatid to bend backward upon themselves within certain minimum distances. This phenomenal where there is increase (negative interference) or decrease (positive interference) in likelihood of a second crossover closely adjacent to another is known as **interference**. The net result of this interference is the observation of fewer double crossover types than would be expected according to map distances.

Coincidence on the other hand is a complement of interference. It is the observed frequency of double crossover (DCO) divided by their expected frequency. When interference is complete, (1.0) no DCO will be observed and coincidence becomes zero. When we observed all the double cross-over that is expected, the coincidence is unity and interference becomes zero. When interference is 30% coincidence becomes 70%.

Example A – B = 10

B – C = 20

Then 0.1 x 0.2 = 0.02 or 2% DCOs in a test cross experiments then coincidence will equal

$$\frac{1.6}{2} = 0.8$$

Therefore, it implies that we observed 80% of the DCO we are expecting. Interference will be 1 – 0.8 = 0.2. Thus 20% of the expected DCO did not form due to interference. Also, the percentage of these DCOs they will probably be observed can be predicted by multiplying the expected DCO by the coefficient of coincidence.

$$= \frac{\% \text{ observed DCOs}}{\% \text{ expected DCOs}}$$