AS-2964

B.A./B.Sc. (Hon's) (Fifth Semester) Examination, 2013
Anthropology and Tribal Development
Paper: Second
(Fundamentals of Human Genetics)

MODEL ANSWER

Section – A

1. Choose the correct answer:

(i) The complete DNA sequence of an organism containing the complete genetic information is called:

(a) Genome (b) Genetic code
(c) Genotype (d) Gene

(ii) A trait that manifests only in homozygous state is known as -

(a) Dominant (b) Co-dominant
(c) Recessive (d) Hemizygous

(iii) Identify the correct sequence -

(a) Diakinesis – Metaphase I – Anaphase I – Telophase I
(b) Metaphase I – Diakinesis – Anaphase I – Telophase I
(c) Diakinesis – Telophase I – Metaphase I – Anaphase I
(d) Anaphase I – Telophase I – Diakinesis – Metaphase I

(iv) The phenomenon called "Synapsis" is observed during the stage of Cell Division

(a) Leptotene (b) Zygotene
(c) Pachytene (d) Diplotene

(v) Blood group alleles in human are referred to as:

(a) Multiple factors (b) Multiple alleles
(c) Polygenes (d) Multigenes

(vi) Identify the correct sequence in the pathway of gene expression –

(a) DNA – RNA transcript – mRNA – Protein
(b) RNA transcript – DNA – Protein – mRNA
(c) mRNA – RNA transcript – DNA – Protein
(d) DNA – mRNA – RNA transcript – Protein

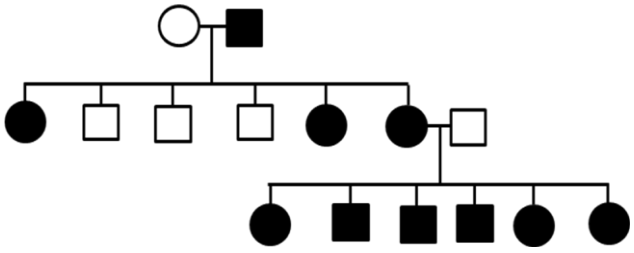
(vii) Individuals having an extra chromosome no. 13 i.e. 13 trisomy is called as

(a) Patau's syndrome (b) Klinefelter's syndrome
(c) Turner syndrome (d) Down's syndrome

(viii) Individuals suffering from Turner's Syndrome has the Karyotype -

(a) XYY (b) XY
(c) XO (d) XXO

(ix) Identify the mode of inheritance pattern from the given pedigree.



(a) autosomal dominant (b) X-linked dominant
(c) X-linked recessive (d) Y-linked

(x) What is RAPD?

(a) randomly amplified polymorphic DNA
(b) repeat amplified polymorphic DNA
(c) random polymorphism
(d) restricted allele polymorphic DNA

Answer Keys

(i) a	(ii) c	(iii) a	(iv) b	(v) b	(vi) d
(vii) a	(viii) c	(ix) b	(x) a		

Section – B

2. Write short notes on:

(i) Down Syndrome (ii) Patau's Syndrome

Answer:

(i) Down Syndrome

Down Syndrome was first detected by Longdon Down in the year 1866. This is the first autosomal abnormality found in man. Karyotype of individual suffering from Down Syndrome shows 47 chromosomes instead of the normal number i.e. 46 chromosomes. Affected individuals posses an extra 21 chromosome, and hence it is also known as Trisomy 21 chromosome. The abnormality is not rare. It occurs approximately 1 out of every 500 to 600 births. Some of the important characteristic features of Down's Syndrome are - epicanthic fold (fold eyelid, therefore known as Mongolism), round and flattened face, long protruding tongue, small ears, short stature, broad fingers and toes, mental retardation, male infertility. Internal organs like heart, thyroid and pituitary are also affected. Correlation exists between age of Mother and incidence of Down's Syndrome.

(ii) Patau's Syndrome

Pstau's Syndrome was first detected by Patau and his colleagues in the year 1960. Affected individuals posses an extra 13 chromosome, so it is also known as Trisomy 13 chromosome. It occurs rarely, approximately 1 out of every 4000 to 10000 births. Some of the important characteristic features of Patau's Syndrome are - various types of eye defects, polydactyly, distal triradius, high frequency of digital arches, malformed ears, cleft palate, cleft lip, mental and physical retardation. More number of females than males is affected. Short life span i.e. dies within one month of age; survive upto 3 years maximum. The risk is more in the older mothers.

3. Describe the inheritance pattern of autosomal traits with a suitable example.

Answer:

The inheritance pattern of any particular trait could be studied under two broad categories such as autosomal inheritance and sex-linked inheritance. Further, autosomal inheritance could be divided into autosomal recessive and autosomal dominant, whereas, sex linked inheritance as X-linked (dominant or recessive) and Y-linked inheritance.

Pattern of Inheritance can be studied through Pedigree analysis. A pedigree shows the inheritance of a trait in a family through multiple generations. It can also be used to deduce genotypes of family members. By analysing a pedigree the nature of inheritance of a particular trait like autosomal dominant inheritance, recessive inheritance, X-linked inheritance, Y-linked inheritance could be ascertained.

(a) Autosomal Dominant Inheritance

Silent characteristic features of autosomal dominant inheritance –

(i) Every affected individual has at least one affected parent
(ii) an affected person has transmitted the trait to almost half of his or her offspring

(iii) Affected males and females appear in each generation
(iv) Affected mothers or father transmit the phenotype to both sons and daughters
(v) Both males and females are affected
(vi) No skipping of generations

Example: Brachydactyly, Wooly Hair, Huntington Disease are good examples of recessive trait

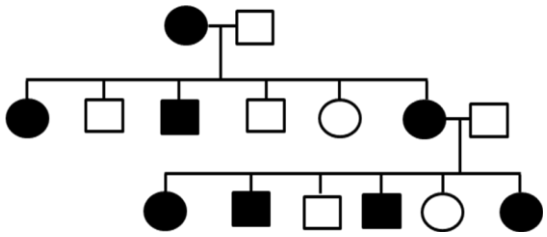


Figure: Pedigree showing diagrammatic representation of autosomal dominant inheritance

(b) Autosomal Recessive Inheritance

Silent characteristic features of autosomal recessive inheritance –

(i) Both the parents of an affected person must carry at least one recessive gene for the trait
(ii) The disease appears in both male and female children of unaffected parents
(iii)Individuals of both sexes are affected
(iv) There is skipping of generations

In this type of inheritance pattern or mating, single sibship with affected persons is usually observed, all other being normal. Some recessive traits are deleterious, when affected persons may not survive. They may be infertile too. The frequency of homozygous recessive individuals is usually very low in comparison to that in the case of dominant allele.

Example: Albinism, phenylketonuria, cystic fibrosis are good examples of recessive trait

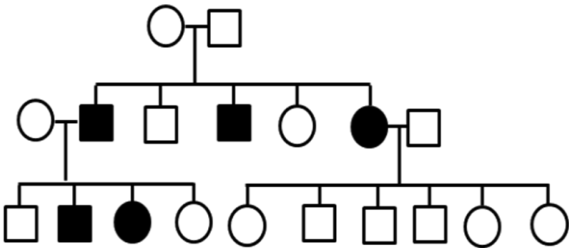


Figure: Pedigree showing diagrammatic representation of autosomal recessive inheritance

4. Give an account on Cell division.

Answer:

A cell is the basic, living, structural and functional unit of the body. It is the building blocks of all plants and animals. All cells come from the division of pre-existing cells. Cells are the smallest units that perform all vital physiological functions. They vary in size and shape. Shape of the cell is determined by its function. Cells can be divided into two types such as Sex/Germ/Reproductive Cells and Somatic (body) cells.

The whole process of cell division may be studied under two broad categories such as – Mitosis (Karyokinesis) and Meiosis (Synapsis).

(a) Mitosis:

Mitosis cell division may be studied under four different stages such as –

(i) Prophase – Cells starts to divide at this first stage. Long, slender and loosely packed chromosome gradually contract and thicken owing to coiling. Each chromosome is seen to be made up of two identical strands lying each other through out their length.

(ii) Metaphase - Nucleolus and nuclear membrane disappear and a spindle-shaped body known as nuclear spindle is formed. Chromosome move towards the equatorial plane of the spindle and become attached to it by the centromere.

(iii) Anaphase - Chromosome begins to separate. Each centromere divides equally. Two centromere and chromatids are pulled apart. The two halves/identical sets of chromatids move to two opposite poles of the spindle.

(iv) Telophase - Two groups of chromatids now become chromosome. That passes towards opposite poles of the spindle. Nuclear membrane, nucleoli reappear and develop. Division of cytoplasm into two parts develops and two daughter cells are formed.

Mitosis cell division is very important because the constituents of the chromosomes are never reduced, but remain identical in all the daughter cells. Thus, the daughter nuclei are similar to the mother nucleus.

(b) Meiosis:

Through Meiosis Cell Division, the chromosome number is reduced to half. It took place shortly before the germ cells are formed. It has two successive divisions – at 1st division the chromosome number is reduced to half while in the 2nd division is mitotic in nature.

1st Division

(i) 1st Prophase:

Leptotene: Chromosome in the form of slender thread in diploid number appears in the nucleus.

Zygotene: Identical chromosomes come close to each other and start pairing throughout the whole length. This phenomenon is called Synapsis. The paired chromosome are said to be in bivalent condition.

Pachytene: The bivalent chromosomes coil around one another and become short and thick. Now, chromosomes are present in haploid number.

Diplotene: Chromosomes starts split longitudinally and as a result chromosome produces two chromatids. Chromosome threads begins to separate. One maternal and one paternal chromatid exchange parts by breakage at corresponding places of the two chromatids. This process is known as crossing over. The point of breakage and rejoining come to lie at right angle forming a cross like structure called "chiasma"

Diakinesis: Chromosomes further coil and become very short and sparsely distributed throughout the nucleus.

(ii) 1st Metaphase: Disappear nuclear membrane and nucleous. Nuclear spindle develops and the bivalent chromosome move towards the equitorial plane.

(iii) 1st Anaphase: Two pairs now separated and they move to opposite poles.

(iv) 1st Telophase: Two daughter nuclei, each with a pair of chromatids are formed at the poles. Both of the daughter nuclei contain haploid number of chromosome.

2nd Division

(i) 2nd Metaphase: The paired chromatids are widely separated and are attached with each other only at the centromere.

(ii) 2nd Anaphase: Same with 1st Anaphase. Chromosome begins to separate. Each centromere divides equally. Two centromere and chromatids are pulled apart. The two halves/identical sets of chromateds move to two opposite poles of the spindle.

(iii) 2nd Telophase: Four daughter nuclei are formed, each with haploid number of chromosomes.

Meiosis cell division maintains a constant number of chromosome in the species. All sexually reproducing plants/animals the Gametes are haploid. Through fertilization i.e. formation of zygot make diploid (i.e. one from egg and one from sperm). Meiosis help in segregation, assortment and recombination of gene. Through the process of meiosis egg and sparm cells are formed.

5. Write a short note on deoxyribonucleic acid (DNA). Describe its function, structure and properties.

Answer:

Deoxyribonucleic acid (DNA) was first identified and isolated by Friedrich Miescher and the double helix structure of DNA was first discovered by James Watson and Francis Crick. DNA is a molecule that encodes the genetic instructions used in the development and functioning of all known living organisms and many viruses. DNA is sometimes called "the blueprint of life" because it contains the code, or instructions for building and organism and ensuring that organism functions correctly. It is the chemical component of chromosomes, which are located in the nucleus of every cell.

Structure:

DNA is usually a double-helix and has two strands running in opposite directions. Each chain is a polymer of subunits called nucleotides, hence DNA is also called as polynucleotide. Each strand has a backbone made up of (deoxy-ribose) sugar molecules linked together by phosphate groups. The 3' C of a sugar molecule is connected through a phosphate group to the 5' C of the next sugar. This linkage is also called 3'-5' phosphodiester linkage. All DNA strands are read from the 5' to the 3' end where the 5' end terminates in a phosphate group and the 3' end terminates in a sugar molecule. Each sugar molecule is covalently linked to one of 4 possible bases like Adenine (A), Guanine (G), Cytosine (C) and Thymine (T). A and G are double-ringed larger molecules (called purines); C and T are single-ringed smaller molecules (called pyrimidines).

Properties:

(a) Physical Properties: In living organisms, DNA exists as a pair of molecules rather than a single molecule. These strands are entwined in the shape of a double helix and the helix is kept stable by hydrogen bonds, which can be found between the bases attached to the two strands. A long polymer, DNA is made up of smaller units called nucleotides.

(b) Base Pairing: In DNA, bases are specific in that an adenine (A) base, for example, only pairs with a thymine (T) base. Following on that premise, a cytosine (C) base will only bond to a guanine (G) base. This base pairing is also known as complementary base pairing.

(c) DNA Grooves: DNA has two kinds of grooves that play important roles in its functioning. Major and minor grooves are structures that allow for necessary proteins in our body to make contact with bases. Some of these proteins are called transcription factors.

(d) DNA Super-coiling: DNA can be in a relaxed or coiled state and it is this coiling that allows our extremely long strands of DNA to fit or 'pack' into the comparatively much smaller cells in our bodies.

(e) DNA Conformations: DNA can exist in different conformations and these conformations interact with enzymes and they are also involved in aspects such as DNA repair.

(f) DNA Sense and Antisense: The antisense strand is the DNA strand that carries important information to make proteins by binding to the RNA. This antisense strand is the key for making proteins. In comparison, the sense strand is the one that does not code for RNA.

Biological Functions:

(a) Transcription and translation: A gene is a sequence of DNA that contains genetic information and can influence the phenotype of an organism. The relationship between the nucleotide sequences of genes and the amino-acid sequences of proteins is determined by the rules of translation, known collectively as the genetic code. The genetic code consists of three-letter 'words' called codons formed from a sequence of three nucleotides (e.g. ACT, CAG, TTT). In transcription, the codons of a gene are copied into messenger RNA by RNA polymerase. This RNA copy is then decoded by a ribosome that reads the RNA sequence by base-pairing the messenger RNA to transfer RNA, which carries amino acids.

(b) Replication: Replication is the process where DNA makes a copy of itself. Cells divide for an organism to grow or reproduce, every new cell needs a copy of the DNA or instructions to know how to be a cell. DNA replicates right before a cell divides. The two strands of the DNA are separated and then each strand's complementary DNA sequence is recreated by an enzyme called DNA polymerase. This enzyme makes the complementary strand by finding the correct base through complementary base pairing, and bonding it onto the original strand. DNA replication is semi-conservative. That means that when it makes a copy, one half of the old strand is always kept in the new strand. This helps reduce the number of copy errors.

6. Write an essay on molecular techniques used in genetic studies with special reference to Polymerase Chain Reaction.

Answer:

Polymerase Chain Reaction (PCR) was invented by Kary B. Mullis for which he was awarded Nobel Prize in chemistry in 1993. The method relies on thermal cycling, consisting of cycles of repeated heating and cooling of the reaction for DNA melting and enzymatic replication of the DNA. PCR allows amplification of a specific target DNA sequence which is then used for further analysis.

Requirements of PCR ingredients:

1. *Primers:* PCR requires specific oligonucleotide primers for amplifying the region of interest,
2. *PCR buffer* for providing a suitable chemical environment for optimum activity and stability of the DNA polymerase,
3. *Magnesium chloride ($MgCl_2$)* for providing Mg^{2+} ion which acts as a catalyst in the reaction
4. *deoxynucleotide triphosphates (dNTPs)* - the building blocks for new DNA strand
5. *Thermus aquaticus (Taq) polymerase* enzyme which catalyzes the reaction of complementary sequence synthesis.

Mechanism of PCR Reaction:

During a PCR, changes in temperature are used to control the activity of the polymerase and the binding of primers. The basic principle of PCR is to make several number of copies of the initial/original DNA sample (or template). A DNA sample can be copied many times (amplified) in vitro and exponential growth of the region of interest is achieved by 3-step cycle such as –

1. Denaturation - Heating the DNA to separate the double-stranded molecule into single strands. It occurs at around 95^0C, where the double stranded DNA will be separated to form single strands. This allows the primer to act on it in order to form complimentary strand.

2. Annealing - Cool the mixture to allow complementary primers to hydrogen bond to the single strands. Annealing takes place generally at around 50-65^{0}C. In this phase primer forms the hydrogen bond with ends of target sequence.

3. Extension - Add DNA polymerase and nucleotides to replicate each strand. Extension occurs at about 72^{0}C. DNA polymerase adds nucleotides to the 3' end of each primer.

Types of PCR - In recent years, modifications or variants have been developed from the basic PCR method to improve performance and specificity, and to achieve the amplification of other molecules of interest in research as RNA. Some of these variants are: Multiplex PCR, Nested PCR, Semi-quantitative PCR, Reverse Transcriptase PCR (RT-PCR), Real time PCR etc.

Applications of PCR - PCR allows amplification of a specific target DNA sequence which is then used for further analysis. Some of the important applications of PCR are - amplification of small amounts of DNA for further analysis, analysis of ancient DNA from fossils, mapping the human (and other species) genome, isolation of a particular gene of interest from whole genome, generation of probes, production of DNA for sequencing analysis, mutations detection, diagnosis of single gene disorders diseases as well as pre-natal diagnosis, detection of microorganisms, detection of microbial genes responsible for pathogenesis or antibiotic resistance. In Forensic Science, PCR is used for genetic identification of suspects from crucial evidence like one human hair, body fluid stain such as blood, saliva, semen etc.

7. Write short notes on:

(i) VNTR

(ii) Biochemical genetics

Answer

(i) VNTR

A Variable Number Tandem Repeat (VNTR) is a location in a genome where a short nucleotide sequence is organized as a tandem repeat. These can be found on many chromosomes, and often show variations in length between individuals. Each variant acts as an inherited allele. The repeats are tandem - they are clustered together and oriented in the same direction. VNTRs were an important source of RFLP genetic markers used in linkage analysis (mapping) of genomes. VNTRs have become essential to forensic crime investigations, via DNA fingerprinting and used for parental identification. VNTR analysis is also being used to study genetic diversity and breeding patterns in populations of wild or domesticated animals. When tested with a group of independent VNTR markers, the likelihood of two unrelated individuals having the same allelic pattern is extremely improbable. There are two principal families of VNTRs: **microsatellites** and **minisatellites**. The former are repeats of sequences less than about 5 base pairs in length (an arbitrary cutoff), while the latter involve longer blocks.

(ii) Biochemical Genetics

Biochemical Genetics is the branch of biology that deals with the formation, structure, and function of macromolecules essential to life, such as nucleic acids and proteins, and especially with their role in cell replication and the transmission of genetic information. It is the study of genes governing the biochemical process. The processes can be explained and exemplified by various serious afflictions such as inborn errors of metabolism, the haemoglobinopathies and immunoglobinopathies. Biochemical Genetics involves the diagnosis and management of inborn errors of metabolism in which patients have enzymatic deficiencies that perturb biochemical pathways involved in metabolism of carbohydrates, amino acids, and lipids. Common metabolic disorders include galactosemia, glycogen storage

disease, lysosomal storage disorders, metabolic acidosis, peroxisomal disorders, phenylketonuria, and urea cycle disorders. Phenylketonuria (PKU) is an autosomal recessive metabolic genetic disorder characterized by a mutation in the gene for the hepatic enzyme phenylalanine hydroxylase (PAH), rendering it non-functional. PAH gene helps in conversion of amino acid phenylalanine to the amino acid tyrosine. Mutation in PAH gene reduced the activity of enzyme causing accumulation of phenylalanine and converted into phenylpyruvate (also known as phenylketone) instead of tyrosine. This Phenylketone can be detected in the urine.

8. Write an essay on single nucleotide polymorphism and discuss its applications in anthropological studies.

Answer:

Genetic polymorphism is the existence of variants with respect to a gene locus (alleles), a chromosome structure (e.g., size of centromeric heterochomatin), a gene product (variants in enzymatic activity or binding affinity), or a phenotype. The term DNA polymorphism refers to a wide range of variations in nucleotide repeats, or single nucleotide variants and they provide the basis for direct physical analysis of genotype using molecular methods.

Single Nucleotide Polymorphism (SNPs)

Single Nucleotide Polymorphisms or SNPs (pronounced "snips") are variations in a DNA sequence that occur when a single nucleotide in the sequence is different from the norm in at least one percent of the population. It can also be defined as a DNA sequence variation occurring when a single nucleotide - A, T, C or G - in the genome (or other shared sequence) differs between members of a biological species or paired chromosomes in a human. SNPs are due to either base change or by deletion/insertion of a base. When SNPs occur inside a gene, they create different variants, or alleles, of that gene. Most polymorphisms of this type have only two alleles (i.e. they are biallelic) and thus, they are sometimes referred to as biallelic markers. The genomic distribution of SNPs is not homogenous; SNPs usually occur in non-coding regions more frequently than in coding regions or, in general, where natural selection is acting and fixating the allele of the SNP that constitutes the most favorable genetic adaptation. SNPs occur in high frequency in the human genome and they occur with very high frequencies – about 1 in 1,200 bases on average, which results in approximately 10 million SNPs in the human genome.

Types of SNP

Single-nucleotide polymorphisms may fall within coding sequences of genes, non-coding regions of genes, or in the intergenic regions (regions between genes). SNPs in the coding region are of two types, synonymous and nonsynonymous SNPs. Synonymous SNPs do not affect the protein sequence while nonsynonymous SNPs change the amino acid sequence of protein. Further, the nonsynonymous SNPs are of two types: missense and nonsense. Missense SNP is a change in DNA sequence that changes the codon to a different amino acid. Not all missense mutations are deleterious, some changes can have no effect. Whereas, nonsense SNP is a change in the genetic code that results in the coding for a stop codon rather than an amino acid. SNPs that are not in protein-coding regions may still affect gene splicing, transcription factor binding, messenger RNA degradation, or the sequence of non-coding RNA. Gene expression affected by this type of SNP is referred to as an eSNP (expression SNP) and may be upstream or downstream from the gene.

Applications of SNP in Anthropological Studies

As anthropology focuses on the study of human evolution and variation, Anthropological genetics examines evolutionary theory of interest to anthropologists while applying genetic methodologies. The field of anthropological genetics utilizes a comparative approach on small, isolated populations and topics such as human variation, evolutionary theory, reconstruction of the human diaspora (out-of-Africa), genetic epidemiology, and forensic sciences. Anthropology uses genetics as a tool to understand human variation and evolution involving focus on health and evolutionary aspects. Genetics is an important aspect, which throws light on the ways of inheritance. The discovery of genetically determined red blood cell polymorphism in the beginning of twentieth century and later on protein polymorphism provided Physical Anthropologist with new tools to study human variation both at the regional and global levels.

Human Genome Diversity: With the advances in statistical methodologies in population genetics and the availability of large scale SNP data, this marker facilitate in the study of prehistoric migration and demographic history of modern humans. Therefore, helps in understanding human population history. It is useful in estimating the contribution of different gene pools to the make-up of present-day populations and test hypotheses about origin of linguistic and historical population movements. The availability of known genomic variations coupled with easy to type technologies facilitated the use of genomic markers for studying intra and inter population variations. Such studies intensively helped in understanding the human evolution and migrations.

Disease Association Studies: SNPs are the major cause of genetic diversity among different individuals facilitating large scale genetic association studies as genetic markers. It is also used in genetic mapping studies to identify DNA markers that are genetically linked to disease genes in the chromosomes in order to pinpoint their location.

Anthropological geneticists started focusing on the genetic variation and susceptibility to various diseases among different populations. The extent of genetic variation and their manifestation are found to vary in different ethnic groups. Some populations are found to be more prone to a particular disease while others are not, as genetic structure of a particular population is shaped by their environmental/geographical position, life style, matting pattern and other genetic factors which are population specific. Anthropological geneticists have been successful in mapping quantitative trait loci involved in biological pathways of diseases such as diabetes mellitus, cancers, obesity, osteoporosis, and coronary heart disease. Therefore, anthropological genetics has emerged as a useful tool for studying various multifactorial complex diseases since the knowledge of human variations and its underlying genetic and environmental factors specific to populations is the primary goal of anthropological geneticists. Moreover, understanding genetic variation in disease risks and mapping candidate genes associated with the complex disease may provide new insight into the disease etiology which could lead to genetic screening programmes to identify the populations at higher risk. On the other hand, forensic anthropologists also used the new techniques on SNPs for identifying suspects. Thus, SNPs has important implications for anthropological studies with respect to evolutionary biology, disease analyses, and forensics.