AU-6317
MODEL ANSWER
M.A./M.Sc. (Third Semester) Examination, 2014
ANTHROPOLOGY
Paper Code: ANT-M303A
(Human Molecular Genetics and Molecular Anthropology)
Time Allowed: Three hours

Maximum Marks: 60 ***Pass Mark: 24***

Note: *Attempt questions of all* ***two*** *sections as directed.*
Distribution of marks is given with sections.

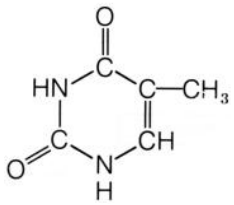
Section – 'A' **Marks 2X10=20**

1. Select one of the most appropriate answer from the following objective questions:

(i) Which enzyme replace the RNA primers in DNA replication?
(a) polymerase I (b) RNA primase (c) polymerase 3 (d) None of them

(ii) Change in genetic sequence that does not change the protein sequence is _____mutation.
(a) Silent (b) Nonsense (c) Both 'a' and 'b' (d) None of them

(iii) Structure of Thymine is _____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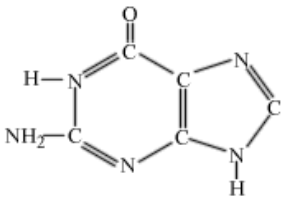
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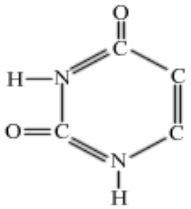
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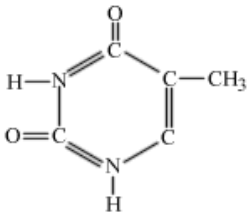

(d)

(iv) Activities of small RNAs on gene expression are collectively known as _____
(a) RNA enhancer (b) RNA silencing (c) RNA transcriptase (d) RNA polymerase

(v) Individuals with _____ received defective gene from both parents.
(a) major thalassemia (b) minor thalassemia (c) mild thalassemia (d) None of the above

(vi) In human there are more than _____ billion of DNA base pairs.
(a) 5 (b) 3 (c) 7 (d) 9

(vii) Base substitution that leads to amino acid substitution is known as _____ mutation.
(a) Silent (b) Missense (c) Nonsense (d) None of them

(viii) Y-chromosomal DNA is inherited through _____ line.
(a) paternal (b) maternal (c) both (d) unknown

(ix) The oldest mtDNA lineage is known as _____
(a) L (b) L0 (c) L1 (d) L2

(x) What is the full form of DSM?
(a) Diagnostic and statistical manual of mental disorders
(b) Diagnostic and statistical manual (c) Diagnosis of mental disorders
(d) Digital system for mental disorder management

KEY ANSWERS:

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

Section – 'B' **Marks 4X10=40**

Note: *Write long answers of the following questions. Attempt any* ***four*** *questions. All questions carry 10 marks.*

2. Write short notes on:

(i) G6PD deficiencies: Glucose-6-phosphate dehydrogenase (G6PD) is a red cell enzyme, which normally metabolizes glucose in the red blood cells. Some persons are deficient of this enzyme. The condition is called G6PD deficiency. G6PD deficiency is inherited through X chromosome. Homozygous females are clearly deficient. But heterozygous females show various degrees of deficiency or none at all. Therefore, it appears to be incompletely dominant. G6PD deficient persons when treated with certain antimalarial drugs, especially primaquine, develop haemolytic anemia. Individuals with such G6PD deficiency are met with in Africa, Southeast Asia, Indonesian, Burma, India and some countries bordering the Mediterranean Sea. Moreover, some individuals when eat fava beans or even if they breathe the pollen, they develop this type of anemia. This disease is also known as 'favism'. These individuals are also deficient of G6PD. However, it is noted that G6PD deficient persons of Africa origin do not get favism, but such persons of European origin get it suggesting existence of different types of G6PD deficiency. For example, in India there are three major types of G6PD deficiency such as - G6PD Mediterranean, G6PD Kerala-Kalyan and G6PD Orissa. Distribution of G6PD deficiency can be correlated with that of falciparum malaria. It is noted that individuals with G6PD deficiency are better protected against malaria infection. The distribution of G6PD deficiency in Indian populations is population specific. The frequency is higher among the tribal than the caste populations.

(ii) 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. Some VNTR sequence segments are found at only a single locus in the human genome. Other VNTR sequence segments occur at many loci in the human genome. These loci are dispersed among the chromosomes. The repeats are tandem - they are clustered together and oriented in the same direction. Individual repeats can be removed from (or added to) the VNTR via recombination or replication errors, leading to alleles with different numbers of repeats. VNTRs were an important source of RFLP genetic markers used in linkage analysis (mapping) of genomes. Now that many genomes have been sequenced, 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 removed from surrounding DNA by the polymerase chain reaction (PCR) technique, and their size determined by gel electrophoresis, they produce a pattern of bands unique to each individual. 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 principle 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. VNTRs with very short repeat blocks may be unstable - dinucleotide repeats may

vary from one tissue to another within an individual, while trinucleotide repeats have been found to vary from one generation to another (see Huntington's disease).

3. Elucidate difference banding techniques used in human cytogenetics.

Specialized staining techniques for the staining of certain sections of a chromosome (bandings) have been develop during the 1960th and 1970th. Depending on the pre-treatment of the chromosome and the used dye or fluorochromes, it is distinguished between Q-, C-, G-, and R-bandings. Most common are:

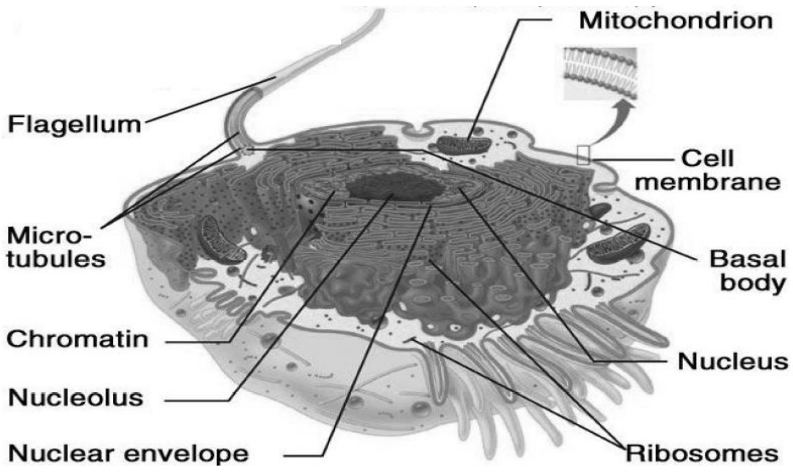
Q-bandings: It result after treatment of the chromosomes with the fluorochrome quinacrin (= atebrin). They can be recognized by a yellow fluorescence of differing intensity. Most part of the stained DNA is heterochromatin. Quinacrin (atebrin) binds both regions rich in AT and in GC, but only the AT-quinacrin-complex fluoresces. Since regions rich in AT are more common in heterochromatin than in euchromatin, these regions are labelled preferentially. The different intensities of the single bands mirror the different contents of AT. Other fluorochromes like DAPI also to characteristic, reproducible patterns. Each of them produces its specific pattern. In other words: the properties of the bonds and the specificity of the fluorochromes are not exclusively based on their affinity to regions rich in AT. Rather, the distribution of AT and the association of AT with other molecules like histones, for example, has an impact on the binding properties of the fluorochromes.

C-bandings: The name is derived from centromeric or constitutive heterochromatin. The preparations undergo alkaline denaturation prior to staining leading to an almost complete depurination of the DNA. After washing the probe the remaining DNA is renatured again and stained with Giemsa solution consisting of methylene azure, methylene violet, methylene blue, and eosin. Heterochromatin binds a lot of the dye, while the rest of the chromosomes absorb only little of it. The C-bonding proved to be especially well-suited for the characterization of plant chromosomes.

G-bandings: They are the result of a staining technique that is well-suited for animal cells but useless with plants. It resembles the C-banding technique without the pre-treatment. Plant chromosomes treated with this technique are uniformly stained.

R-banding: Reverse banding are the results of a technique that stains regions rich in GC that are typical for euchromatin.

4. Draw and level structure of human cell and describe cell theory and its implication.



The cell was discovered by Robert Hooke in 1665. The cell theory, first developed in 1839 by Matthias Jakob Schleiden and Theodor Schwann, states that all organisms are composed of one or more cells, that all cells come from pre-existing cells, that vital functions of an organism occur within cells, and that all cells contain the hereditary information necessary for regulating cell functions and for transmitting information to the next generation of cells.
Generally accepted parts of Modern Cell Theory -
(i) All known living things are made up of one or more cells
(ii) All living cells arise from pre-existing cells by division
(iii) The cell is the fundamental unit of structure and function in all living organisms.
(iv) The activity of an organism depends on the total activities of independent cells
(v) Energy flow (metabolism and biochemistry) occurs within cells
(vi) Cells contains DNA which is found specifically in the chromosome and RNA found in the cell nucleus and cytoplasm.
(vii) All cells are basically the same in chemical composition in organisms of similar species.
Some of the important implications of Cell theory are - cells is the fundamental structural unit in all organisms, and all species are related by common ancestors and change over time in response to natural selection. If all cells come from pre-existing cells, than all individuals in a population of single - called organisms must be related by similar ancestor. In multicellular organisms, all cells trace back to fertilized egg. Therefore, it helps in understanding the evolutionary studies as well as clinical genetic studies.

5. Write an essay on transposable elements with special reference to LINE and SINE.

The human genome contains interspersed repeat sequences that have largely amplified in copy number by movement throughout the genome. These sequences are referred to as transposable elements. LINEs and SINEs are the primary families of transposable elements in the human genome. The terms SINE and LINE were coined by Maxine Singer in 1982. By that time, the term "junk DNA" (Ohno 1972; Comings 1972) had been in circulation for a decade, and this was also two years after the "selfish DNA" hypothesis was put forward by Orgel and Crick (1980) and Doolittle and Sapienza (1980).

(i) Long Interspersed Repeated Sequences (LINEs)

LINEs are sometimes referred to as non-LTR retrotransposons because sequences in the elements code for enzymes utilized in the retroposition process. Long interspersed elements are a group of genetic elements that are found in large numbers in eukaryotic genomes. They are transcribed (or are the evolutionary remains of what was once transcribed) to an RNA using an RNA polymerase II promoter that resides inside the LINE. LINEs code for the enzyme reverse transcriptase, and many LINEs also code for an endonuclease (e.g. RNase H). The reverse transcriptase has a higher specificity for the LINE RNA than other RNA, and makes a DNA copy of the RNA that can be integrated into the genome at a new site. The Endonuclease encoded by non-LTR retrotransposons may be AP (Apurinic/Pyrimidinic) type or REL (Restriction Endonuclease Like) type. R2 group of elements have REL type endonuclease which shows site specificity in insertion. The 5' UTR contains the promoter sequence, while the 3' UTR contains a polyadenylation signal (AATAAA) and a poly-A tail. Because LINEs move by copying themselves (instead of moving, like transposons do), they enlarge the genome. The human genome, for example, contains in the human genome are actively transcribed and the associated LINE-1 RNAs are tightly bound to nucleosomes and essential in the establishment of local chromatin environment.

(ii) Short Interspersed Repeated Sequences or Short Interspersed Nuclear Elements (SINEs)
Short interspersed elements are short DNA sequences (<500 bases) that represent reverse-transcribed RNA molecules originally transcribed by RNA polymerase III into tRNA, rRNA, and other small nuclear RNAs. SINEs do not encode a functional reverse transcriptase protein and rely on other mobile elements for transposition. The most common SINEs in primates are called Alu sequences. Alu elements are 280 base pairs long, do not contain any coding sequences, and can be recognized by the restriction enzyme AluI (hence the name). Alu elements are the most common single type of non-coding DNA element in the human genome. These sequences are now recognized as a type of transposable element that uses an RNA intermediate (i.e., undergoes retrotransposition) but which cannot do so without borrowing (some say parasitizing) the molecular transposition apparatus of other elements, namely long interspersed repeated sequences (LINEs). LINEs are not as common in the human genome as SINEs, but as they are much larger, they make up more of the total DNA. Whereas there are about 1.5 million SINEs (1 million of them Alu) making up about 13% of the genome sequence, the 870,000 or so copies of LINE elements (more than 500,000 of them LINE-1) constitute more than 20% of human DNA. While historically viewed as "junk DNA", recent research suggests that in some rare cases both LINEs and SINEs were incorporated into novel genes, so as to evolve new functionality. The distribution of these elements has been implicated in some genetic diseases and cancers.
LINE and SINE are very useful for ascertaining phylogenetic relationships. Therefore, if two different species share the same SINE or LINE sequences, they probably inherited them from a common ancestor. They therefore are almost certainly more closely related to one another than either of them is to a third species that lack these inserted sequences. Approximately 2000 Alu elements have integrated within the human genome subsequent to the divergence of humans from the great apes. About 25% of the more recent Alu integrations have yielded presence/absence insertion polymorphisms that are useful as DNA markers for the study of forensics and human population genetics.

6. Write an essay on origin of modern humans with special reference to Y chromosomal DNA.

Origin of modern human can be studied from two broad aspects such as mtDNA and Y chromosomal DNA. According to research, Y-DNA is passed solely along the patrilineal line, from father to son, while mtDNA is passed down the matrilineal line, from mother to offspring of both sexes. It is believed that neither recombines, and thus Y-DNA and mtDNA change only by chance mutation at each generation with no intermixture between parents' genetic material. Anthropologists studied haplogroups to understand the genetic structure of the population. Haplogroups is a group of similar haplotypes that share a common ancestor having the same single nucleotide polymorphism (SNP) mutation in all haplotypes. It pertains to deep ancestral origins dating back thousands of years. In human genetics, the haplogroups most commonly studied are Y-chromosome (Y-DNA) haplogroups and mitochondrial DNA (mtDNA) haplogroups, both of which can be used to define genetic populations. All individuals in a given haplogroup have a common ancestor at some point in time. If a sufficient number of individuals are examined for their haplotypes, maps can be created,

showing the distribution of various haplogroups across the world. These maps are called Haplotype Maps.

Using haplotype maps, it is possible to trace the last common ancestor of all men today, sometimes called the "**Y-chromosomal Adam**". Note that the last common ancestor is not the "first" man who ever lived. Indeed, evolution says that there was no such thing as "first man". A species does not start from a single individual, but rather from a sub-population that becomes geographically separated from its parent population, and evolves separately from it, gradually accumulating sufficient differences from the parent population over time so that it can be called a new and different species. Y-chromosomal Adam lived about 60,000-90,000 years ago in Africa. The date is very approximate, since such calculations are not exact. But even allowing for a large fudge factor, it can be seen that this was a long time after humans first evolved. Modern humans first appeared in Africa sometime between 195,000 to 160,000 years ago. So humans had been around for about a hundred thousand years before the lifetime of Y-chromosomal Adam. The concept of "Y-chromosomal Adam" simply means that all men today are descended from a single male ancestor who lived in Africa about 60,000 - 90,000 years ago.

Haplogroups A and B are found only in Sub-Saharan Africa. These haplogroups are the oldest haplogroups and they are found where humans first originated. The first haplogroup that branched off was **Haplogroup A**, with the defining mutation M91. Humans who are not Haplogroup A are lumped into **Haplogroup BT**, which is composed of Haplogroups B and CT. The super-group BT is defined by mutations M42, M94, M139 and M299, all of which date to about 55,000 years ago. **Haplogroup B** was the next to diverge, defined by mutation M60, and is today found in Africa among the Pygmies and Hadzabe people in central Tanzania. Individual who doesn't belong to Haplogroup A or B belongs to the super-group CT, which is defined by mutations M168 and M294. This is the branch of humanity that first left Africa, although the mutation that led to CT probably happened in Africa about 50,000-60,000 years ago, in a man from East Africa, who's been called the "Eurasian Adam", since his descendents include all Eurasian and Asian people today. **Haplogroup CT** was probably the group involved in the early migration out of Africa, which spread along the southern coast of the Arabian peninsula, Iran, Pakistan, India, and all the way to southeast Asia. **Haplogroup CF** diverge and is defined by mutation P143. ***Haplogroup C*** emerged from CT, via CF, and is defined by mutations M130 and M216. It's divided into various subgroups: C1 (M8, M130, M216) - presently found in Japan; C2 (M38) - presently found in southeast Asia, Polynesia; C3 (M217, P44): presently found in native Americans, and groups related to them in Asia, such as Mongols, Kazakhs, Eskimos and other Asian people of the far north, and paleo-Siberians; C4 (M347) - presently found in the aboriginal inhabitants of Australia; C5 (M356) - found in some parts of India. ***Haplogroup R*** is defined by the M207 mutation, and first arose about 27,000 years ago in south or western Asia, with the probable origin being likely either in India, Pakistan or Iran. This group is divided into two major subclasses, R1 and R2. R1 is further divided into R1a and R1b.

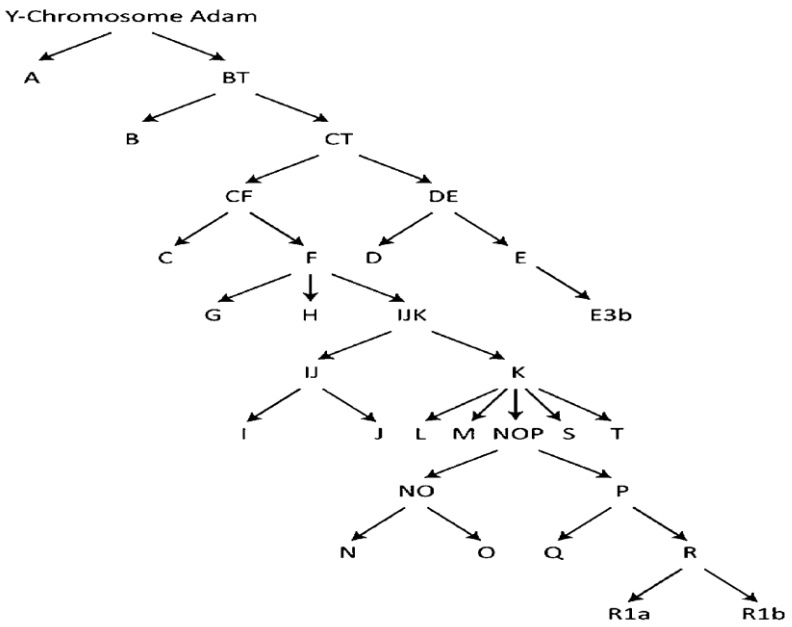


Figure: Haplotype map of Y chromosome haplogroups

7. Give an account on ethical guidelines in human genome research.

Human Genome Research focuses on wide range of genetic studies including trial, clinical, case-control, edpidemiological, genome wide association studies etc. for understanding different aspect of human beings. It could be broadly divided into two main branches like – (i) studying human evolutionary & migratory routes/systems, (ii) health and disease.

Some of the important guidelines in Human Genome Research include –

Guideline 1: Acceptability of purpose for which human genetic data is collected

(a) Human genetic data may only be collected, processed, and stored and processed for the following purposes:

- the provision of health care; research intended to further understanding of the structure and function of the human genome; the identification, in accordance with the provisions of national law, of those suspected of involvement in crime; the identification in the context of military service or for the purpose of identifying the victims of accidents or disasters, or for any other identification purpose authorised by national law and which is in conformity with the principles of international human rights law.

(b) Human genetic data may not be collected, stored or communicated for any purpose which is inconsistent with the principles set out in the Universal Declaration on the Human Genome and Human Rights.

Guideline 2: Cultural Issues

(a) The human tissue from which genetic data are obtained, and genetic data itself, may be the subject of moral, social or religious beliefs. Those who collect human genetic data from communities holding such beliefs must give these convictions all due respect, endeavouring to do nothing to or with the genetic data, or the samples from which the data are derived, that would give offence to those from whom the samples and the data have been obtained.

(b) National authorities promoting the collection of human genetic data from their populations should take into account the sensitivities of social, religious or ethnic groups within the population at large. Researchers must also observed the laws of the country in

which their studies are conducted, as well as implementing the standards under which they work in their own country.

Guideline 3: Collection of samples from indigenous peoples

The collection of samples from indigenous peoples must only be undertaken after appropriate consultation with those peoples according to their customs and protocols and according to both the laws of their own country and the laws of the country of the researcher.

Guideline 4: Free and informed consent in research; Guideline

(a) A research sample may be collected from a person only after the person has first been given a sufficient explanation in an appropriate style and language of:

- the purpose for which the sample is collected
- the source of funding for the research
- the type of use which will be made of the sample or any information derived from it; and
- any other implications which the collection and subsequent use of the sample might reasonably be expected to have for the person providing it.

(b) The consent should be expressed in writing unless there are cultural reasons for not doing so, in which case other possibilities of publicly recording consent should be explored.

(c) Donors of samples for research purposes should not be subjected to any pressure or improper inducement in order to secure their consent. A person who refuses to consent should not suffer any adverse consequences as a result of this refusal, and all potential donors should be given an assurance to this effect.

Samples donated for research purposes should not be made available for other purposes, such as police use, and national legislation should seek to prevent such use.

Guideline 5: Withdrawal of informed consent

Providing samples and derived data have been stored in an identifiable manner, donors may request that those samples and any human genetic data derived from them be returned to them or destroyed.

Guideline 6: Confidentiality or Anonymity

Donor of the samples for genetic testing, both individuals and communities, should be informed prior to giving consent whether their samples and genetic data will be identified, coded but identifiable or not identifiable (anonymized), and the meaning of these terms should be clearly explained.

Other ethical guidelines includes the following heads - Guideline 7: Counselling; Guideline 8: Validity and reliability; Guideline 9: Limitation of use; Guideline 10: Informed consent to diagnostic testing; 11: Obtaining research samples from those unable to consent; Guideline 12: Transparency of purpose; Guideline 13 & 14: Role of education; Guideline 15: Fate of material; Guideline 16: Sharing information; Guideline 17: Post-mortem samples; Guideline 18: Historical or archived collections; Guideline 19: Rights of children; Guideline 20: Collection of samples in other countries; Guideline 21: Public consultation and involvement

8. Write an essay on mechanism of gene expression.

In genetics, gene expression is the most fundamental level at which the gives rise to the phenotype. The genetic code stored in DNA is ‘interpreted’ by gene expression and the properties of the expression give rise to organism phenotype. Such phenotypes are often expressed by the synthesis of proteins that control the organism shape or that act as enzymes

catalysing specific metabolic pathways characterising the organism. Gene expression is the process by which information from a gene is used in the synthesis of a functional gene product. These products are often proteins. The process of gene expression is used by all known life eurokaryotypes, prokaryotypes, and viruses, to generate macromolecular machinery for life. Some of the important steps in the gene expression process may includes the transcription, RNA splicing, translation and post-translational modification of protein.

DNA Transcription: The process by which RNA is created from DNA template. During the process of transcription, DNA sequence is read by RNA. Some of the important steps involved in DNA transcription includes:

(i) An RNA polymerase binds to the promoter side of the DNA strand in-order to begin DNA transcription. (ii) It combines with Transcription Factors to form the Transcription Initiation Complex. (iii) As it moves along the DNA strand, the RNA polymerase breaks hydrogen bonds between the complementary nucleotides and separated. (iv) Only one strand is copied during the process of transcription. (v) RNA nucleotides paired with complementary DNA nucleotides in order to formed a RNA strand called mRNA. (vi) mRNA is the copy of the message contained in the gene. (vii) DNA transcription ends when the RNA polymerase reaches the termination site of the DNA. (viii) DNA strands binds together once again and mRNA polymerase moves away. (ix) The new mRNA molecules is than released from the RNA polymerase and is ready to be used in the transcription of protein.

Translation (Protein Synthesis): In Prokaryotic Cell, the process of translation is initiated by the formation of initiation complex consisting of the following compound such as: 30S ribosomal subunit, Formyl-methionyl tRNA and mRNA. This Translation Initiation Complex is than joint by 50S ribosomal subunit along with Protein called Initiation Factors. 50S ribosomal subunit has two sites to its tRNA carrying amino acids can bind. One is called P-Site (Peptidal Site) for transfer and A-Site (Acceptor Site) to accept or bind the amino acids. There is also another third site called E-Site (Exit Site) where tRNAs are released. Important Steps involved in Translation can be summarised as follows:

(i) The initiating tRNA carrying formyl-methionyl binds to the P-Site.

(ii) A tRNA that recognised that next CODON and carry the 2^{nd} amino acid than moves into the A-site. The formyl-methionyl carried by tRNA in P-site is than joined to the amino acid carried by the tRNA that just enter into the A-site by a Peptide bond.

(iii) The ribosome now shift down a distance of one CODON and tRNA that carry the formyl-methionyl is release at the E-site. A tRNA carrying the next amino acid is now moves into the A-site where the ANTI CODON on the tRNA matches the CODON on the mRNA.

(iv) The ribosome shifts down by a distance of one CODON. As the shift occur the two amino acid on the tRNA in the P-site are transfer to the new amino acid at the 2^{nd} tRNA is release at the E-site. The ribosome continues to move along the mRNA and new amino acids are added to the growing polypeptide chain.

(v) Elongation of the polypeptide is terminated when a STOP CODON moves into the A-site. The STOP CODON do not specified amino acid and does not have corresponding tRNA. The ribosome dissociates into the 30S and 50S subunit and mRNA and protein are released.