International Conference on Latest Innovation in Engineering Science and Management
Buddha Institute of Technology, GIDA, Gorakhpur (UP)
30th - 31st March 2019 www.conferenceworld.in ISBN : 978-93-87793-80-4

Human molecular genetics

Aryan Pathak[1]

[1]Undergraduate, Biotechnology Department, Jaipur National University, (India)

ABSTRACT

This is expected introduce the rapid advancements in our understanding the role of human genome in health and disease, to introduce key concepts of inheritance of human traits, pedigree analysis, and chromosome organization. Molecular biology tools used for understanding the genome, gene structure and gene mutations, gene mapping and gene cloning strategies will also be covered. Also discussed about DNA finger printing & RFPL analysis. This including pedigree constructions for human genetic traits by tracing their segregation in families and also introduce concepts for determining the dominant and recessive alleles (genotypes), and autosomal versus sex chromosomal inheritance. basic principles of molecular biology tools used in gene cloning, and mutational detection. discussing about the mutational process, genetic basis of mutational hot-spots, and on "loss-of-function" mutations. molecular basis of mutations and will providing some examples from the human genetic disorders.

Keywords: DNA, gene,genome, mutation

1.INTRODUCTION

A central dogma system consists the conversion id DNA to RNA to protein with the known transcription & translation process. A genotype is responsible for the phenotype. As in case if alkaptonia, accumulation of homogenetesic acid results in pigments due to defect in Homogenetesic acid oxidase. But other enzyme can also takes it place for the continuation of process. A DNA is a double strand structure having phosphate, sugar & nitrogenous base. The background of it consisting phosphate sugar. A DNA is differ from RNA because of absence of O in 2' carbon of sugar while OH is present at 2' C of sugar in RNA. thisexons & introns are in DNA but introns are remove during splicing & exons are present in mRNA. A cap is at 5' &poly(A) tail at 3' and form

ISBN : 978-93-87793-80-4

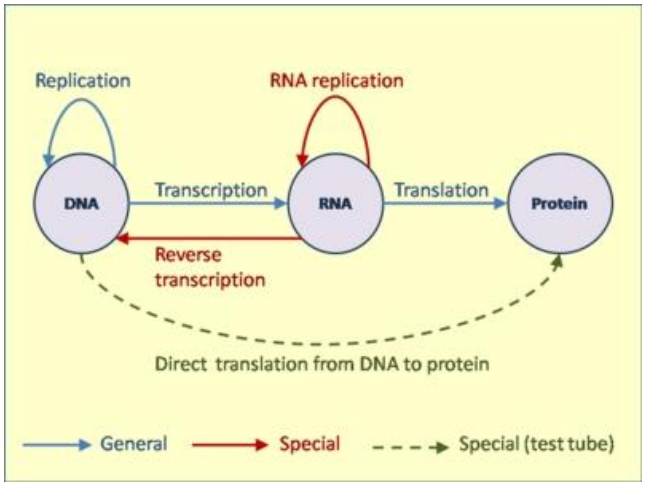


Figure 1. central Dogma

protein during translation in cytoplasm. A chromosome consists DNA and segment of DNA known as Gene with bases.

2.The genetic code

A, U, G, C code for all types of amino acids. The genetic sequence is not easy to read therefore forms codon that can easily read by ribosomes &form different amino acids. Reverse transcription in virus is followed as RNA >DNA >RNA >Protein. Both DNA & RNA go through replication & proteins also goesself-propagation. . But all these exceptions are rare event, hence central dogma still hold true fir great majority of species. RNA functions as regulatory factor(non-coding sequence).

3.Mutations

Mutation is permanent alteration in bases DNA. It is caused by mutagenic agents such as chemicals and radiation. They are often called variation and seed new characters. Cells do have repair mechanism for correct Mutation but error escape from it and come to population. Mutation generates new allele such as A to G. Mutation is different from Variation. Variation makes us better and do not threatening to life whereas mutationhaving impact on life and individual survival . we are unable to digest milk in adulthood but in variation of promoter of gene coding for lactase able us to digest milk by breakdown of it. Majority having wild-type allele & having different types of mutant allele. It can be point, deletion, insertion. Point type result in change in base while insertion result in frame shifting of sequences.

ISBN : 978-93-87793-80-4

Figure 2.variation

4.TYPES

Wild type sequence is present in most of the population. They code for different amino acids.Inmissrnse, a particular allele is replaced with other that code for some other amino acid. In nonsense sequence, allele is replaced with may act as stop codon that resist the translation of sequence further. Frame shifting by addition or deletion of allele result in frame shifting that code for other amino acid or can even stop sequencing strand. A to T Mutation in missense sequencing result in sickle cell anaemia while nonsense & frame shifting lead to Duchenne muscular dystrophy.

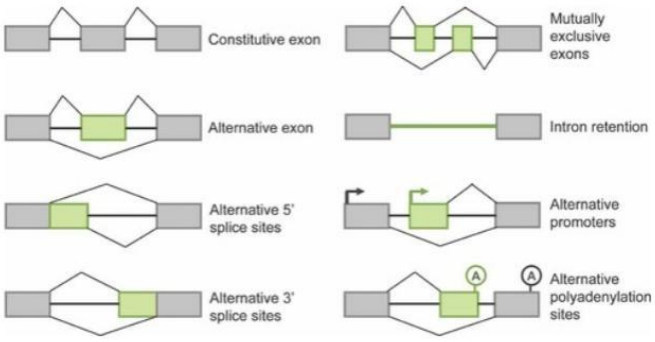
5.Exception

Not all changes in coding region affect the protein function. Such as in silent , a change in allele can again code for same amino acid & in nonsense, mutant allele code for stop &in missense, mutant allele code for different amino acids. Missense can be conservative and non conservative.

6.Splicing

snRNPs and other protein combine to form spliceosome that remove introns. These proteins bind to adjacent site in introns. Excised introns &spliceosome components are removed from mRNA. Some proteins can't bind to introns&introns retained in mRNA and result in frame shifting that Can't code for protein. Alternative Splicing can also occur in which different exons sequence bind together to form protein isoforms. Spinal muscular atrophy caused Mutation in gene coding for protein. Ret syndrome caused due to defect in gene responsible for transcription factor.

ISBN : 978-93-87793-80-4



7.Human chromosomes Figure3.

We have 23 pair of chromosome, 22 autosomes&1 sex chromosome. These arrangements of chromosome are called Karyotype. Generally errors in meiosis can occur & Karyotype help to identify the error in which

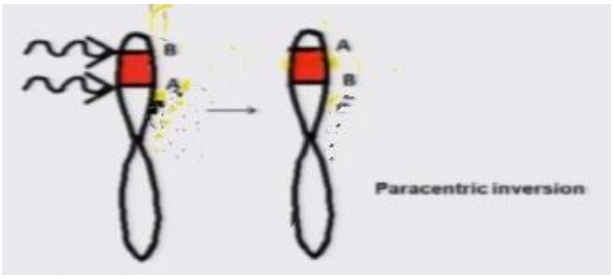


Figure 4.

chromosome. Down syndrome can occur because of triplets if chromosome 21. Turner syndrome is due to deletion of X chromosome having 45 chromosome. In meiosisII, 2 sister chromatin can occur in single cell. Klinefelter syndrome is due to additional copy of X chromosome. Sometimes pieces od chromosome are lost or rearranged during meiosis. This happens during recombination step, maternal & paternal pieces swap pieces. One break on chromosome can occur results in deletion of segment of chromosome such as in Cri-du-chat syndrome, deletion of region in 5 pair chromosome. 2 break in one chromosome or in different chromosome, Three break on chromosome can orrur.Ring chromosome can be formed, ring is formed due to fusion of breakpoints.

8.Mode of inheritance

A test cross is used to identify the dominant character by crossing unknown genotype with known genotype. Inheritance can really defined in pedigree.

ISBN : 978-93-87793-80-4

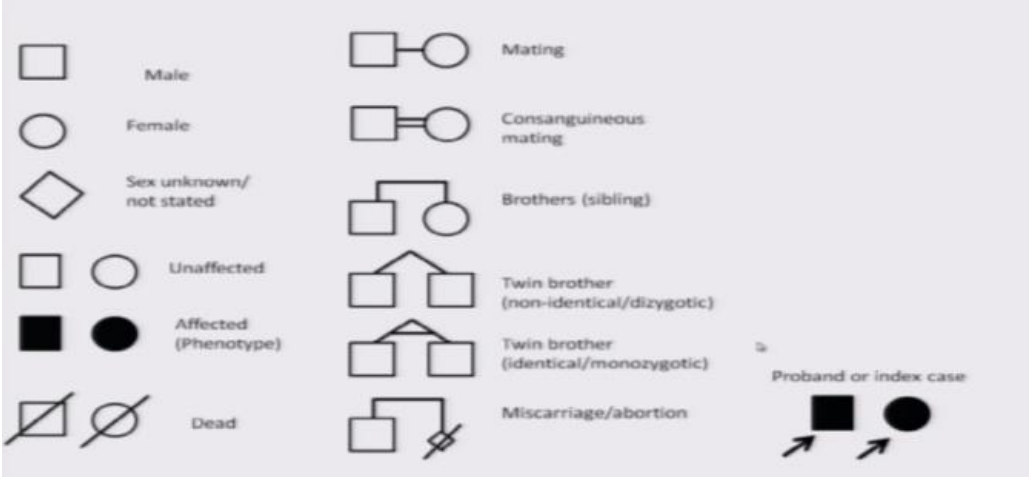


Figure 5. Pedigree sequence

8.1.Autosomal dominant inheritance

An affected person usually having one affected parent. It effects either sex& transmitted by either sex. A child having one affected parent and one non affected parent has 50% chance if being affected.

8.2. Autosomal recessive inheritance

Affected person born to unaffected parent. Parent of affected person are carriers. It affect either sex. After the birth of affected child, each subsequent child having 25% chance of being affected. There is increased incidence of paternal consanguinity.

8.3X linked recessive condition

It affects mainly male. Affected males are usually born to unaffected parents. There is no male to male transmission in the pedigree. Female may be affected of father is affected & mother is carrier. The mother is the carrier and may have male affected relatives.

8.4 X linked dominant

It affect either sex but more females than males. Usually at least one parent is affected. Females are more often mildly. For affected males, all daughters but no males are affected. The child of an affected female has 50% chance of being affected.

8.5 Y linked inheritance

It affects only male. Affected males always have affected father. All sons of affected males are affected.

8.6 Mitochondrial inheritance

It affects both sexes. It is usually inherited from affected mother. Can be caused by de nevo Mutation with mother unaffected. It is not transmitted by father to his children. There are highly variable clinical manifestation.

ISBN : 978-93-87793-80-4

9. Complication in pedigree

Incomplete penetrance. Phenotype skip a generation in autosomal dominant trait. Variable expression, serve to moderate. Mutation in two different gene can rescue the phenotype. With every generation, the age at onset decrease & the severity of the disease increases.

10. Genomics DNA Library

DNA is isolated from cell & digested with restriction enzymes. It forms segments of DNA. DNA fragments are inserted into cloning vector. The cloning vector is usually the Plasmid. Bacterial cells are transformed with vector which are further stored in boxes. A restriction enzyme is a protein that is coded by bacterial species. It recognize &

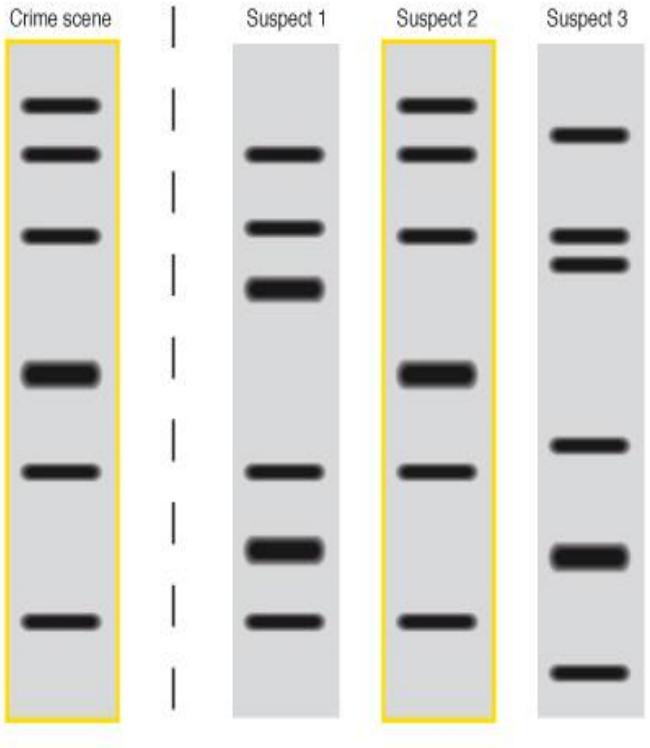


Figure6. DNA finger printing

cut DNA at specific sequence of nucleotide. If EcoRI is in insufficient amount then it cut DNA in abnormal form in overlapping fragments. DNA ligase is use to join the fragments with circular DNA of Plasmid. It can join blunt & sticky ends. Cloning vector having ORI, amp, & region into which DNA can be inserted.

11. Conclusions

The principle behind the use molecular biology tools in pedigree analysis. This includes DNA fingerprinting &RFPL analysis. DNA profiling decides whether a sequencing variant is causative for the disease could be daunting task. In 'loss of function ' Mutation, Mutation affects the protein. In 'gain of function' Mutation, gain of function for a protein. DNA finger printing is helpful to identify the DNA matching with parental DNA.

ISBN : 978-93-87793-80-4

DNA is run through gel in electrophoreses that gives us fragments if DNA with bases that can be match with others. In RFPL, the wild type sequence is present in population but mutant sequence cut the strands with different bases that can easily visualize under gel electrophoreses.

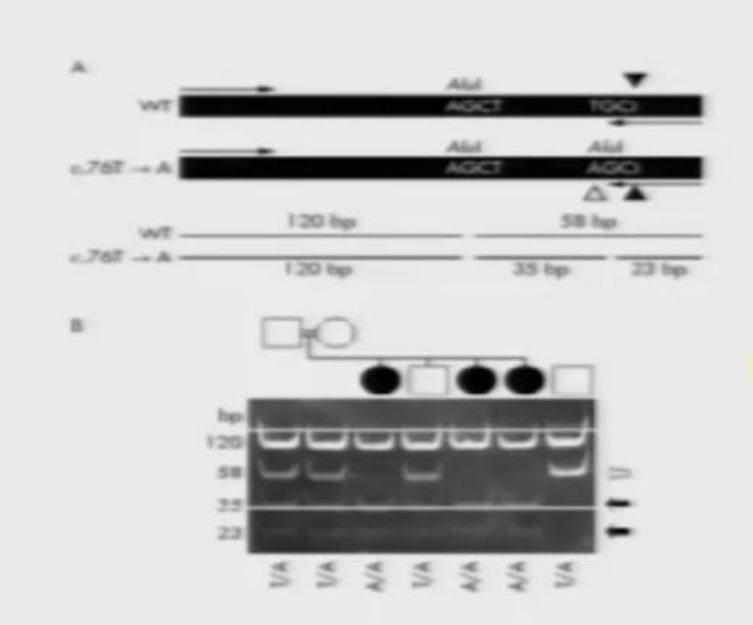


Figure 7.

A few Mutation are frequent in population than rests. This can be due to the deletion, point-mutation or due to founder effect. A population with wild-type & mutant allele can migrate to form isolates or a population having wild-type allele later develops mutant allele in isolate.

References

[1] hum mol genet. 2009 Apr 15;18(R1)R9-17

[2] J Pathol. 2010 Jan;220(2): 152-163

[3] Redrawn form HMG, Tom Stachan and Andrew P. Read

[4] J Med Genet. 2006 Sep;43(9):e48