Indian Journal of Dental Sciences.
October 2011
Supplementary Issue
Issue:4, Vol.:3

www.ijds.in

Review Article

Indian Journal
of Dental Sciences

E ISSN NO. 2231-2293
P ISSN NO. 0976-4003

Game Of Genes In Health And Disease

[1] Abhiney Puri
[2] Sucheta Bansal
[3] Sanjeev Joshi
[4] Priti Gupta

[1] MDS (Professor & HOD)
[2] MDS (Senior Lecturer)
Department of Oral and Maxillofacial Pathology
[3] Reader, Department of Prosthodontics
[4] Professor, Department of Conservative Dentistry
Himachal Institute Of Dental Sciences And Research
Paonta Sahib, Himachal Pardesh, India

Address For Correspondence:
Dr. Sucheta Bansal MDS (Senior Lecturer)
Department of Oral and Maxillofacial Pathology,
HIDS, Paonta Sahib, Himachal Pardesh, India
E-mail: suchetabansal@gmail.com
Date of Submission : 04/10/2010
Date of Acceptance : 06/10/2010

Abstract
Genetics is the study of heredity, the process by which characters are passed from parents to their offsprings, so that all offsprings resemble their parents. The characteristics in the organism, thus, depend upon the kind of genes or DNA they receive from their parents. Mutation is any sudden heritable structural change in DNA.

Key Words
genes genetics DNA RNA

INTRODUCTION

The term genetics was introduced by Bateson in 1906, derived film Greek word Gene, which means 'to become' or "to grow into" therefore genetics is the science of 'coming into being'. Genetics is the study of heredity, the process by which characters are passed from parents to their offsprings, so that all offsprings resemble their parents. This phenomenon of transmission of characters from parents to the offsprings is called *Heredity*[1].

According to the concept of genetics, heredity is controlled by large number of genes that are located on chromosomes which are called *Hereditary Vehicles*. Chromosomes are composed of deoxyribonucleic acid (DNA) and protein. The characteristics in the organism, thus, depend upon the kind of genes or DNA they receive from their parents[2].

During 1930s, biochemical and biophysical methods were first applied to study the chemical nature of a gene. This led to the new branch of genetics- *Molecular Biology*[2].

Due to the close association and interdependence between genetics and molecular biology the term *Molecular Genetics* is now used. It is that branch of biology that is concerned with the study of genetic material, deoxyribonucleic acid (DNA), its replication to produce more DNA, its transcription into ribonucleic acid (RNA), and the translation of RNA into protein in the form of polypeptide chains[1].

DISCUSSION

STRUCTURE OF DNA

The three dimensional structure of DNA was deduced by James Watson and Francis Crick in the year 1953. DNA molecule is composed of two long, parallel, polynucleotide chains, which are twisted in the form of a double helix with sugars and phosphates forming its backbone[3]. DNA consists of 2 different classes of nitrogenous bases:

* 2 Purines-Adenine (A) and guanine (G) &
* 2 Pyrimidines- Cytosine (C) and thymine (T) (uracil in RNA).

The two strands are complementary and have an antiparallel orientation held together by hydrogen bonds between A or G of one chain and T or C of the other respectively **(Fig. 1).**

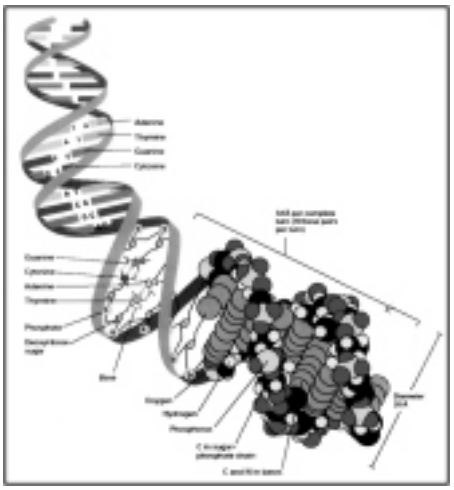


Fig. 1 Double helical structure of DNA.

- DNA precursors contain the pentose deoxyribose and the RNA precursors contain ribose instead. NUCLEOSIDE: Sugar + Nitrogenous base
- The nucleosides can serve as elementary precursors for DNA or RNA synthesis only when they become complexed with a phosphate group to form a nucleotide. NUCLEOTIDE: Sugar + Nitrogenous base + phosphate
- This phosphate group, is bound to the 5' carbon of the pentose sugar on one nucleotide, and bound to the 3' carbon of the sugar of the next nucleotide, so that a series of 5'-3' phosphate linkages, holds the nucleotides together along the length of the polymer.
- The phosphate bonds also called phosphodiester bonds are covalent bonds and so are extremely strong.

Types of DNA[3,4]

1. A- DNA- Right handed, with 11 base pairs per helical turn.
2. B- DNA- Right handed, with 10 base pairs per helical turn.
3. C- DNA and E- DNA- Right handed with slightly different configuration. Seen under very special environmental circumstances.

4. Z- DNA- Left handed, with 12 base pairs per helical turn. **(Fig. 2)**

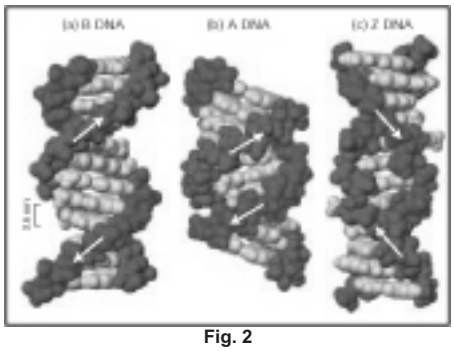


Fig. 2

Since the two chains are complementary, each synthesizes a second chain identical to one from which it had been separated, and the end result is two complete chromosome molecules, each identical to the original, this is referred to as *Semiconservative replication.* **(Fig. 3)**

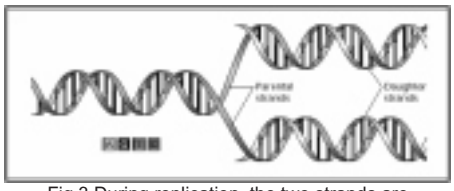


Fig.3 During replication, the two strands are unwound and used as templates to produce complementary strands. The outcome is two copies of the original double helix, each containing one of the original strands and one new daughter (complementary) strand.

STRUCTURE OF GENE

Gene is a segment of DNA that codes for a particular protein. There are two types of gene in the human genome:

1. Non-coding genes - will be transcribed but not translated (RNA genes).

2. Coding genes - will be transcribed and translated (Protein coding).

Genetic code[5,6]
The genetic code is the set of rules by which information encoded in genetic material is translated into proteins.

Salient features of genetic code [6,7]:
- Triplet i.e. comprises of 3 nitrogenous bases.
- Commaless i.e. there is no punctuation between the adjacent codons.
- Genetic code is universal. i.e., the same amino acids are coded for by the same codons, in all organisms studied, from bacteria to man.
- It has non-overlapping sequences.
- Genetic code is degenerate i.e. most amino acids are coded for by more than one triplet. This multiple system of coding is known as degenerate system. **(Fig.4)**

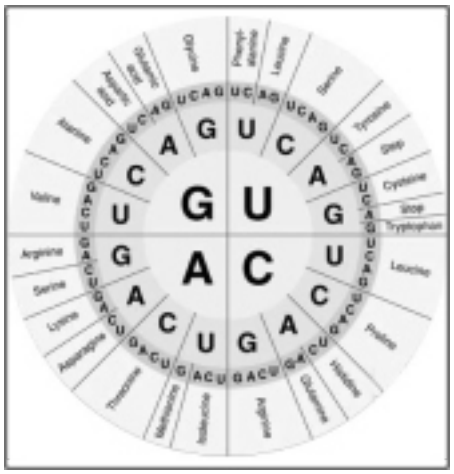


Fig.4 Genetic Code

DNA directs the synthesis of proteins which are molecules made up of amino acids arranged in a specific linear sequence. As there are 20 different amino acids, it is necessary for DNA to provide a code for each one of these. DNA has only 4 nitrogenous bases, which, taken one at a time, could code for only four amino acids. If two sequential bases would code for one amino acid there would be 4 x 4 or 16 possible combinations which are inadequate for 20 amino acids. The sequence in which amino acids are incorporated into a polypeptide chain is determined by the order of the corresponding triplets of bases. The coding region begins with the initiation codon, which is normally ATG. It ends with one of three termination codons: ATT, ATC, ACT. The synthesis of a polypeptide chain "Stops" when these codons have been read through.

RNA[5]
RNA (ribonucleic acid) - is composed of a single polynucleotide chain. It is synthesized on a DNA template by a process known as transcription which takes place in the presence of the enzyme RNA polymerase. **(Fig. 5)**

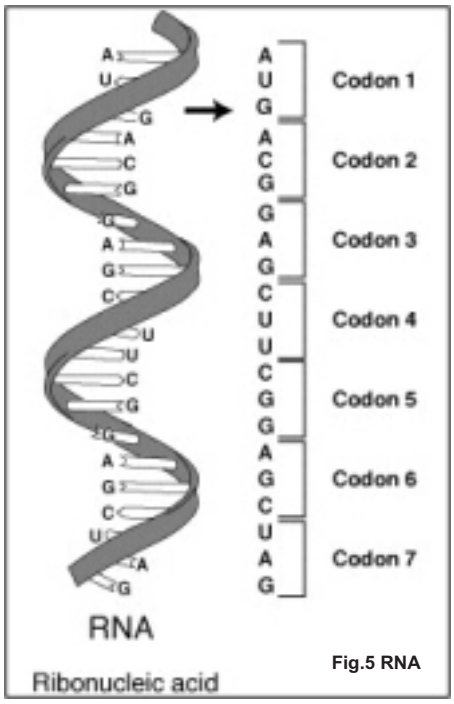


Fig.5 RNA

Three types of RNA concerned with protein synthesis: Messenger RNA, Transfer RNA and Ribosomal RNA.

Messenger RNA (mRNA):
It is produced in the nucleus. It represents a strand complementary to the DNA template; with the difference that uracil replaces thymine. It passes out from the nucleus to the cytoplasm and it dictates the sequence in which amino acids are incorporated into a polypeptide.

Transfer RNA (tRNA):
It is also known as **soluble RNA** (sRNA) or as **adaptor RNA.** It is concerned with bringing amino acids from the cytoplasm to their required places along the mRNA template. The tRNA molecule has an **anticodon** which is complementary to and reads a specific codon on the mRNA chain. The amino acid-tRNA complex is placed in the correct position on the linear mRNA molecule by the matching of codon and anticodon.

Ribosomal RNA (rRNA):
Ribosomes are made up of protein and nonspecific RNA (rRNA) in about equal proportions. The ribosomes are concerned with **reading the code** on mRNA and bringing amino acid-tRNA units into line at the appropriate codons. Ribosomes adhere to mRNA and then proceed along it. Ribosomal enzymes form peptide bonds between the **amino** acids. Once the peptide bond is formed, the polypeptide chain

breaks off from its ribosome. A ribosome takes about 10 seconds to read the length of an mRNA molecule.

Introns: In a single gene, there are five or more silent regions, the effects of which never appear in the final gene product, known as 'Introns'.

Exons: The functioning inter-intronic regions are called exons.
Introns are removed from the initial RNA formed by transcription and the exon-sequences are precisely joined or spliced together, by a process called **mRNA splicing,** to form a functional messenger RNA (mRNA). **(Fig. 6)**

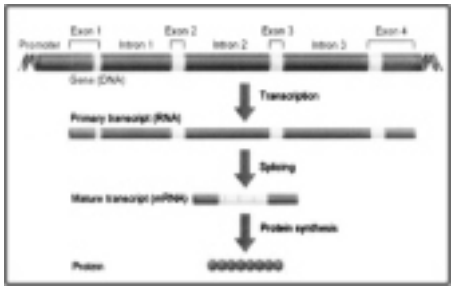


Fig.6 mRNA splicing

MUTATIONS

Mutation is any sudden heritable structural change in DNA. It also refers to the process by which a gene undergoes a structural change.
Mutations may be subdivided according to:[8, 9, 10]

A). Cause of mutation
1) Spontaneous mutations
2) Induced by exogenous agents

B). Type of change brought about by a mutation
1) Genome mutations (numerical chromosomal aberrations)
2) Chromosome mutations (structural chromosomal aberrations)
3) Gene or point mutation (alteration in the DNA at the molecular level)

C). Place at which a mutation occurs
1) Somatic mutations (occurring in body cells)
2) Germ cell mutations (occurring in germ cells - gametes)

SPONTANEOUS MUTATIONS[9]

- The mutational change may occur spontaneously, i.e. without exposure to mutagenic agents, or it may be induced by such mutagenic agents, eg. penetrating ionizing radiation or chemicals like mustard gas etc.

CHROMOSOMAL DISORDERS[8, 9, 10]

- These diseases are the result of the addition or deletion of entire chromosomes or part of chromosomes. Major chromosome disorders are characterized by growth retardation, mental retardation and a variety of somatic abnormalities. For eg. Down syndrome, caused by trisomy of chromosome 21. Clinically significant chromosomal abnormalities occur in nearly 1% of live born babies and accounts for about 1 % of pediatric hospital admission and 2.5% of childhood disease.

Types of chromosomal abnormalities:

I. Numerical
a) Euploidy: exact multiples of haploid no. of chromosomes. E.g. Diploid (46).

b) Polyploidy: multiples of haploid number of chromosomes other than diploid.
Triploidy - 69 chromosomes,
Tetraploidy - 92 chromosomes

c) Aneuploidy: chromosome number differing by 1 or more from an exact multiple of the haploid number.
Monosomy - loss of single chromosome,
Trisomy - gain of homologous chromosome
Tetrasomy - gain of 2 homologous chromosomes

II. Structural
a)Translocation: transfer of genetic material from one chromosome to another

Reciprocal - is formed when a break occurs in each of 2 chromosomes with the segments being exchanged to form 2 new derivative chromosomes.

Robertsonion - is a particular type of reciprocal translocation in which the breakpoints are located at or close to centromeres of 2 acrocentric chromosomes.

b)Deletion/Deletion: loss of part of chromosome resulting in monosomy for that segment.

Microdeletion- deletions of only a few genes at closely placed loci and are very small.

Ring chromosomes - when a break occurs on each arm of a chromosome leaving 2 sticky ends on the central portion which reunites as a ring.

c) Insertion: a segment of one chromosome becomes inserted into another chromosome.

d) Inversions: is a 2-break rearrangement involving a single chromosome in which a segment is reversed in position.

Pericentric: if the inversion segment involves the centromere.

Paracentric: if it involves only one arm of chromosome.

f) Isochromosomes: loss of one arm with duplication of the other E.g.: Turner's syndrome

g) Duplication: presence of a portion of chromosome more than once in a gamete or more than twice in a zygote.

III. Different cell lines (myxoploidy)
a) Mosaicism: Defined as presence in an individual or in a tissue of two or more cell lines which differ in their genetic constitution but are derived from single zygote. E.g.: Down's syndrome, Duchenne muscular dystrophy

b) Chemarism: Defined as the presence in an individual of two or more genetically distinct cell lines derived from more than one zygote. [Word 'chimaera' derived from Greek mythological monster which had a head of a lion, body of a goat and tail of a dragon].

SINGLE GENE DISORDERS/ POINT MUTATION[9]

- They are the alteration in the DNA at molecular level caused by a single mutant gene with a large effect on the patient's health. They account for approximately 5 - 10 % of pediatric hospital admissions and childhood mortality.

Examples:
a). Familial breast cancer and hereditary colon cancer occurs 1 in 300 individuals.

b). Sickle cell anemia occurs, 1 in 400 blacks in U.S.A.
- Mutations can also occur in genes on the mitochondria chromosomes, which are inherited in a uniquely maternal fashion.

Subclassification of gene or point mutation (Fig. 7):

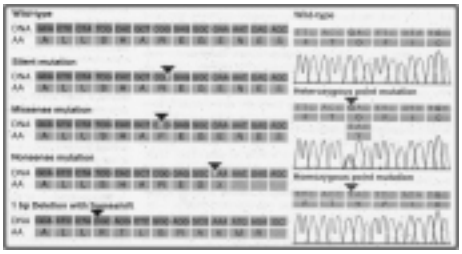
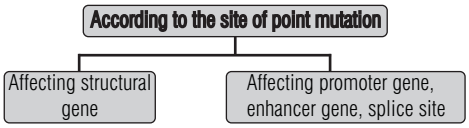
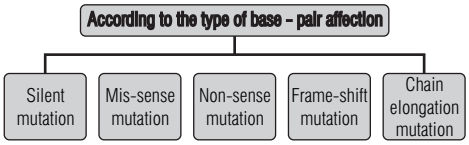


Fig.7 Examples of mutations. The coding strand is shown with the encoded amino-acid sequence.





Silent mutations: Because of the degeneracy of genetic code, many single base pair mutations do not change the amino acid sequence thereby exercising no effect. Such mutations are called silent substitutions.

Mis-sense mutations: These are type of base-pair substitutions which produce a change in a single amino acid.

Non-sense mutations: The base-pair substitutions which produce one of the three stop codons in the mRNA, altering the length of polypeptide either by shortening or lengthening.

- When a purine base is substituted for a pyrimidine base, it is called **transversion.**
- Substitution of one purine base for another purine base or a pyrimidine base for another pyrimidine base is known as **transition.**

Frame shift mutation: When deletion or insertion of base-pair is not a multiple of three, such insertions or deletions alter all the downstream codons.

POLYGENIC OR MULTIFACTORIAL DISORDERS[9]

- Results from the interaction of multiple genes, some of which have a major effect, but many of which have a relatively minor effect. Examples of such disorders are diabetes mellitus, hypertension, coronary heart diseases, schizophrenia, cleft lip and palate, congenital heart diseases etc.
- These diseases accounts for 25-50% of pediatric hospital admission and approximately 25-35% of childhood mortality.

SOMATIC CELL GENETIC DISORDERS[9]

- In the above three categories, there is abnormality in DNA of all cells in the body including germ cells and can be transmitted to subsequent generations.
- Cancer is a consequence of mutations in genes that control cellular growth; the most common genetic disease.

CONCLUSION

DNA molecule is composed of two long, parallel, polynucleotide chains, which are twisted in the form of a double helix with sugars and phosphates forming its backbone. Mutation is any sudden heritable structural change in DNA. Types of mutation include point mutations, deletions, insertion, rearrangements and duplications. The effect can be produced at any stage in transcription or translation.

In point mutations the change is in one base pair of the DNA molecule. Deletions can remove part of a gene, and if a deletion affects only part of a codon this will alter a reading frame, which results in a marked effect on transcription and subsequent translation. An example of this is a deletion in the dystrophin gene leading to a frame shift, resulting in Duchenne's muscular dystrophy. Sickle cell anaemia is an example in which a simple point mutation leads to modification of the mRNA.

The study of genetically determined conditions in which the defective enzyme alters the expected effect of a drug is termed pharmacogenetics.

REFERENCES

1. Dhami PS, Mahindru RC. Nature and scope of biology. In: A textbook of biology, 8th ed. Jalandhar: Pradeep publications, 1996. p. I-6.
2. Rastogi VB. Origin of genetics and molecular biology. In: A textbook of genetics, 9th ed. New Delhi: Kedar Nath Ram Nath publications, 1992. p. 3-4.
3. Rastogi VB. Molecular structure of genetic material. In: A textbook of genetics, 9th ed. New Delhi: Kedar Nath Ram Nath publications, 1992. p. 300-311.
4. Lodish, Berk, Matsudaira, Kaiser, Krieger, Scott. Structure of nucleic acids. In: Molecular cell biology 5th ed. p. 103-5.
5. Bhatnagar SM, Kothari ML, Metha LA. Molecular genetics: The genetic basis of inheritance. In: Essentials of human genetics, 4th ed. Orient Longman: 2004. p. 44-65.
6. Rastogi VB. Genetic code. In: A textbook of genetics, 9th ed. New Delhi: Kedar Nath Ram Nath publications, 1992. p. 342-50.
7. Friedman JM, Dill FJ, Hayden MR. Nature of genetic material. In: Friedman JM, Dill FJ, Hayden MR, McGillivray BC, editors. Genetics, 2nd ed. New Delhi: Waverly International, 1996. p. 8-18.
8. Sandberg AA. The chromosomes in human cancer and leukemia. North Holland, New York: Elsevier, 1980.
9. Bhatnagar SM, Kothari ML, Metha LA. Genetic basis of variation: Polymorphism and mutation. In: Essentials of human genetics, 4th ed. Orient Longman, 2004. p. 85-94.
10. www.genetics.edu.au/ The Australasian Genetics Resource Book - © 2007

Source of Support : Nill, **Conflict of Interest** : None declared