Lec(1) Genetic diseases

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Objectives:

To Describe nature of genetic abnormalities and types of mutations

Meaning

The term Genetics was introduced by Bateson in 1906. It was derived from Greek word “Gene” which means 'to become' or 'to grow into'.

Therefore, genetics is the science of coming into being.

"Genetics is that branch of biological sciences which deals with the transmission of characteristics from parent to off spring

Terminology

1. Gene: The fundamental physical and functional unit of heredity. an ordered sequence of nucleotides located in a particular position on a particular chromosome that encodes a specific functional product.

2. Heredity: The handing down of certain traits from parents to their offspring. The process of heredity occurs through the genes.

3. Allele: Alternative form of a (gene) genetic locus; a single allele for each locus is inherited separately from each parent

4. Genome: All the genetic material in the chromosomes of a particular organism

5. Autosome: A chromosome not involved in sex determination.

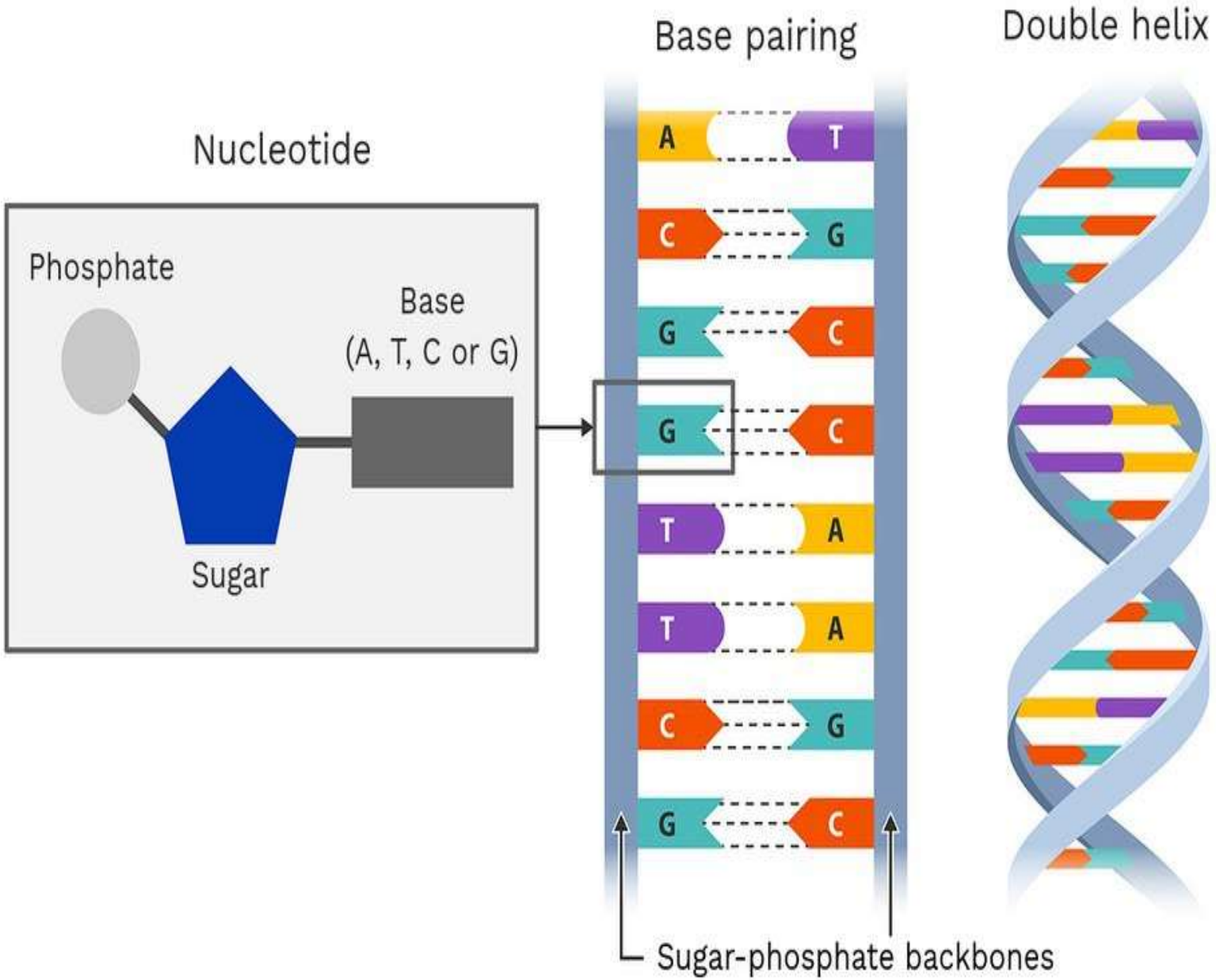
The diploid human genome consists of 46 chromosomes, 22 pairs of autosomes

6. Sex Chromosome: The X or Y chromosome in human beings that determines the sex of an individual. Females have two X chromosomes in diploid cells; males have an X and a Y chromosome.

7. Locus : The specific physical location of a gene on a chromosome.

What is DNA?

Deoxyribonucleic acid (abbreviated DNA) is the molecule that carries genetic information for the development and functioning of an organism. DNA is made of two linked strands that wind around each other to resemble a twisted ladder — a shape known as a double helix. Each strand has a backbone made of alternating sugar (deoxyribose) and phosphate groups. Attached to each sugar is one of four bases: adenine (A), cytosine (C), guanine (G) or thymine (T). The two strands are connected by chemical bonds between the bases: adenine bonds with thymine, and cytosine bonds with guanine.


Nucleotide
Phosphate
Base
(A, T, C or G)
Sugar
Base pairing
A
T
C
G
G
C
G
C
T
A
T
A
C
G
G
C
Sugar-phosphate backbones
Double helix

What Is a Gene?

A gene is a distinct portion of a cell's DNA.

- Genes are coded instructions for making everything the body needs, especially proteins.

Gene hold the information to maintain their cells and pass genetic traits to off springs

- Human beings have about 25,000

- A dominant allele produces a dominant phenotype in individuals who have one copy of the allele, which can come from just one parent.
- For a recessive allele to produce a recessive phenotype, the individual must have two copies, one from each parent.

- An individual with one dominant and one recessive allele for a gene will have the dominant phenotype. They are generally considered "carriers" of the recessive allele: the recessive allele is there, but the recessive phenotype is not.

Homozygous-an organism in which 2 copies of genes are identical i.e. have same alleles

Homozygous means you carry two genes that are the same for each trait.

Heterozygous-an organism which has different alleles of the gene or Heterozygous means you carry two different genes for each trait Heterozygous-an organism which has different alleles of the gene

A phenotype (from Greek phainein, meaning "to show", and typos, meaning "type") is the composite of an organism's observable characteristics or traits, such as its morphology, development, biochemical or physiological properties, phenology, behavior and products.

What are chromosomes

Chromosomes are threadlike structures made of protein and a single molecule of DNA that serve to carry the genomic information from cell to cell. In plants and animals (including humans), chromosomes reside in the nucleus of cells..

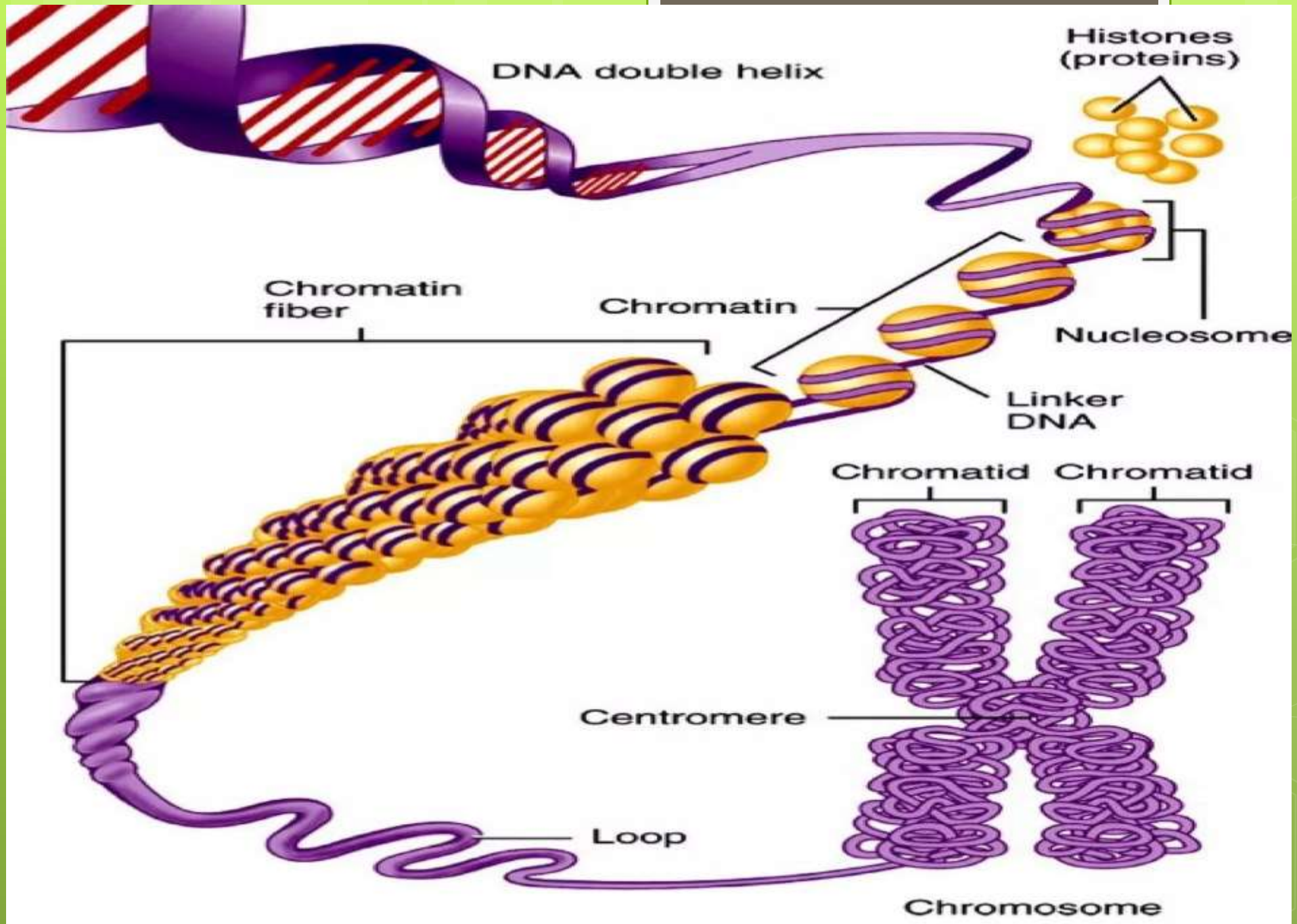


Figure 03.25 Tortora - PAP 12/e

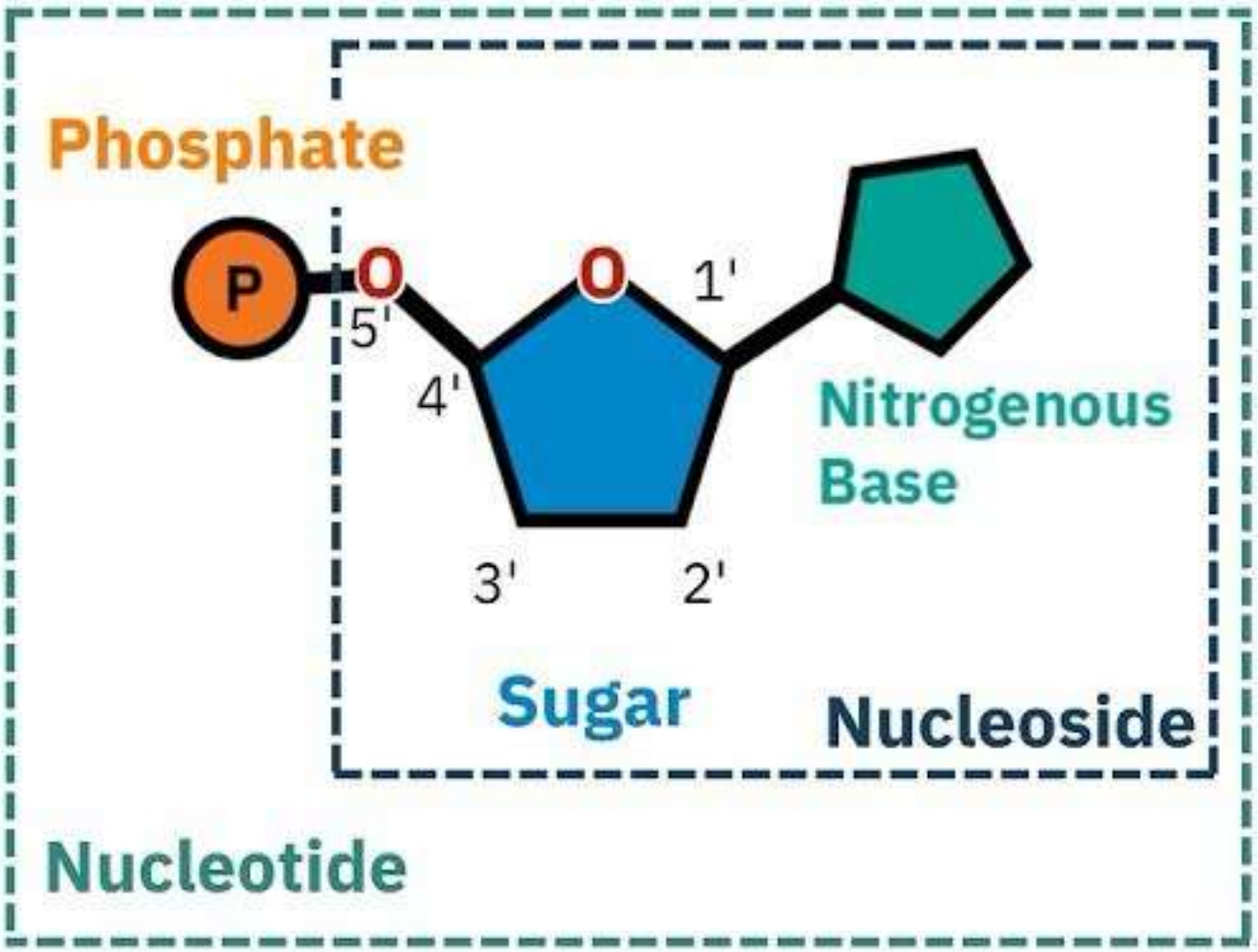
Chromatin: made up of DNA, RNA & proteins that make up chromosome, Chromatin is located in the nucleus of a cell.

Chromatids: one of the two identical parts of the chromosome.

Centromere: the point where two chromatids attach

NUCLEOTIDE: group of molecules that when linked together, form the building blocks of DNA and RNA; composed of phosphate group, the bases: adenosine, cytosine, guanine and thymine and a pentose sugar. In case of RNA, thymine base is replaced by uracil.

CODON: series of three adjacent bases in one polynucleotide chain of a DNA or RNA molecule which codes for a specific amino acid.

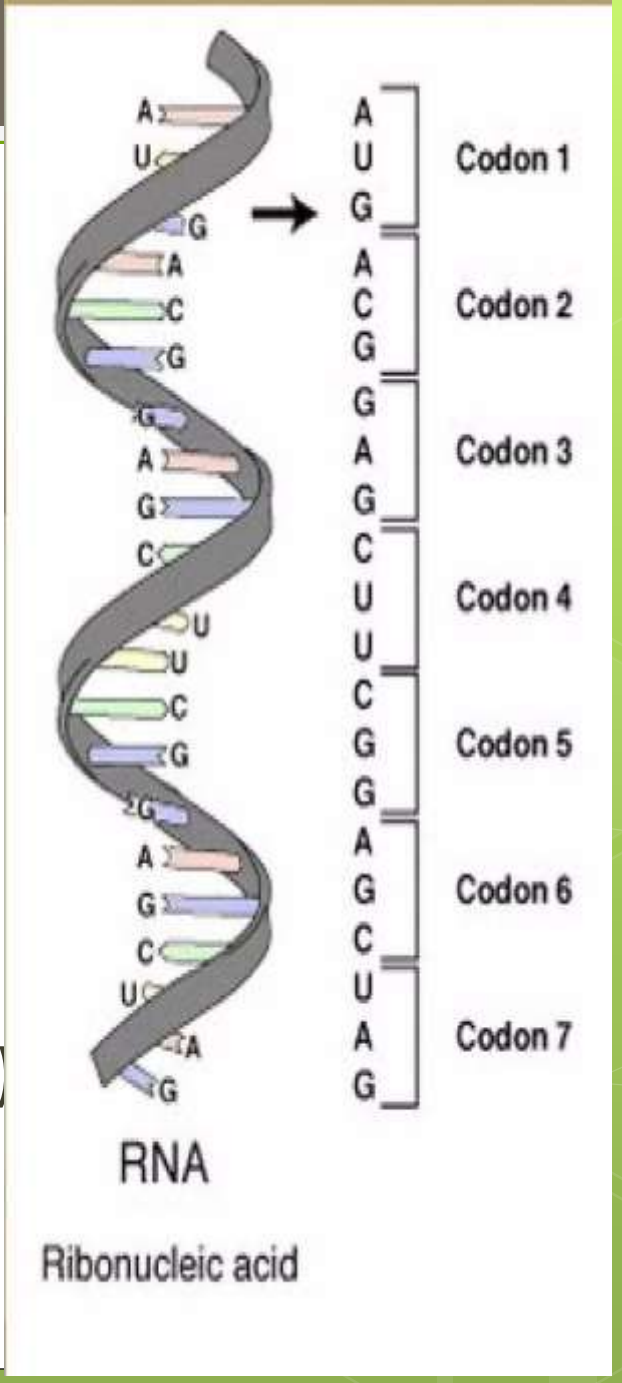

Phosphate
P
O
O
5'
4'
1'
3'
2'
Nitrogenous Base
Sugar
Nucleoside
Nucleotide

A series of codons in part of a mRNA molecule.

Each codon consists of three nucleotides, usually representing a single amino acid.

The nucleotides are abbreviated with the letters A, U, G and C.

This is mRNA, which uses U (uracil) DNA uses T (thymine) instead.



Congenital Disease.

Diseases which are present at birth.

Hereditary/Familial Disease. .1

Diseases which are derived from one's parents and transmitted in the gametes through the generations.

Not all congenital diseases are genetic and not all genetic diseases are congenital. .1

Genetic mutations Definition

A permanent heritable change in a gene or chromosomal structure and are important in the causation of cancer and some congenital diseases. .1

Causes of Mutations

- Chemicals
- Nitrous acid
- Alkylating agents
- 5- bromouracil
- Antiviral drug iododeoxy uridine
- X-Rays and Ultaviolet light
- Certain viruses
- Benzpyrene in tobacco smoke

Types of Genetic Mutations

1. Point Mutation
   - A. Silent
   - B. Missense
   - C. Nonsense

2. Frame shift Mutations
   - A. Deletion
   - B. Addition

Point mutation

1. Substitution of a single nucleotide base by different base 2.

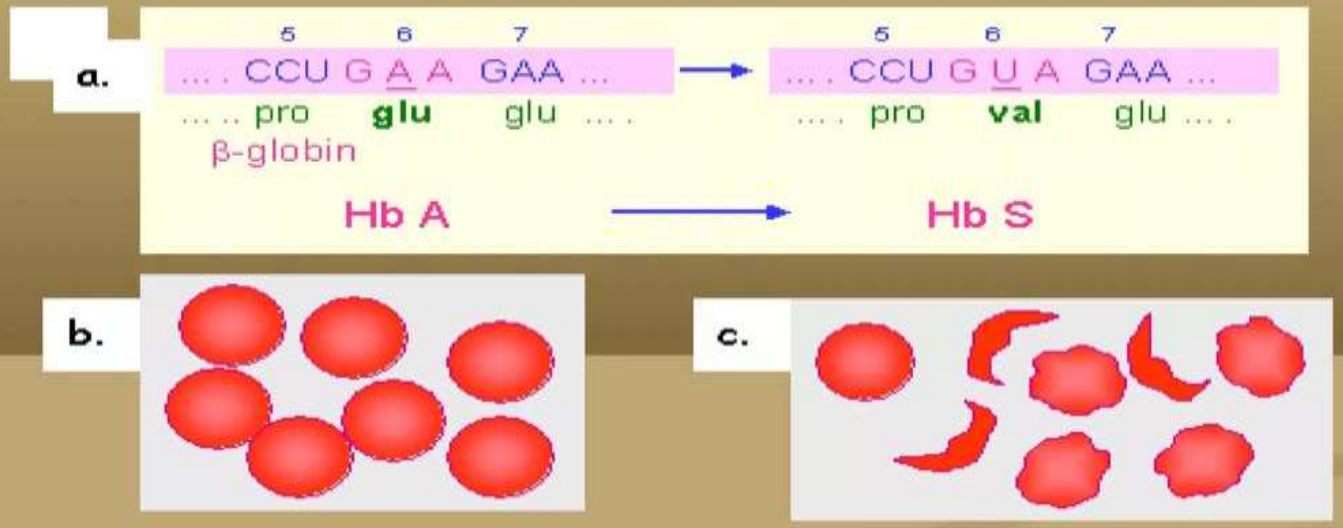


Fig. 5.1 (a) Point mutation in codon number six of the beta β-globin gene results in the substitution of the amino acid number glutamine with valine and the formation of haemoglobin S (HbS); (b) Red blood cells in a smear of normal blood containing HbA; (c) crenated and sickle-shaped red blood cells in sickle cell anaemia.

- Sickle cell anaemia is the result of a point mutation in codon 6 of the b-globin gene resulting in the substitution of amino acid glutamic acid by valine.

- b-globin is a major component of adult haemoglobin (HbA). The single amino-acid substitution results in a type of haemoglobin termed HbS, which has different properties from the normal HbA.

Silent mutation

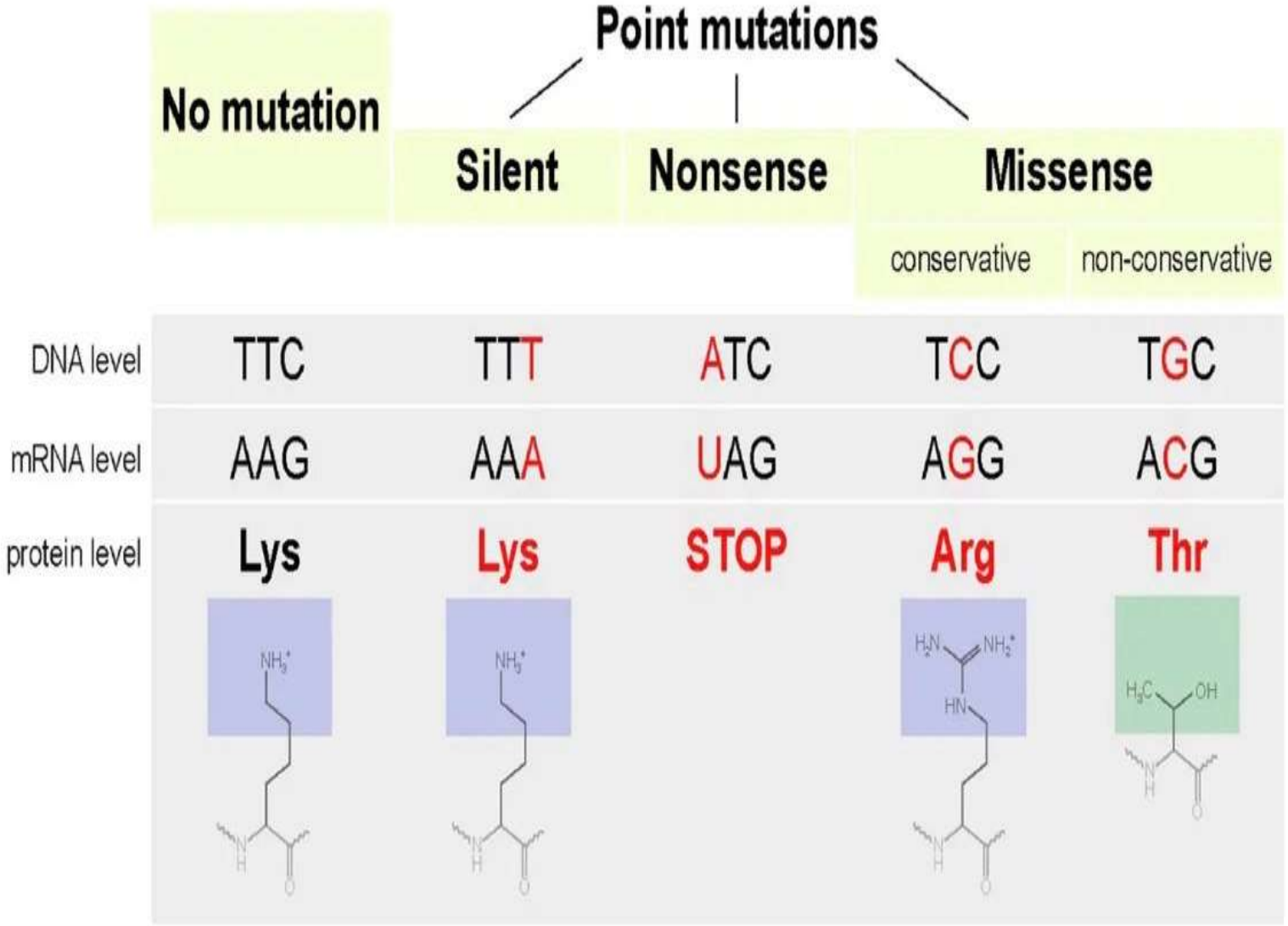
Silent mutations are mutations in DNA that do not have an observable effect on the organism's phenotype. They are a specific type of neutral mutation. .1

Nonsense mutation

- A nonsense mutation is also a change in one DNA base pair. .1
- Instead of substituting one amino acid for another, however, the altered DNA sequence prematurely signals the cell to stop building a protein. .2
- This type of mutation results in a shortened protein that may function improperly or not at all. .3

Missense mutation

This type of mutation is a change in one DNA base pair that results in the substitution of one amino acid for another in the protein made by a gene. .1


Point mutations
No mutation
Silent
Nonsense
Missense
conservative
non-conservative
DNA level
TTC
TTT
ATC
TCC
TGC
mRNA level
AAG
AAA
UAG
AGG
ACG
protein level
Lys
Lys
STOP
Arg
Thr

Frameshift mutation

This type of mutation occurs when the addition or loss of DNA bases changes a gene's reading frame. .1

- A reading frame consists of groups of 3 bases that each code for one amino acid. .2

- A frameshift mutation shifts the grouping of these bases and changes the code for amino acids. .1

- The resulting protein is usually nonfunctional. .1

- Insertions, deletions, and duplications can all be frameshift mutations.

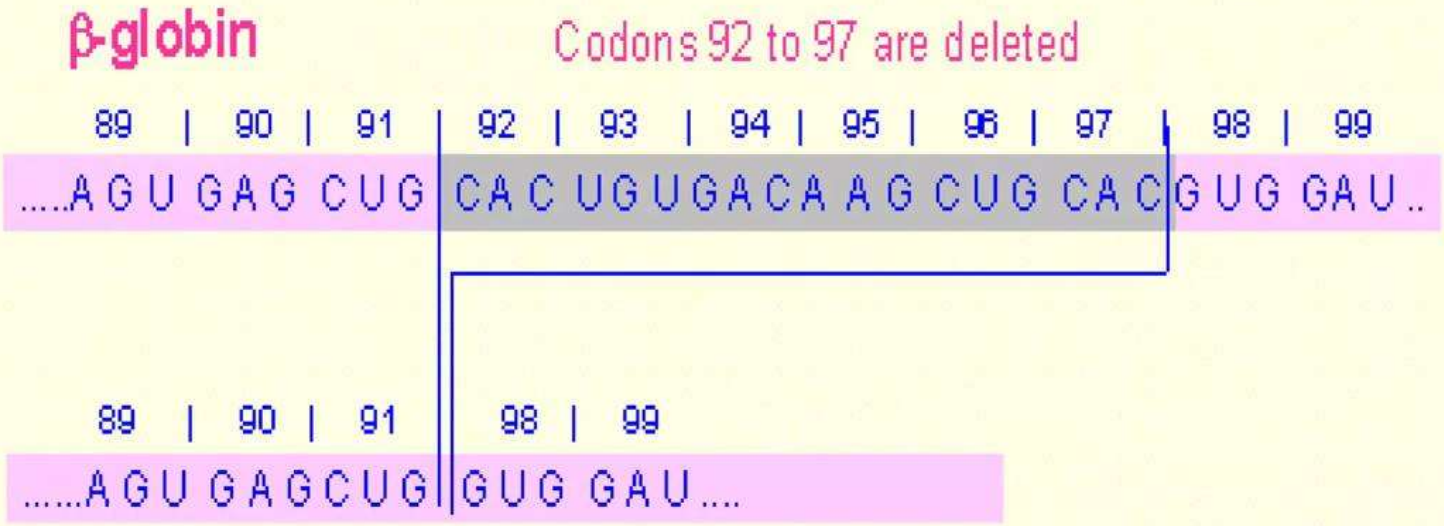


Fig. 5.5. Deletion of codons 92 to 97 in the β-globin gene.

Fig 5.6. Insertion of a 3.8 Kilo base segment in the factor VIII gene is the most common mutation in haemophilia A

Deletion

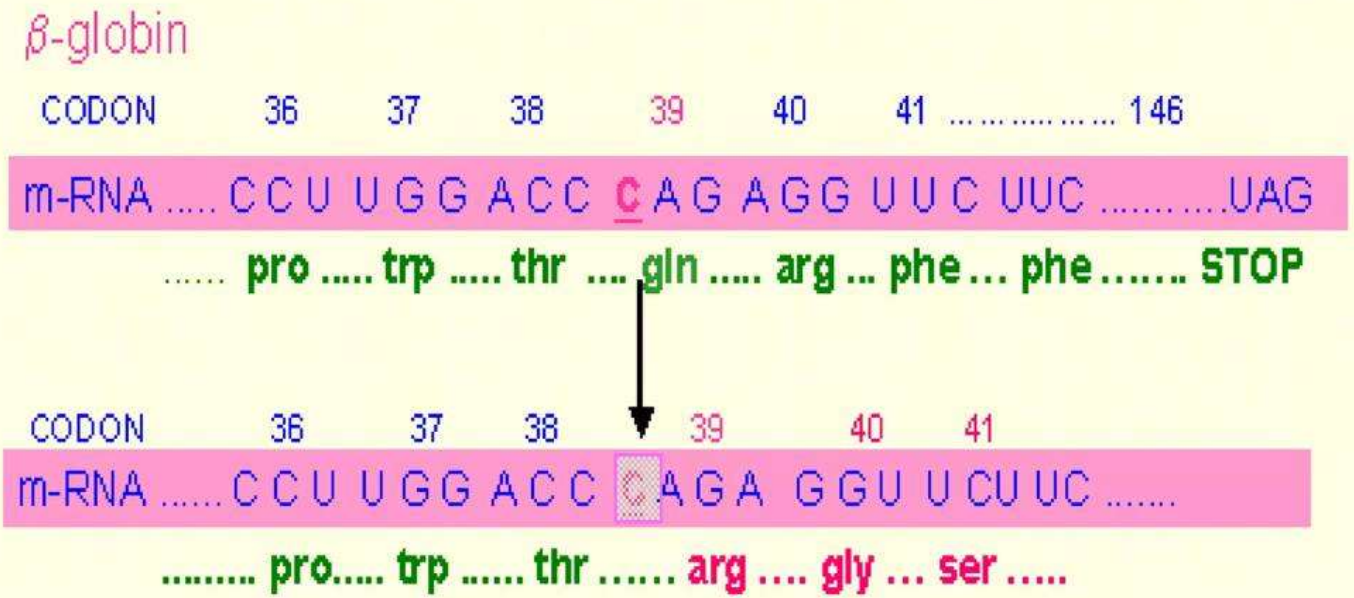


Fig 5.7. Deletion of a single nucleotide completely alters the subsequent reading frame and results in a non-sense sequence of amino acids.

Insertion

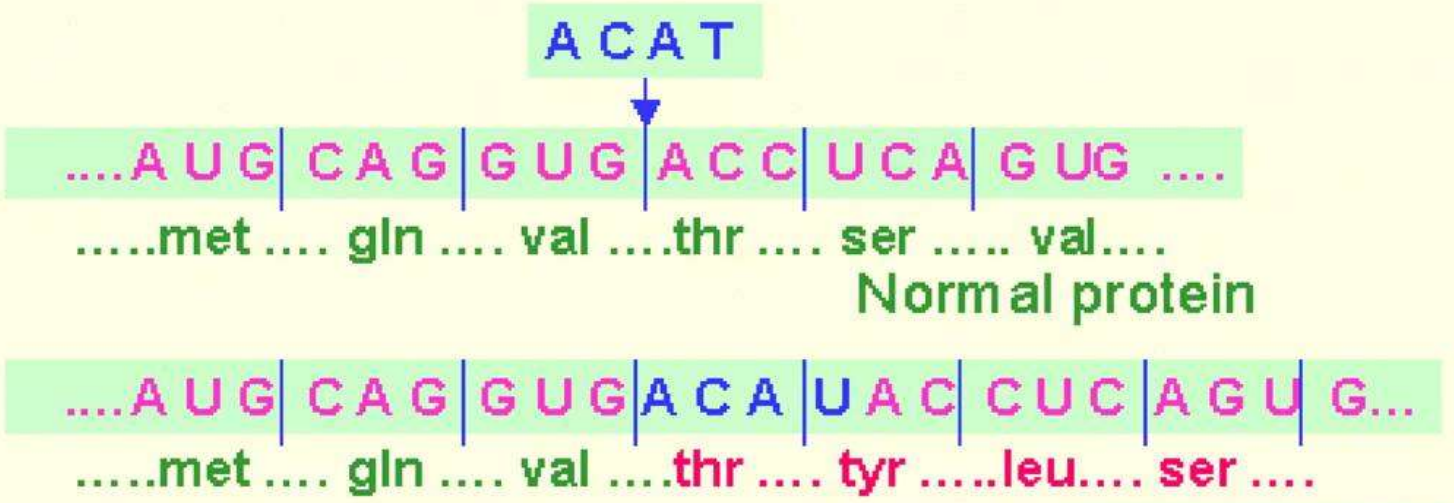


Fig 5.8. Insertion of 4 bp in the hexoseaminidase gene results in a frame shift mutation causing Tay Sach's disease.

- Tay-Sachs disease is a rare inherited disorder that progressively destroys nerve cells (neurons) in the brain and spinal cord

Thanks