Chap.3 Doc.2 Mutations and Multiple Alleles

- Mutation is a sudden and unpredictable change in the sequence of nucleotides of DNA to produce a new allele that will result in a new phenotype that may be beneficial or harmful.

-Types of mutation:

A. Genetic mutation
B. Chromosomal mutation(chap.5)

A. Types of genetic mutations:
   1. Mutation by substitution or replacement
   2. Mutation by deletion or elimination
   3. Mutation by insertion or addition

- If mutation occurs at the level of one nucleotide, it is called point mutation.
- If mutation occurs at the level of more than one nucleotide, it is called stretched mutation.

1. **Mutation by substitution**

a. **Mutation by substitution (missense mutation)** :

…CCA – GAG – ACT… Non-transcribed strand of DNA(normal allele)
…CCA –GAG - ACU… mRNA
…Pro - Glu - Thr … Sequence of amino acids→ Normal functional protein →Normal phenotype

…CCA – GTG- ACT …. Non-transcribed strand of DNA (mutant allele)
…CCA - GUG – ACU… mutated mRNA
…Pro - **Val** - Thr … Sequence of amino acids (missense mutation: leads to a change in the sequence of one amino acid, but the total number of amino acids is conserved)→Non-functional protein →Abnormal phenotype

Site of mutation: 2nd codon,2nd nucleotide
Type of mutation: Substitution missense mutation, where the 2nd nucleotide of 2nd codon of base A is replaced by another nucleotide of base T.
Modification:

- Change in the sequence of nucleotides of DNA of the normal allele
- Change in the sequence of nucleotides of mRNA of the normal allele
- Change in the sequence of amino acids

Consequence:

- It results in a mutant allele
- The synthesis of non-functional protein that leads to appearance of an abnormal phenotype "defect"

b. **Mutation by Substitution (silent mutation)**:

… CCA – GA**A** – ACT… Non-transcribed strand of DNA (mutant allele)
….CCA - GAA –ACU… mutated mRNA
….Pro – **Glu** - Thr…..Sequence of a.a
Site of mutation: 2nd codon, 3rd nucleotide
Type of mutation: Substitution, where the 3rd nucleotide of 2nd codon of base G is replaced by another nucleotide of base A
Modification: - change in the sequence of nucleotides of DNA of normal allele
-change in the sequence of nucleotides of mRNA
- **No** change in the sequence of amino acids

Consequence: - It results in a mutant allele

-The synthesis of same functional protein

So **silent mutation** is the change in the sequence of nucleotides of DNA that doesn't affect the sequence of amino acids in the produced protein (Such modifications have no effect on the phenotype).

c. Mutation by substitution (Nonsense mutation)

CCA – **T**AG – ACT Non-transcribed strand of DNA (mutant allele)

CCA – UAG… mRNA

Pro – Stop……(incomplete polypeptide)

2. Mutation by deletion:

9 10 11 12 13 14 15 16

… TAC –**A**CC –ACG –A… non-transcribed strand of DNA (normal allele)

… UAC – ACC-ACG -A …. mRNA

…. Tyr – Thr – Thr - sequence of amino acids →normal functional active protein→Normal phenotype

….TAC – CCA – CGA -…. Non- transcribed strand of DNA of mutant allele

….UAC – CCA – CGA … mutated mRNA

… Tyr – **Pro - Arg** Sequence of amino acids (Frameshift mutation: change the whole sequence of amino acids from the site of mutation and after)

Site of mutation : Elimination of 12th nucleotide of base A

Type of mutation: Deletion, where 12th nucleotide of 2nd codon of base A is eliminated.

Modification: - change in the sequence of nucleotides of DNA of normal allele.

-change in the sequence of nucleotides of mRNA of normal allele

-change in the sequence of amino acids

Consequence: - It results in mutant allele

-The synthesis of non-functional protein which leads to the appearance of abnormal phenotype.

3. **Mutation by insertion**:

… TAC – ACC – ACG –A… Non-transcribed strand of DNA (normal allele)

… UAC –ACC – ACG – A… mRNA

…. Tyr – Thr – Thr Sequence of amino acids →Active normal functional protein→Normal phenotype

……TAC –**G**AC – CAC- GA…. Non-transcribed strand of DNA (mutant allele)

….. UAC –GAC –CAC –GA … mutated mRNA

….. Tyr – **Asp – His** Sequence of amino acids (frameshift mutation)

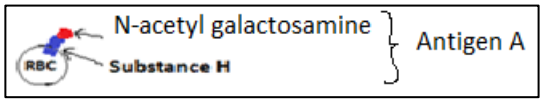
Genes and multiple alleles(p.61 doc.c,d and e)

Genetic polymorphism is the presence of many functional alleles of the same gene.It is due to mutation of the gene which results in diversity of alleles.

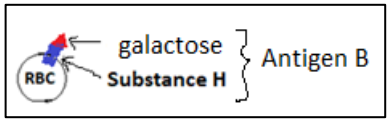
Applications on genetic polymorphism:

- Gene of blood group in humans:

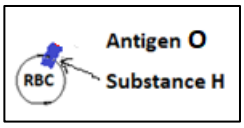
Blood grp A has molecule A on the surface of Red blood cells



Blood grp B has molecule B on the surface of RBC



Blood grp O has molecule O on the surface of RBC



The 3 molecules (A,B and O) have common structure (substance H)
but molecule A has in addition a sugar called N-acetyl galactosamine ,
molecule B has in addition a sugar called galactose
and molecule O has no added sugar.
Sugar addition is controlled by an enzyme "transferase" which is coded by 3 allelic genes , A, B and O that derive from different mutations of the same gene.

Ancestral gene of the blood group: wild allele

Substitution mutation	Substitution mutation	Mutation by deletion
Allele A	**Allele B**	**Allele O**

Allele A By transcription and translation **Protein A (active Transferase enzyme A) [EA]**
Allele B **Protein B (active Transferase enzyme B) [EB]**
Allele O **Protein O (inactive enzyme EO)**

Substance H + N-acetylgalactosamine Transferase enzyme A Antigen A

Substance H + galactose Transferase enzyme B Antigen B

Substance H Truncated enzyme O Antigen O

*Note: substance H is coded by a gene composed of 2 alleles H and h where H dominates h ;so the genotype is HH,Hh or hh. Therefore if an individual has the genotype HH or Hh, he can synthesize substance H ; but if he has the genotype hh and both alleles AA for example , his blood grp is O (Bombay group) because he can't synthesize substance H.