PROPERTIES OF GENETIC CODE.

- DEGENERACY-
- Degeneracy means that an amino acid is coded by more than one codon even though each codon is sepecific for one amino acid.
- For example arginine, is coded by six codons but each of six codon code for only arginine.

Wobble Hypothesis.

- Methionine is coded only by one codon.

- It is due to wobble phenomenon described below.
- WOBBLE HYPOTHESIS---
- Single tRNA recognises more than one codon. All such codons have their third nucleotide different from each other but first the two codon are same.
- This is called Wobble Hypothesis.

Degeneracy of codon.

Amino acids	Number of codon
Arginine, leucine, serine	*6 each*
Alanine, glycine, proline and threonine	*4 each*
Isoleucine	*3 each*
Aspartate, glutamate, cysteine, histidine, lysine, phenylalanine, asparagine, glutamine	*2 each*
Methionine and tryptophan	*1 each*

- The first two bases of a wobble codon makes strong base pairings of the with the corresponding bases anticodon on tRNA.
- This confers most of the coding specificity. The third base of the codons forms a loose/weak pairings with the corresponding base on anticodon.
- This third base is called wobble (unsteady or unstable).
- It permits rapid dissociation of the tRNA from the codon during protein synthesis.

FEATURES OF GENETIC CODE.

- ***UNIVERSALITY-***

  Genetic code is considered to be universal because the aminoacid are coded by the same codons in the proteins of all the living organism.

- ***SPECIFICITY---***

  A particular codon always codes for the same aminoacid.eg.-UGG always codes for only tryptophan.

- ***NON-OVERLAPPING—***

  The genetic code is read on mRNA 5' to 3' end in a continuous , comma-less pattern.The codon does not overlap and once the translation started , there is no punctuation and it is read in a continuing sequence until a stop codon is encountered.

  The addition or deletion of one or more bases alters the message sequence in mRNA result in different protein synthesis.(Mutation).

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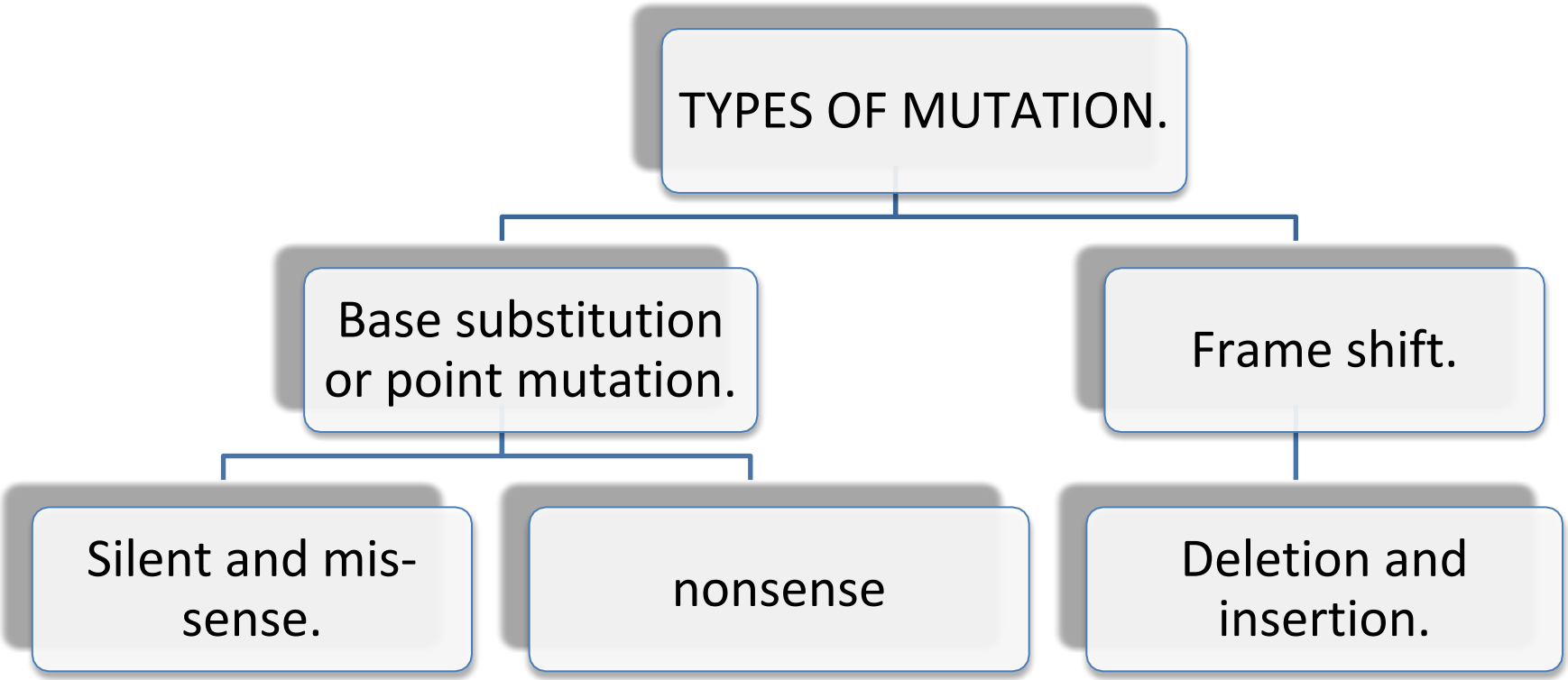
MUTATION.

- Mutations are defined as change in nucleotide sequence of DNA which act as templates for transcription and transmission of genetic information.

TYPES OF MUTATION.



Introduction.

- Sudden heritable change in genetic material or character of an organism is known as mutation.
- Individuals showing these changes are called mutants.
- Factors or agent causing mutation are known as mutagens.
- Mutation which causes change in base sequence of a gene are known as gene mutation or point mutation.

POINT MUTATION

- Point mutation results from change in single nucleotide in the sequence. They may be due to the following changes.

Only one base is altered.

Protein with abnormal AA sequence.

Types-

Transition

Transversion.

or substitution of one nucleotide in a gene.

Sickle cell disease is the result of nucleotide substitution.

Ocurs in Haemoglobin gene.

- ***INSERTION-***

  Trinucleotide expansion-

- ***In Huntington's chorea , CAG trinucleotides are repeated 30 to 300 times leads to polyglutamines repeat in protein.***

- ***Duplication---Gene duplication results from unequal crossing over of chromosomes during meiosis and plays an important role in evolution.***

Point mutation.

- **Transition—**
- in which one purine base (A) is changed by another purine (G).

- Similarly, a pyrimidine base (C) may be changed by other pyrimidine base (T).

Point mutation.

- Purine is never changed by pyrimidine or vice versa.

- *Transversion--* in which a purine base is changed by a pyrimidine and vice versa.

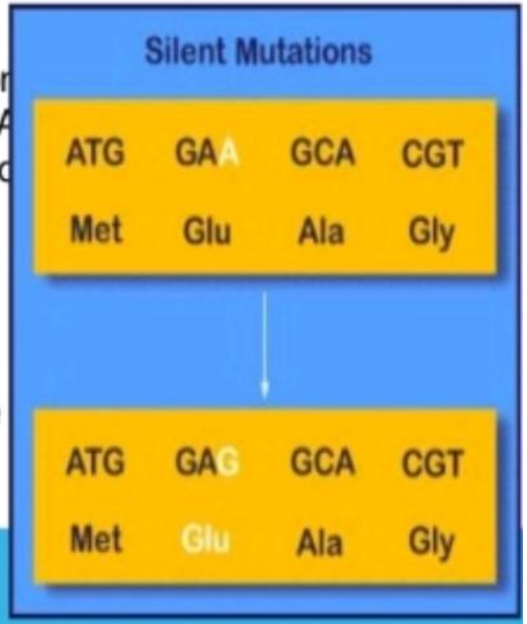
SPECIFIC DISEASES CAUSED BY POINT MUTATIONS

- **Cystic fibrosis**
- A defect in the cystic fibrosis transmembrane conductance regulator (CFTR) gene causes cystic fibrosis (CF). A protein made by this gene controls the movement of the water and salt in and out of the body's cells. Genes in people with CF incorrectly code proteins. This causes thick, sticky mucus and very salty sweat.
- **Neurofibromatosis**
- Neurofibromatosis is caused by point mutations in the Neurofibromin 1or Neurofibromin 2 gene.
- **Sickle-cell anemia**
- Sickle-cell anemia is caused by a point mutation in the β-globin chain of haemoglobin, causing the hydrophilic amino acid glutamic acid to be replaced with the hydrophobic amino acid valine at the sixth position.
- **Color blindness**
- People who are colorblind have mutations in their genes that cause a loss of either red or green cones

Effects of Point Mutations.

- ***Silent Mutation(no change in sequence)--***
- Mutation may not lead to any change in sequence of resulting protein due to degeneracy or wobble effect of genetic code.
- This is most likely if the change of nucleotide falls in the third nucleotide of the codon.

- **Silent mutations:**
- Code for the same amino acid. A silent mutation has no effect on the functioning of the protein. A single nucleotide can change, but the new codon specifies the same amino acid, resulting in an unmutated protein.
- This type of change is called synonymous change, since the old and new codon code for the same amino acid. This is possible because 64 codons specify only 20 amino acids.



Point mutation.

- ***Missense Mutation-(change in sequence)-***

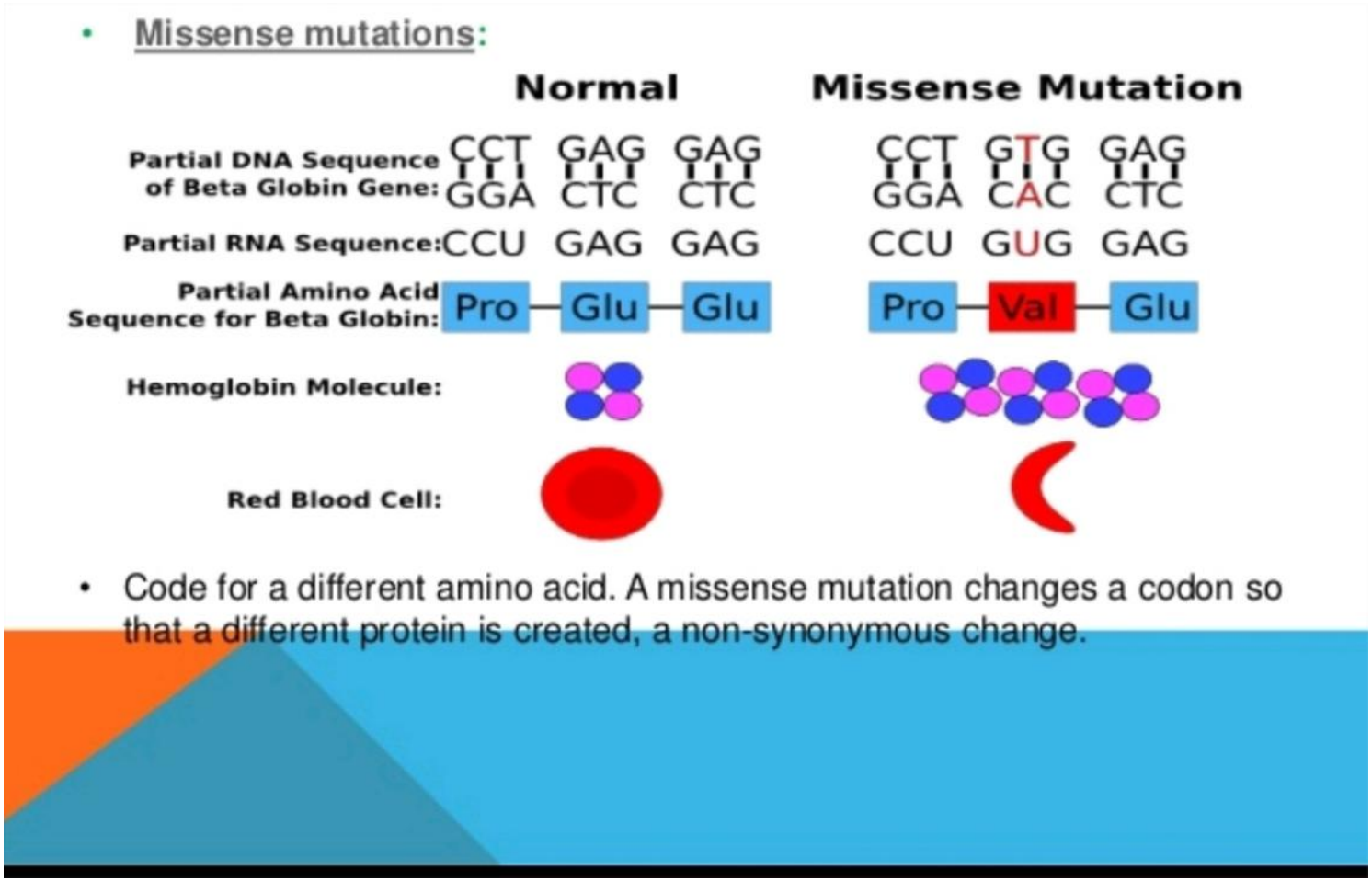
Mutation which results in change in sequence leading to a different amino acid being incorporated in the protein is called missense mutation.

It can be acceptable, partially acceptable or unacceptable.

Point Mutation

- **Sickle Cell disease** is the result of one nucleotide substitution
- Occurs in the **hemoglobin gene**

- Missense mutations:



- Code for a different amino acid. A missense mutation changes a codon so that a different protein is created, a non-synonymous change.

- This wrong or missense amino acid may or may not have any effect on the function depending upon its position in the protein. Its can be classified as:

- *Acceptable missense mutation:*
- When the changed amino acid does not alter the function, it is called acceptable missense mutation e.g. hemogglobin Hikari.
- *Hb-Hikari– Asp replaces Lys at 61th position of Beta chain—normal function unaltered.*

- *Partially acceptable missense mutation:*

- When the changed amino acid alters the function partically which is compatible with life e.g Hemoglobin S, it is called partially acceptable missense mutation.
- *Sickle cell disease-Beta 6 GLU- Val.*

- *Unacceptable missense mutations:*

- When the changed amino acid alters the function drastically or abolishes it completely so that the protein can not perform its normal function and is not compatible with life.

- It is called unacceptable missense mutation.

- Methemoglobin which cannot tranport O2 is an examples.
- *Alpha 58His---Tyr, non functional Hb.*

Nonsense Mutation- (no protein synthesis)--

- Nonsense mutation which result in the formation of a stop codon also called nonsense codon or termination codon.

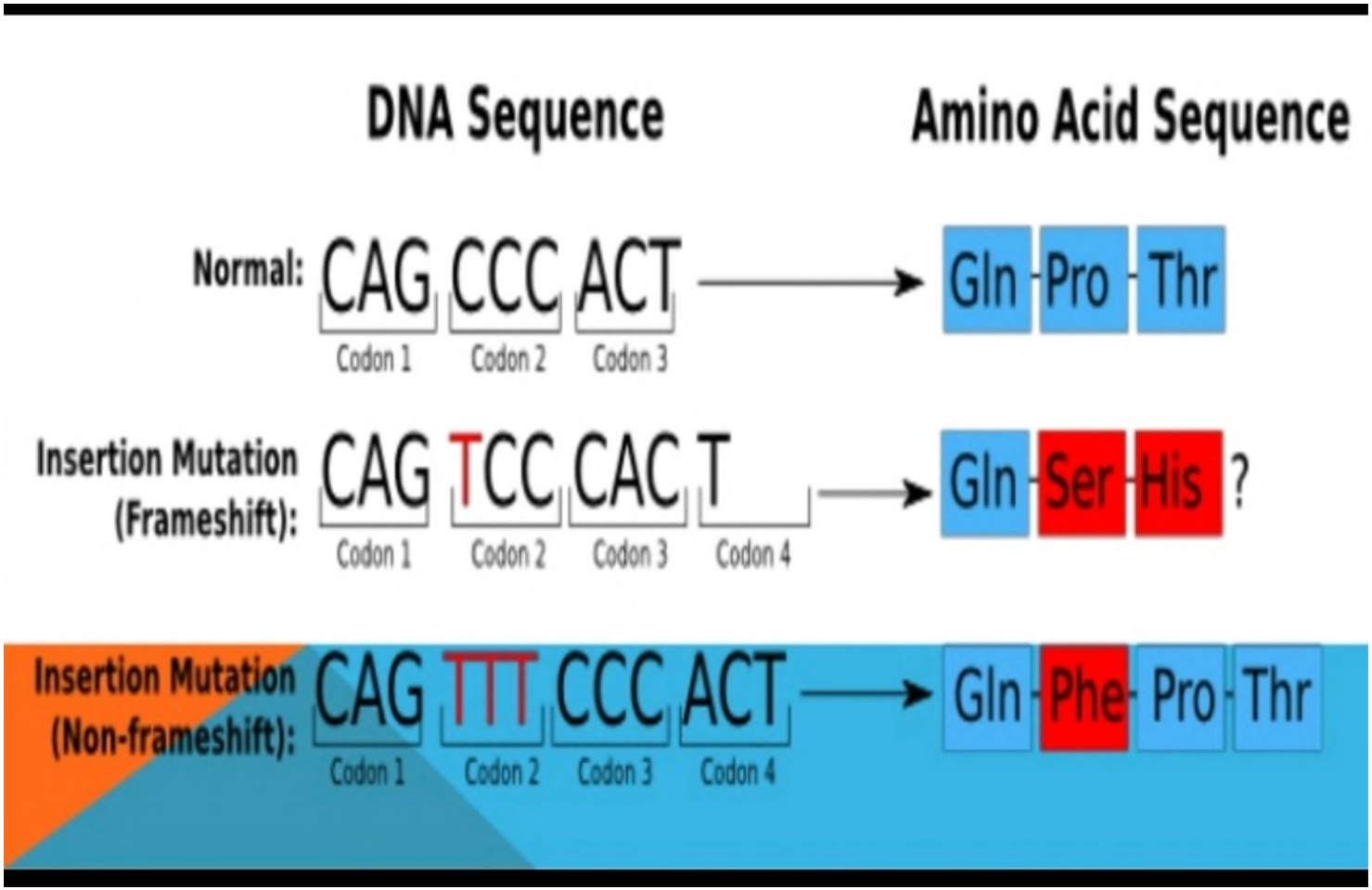
This leads to the production of only a part of protein, i.e. Incomplete protein which is not functional.

- *FRAME SHIFT MUTATION –*

- **The mutation due to an addition or removal of one, two and more (non multiples of three)nucleotides in the gene leading to the change in the reading of nucleotides sequence is called frame shift mutation.**

Frame shift Mutation.

- Insertion or deletion of one or two nucleotides in DNA.
- Whole reading frame alters.
- Deletion frame shift mutation-cystic fibrosis of pancreas.
- Insertion frame shift mutation-Thalassaemia.



EFFECT OF FRAMESHIFT MUTATION.

- ***Premature Termination of Synthesis—***
- **At times, the insertion or deletion of a nucleotide changes the original codon to a stop codon. In this case, as the reading frame reaches the stop codon, the protein synthesis stops abruptly leading to incomplete protein synthesis due to its premature termination.**

MUTAGEN AND MUTAGENESIS.

- Any agent which will increases DNA damage.

- X-ray, UV-rays, acridine orange etc are well known mutagens.
- Lethal Mutations–

  The alteration is incompatible with life of cell or the organism.
- Examples-a mutation which does not produce alpha chain(4 gene deletion) will result in intrauterine death of embryo.

- Silent mutation–
- Alteration at an insignificant region of protein may not have metabolic effect.
- Beneficial mutation--Normal maize is dificient in tryptophan. Tryptophan – rich maize varities are now available for cultivation.

- Carcinogenic Effect-

Mutation may not be lethal but alter regulatory mechanism. Such a mutation in a somatic cell may results in uncontrolled cell division leading to cancer.