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FACULTY OF ENGINEERING &TECHNOLOGY

DEPARTMENT OF BIOTECHNOLOGY

# DNA Damage:

- Due to by physical, chemical & environmental agents.
- Broadly classified into four categories.

1. Single base alterations (e.g. depurination, deamination).
2. Two-base alterations (e.g. pyrimidine dimer)
3. Chain breaks (e.g. ionizing radiation)
4. Cross-linkages (e.g. between bases).

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- Cytosine gets deaminated to form uracil while adenine forms hypoxanthine.
- Spontaneous depurination, due to cleavage of glycosyl bonds (that connect purines to the backbone).
- The depurinated sites are called as abasic sites.

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- They were detected in purines & called apurinic sites (AP sites) which represent lack of purine.
- The term AP sites is generally used to represent any base lacking in DNA.

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- The production of reactive oxygen species is often associated with alteration of bases e.g. formation of 8-hydroxy guanine.
- Free radical formation & oxidative damage to DNA increases with advancement of age.

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- Ultraviolet radiations result in the formation of covalent links between adjacent pyrimidines along the DNA strand to form pyrimidine dimers.
- DNA chain breaks can be caused by ionizing radiations (e.g. x - rays).

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# Mutations

- Mutation refers to a change in the DNA structure of a gene.
- The substances (chemicals) which can induce mutations are collectively known as mutagens.
- The changes that occur in DNA on mutation are reflected in replication, transcription & translation.

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# Types of mutations

- Two major types

1. Point mutations
2. Frameshift mutations

- Point mutations:
- The replacement of one base pair by another results in point mutation.

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- They are of two sub-types.
- **Transitions:**
- In this case, a purine (or a pyrimidine) is replaced by another.
- **Transversions:**
- These are characterized by replacement of a purine by a pyrimidine or vice versa.

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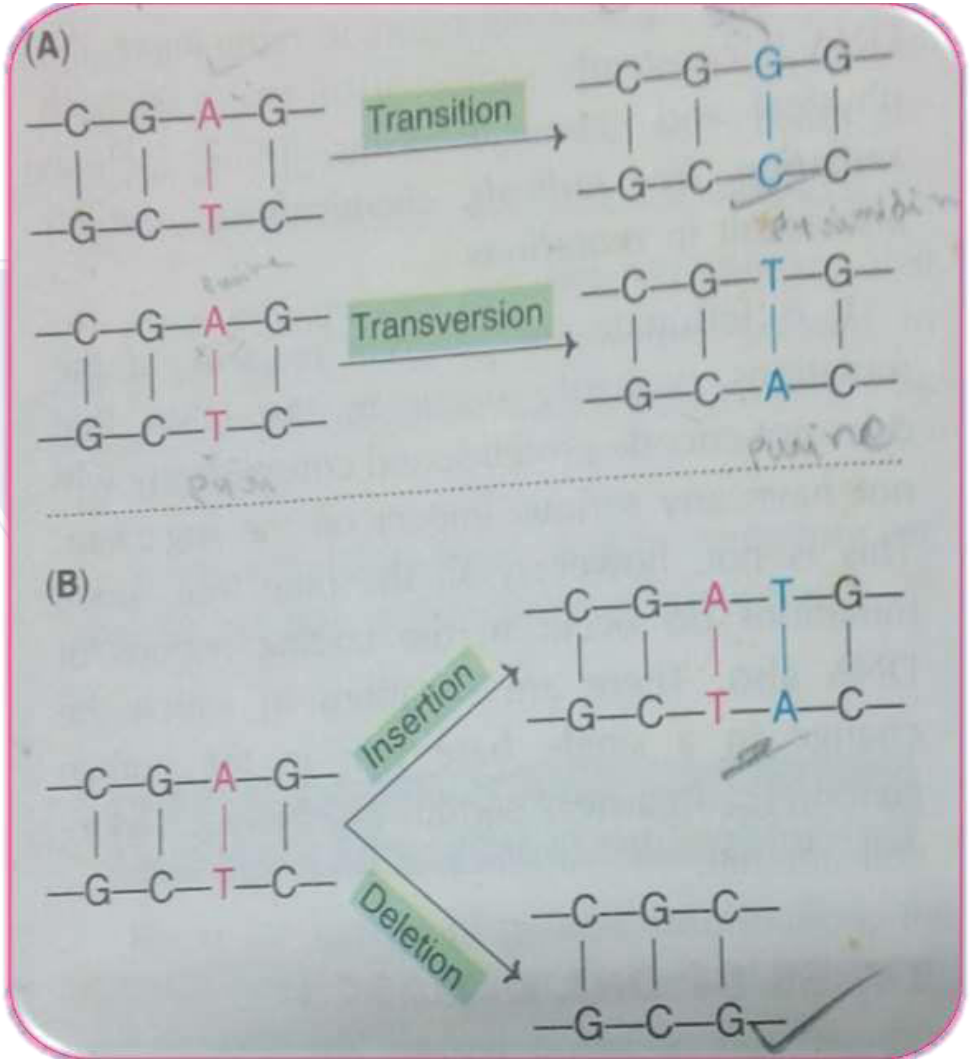
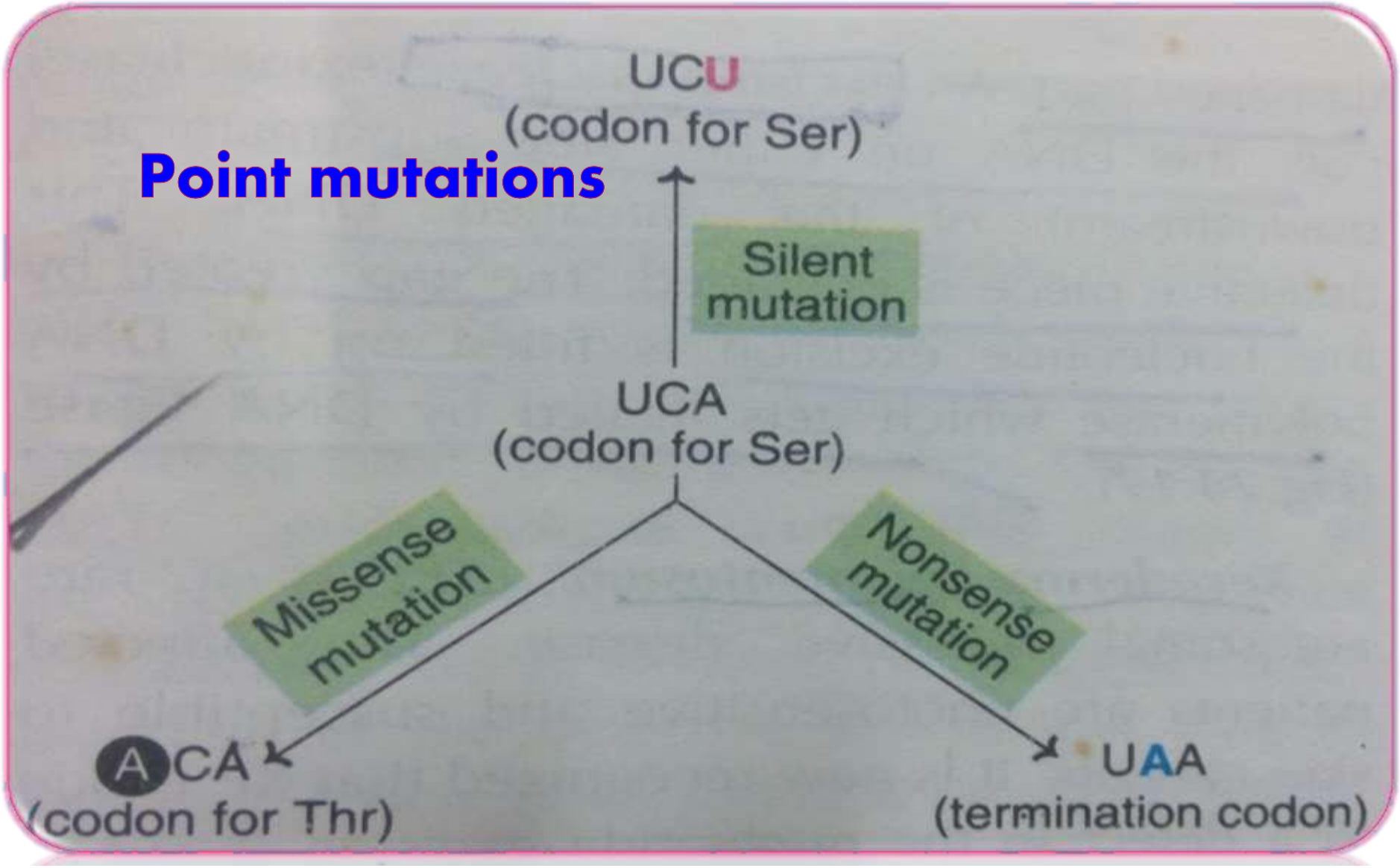
# Point & frameshift mutations



# Point Mutations



# Consequences of point Mutations

- **Silent mutation:**
- The codon (of mRNA) containing the changed base may code for the same amino acid.
- UCA codes for serine & change in the third base (UCU) still codes for serine.
- This is due to degeneracy of the genetic code.
- There are no detectable effects.

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# Missense mutation:

- In this case, the changed base may code for a different amino acid.
- UCA codes for serine while ACA codes for threonine.
- The mistaken (or missense) amino acid may be acceptable, partially acceptable or unacceptable with regard to the function of protein molecule.
- E.g. Sickle-cell anemia.

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# Nonsense mutation:

- The codon with the altered base may become a termination (or nonsense) codon.
- Change in the second base of serine codon (UCA) may result in UAA.
- The altered codon acts as a stop signal & causes termination of protein synthesis.

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# Frameshift mutations:

- **These occur when one or more base pairs are inserted in or deleted from the DNA, respectively causing insertion or deletion mutations.**

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## Consequences of framshift mutations

- The insertion or deletion of a base in a gene results in an altered reading frame of the mRNA.
- The machinery of mRNA (containing codons) does not recognize that a base was missing or a new base was added.
- No punctuation in the reading of codons, translation continues.
- The result is that the protein synthesized will have several altered amino acids and/or prematurely terminated protein.

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