MUTATIONS

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Mutations

- Any change in the DNA sequence of an organism is a mutation.
- Mutations are the source of the altered versions of genes that provide the raw material for evolution.
- Most mutations have no effect on the organism, especially among the eukaryotes, because a large portion of the DNA is not in genes and thus does not affect the organism's phenotype.
- Only a small percentage of mutations causes a visible but non-lethal change in the phenotype.

- Mutation = change(s) in the nucleotide/base sequence of DNA; may occur due to errors in DNA replication or due to the impacts of chemicals or radiation to the DNA molecule

- Mutation may result in coding sequences for new amino acids in proteins or not!

Somatic Vs.Germinal Mutations

Some people may have mutations in their skin cells or hair. Such mutations are termed Somatic.

Germ mutations occur only in the sex cells& called Germinal Mutations

These mutations are more threatening because they can be passed to offspring (forever).

Somatic Mutation

- In normal body tissue
- May have vast effects on individual
- Not passed on to offspring
  - Not of evolutionary significance

Germinal Mutation

- Germinal or germ line
  - Gametes or cells producing gametes
  - Little or no effect on individual originating mutation
  - Passed on to all cells of zygote formed
    - Passed on to subsequent generations
    - Source of new alleles

Mutation

- Not necessarily harmful!
  - Dependent on: 1) nature of mutation
    2) environment
- Spontaneous
  - occur randomly throughout genome
  - rates: 10^{-6} - 10^{-4} /gene/cell
- Reversible

Types of Mutations

- Point Mutations
  - Base Pair Substitutions
    - Silent
    - Missense – new protein (Amino Acid Substitutions)
    - Nonsense – stop codon
  - Base Pair Insertions and deletions
    - Frameshift Mutations

Point mutations

- Base subsitution :
  - neutral
    - no change in final protein
  - silent
    - no change in amino acid
  - missense
    - amino acid substitution
  - nonsense
    - stop codon substitution

Types of Mutations

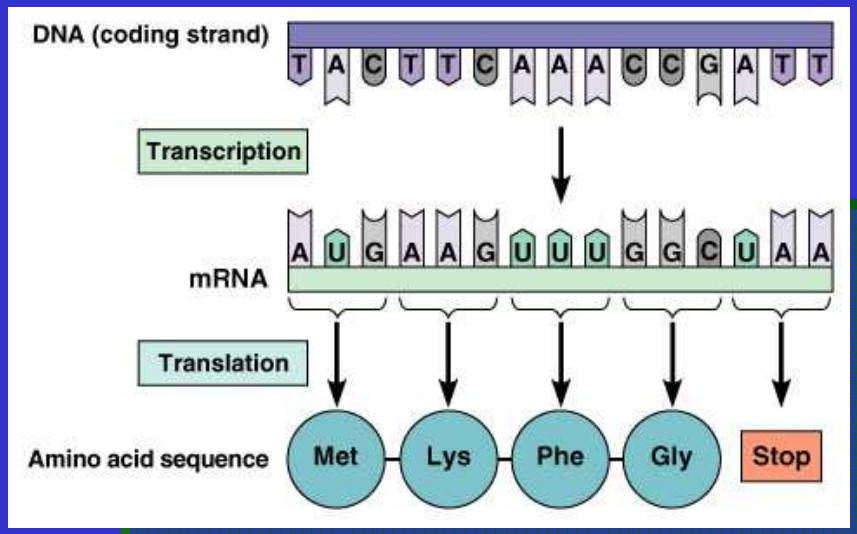
- Why are these mutations important?
  - They can affect mRNA and protein production, eventually determining the phenotype.
- Silent mutations – produce no change in amino acid sequence (due to degeneracy of the genetic code.) (aka synonymous mutations).
  - CUU codes for leucine, but so does CUC, CUA, CUG, UUA, and UUG.

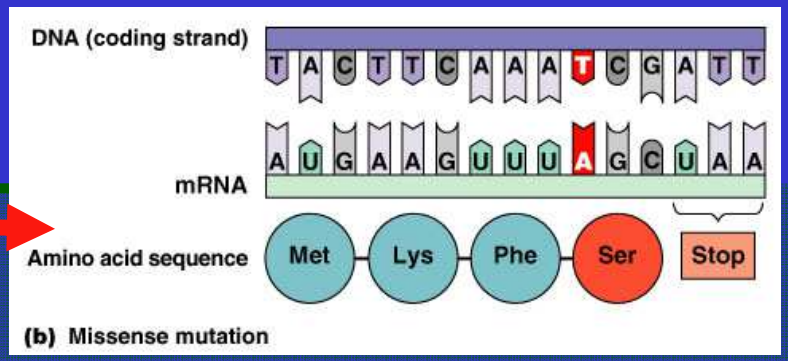
1. Point mutations affect single sites on DNA

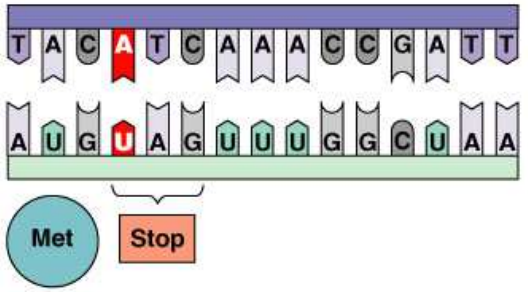
- Substitution of 1 base for another
- Deletion/addition of a single base
- Deletion/addition of a small number of bases

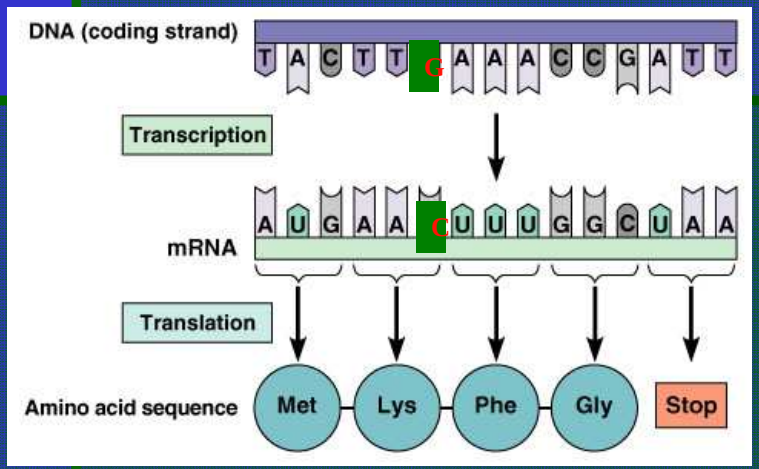
- If purine (A/G) or pyrimidine (T/C) substitutes for itself = transition substitution
- If purine substitutes for pyrimidine or vice versa = transversion substitution

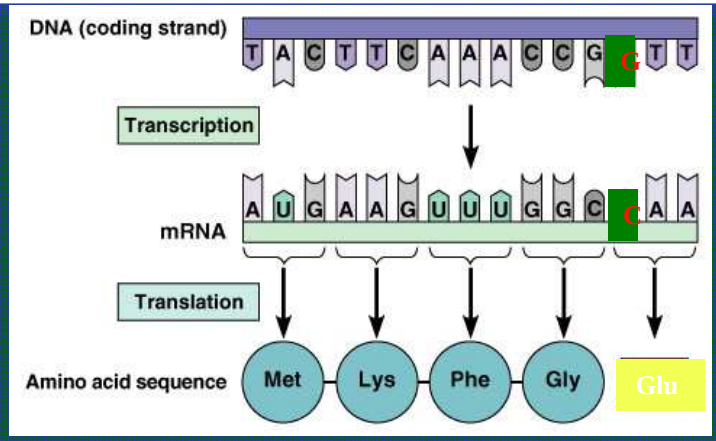
Point Mutations:











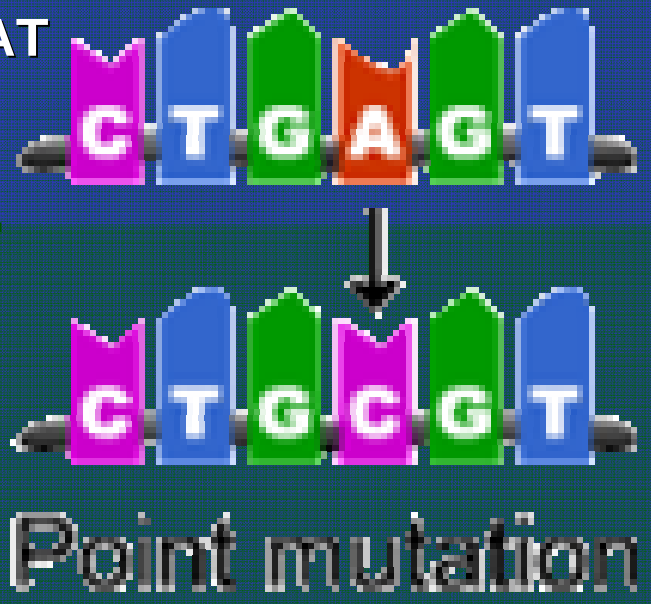
Point Mutations

changes in one or a few nucleotides

- Substitution

THE FAT CAT ATE THE RAT

THE FAT HAT ATE THE RAT



Point Mutations

- **Frameshift Mutations** – shifts the reading frame of the genetic message so that the protein may not be able to perform its function.
  - **Insertion**

    THE FAT CAT ATE THE RAT

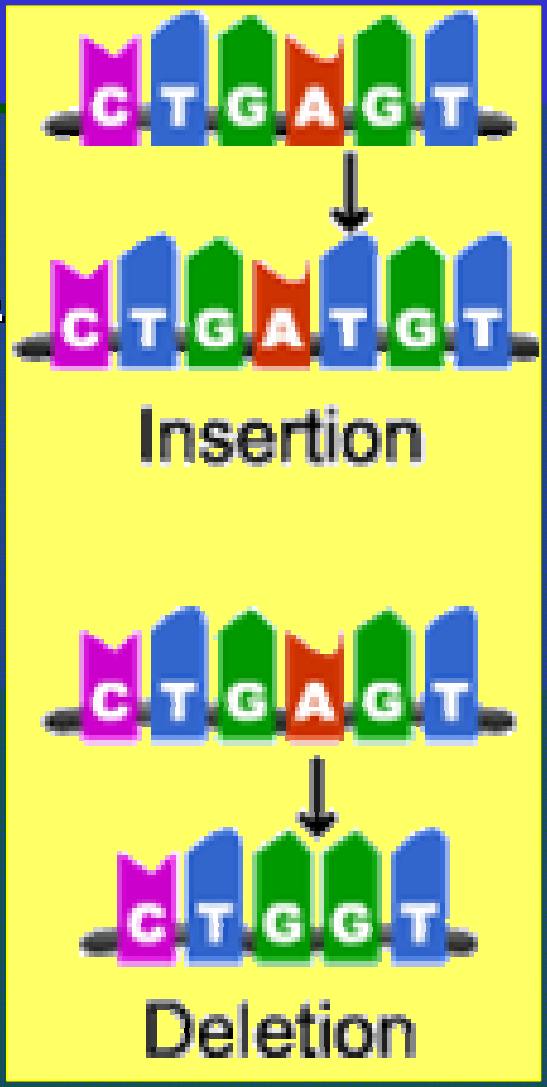
    THE FAT HCA TAT ETH ERA T

  - **Deletion**

    THE FAT CAT ATE THE RAT

    TEF ATC ATA TET GER AT

    H

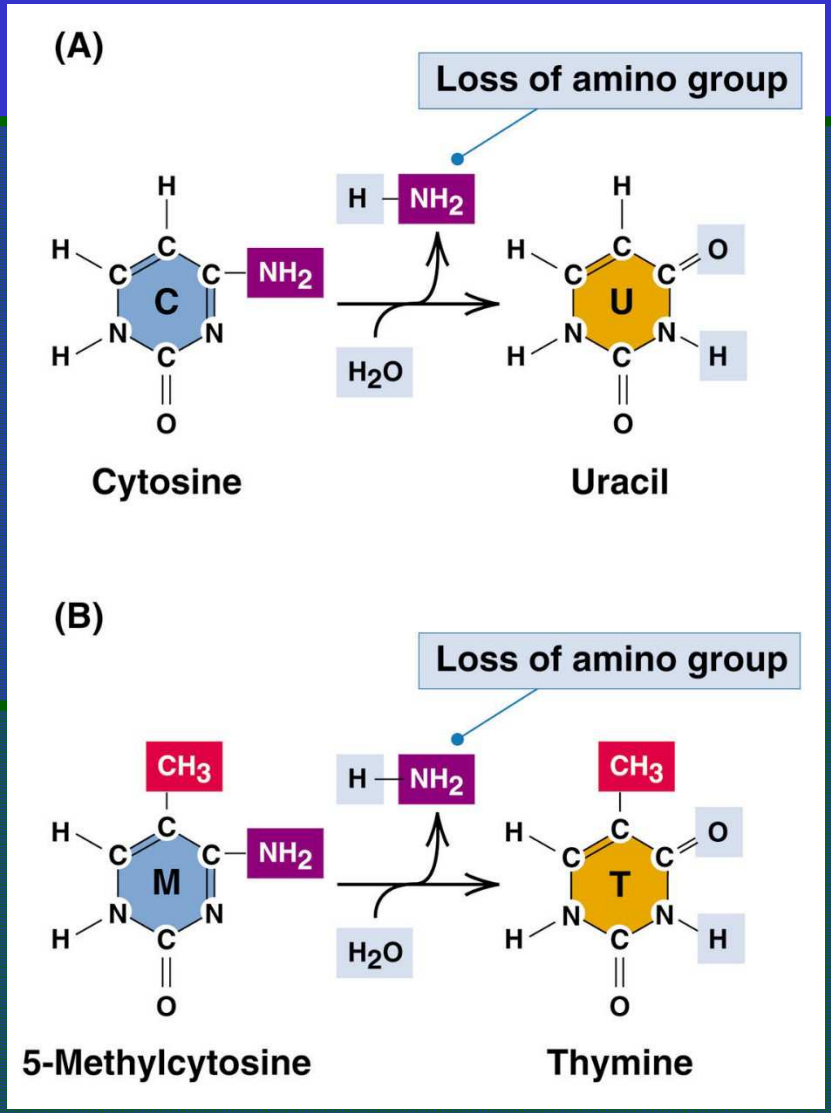


Types of Mutations

- Most common – base-pair substitutions
  - Transition mutations – Pu to Pu, Py to Py.
    - G→A & A → G
    - T → C & C → T
  - Transversion mutations – Pu to Py or Py to Pu.
    - A → T, A → C, G → T, or G → C.
    - T → A, T → G, C → A, or C → G.

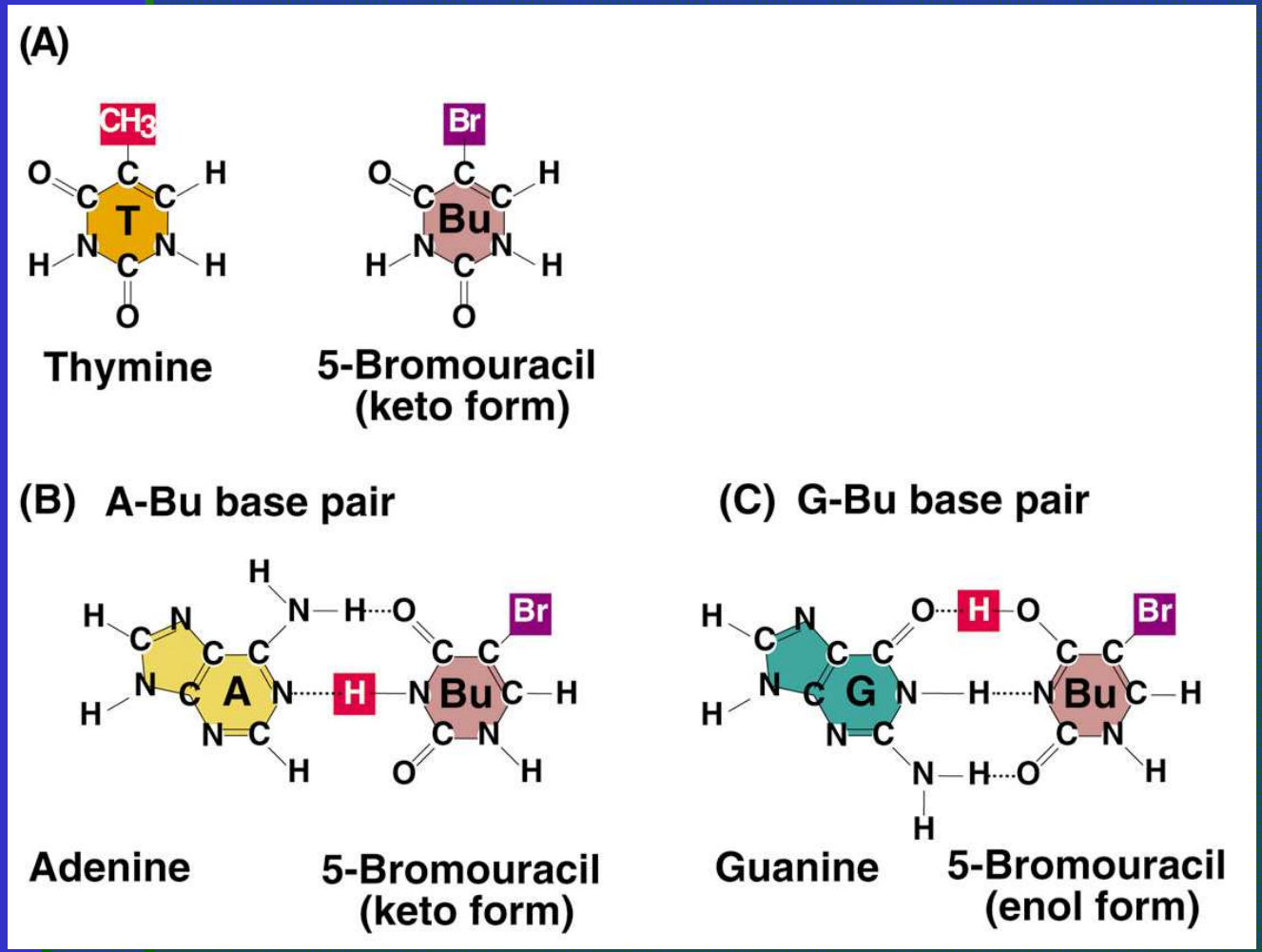
5-methylcytosines are hot spots of mutation-2

Deamination of cytosine leads to uracil
while deamination of 5-methyl-cytosine leads to thymine



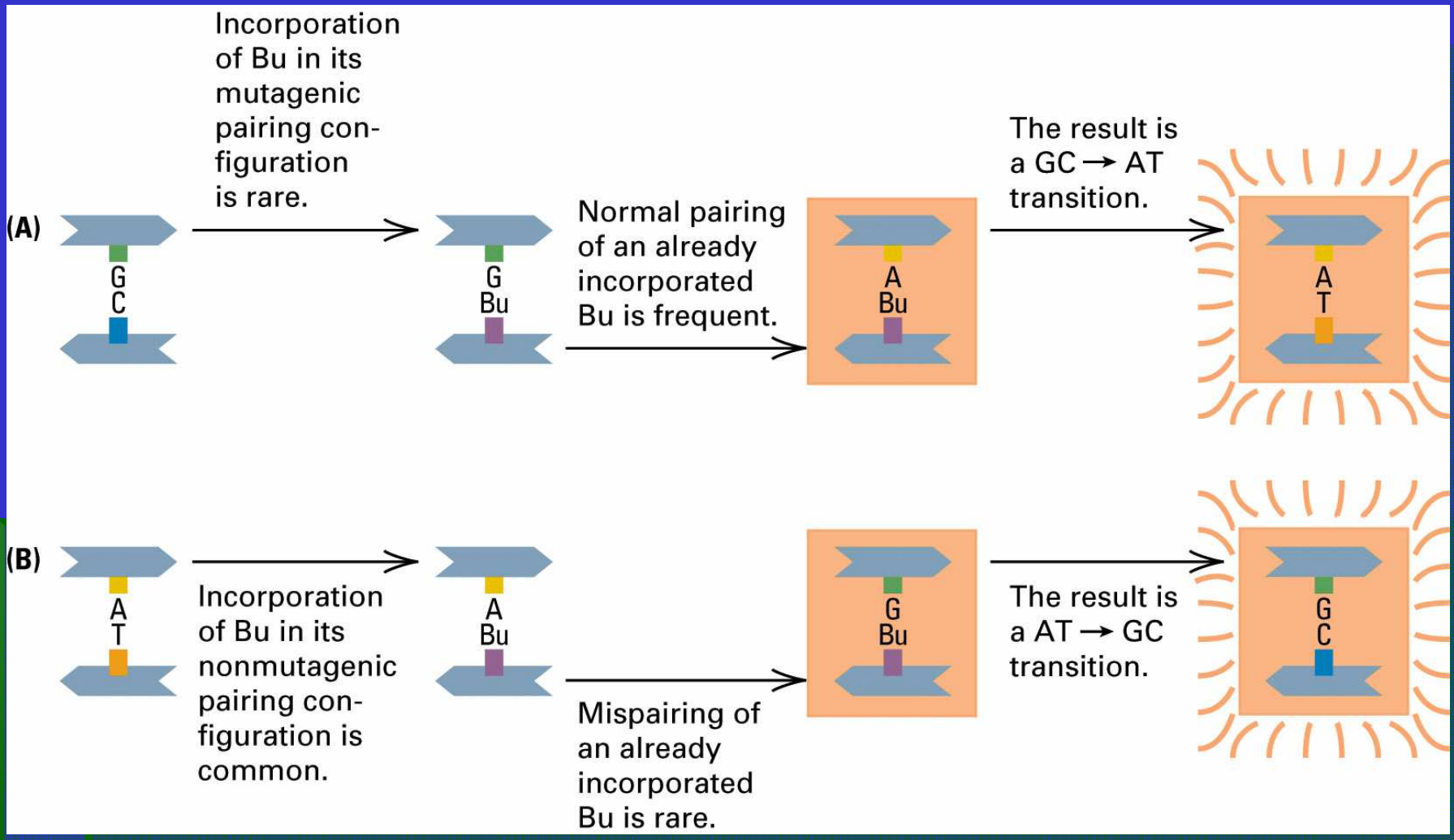
Uracil is not a normal component of DNA and can be recognized and removed. Thymine is a normal component of DNA and is not recognized as a source of potential mutation.

Mechanism of mutagenesis by the tautomerization of the thymine analog 5-Bromouracil

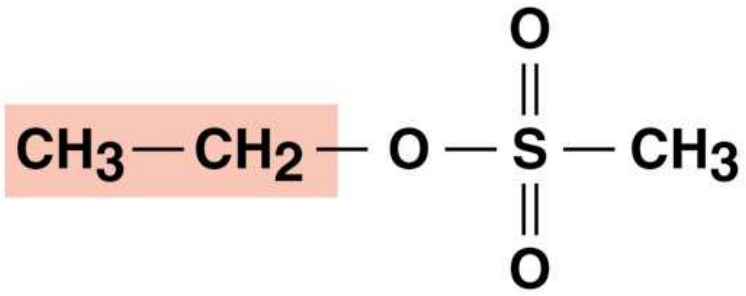


The keto and enol forms of DNA bases are called tautomers. Both thymine and 5-bromouracil can assume these 2 alternative states.

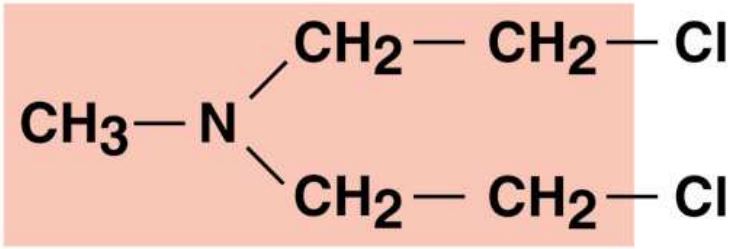
Base analogs like 5-bromouracil can induce mutations



Structure of 2 alkylating mutagens

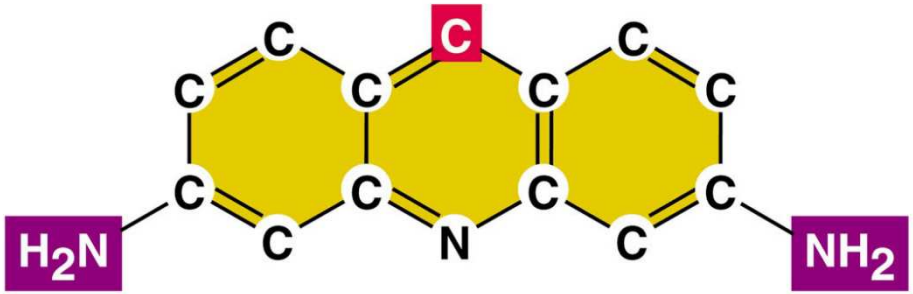


Ethyl methanesulfonate



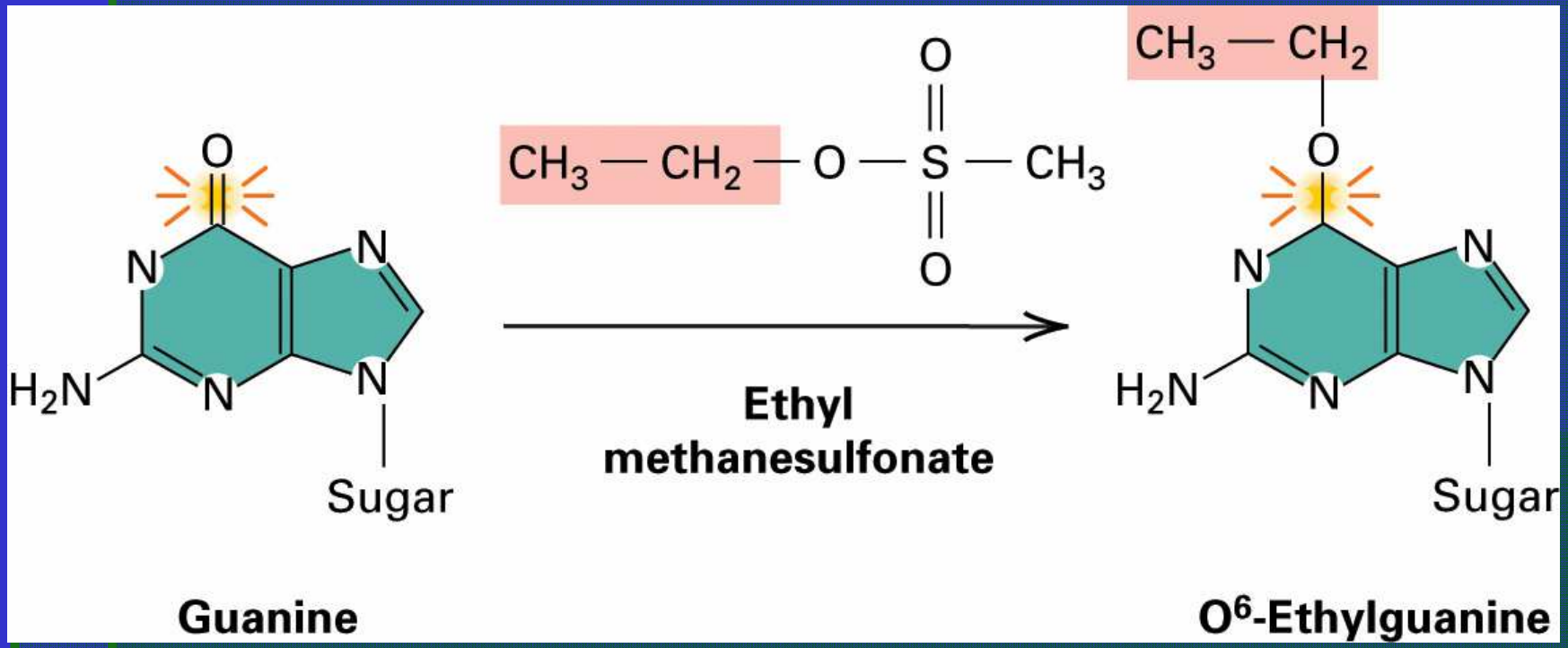
Nitrogen mustard

Structure of a frameshift mutagen

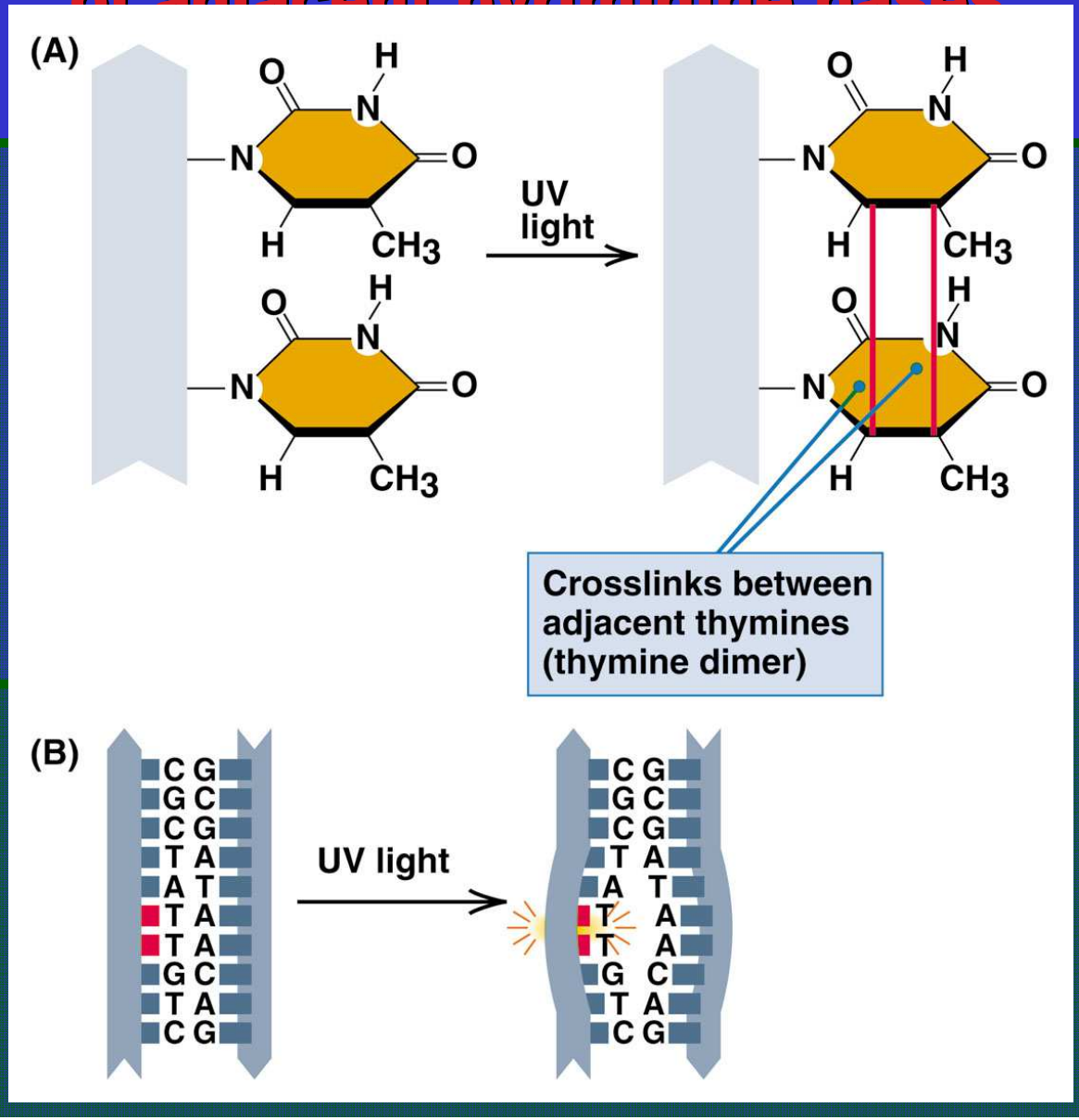


Proflavin

It resembles a base pair


O
N
N
N
N
H_2N
Sugar
Guanine
$CH_3 — CH_2 — O — S — CH_3$
O
O
Ethyl
methanesulfonate
$CH_3 — CH_2$
O
N
N
N
N
H_2N
Sugar
O^6-Ethylguanine

Ultraviolet light causes joining (crosslinking) of adjacent pyrimidine bases

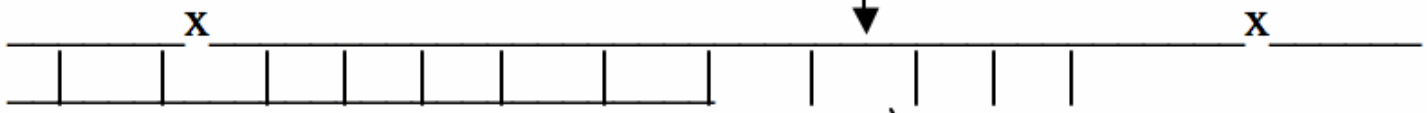


Summary of Mutation Types

DNA type mutations

Point mutation
(Substitution of one nucleotide for another)

Insertion or Deletion
(Addition or loss of nucleotides)



Results in:

Protein type mutations

Silent mutation
No change in amino acid sequence or composition

Missense mutation
One amino acid changed to another

Frameshift mutation
All amino acids after mutation point are changed

Nonsense mutation
Polypeptide is truncated because of a new stop codon


Thank
You!