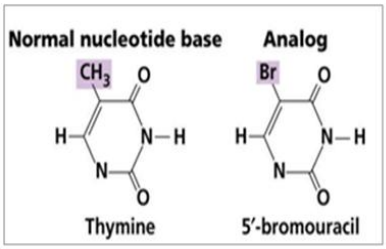
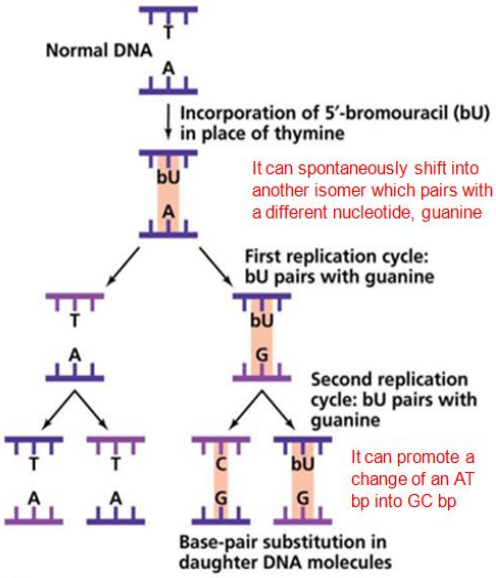
Unit II – Problem 2 – Genetics: Mutations

- **What are mutations?**
  - They are changes in the genetic material resulting in abnormal phenotypes. They can occur at a specific gene (part of a chromosome) or involve a whole chromosome! Notice that most of mutations are harmful.
- **There are two types of mutations:**

Somatic	• Genetic alterations acquired by cells after the formation of the zygote. • They are not transmitted to offspring (not inherited).
Gonadal	• Genetic alterations acquired by germ cells. • They are transmitted to offspring (inherited).

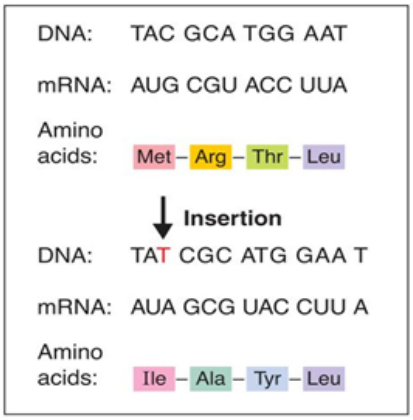
- **Mutations can be spontaneous or induced:**
  - **Spontaneous mutations (most common):** occurring naturally in the absence of mutagens (agents which cause mutations).
  - **Induced mutations**: occurring due to exposure to mutagens:
    - ✓ Chemicals:
      - ❖ *Base analogs*: derivatives of normal bases incorporated in the DNA, substitute for normal nucleotide and alter base pairing properties.





      - ❖ *Intercalating agents:* can be inserted between bases in the DNA, resulting in structural changes of the DNA
      - ❖ *Base modifiers:* change the structure of DNA bases resulting in mismatch pairing (e.g. metals or Reactive Oxygen Species).
    - ✓ Radiation: X-ray (causing breaks in double stranded DNA) or UV-light (causing cross link of thymidine).
- **Gene mutations:**
  - **Single base substitution:**
    - ✓ Substitution of a single nucleotide with a different one:
      - ❖ *Transition*: substitution of one base with a different base of the same chemical category (i.e. purine to purine or pyrimidine to pyrimidine).
      - ❖ *Transversion*: substitution of one base with a different base of other chemical category (i.e. purine to pyrimidine or pyrimidine to purine).
    - ✓ Types of mutations which can result:
      - ❖ *Missense mutation*: translation of a different amino acid. Example include: galactosemia and sickle cell disease (valine instead of glutamic acid in the 6^{th} amino acid position of β-globin chain).
      - ❖ *Nonsense mutation*: resulting in a stop codon (UAG or UGA or UAA). Example: β-thalassemia.
      - ❖ *Silent mutation*: doesn't cause any changes in amino acid sequence.

- **Insertions or deletions:**
  - ✓ Extra base pairs might be added (insertion) or removed (deletion) from the DNA sequence of a gene and this can result in what is known as "frameshift mutation".



- **Triplet repeat expansion:**
  - ✓ DNA mutation caused by expansion of a DNA sequence by the addition of trinucleotides resulting in a trinucleotide repeat.
  - ✓ Example: Huntington's disease in which there is excessive repeat of the trinucleotide CAG → adding series of glutamine to the resulting protein.

- **Chromosomal mutations:**
  - **Stractural:**
    - ✓ Deletion: a segment of the chromosome breaks-off and will be lost.
    - ✓ Inversion: a segment of the chromosome breaks-off → flips 180 degrees and then reattaches.
    - ✓ Duplication: extra copy of a part of the chromosome is formed.
    - ✓ Translocation.
  - **Numerical (aneuploidy):** trisomies are considered as an example.
- **Functional effect of mutations:**
  - **Loss of function**: reduced activity of the gene product; associated with recessive mutations.
  - **Gain of function**: confer a new function of gene product; associate with dominant mutations.
- **What are the methods which can be used to detect mutations?**
  - **Direct PCR.**
  - **Real-time PCR.**
  - **RFLP.**
  - **Hybridization.**
  - **DNA sequencing.**