MUTATIONS

TYPES OF MUTATIONS

1 Gene Mutation

- Point Mutation
  - Silent
  - Missense
  - Nonsense
- Frameshift Mutation
  - Addition
  - Deletion

2 Chromosome Mutation

- Deletion
- Duplication
- Inversion
- Translocation

TYPES OF MUTATIONS

3 Genome Mutation

- Aneuploidy
- Polyploidy
- Autopolyploidy
- Allopolyploidy

1 GENE MUTATION

Point Mutation

Frame shift

GENE MUTATION

- Involve **insertion** or **removal** of 1 or more base pairs

- Gene mutation is a change in single base pair within DNA sequences

EFFECTS OF GENE MUTATIONS

- Most mutations are **neutral** - they have no effect on the polypeptide.
- Some mutations result in a **less active product**;
- Less often an **inactive product**;
- Very few mutations are **beneficial**.

EFFECTS OF GENE MUTATIONS(cont)

- Affects molecular changes in the DNA sequence of a gene
- Alter the coding sequence within a gene
- Causes **permanent change** in DNA sequence

BODY (SOMATIC) AND GAMETE (GERM)MUTATION

- **Body cell** mutations can cause **cancer**.
  - only the individual is affected

- **Gamete cell** mutations affect the **egg and the sperm**.
  - all offspring of the individual can be affected.

GENE MUTATION: The Types

1. **Point mutations** - a one base change in DNA.

2. **Frame Shift Mutations** - the addition or deletion of **1 or more bases**. These are due to powerful mutagens; chemical or physical.

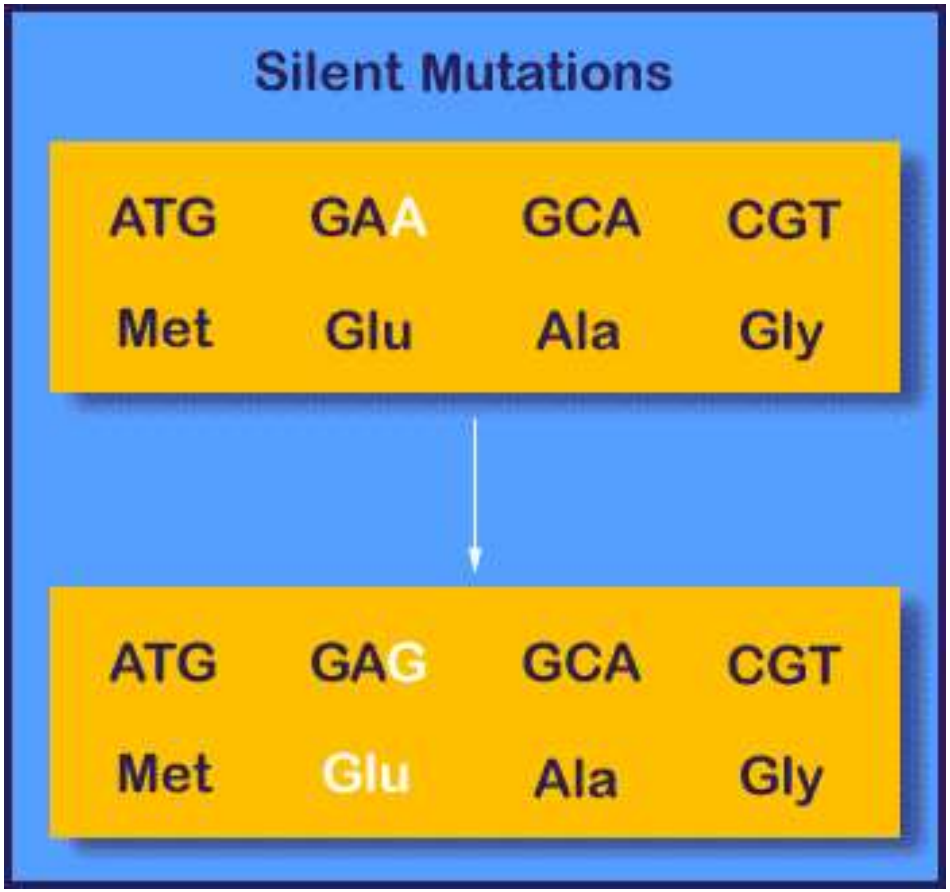
1. POINT MUTATION (PM)

3 TYPES:

- **silent mutation** - single base substitution in the 3rd base nucleotide position of a codon. This results in NO change in amino acid. Note that the first 2 letters of the genetic code are the most critical.
- **missense mutation** - single base substitution in 1st or 2nd base nucleotide position. This results in changed amino acid.
- **nonsense mutation** - single base substitutions that yield stop codon. Note: there are 3 nonsense codons in the genetic code = NO PROTEIN

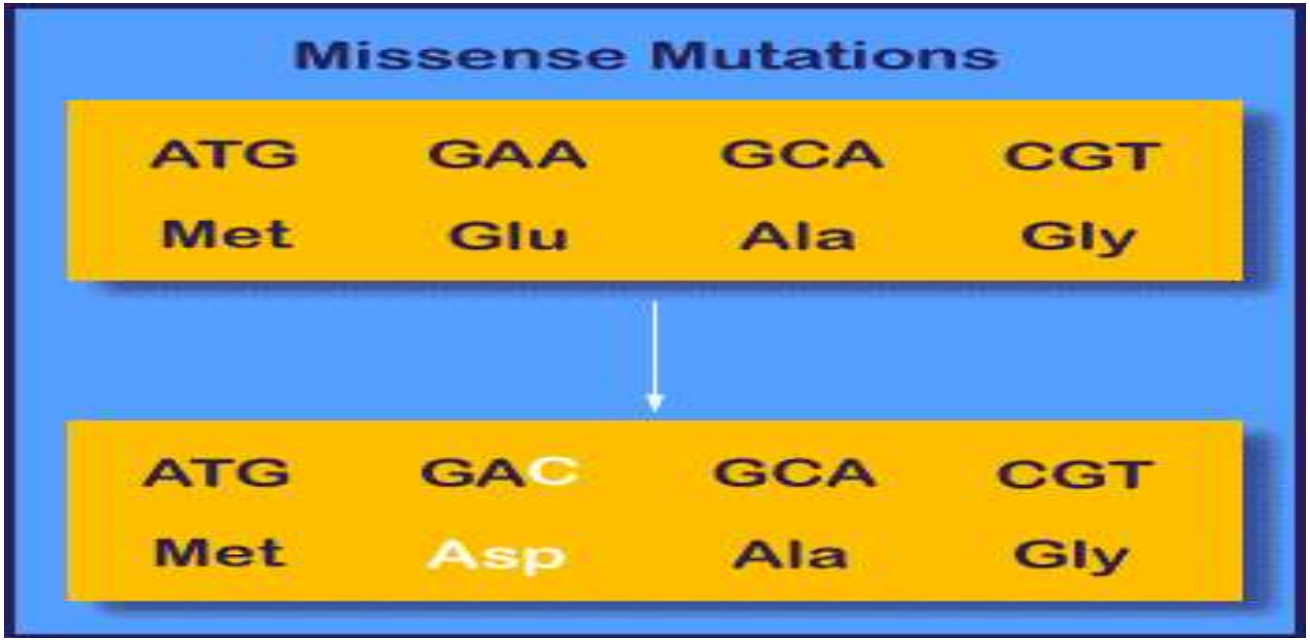
PM: Silent mutation

single base substitution in the 3rd base nucleotide position of a codon. This results in NO change in amino acid. Note that the first 2 letters of the genetic code are the most critical.



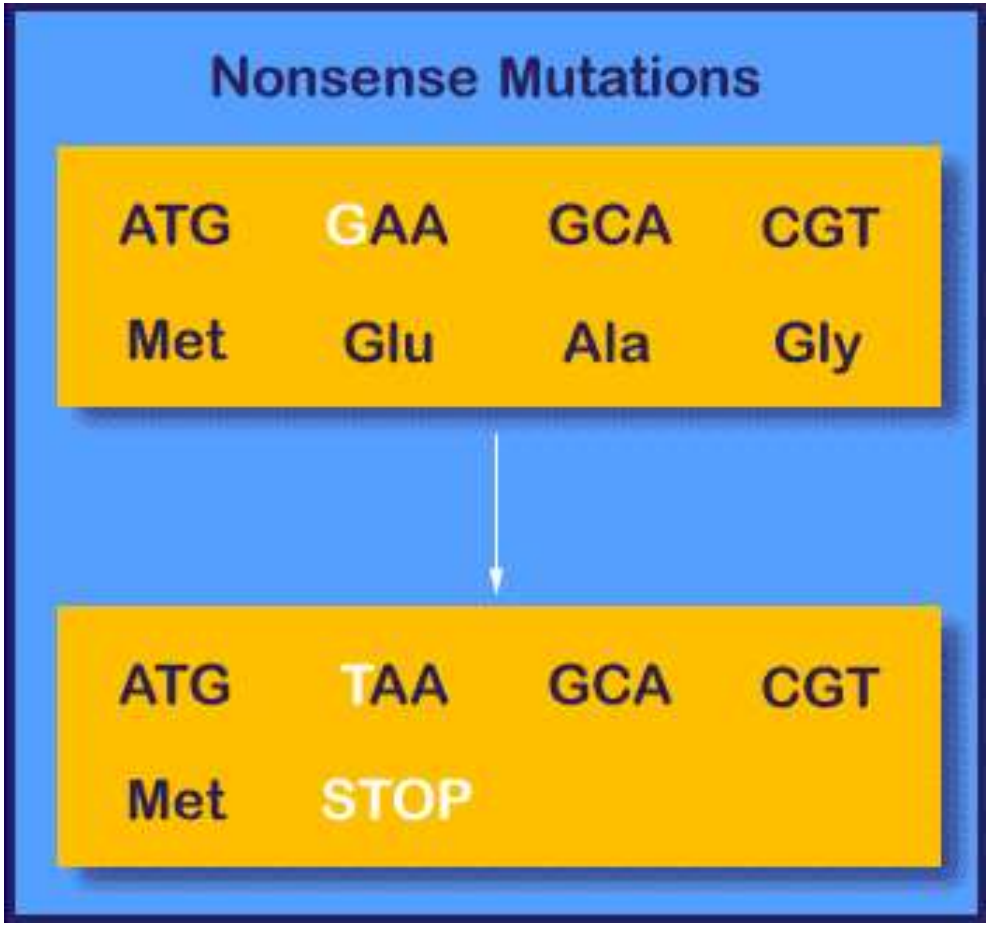
PM: Missense mutation

Single base substitution in 1st or 2nd base nucleotide position. This results in changed amino acid.

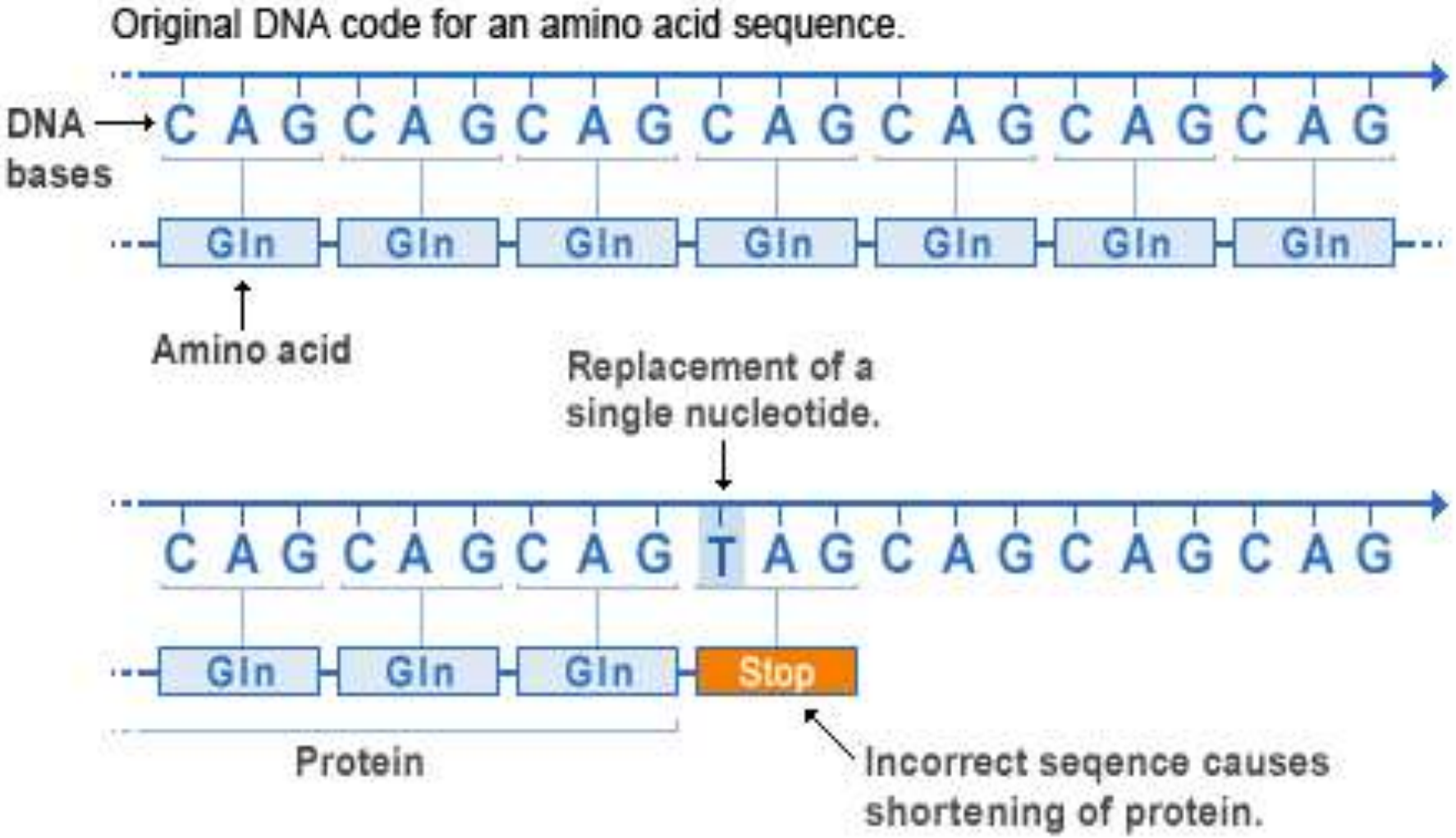


PM: Nonsense mutation

single base substitutions that yield/become **stop codon**. Note: there are 3 nonsense codons in the genetic code = NO PROTEIN



Nonsense mutation



2. FRAME SHIFT MUTATIONS

Gene addition or deletion

One or more bases are **added** or **deleted**, the equivalent of inserting or removing letters in a sentence. But because our cells read DNA in three letter "words", adding or removing one letter changes each subsequent word. This type of mutation can make the DNA **meaningless** and often results in a **shortened protein & non-functional.**

2. FRAME SHIFT MUTATIONS

Additions

Normal gene

GGTCTCCTCACGCCA

↓

CCAGAGGAGUGCGGU

Codons

↓

Pro-Glu-Glu-Cys-Gly

Amino acids

Addition mutation

GGT**G**CTCCTCACGCCA

↓

CCA**C**GAGGAGUGCGGU

↓

Pro-**Arg-Gly-Val-Arg**

2. FRAME SHIFT MUTATIONS

Deletion

Normal gene

GGTCTCCTCACGCCA

↓

CCAGAGGAGUGCGGU

Codons

↓

Pro-Glu-Glu-Cys-Gly

Amino acids

Deletion mutation

GGT**C/C**CTCACGCCA

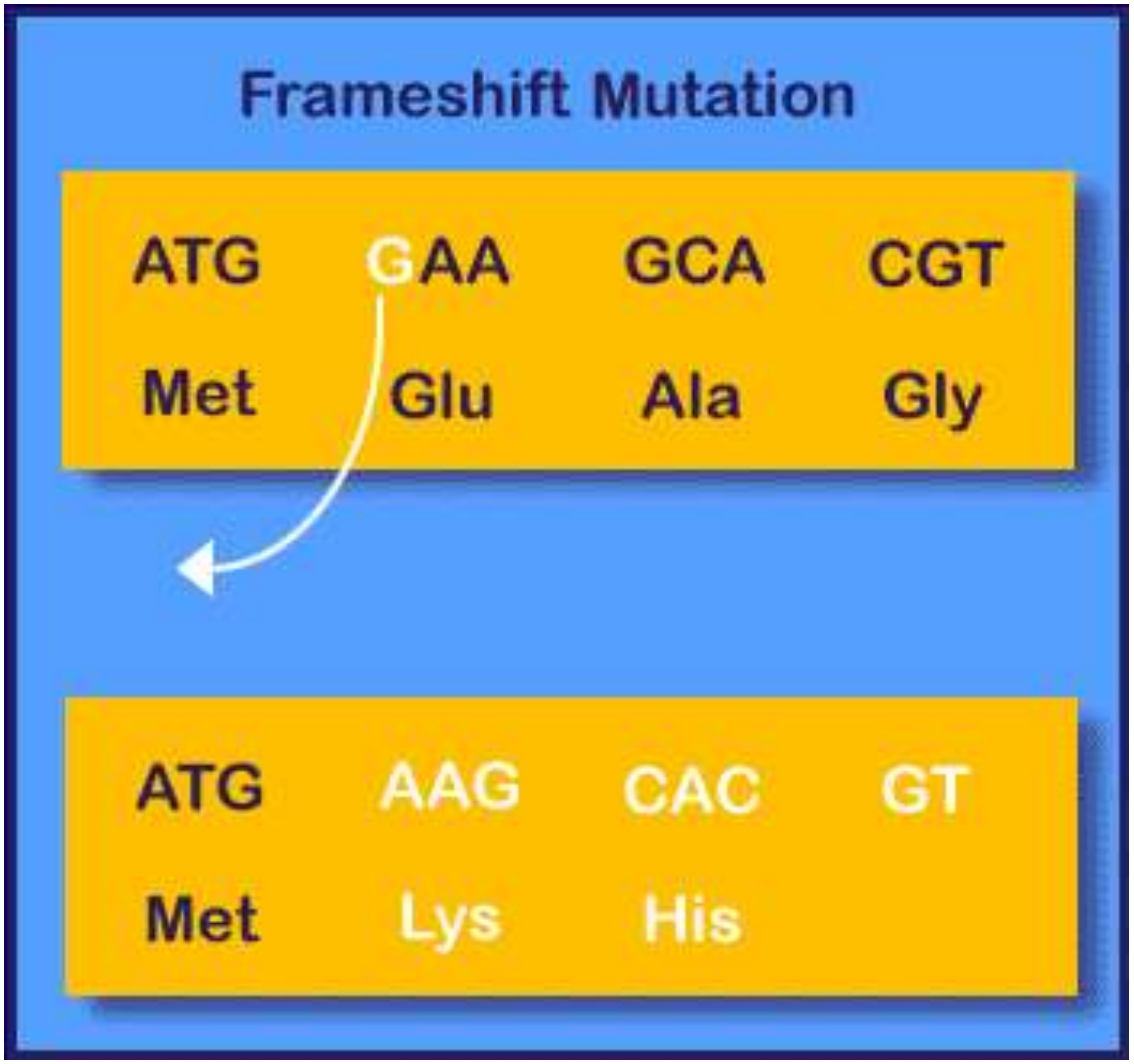
↓

CCA**GG**GAGUGCGGU

↓

Pro-**Gly-Ser-Ala-Val**

2. FRAME SHIFT MUTATIONS



MUTATIONS CAN BE NEUTRAL

- They may have **little** or **no effect** on the survival of an organism or on its ability to reproduce.

- They may result in the same kind of organism - meaning that the change still tells the cell to do what it should, so there is no difference.

- It is estimated that the average human has 50-100 mutations within their DNA - most (if not all) are neutral or beneficial

MUTATIONS CAN BE NEUTRAL (cont)

- Bacterial resistance to antibiotics
- Insecticide resistance in bugs
- Rapid mutation rates in virus's proteins allowing them to adapt to new "hosts"

MUTATIONS CAN BE BENEFICIAL

- In humans, it can be a different set of circumstances… Here's an example:
- **Sickle-Cell Anemia** is a genetic disorder in which there is a defect in the structure of red blood cells. This leads to fatigue and anemia when not treated.
- However, it has been found that people who are **carriers** for Sickle-Cell Anemia also has some **genetic protection** against another disease, **malaria**.

MUTATIONS CAN BE BENEFICIAL (cont)

- In evolutionary studies, scientists have connected the presence of a brain chemical microcephalin (a proposed mutation) with the human's development of art, music, and complex tool-making practices
- This same research indicates that the human brain is still evolving and becoming more and more capable of more complex tasks
- Some humans have been found to have mutations that protect them from other diseases, such as AIDS

2 CHROMOSOME MUTATION

Deletion
Duplication
Inversion
Translocation

CHROMOSOME MUTATION

Chromosome structure become influenced by;

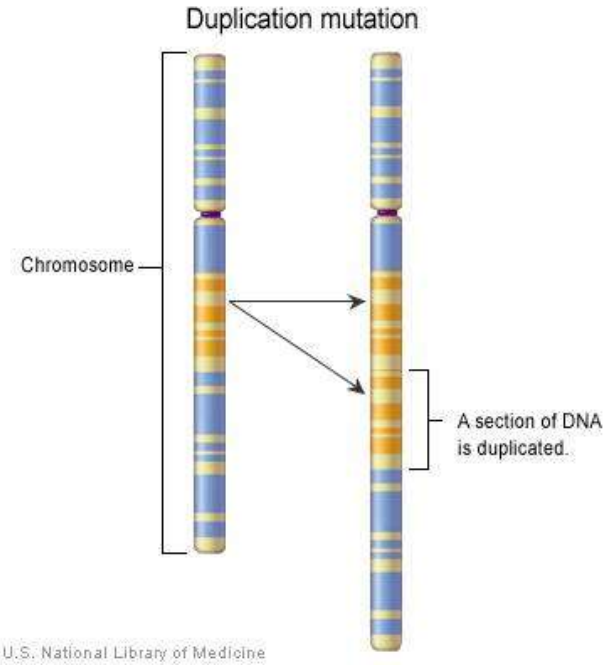
1. **Change in amount** of genetic information in chromosome because of
   - Deletion
   - Duplication
2. **Similar amount** of genetic information but the materials are rearranged
   - Inversion
   - Translocation

CHROMOSOME MUTATION (cont)

- **Deletion**
  - Loss of chromosomal segment
- **Duplication**
  - Repetition of chromosomal segment. Gain of segment.
- **Inversion**
  - A change in the direction of the genetic material along a single chromosome. Reversal of region.
- **Translocation**
  - A segment of one chromosome becomes attached to a different chromosome
  - Simple translocation
    - One way transfer
  - Reciprocal translocation
    - Two way transfer

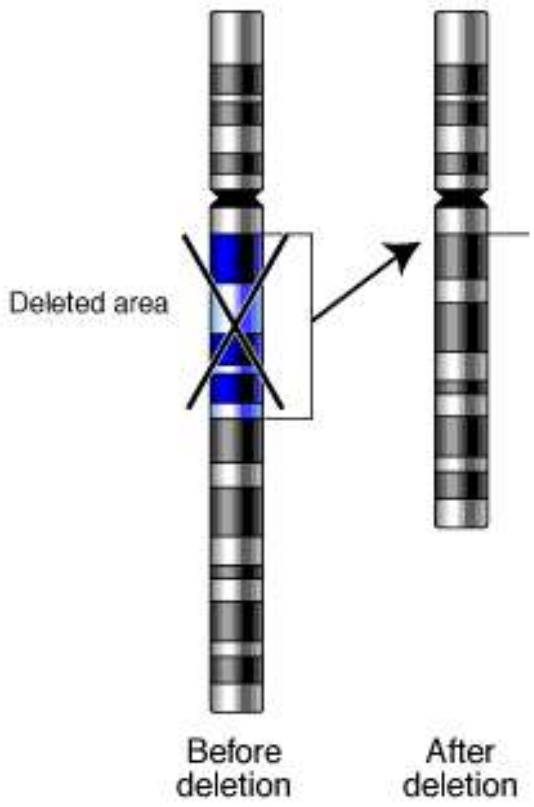
Duplications

- In this mutation, some genes are duplicated and displayed twice on the same chromosome. Gain of segment of DNA.
- Insertion of an extra copy of a region of a chromosome into a neighboring position.
- Zygotes produced from gametes involving duplications are often viable and may or may not have any serious problems.
- Various sorts of duplications are related to color vision conditions many of which are quite subtle in their effects e.g certain anemias involving abnormal hemoglobins called the thalassemias.



Deletions

- Deletions result when a gene mistakenly removed from chromosome, as a resu of unequal crossing over.
- Often zygotes produced b gametes involving deletions ar not viable since they do not hav the full compliment of genes.



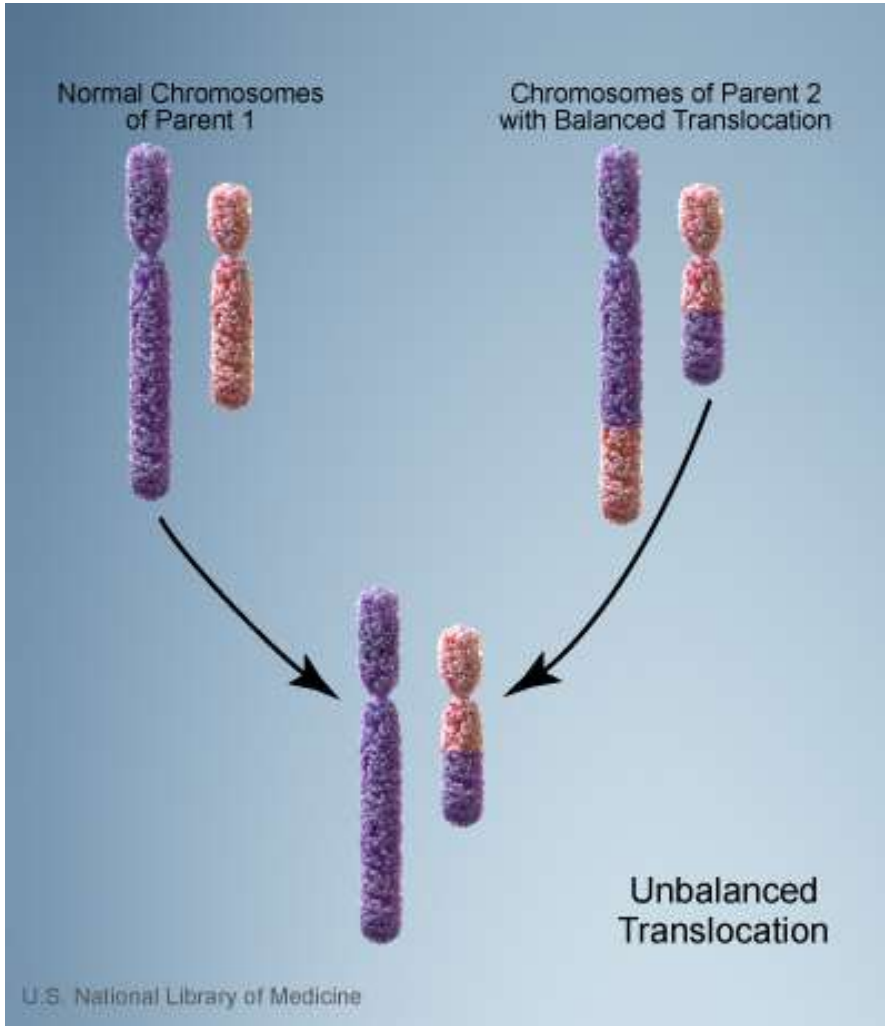
Translocation

- Movement of part of a chromosome to another part of the genome.
- May happen with the same chromosome.
  - translocation is an intrachromosome translocation.

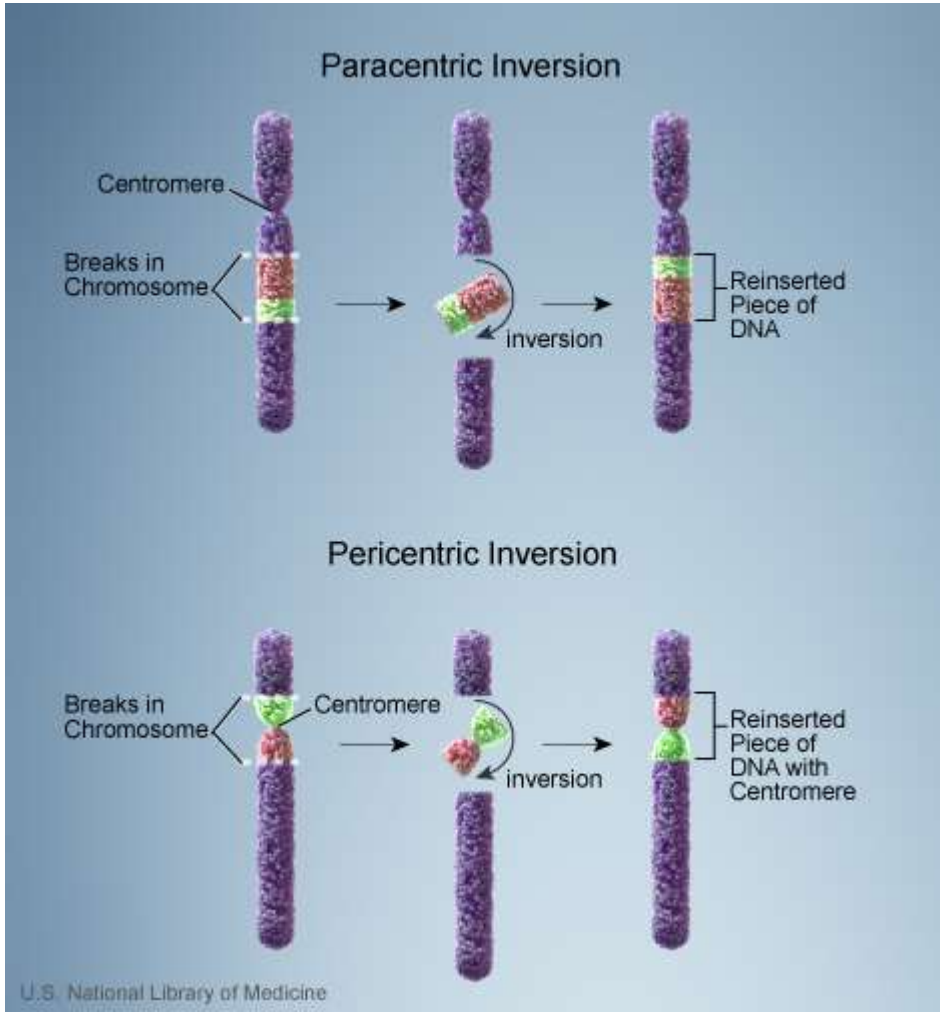
Inversion

- Inversions happen when a whole region of genes on a chromosome gets flipped around .
- 2 types of inversions.
  - **paracentric** inversions the centromere is not included in the inversion.
  - **pericentric** inversions, the centromere is involved in the inversion.

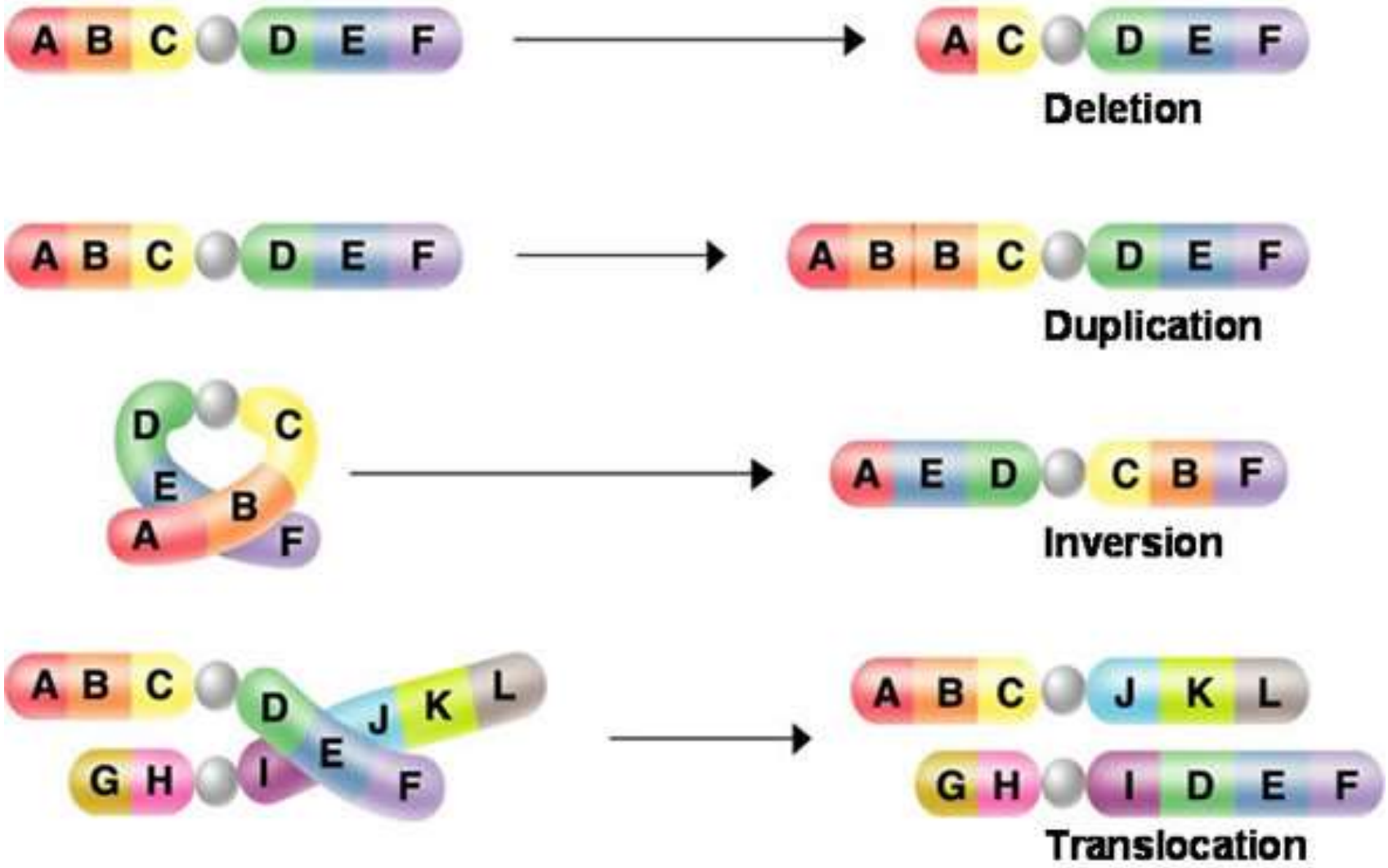
TRANSLOCATION



INVERSION



CHROMOSOME MUTATION



3 GENOME MUTATION

Aneuploidy
Polyploidy
Autopolyploidy
Allopolyploidy

- Normal organism is **euploid** with exact chromosome number that is multiple of chromosome set (2n).
- E.g *Drosophila melanogaster* normally with 8 chromosome. The species is diploid, having two sets of 4 chromosomes each.

Rare occasion where abnormal fruit fly produce 12 chromosomes, containing 3 sets of 4 chromosomes each. This alteration is called triploid fruit fly with 12 chromosomes. What about triploid individual?

Chromosome numbers can vary in 2 ways

Polyploid

- An increase in the number of the complete sets of chromosome
- In animals and plants

Aneuploid

- Abnormal number of chromosomes within a set
- Variations are less common

CHANGES IN CHROMOSOME NUMBER

a. Aneuploidy
b. Polyploidy

a. Aneuploidy

- Normally 2N (haploid individual) ends up either with **extra copies** of homologous chromosomes or **fewer than the normal diploid number**.

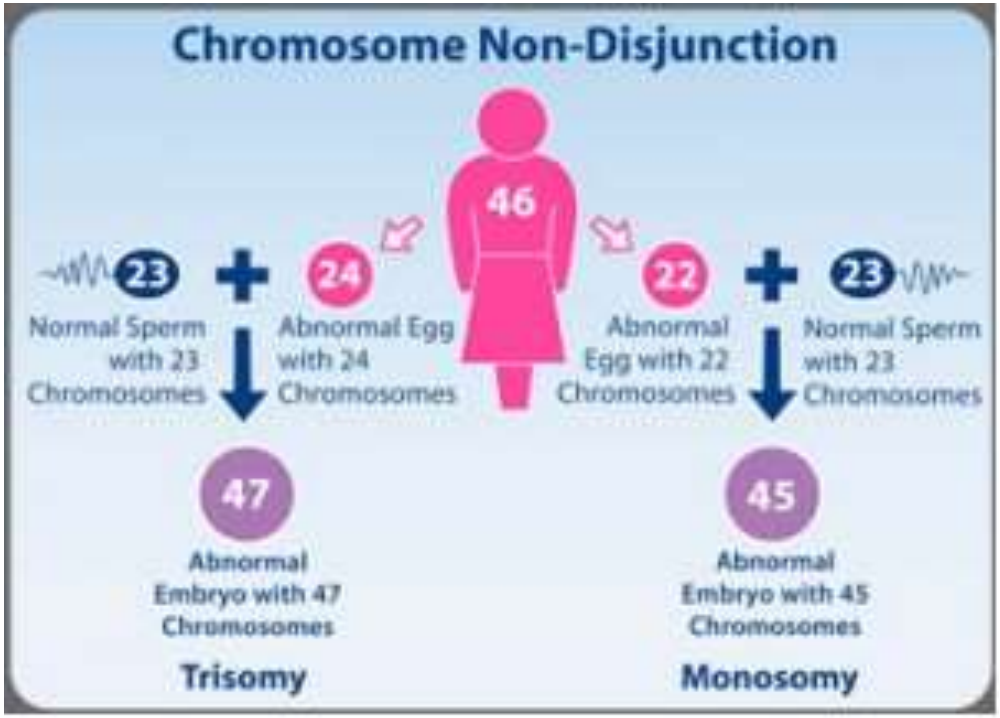
- Happens when homologous chromosomes fail to segregate properly during meiosis (non disjunction).

- **Monosomy (2n-1)** in which the diploid individual has only one member of a certain homologous chromosome.

- The other common type of aneuploidy is called **trisomy (2n+1)** because the individual has three copies of the particular chromosome.

a. Aneuploidy (cont)

- Happens when homologous chromosomes fail to segregate properly during meiosis (non disjunction).



a. Aneuploidy (cont)

- Aneuploidy leads to a number of syndromes in humans. For example **trisomy 21** leads to Down syndrome, characterized by mental retardation and other abnormalities.

- Aneuploidy involving the sex chromosomes is common. **XYY males** are normal but…

- **XXY males** and **XXXY males** have a syndrome called **Klinefelter syndrome**. These males are often actually intersexed or hermaphroditic with partially developed sexual organs of both genders. These individuals are sterile and are often subjected to hormones and surgery to bring them into conformance with social gender roles.

The ‘XYY’ Jacob’s syndrome men

- 47,XYY ; an extra copy of the Y chromosome
- Taller than average, but typically causes no unusual physical features. Most have normal sexual development and are able to father children.
- Associated with the risk of learning disabilities and delayed development of speech and language skills. Delayed development of motor skills (such as sitting and walking), weak muscle tone (hypotonia), hand tremors or other involuntary movements (motor tics), and behavioral and emotional difficulties are also possible.
- A small percentage of males with 47,XYY syndrome are diagnosed with autistic spectrum disorders, which are developmental conditions that affect communication and social interaction.

b. Polyploidy

- 3N/sets or more of chromosomes in a nucleus.
- Can happen because of a failure of the spindle fibers in mitosis or meiosis to segregate chromosomes into separate groups.
- Many organisms have specialized polyploid tissues even organisms we typically consider as diploid.
  - For example in plants a so called double fertilization leads to the genesis of a diploid zygote from the union of two gametes produced by the haploid gametophytes, but also a specialized triploid tissue (3N) called endosperm. This tissue is produced when a male gamete fertilizes special diploid tissue from the flower. In mammals, cells of the liver are typically polyploid.

b. Polyploidy (cont)

- Individuals with **triploid syndrome** have three of every chromosome for a total of sixty-nine rather than the normal forty-six chromosomes.
- Babies with Triploid Syndrome usually are lost through early miscarriage. However, some infants have been born and survived as long as five months. Affected infants are usually small and have multiple birth defects.
- Those that survive are usually mosaic, meaning that some cells have the normal number of 46 chromosomes and some cells have a complete extra set of chromosomes.

FACTORS CAUSING MUTATIONS

Factors that causes mutation

2 Factors that contribute to mutation

- Error in DNA replication.
- Damaging effects of mutagens
  - CHEMICALS: Alkylating agents like nitrosoguanidine, nitrosamine, etc.
  - RADIATIONS: X-rays, U.V.rays, etc.

Error in replication

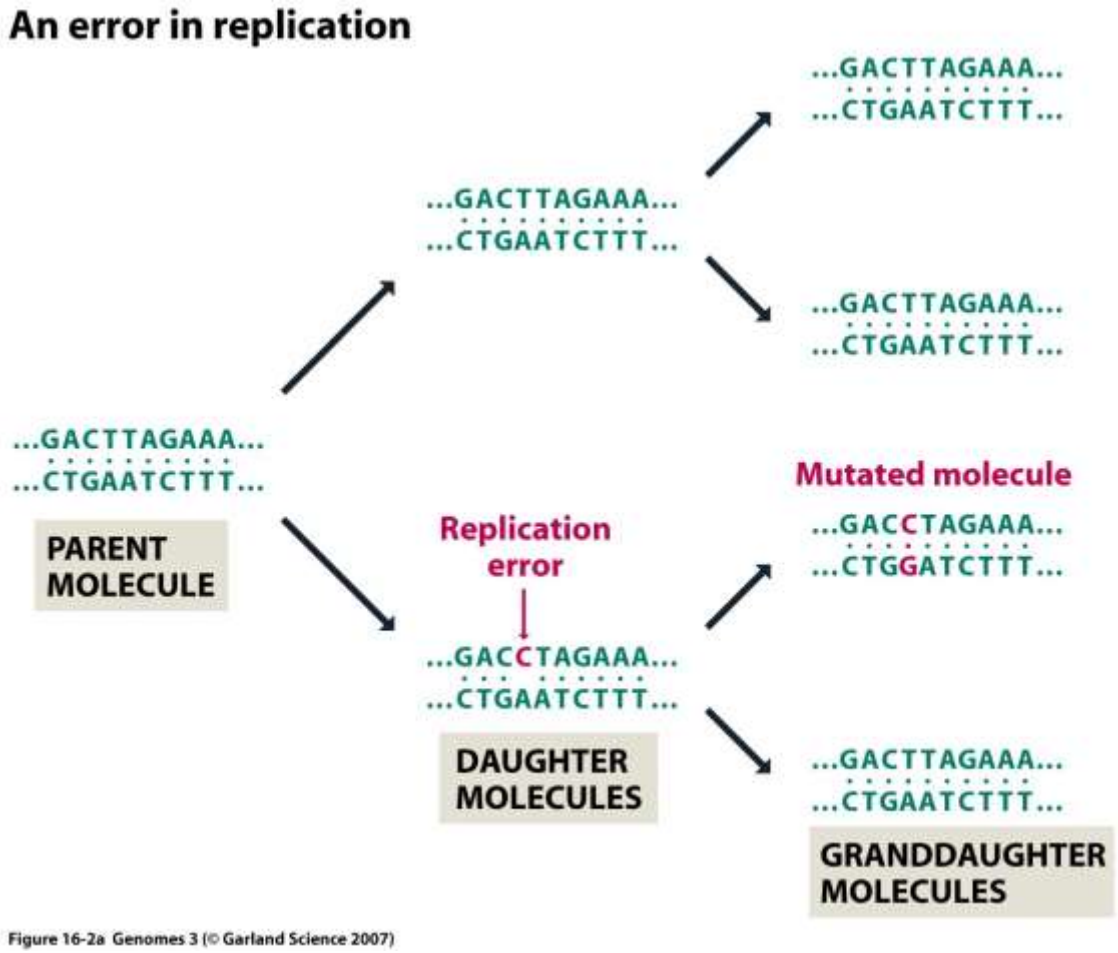


Figure 16-2a Genomes 3 (© Garland Science 2007)

Factors that causes mutation

Chemical mutagens - used in research to study mutagenesis. There are 3 kinds of chemical mutagens.

1. **Alkylating agents.**
   - Adds alkyl group, such as methyl group CH_3 CnH(2n+1), result in mispairing bases in DNA replication
   - Pairing with wrong bases; methyl group bond with G, it will pair with thymine instead of cytosine.

2. **Intercalating agents.**
   - Inserts into DNA and pushes bases apart.
   - Eg. Benzopyrene – from smoke causing frameshift mutation.

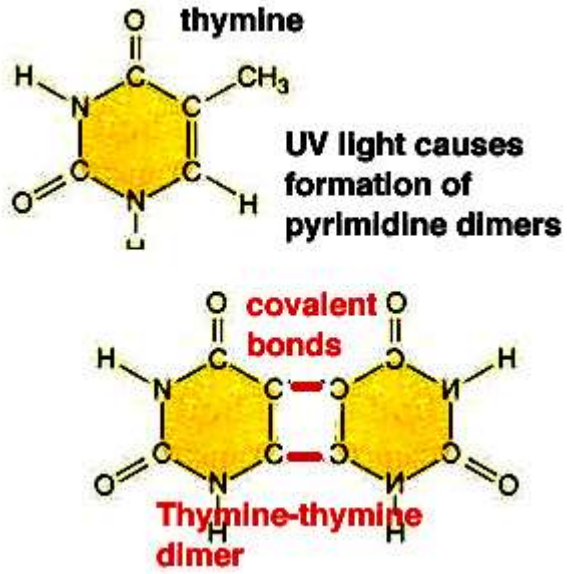
3. Base analogs.

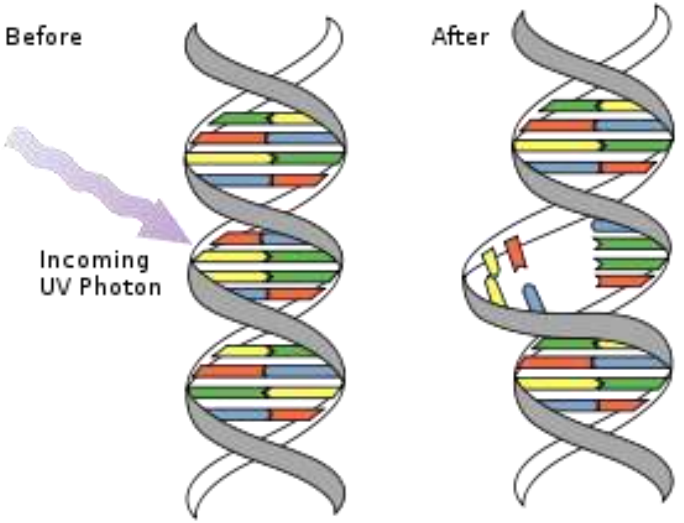
- Mimics a nitrogenous base. Eg. AZT is a modified sugar that substitutes for T.
- Eg. 5 - bromouracil binds with A or G.

Factors that causes mutation (cont)

Physical mutagens:

1. **Nonionizing radiation**
   - Causes the formation of T= T dimers. UV light @ 260 nm.
   - Affecting formation harmful covalent bonds between pyrimidine (T and C).
   - Forming gap in in DNA strand = no pairing, no replication = cell death





2. Ionizing radiation

- damages DNA by causing the formation of “free radicals” leading to mutations.
- Eg. X-rays. Gamma rays from radioactive fallout penetrates the body. Alpha rays from inhaled dust containing radioactive fallout.

Questions