Elective Virology Course E007

Lecture Series IV

Virus Genetics and Evolution

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Genetic Changes

- Mutation
- Recombination
- Interaction between viral Gene Products

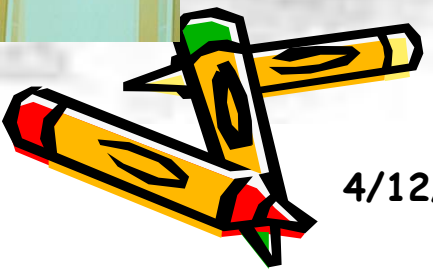
Mutation

Definition:

Is a change in the nucleotide sequence either due to mistakes when NA is copied or as a result of environmental factors.

Wild-type Virus: Naturally occurring non-mutant strain of the virus (original – street – parental).

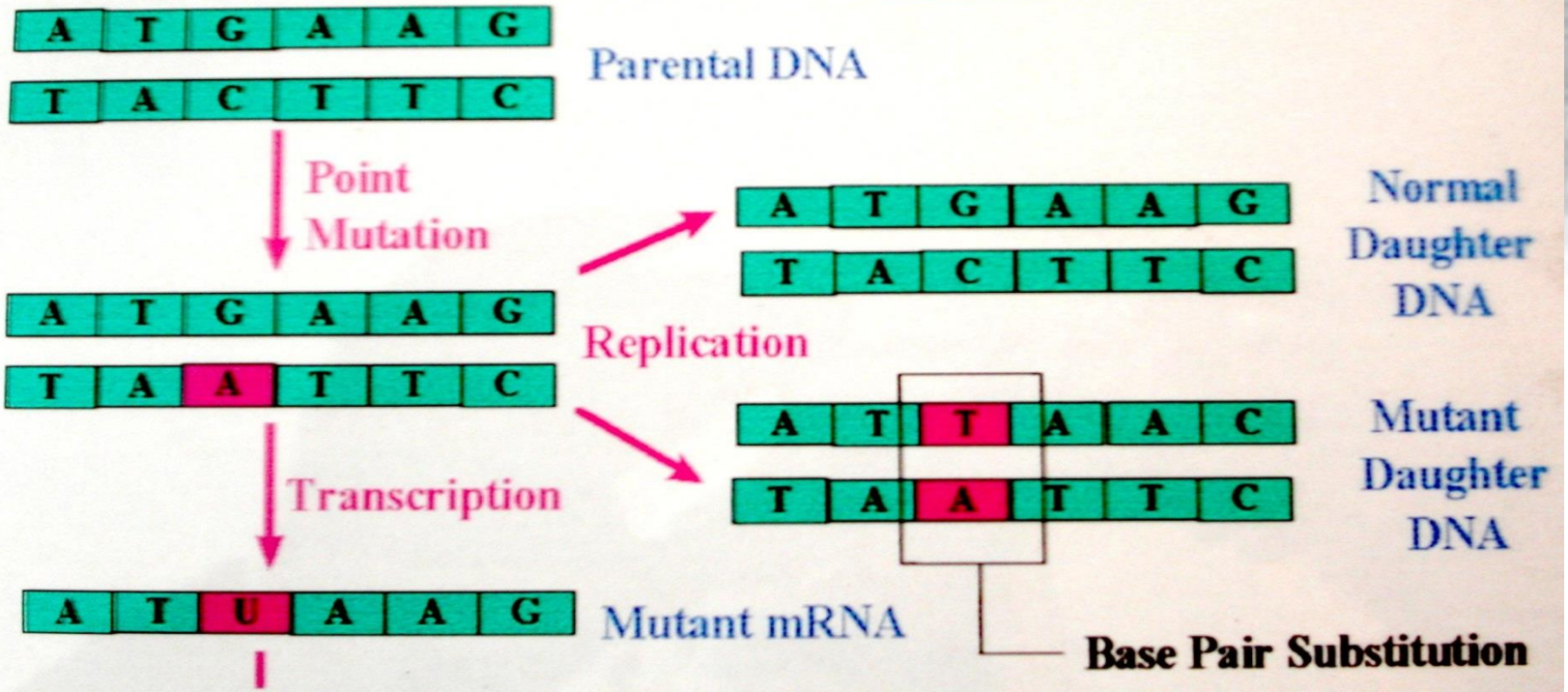
Mutant Virus: A virus with an alteration in its nucleotide sequence (variant).



Types of Mutation

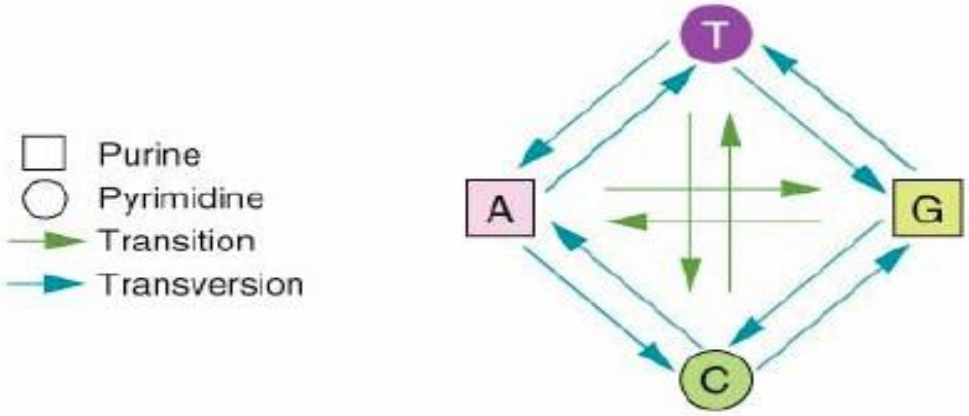
A. Genotypic

1. **mutation, also called a base substitution, occurs when a single nucleotide is replaced with a different nucleotide. A point mutation results in a base pair substitution after replication and possibly a mutant protein after transcription and translation.**



Types of Mutation (Cont.)

Base substitutions



(*a*) Twelve different base substitutions can occur in DNA.

Two main types of base subst.:

1) Transition (purine—>purine or pyrimidine —>pyrimidine) Ex.- A—>G or T—>C

2) Transversion (purine—>pyrimidine or pyrimidine —>purine)

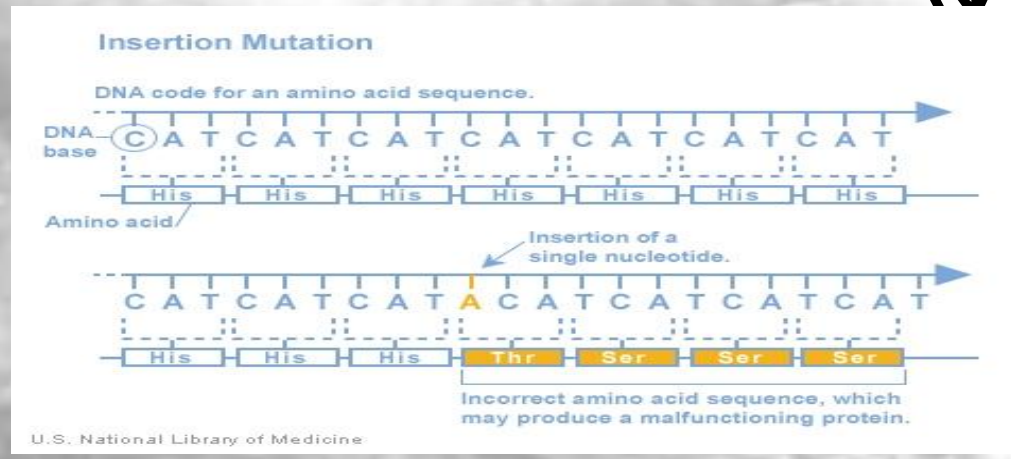
Transitions are more common.

Types of Mutation

A. Genotypic

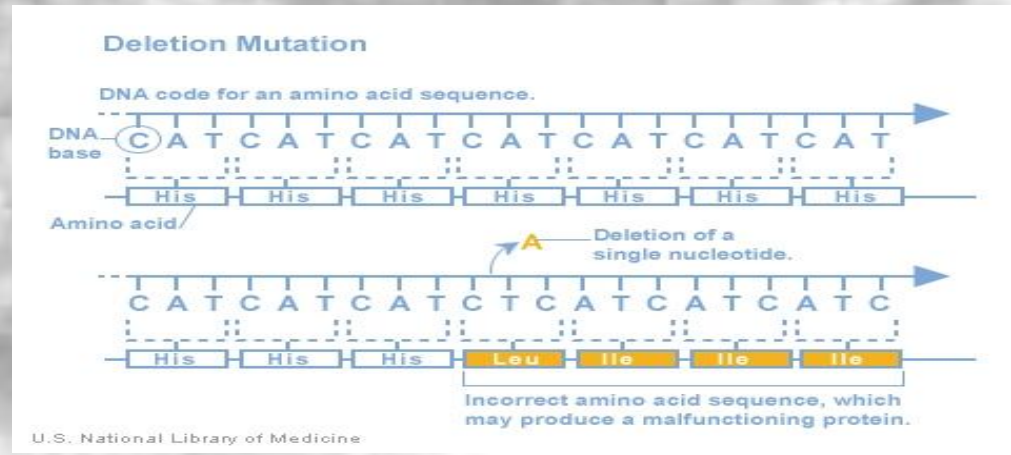
2. Insertion mutations:

Extra base pair(s) are inserted into a new place in the DNA



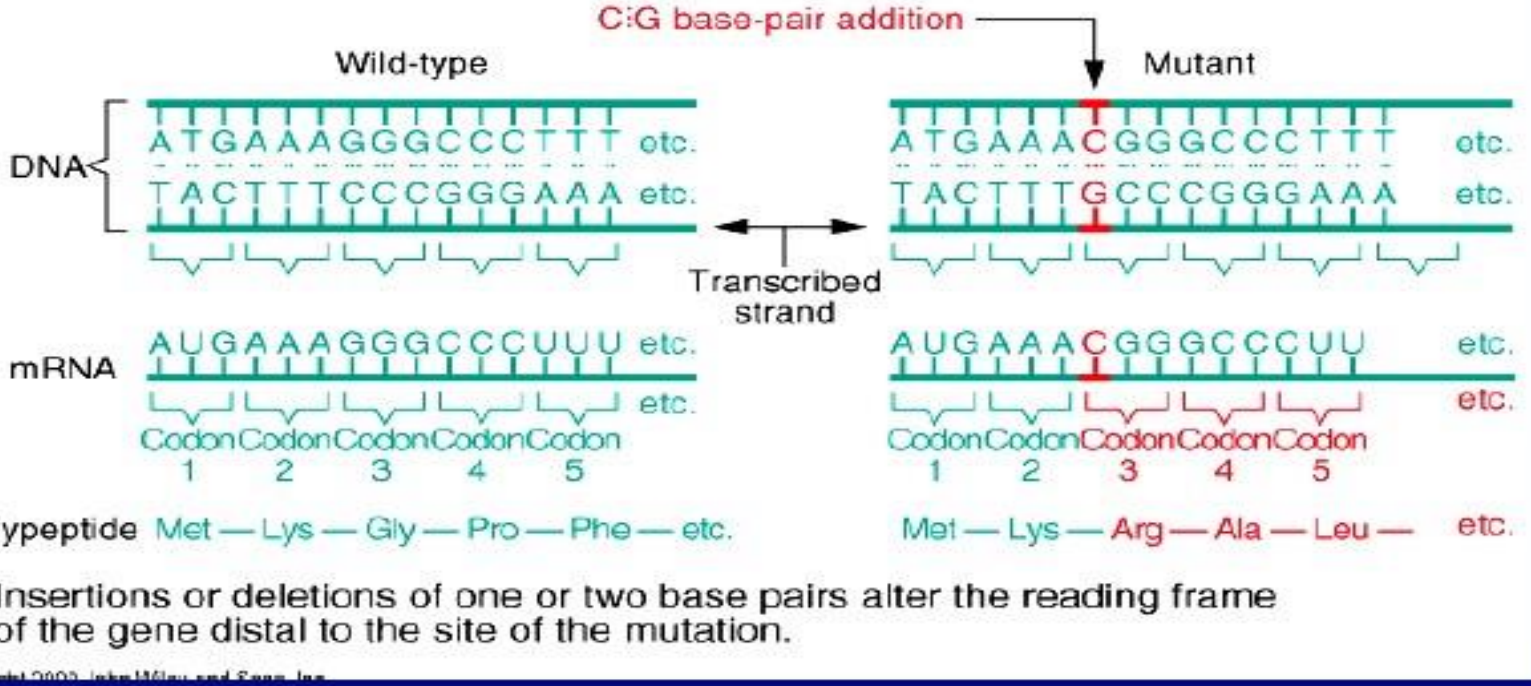
3. Deletion mutations:

One or more of base pairs are deleted.



Types of Mutation (Cont.)

Insertion and deletion mutations



(*b*) Insertions or deletions of one or two base pairs alter the reading frame of the gene distal to the site of the mutation.

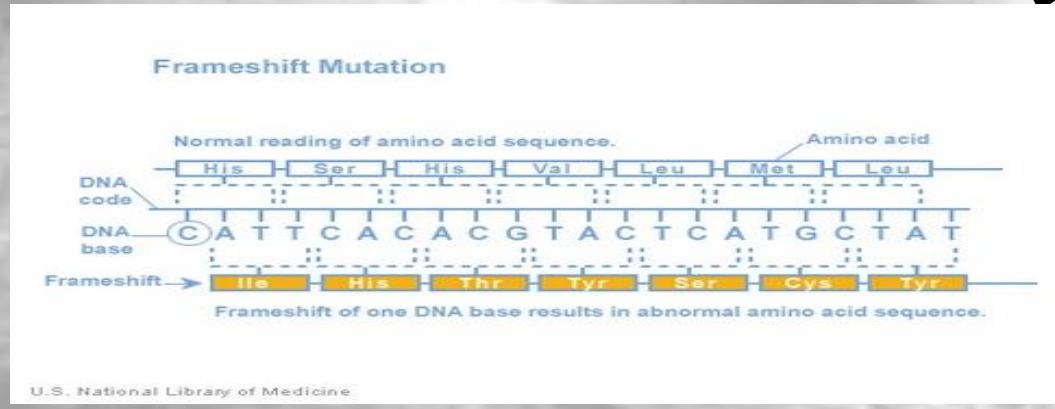
Insertion or deletion of one or two bases changes the reading frame. +1, +2, -1, or -2 Frameshift.

Types of Mutation (Cont.)

A. Genotypic

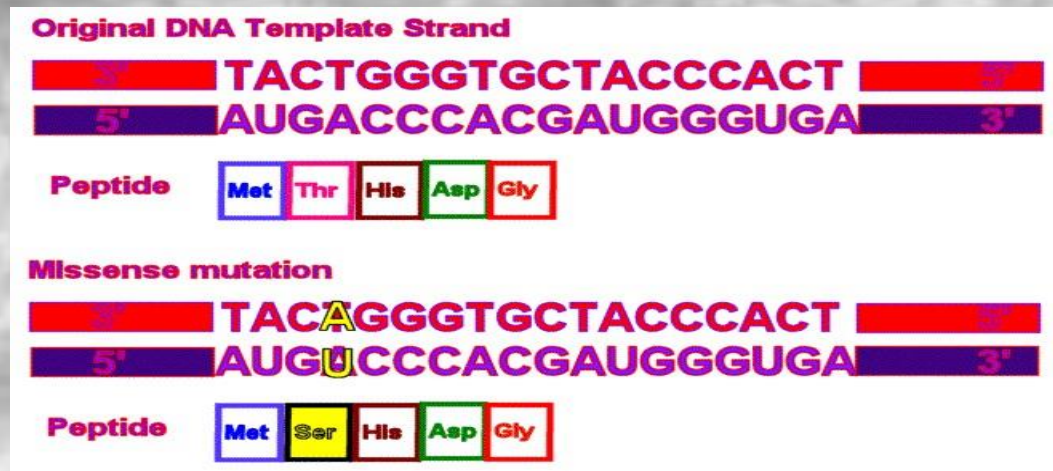
Frame-Shift Mutation:

Error occurs at the DNA level, causing the codons to be parsed incorrectly.



Missense Mutation:

Substitution of a single base pairs results in codon change, thus giving a single A.A. substitution.



Types of Mutation (Cont.)

B. Phenotypic Changes:

1. CONDITIONAL LETHAL:

Multiply under some conditions but not others

Wild-type (wt) grows under both sets of conditions

Examples:

- temperature-sensitive (ts) mutants do not grow at higher temperature.
- host-range mutants do not grow in all the cell types that the wt does.

Types of Mutation (Cont.)

B. Phenotypic Changes (Cont.):

2. *Plaque Mutants:* a mutant may produce a different type of plaques in a cell monolayer

3. *Antibody escape mutants:* may become resistant to neutralization by antibody raised against the wild type (e.g.In horse persistently infected with equine infectious anemia virus "EIA").

N.B. A prominent example of mutations affecting viral antigenicity is the antigenic drift of Influenza Viruses.

Types of Mutation (Cont.)

B. Phenotypic Changes (Cont.):

4. *Hot Mutants:* grow better at elevated temperature than wt and less susceptible to host fever response.

5. *Attenuated Mutants*:
   - milder (or no) symptoms.
   - vaccine development.
   - Pathogenesis.

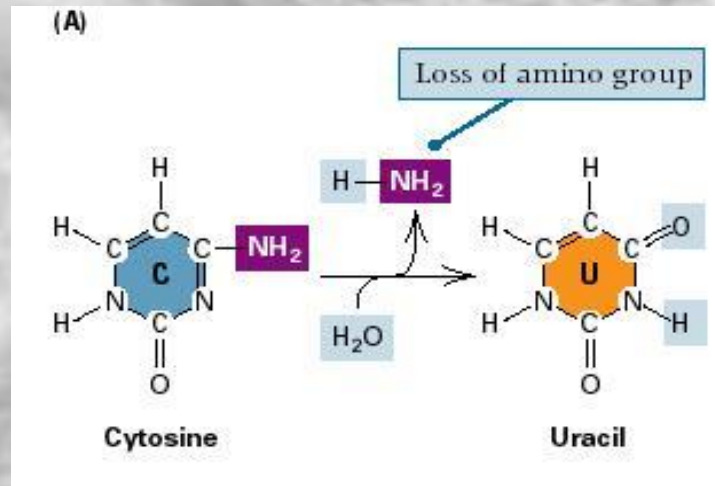
6. *Defective Interfering Viruses:* demonstrated in most families (specially RNA Viruses) and need the presence of the wild-type virus (e.g Influenza Viruses)

Mutagenesis

A. Spontaneous Mutation:

1. ***Errors in Replication:***
   Transitions and Transversions that occur during replication.

2. ***Spontaneous Lesions:***
   - Depurination.
   - Deamination.
   - Oxidative Damage to DNA.



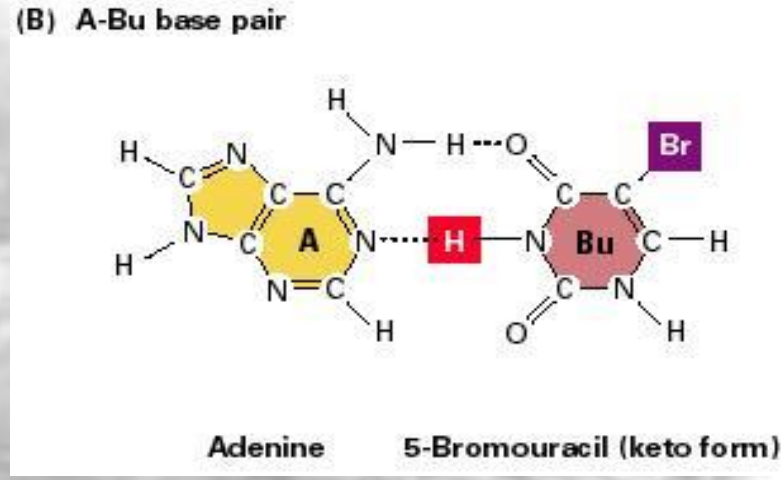
Mutagenesis

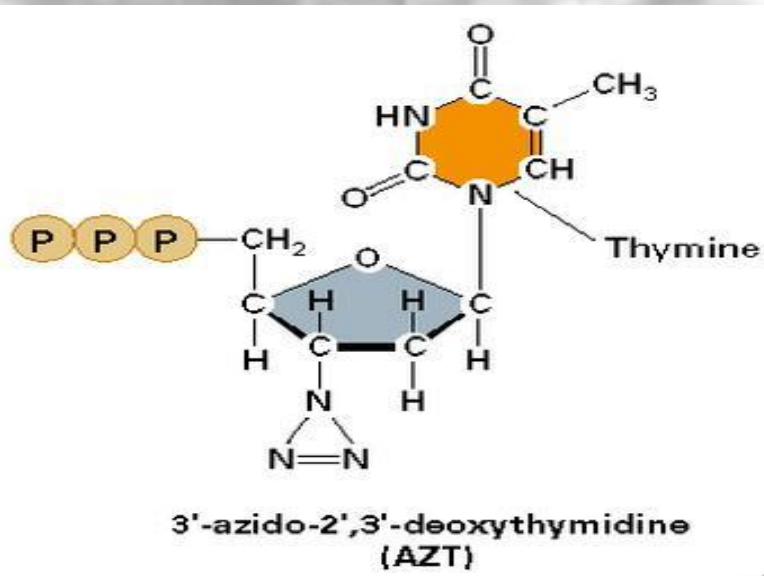
B. Induced Mutation:

1. Base-Analog Mutagens:

5-Bromo-uracil can substitute for T, and then wind up binding with G (B) and results in miscoding.

AZT a nucleotide analog that can result in Chain Termination.





Mutagenesis

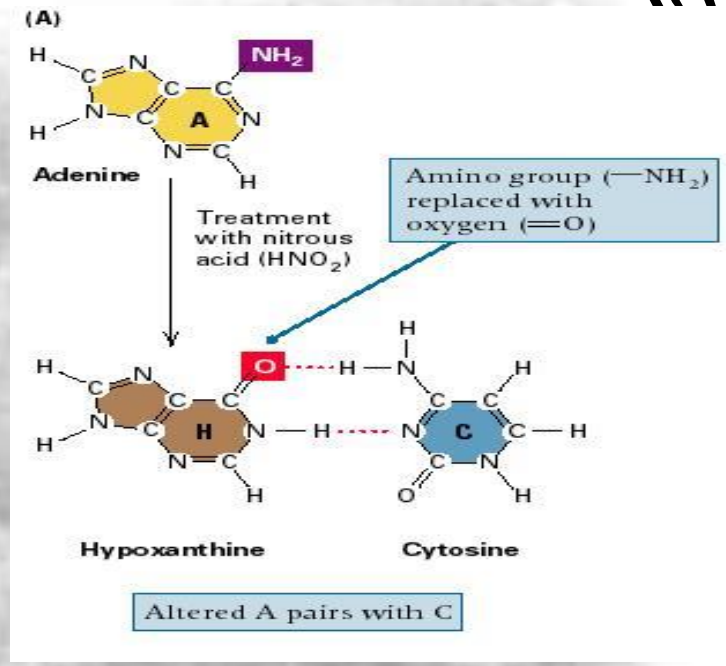
B. Induced Mutation:

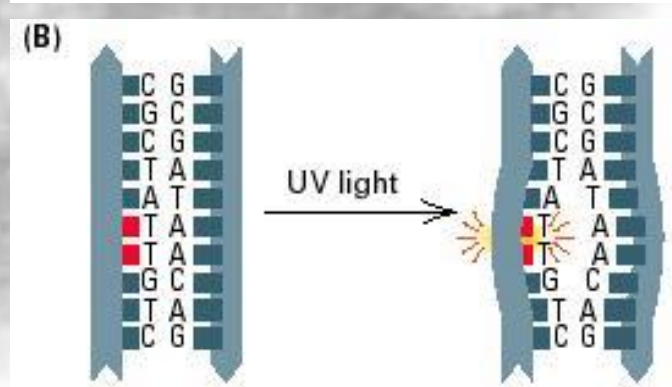
2. Chemical Agents:

Such as nitrous oxide or nitrosoguanidine.

3. UV and Ionizing Irradiation:

Crosslinks between adjacent thymines (thymine dimer)



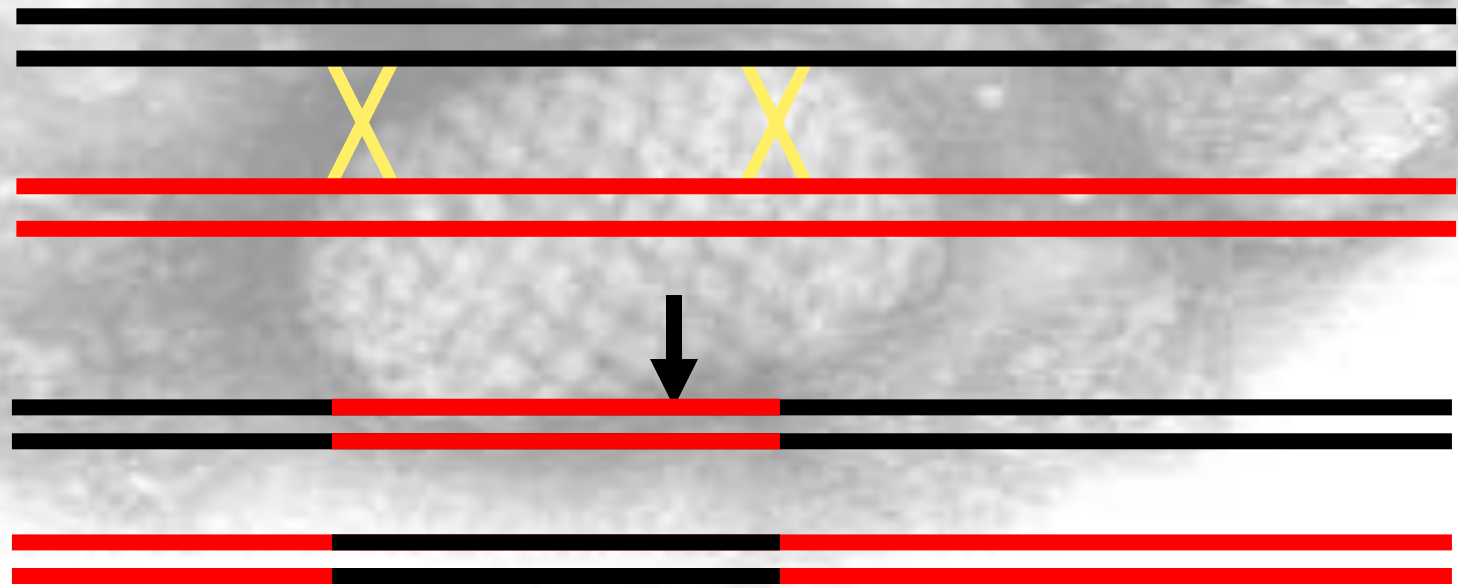


RECOMBINATION

Exchange of information between two genomes.

1. Intramolecular Recombination:

It involves the exchange of nucleotide sequence between different-but usually closely related-viruses during replication, e.g. as in Picornaviruses, Coronaviruses and Togaviruses)

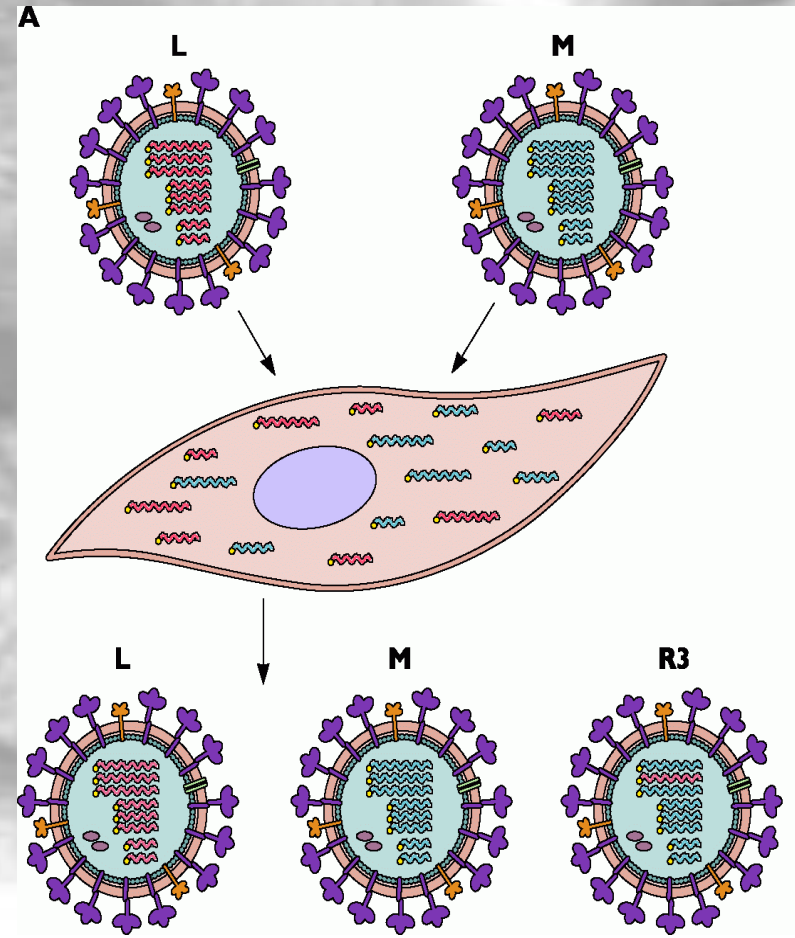


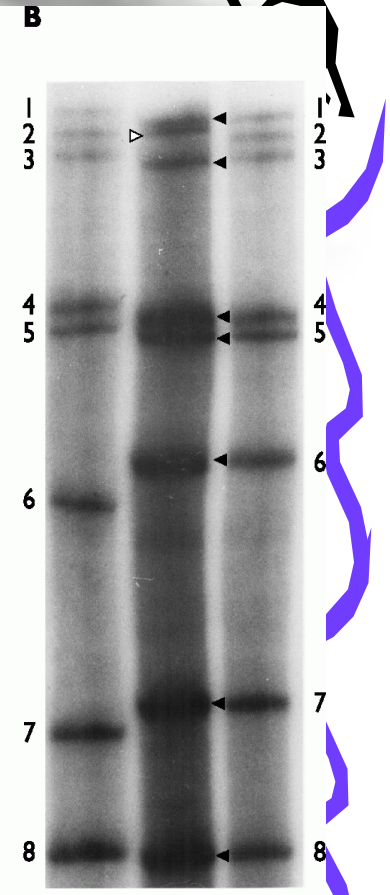
RECOMBINATION (Cont.)

2. Genetic Reassortment:

* Observed in RNA Viruses with segmented genomes (e.g Bunyaviridae "RVFV", Orthomyxoviridae "Infl.", and Reoviridae "Rotaviruses and Blue Tongue Virus",

* Exchange of segment may occur when cell are infected simultaneously with two related viruses.



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