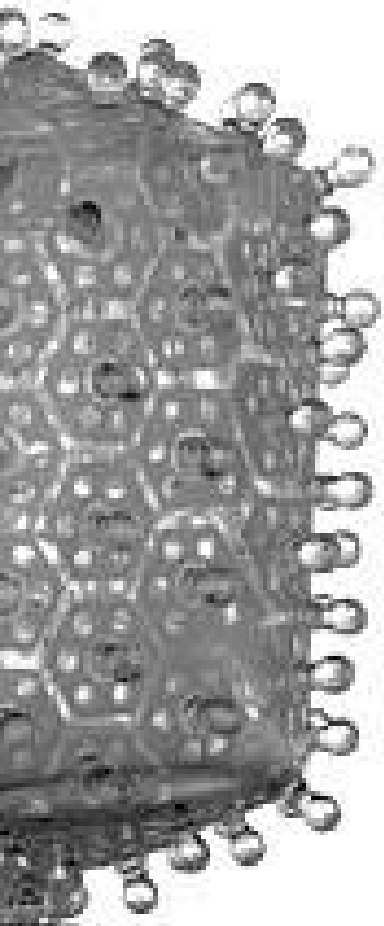
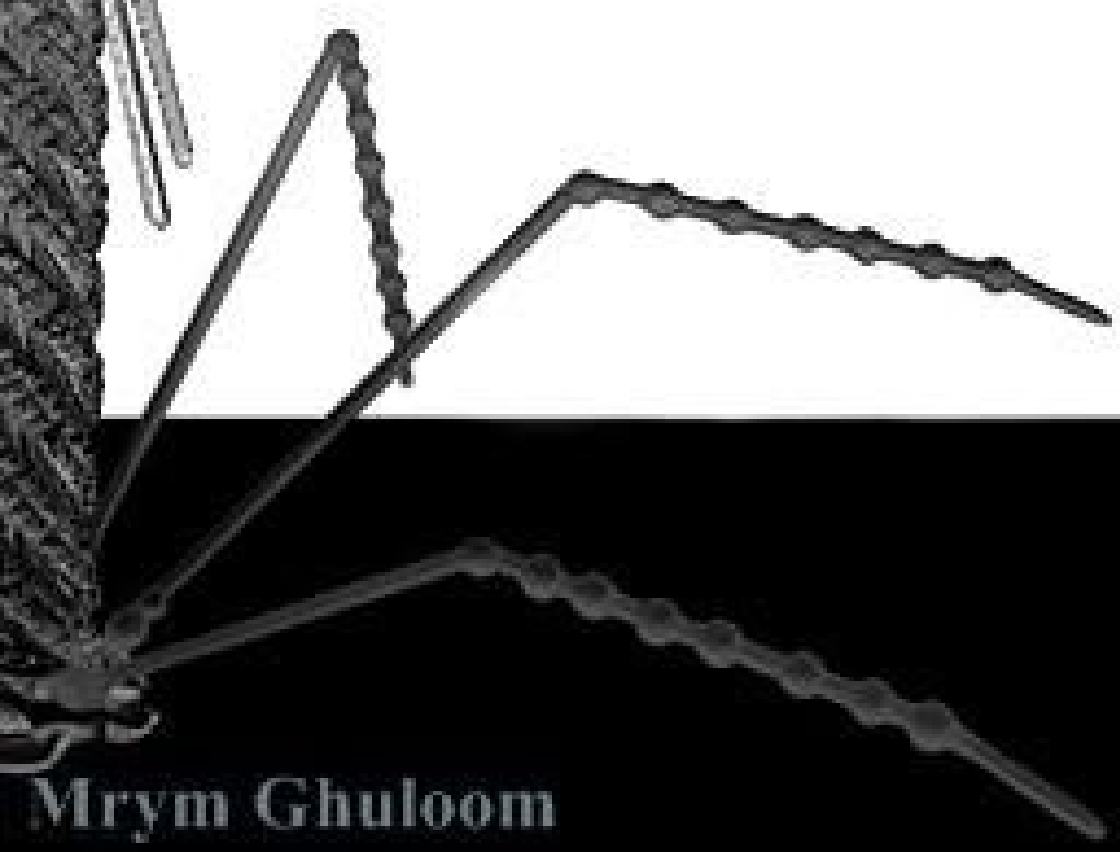


Microbiology

Lecture No:.3.....

Dr Name:..Hamed Al Zoubi

Sheet ☐ Slide ■



Mrym Ghuloom

Virology – Introduction
JU- 2nd Year Medical Students
2014

By

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Virology – replication and genetics

- **Formation of viral mRNAs**
- Synthesis of mRNA is a crucial step in replication

✓ mRNA is transcribed from dsDNA using cellular DNA dependent RNA polymerase (POXVIRUS?)

✓ +ve ssRNA recognised as mRNA and translated directly by cellular ribosomes (POLIOVIRUS, FLAVIVIRUS)

- directly infectious to cells by itself

✓ -ve ssRNA? antigenome (RABIES, INFLUENZA)

Virology – replication and genetics

- For many other viruses, translation is not straightforward:

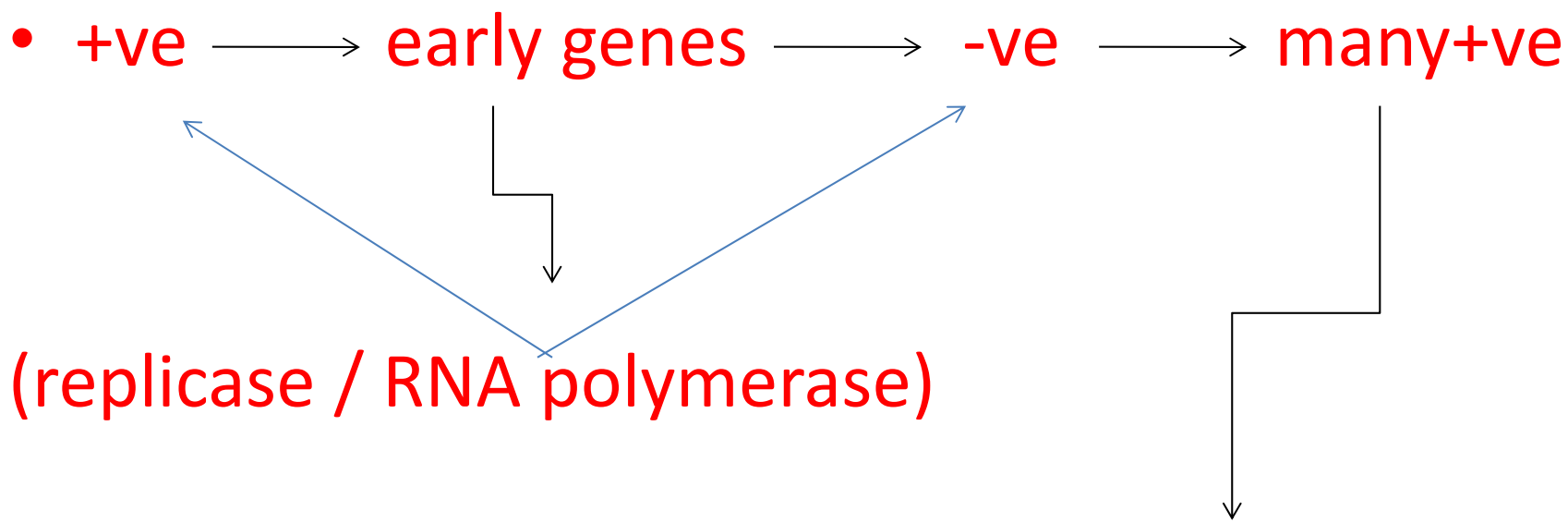
1. Poxviruses replicate in the cytoplasm where no cellular RNA polymerase is available to transcribe the DNA genome > therefore, poxviruses carry its DNA dependent - RNA polymerase with it.

2. No cellular machinery exists that can use either single-stranded DNA or double-stranded RNA as a template to synthesize mRNA.

Replication

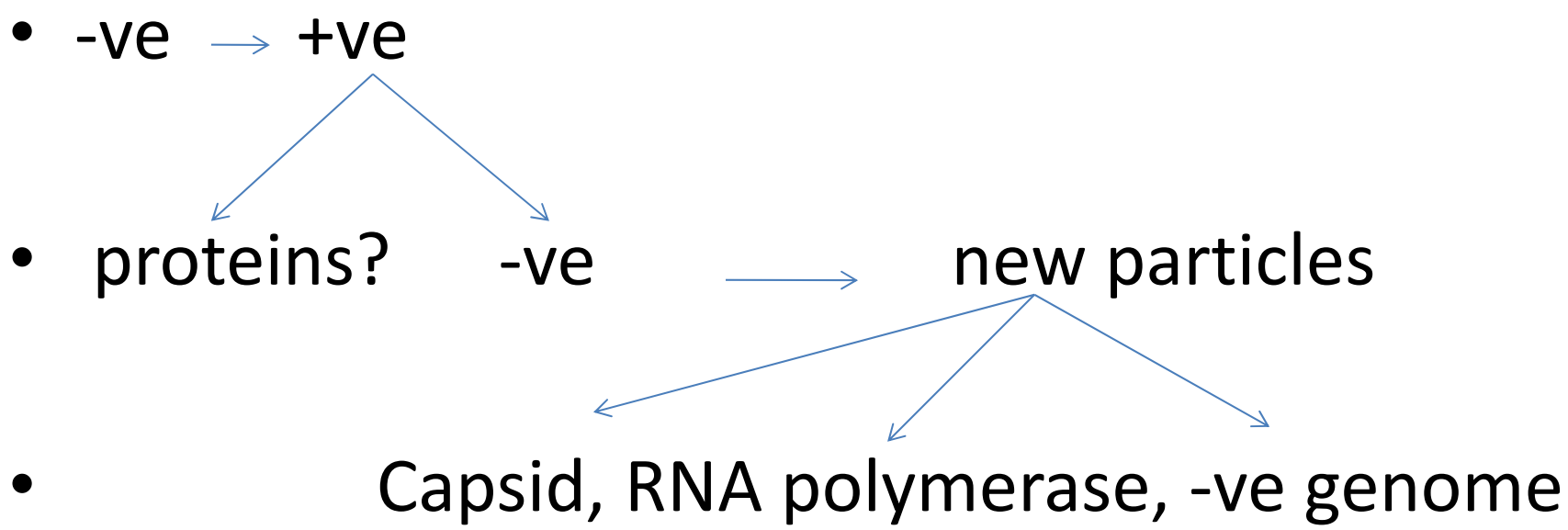
- +RNA VIRUSES (homologus to mRNA/Baltimore):
- Cap and poly A tail
- +: produce early proteins (RNA polymerase or replicase) THEN:
- Replicase will synthesize complementary –ve copy (transient replicative intermediates/unstable) from which many +ves copies will be synthesized
- The +ve copies now used for structural proteins and
- For the offspring genome
- ERRORS MAY HAPPEN DURING TRANSCRIPTION

What is this?


+ve
early genes
-ve
many+ve
(replicase / RNA polymerase)
(structure and offsprings)

Replication

- -ve RNA viruses



DNA viruses

- Use cellular DNA dependent polymerase but poxvirus (has its polymerase)
- Replication fork
- In cases of ssDNA: a transient dsDNA intermediate is synthesized
- Early proteins (from viral DNA copy) late proteins (from newly synthesized copies)

dsRNA (Reoviruses):

- The viruses carry dsRNA dependent RNA polymerase > mRNA

+ss Retrovirus RNA:

- ssRNA > dsDNA by the viral reverse transcriptase (RNA-dependent DNA polymerase) > integrated into host genome > then mRNA will be transcribed using the cellular DNA-dependent RNA polymerase

- Partially ds hepadnaviruses DNA

- The genome will be completed into complete dsDNA using the viral DNA polymerase (reverse transcriptase) > then the mRNA will be transcribed using the cellular DNA-dependent RNA polymerase

- Parvovirus: ? HAIRPIN mechanism.....

Control of viral replication

✓Transcription:

- Might be virally blocked by M proteins
- Enhanced by some viral signals or structures such as:

  Overlapping reading frames or primary RNA transcript splicing

Control of viral replication

✓Translation:

- Binding to ribosomes (competing the host mRNA) by structural proteins at the Internal ribosome entry sites

  E.g poliovirus, hepatitis A and C

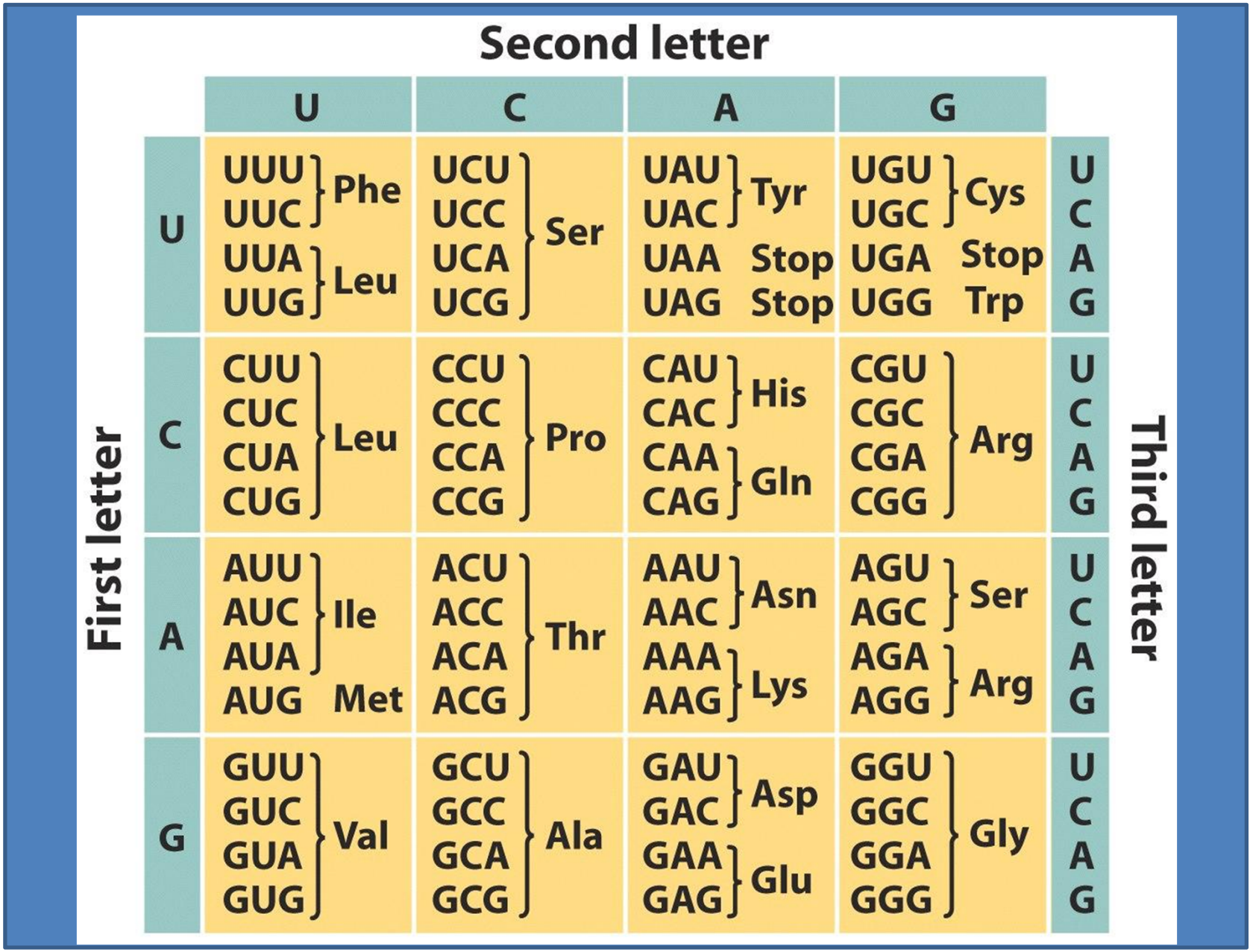
- Expressing immediate early proteins that will activates further expression of early and late proteins e.g Adenoviruses

Synthesis of viral proteins

- Start and stop codons

- Mutations:

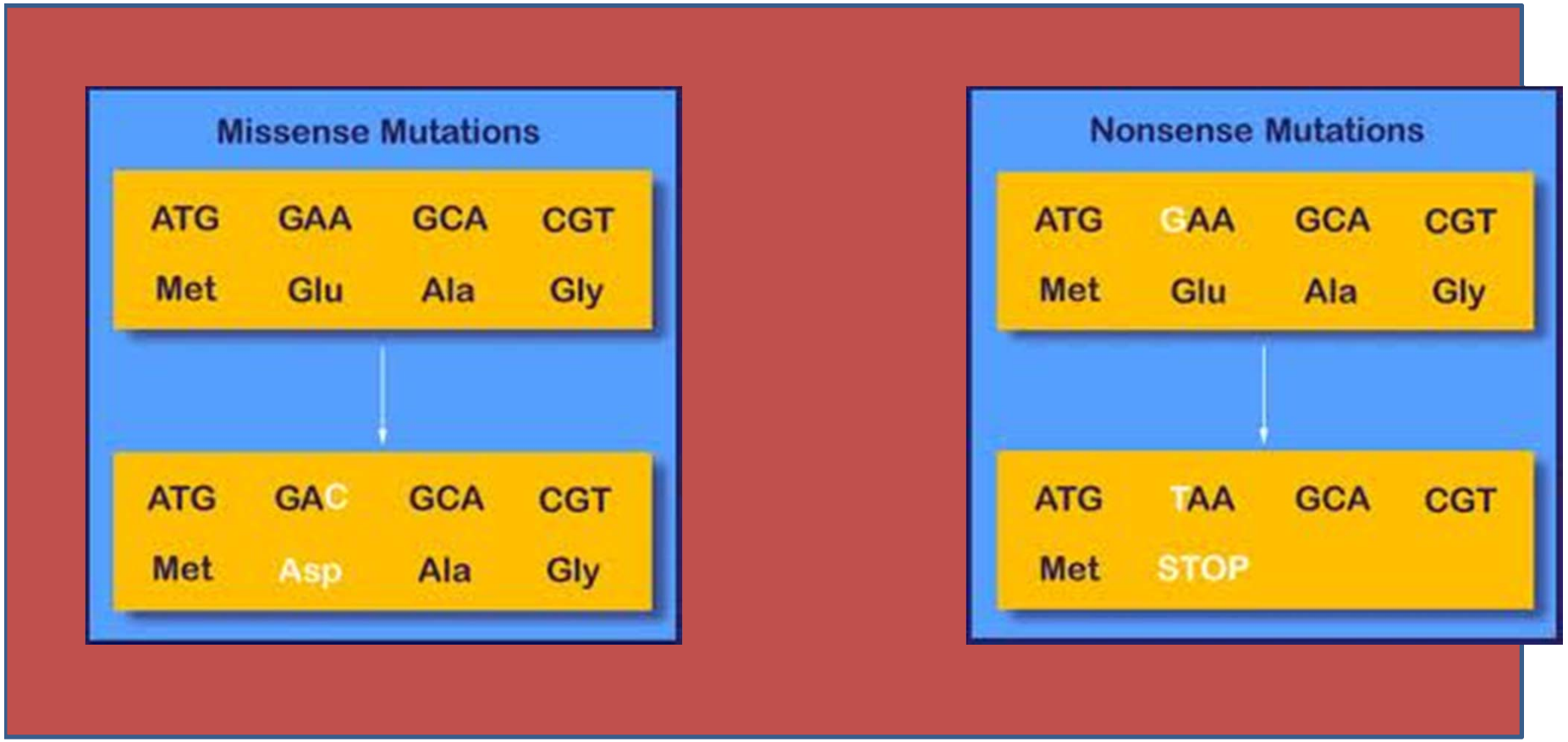
✓Silent, nonsense, missense and frame shift


Second letter
U
C
A
G
First letter
Third letter
U
UUU Phe
UUC
UUA Leu
UUG
UCU Ser
UCC
UCA
UCG
UAU Tyr
UAC
UAA Stop
UAG Stop
UGU Cys
UGC
UGA Stop
UGG Trp
U C A G
C
CUU Leu
CUC
CUA
CUG
CCU Pro
CCC
CCA
CCG
CAU His
CAC
CAA Gln
CAG
CGU Arg
CGC
CGA
CGG
U C A G
A
AUU Ile
AUC
AUA
AUG Met
ACU Thr
ACC
ACA
ACG
AAU Asn
AAC
AAA Lys
AAG
AGU Ser
AGC
AGA Arg
AGG
U C A G
G
GUU Val
GUC
GUA
GUG
GCU Ala
GCC
GCA
GCG
GAU Asp
GAC
GAA Glu
GAG
GGU Gly
GGC
GGA
GGG
U C A G

- Types of mutation:

1. base substitution:

- DNA polymerase error or due to mutagens
- Missense vs nonsense mutations
- silent

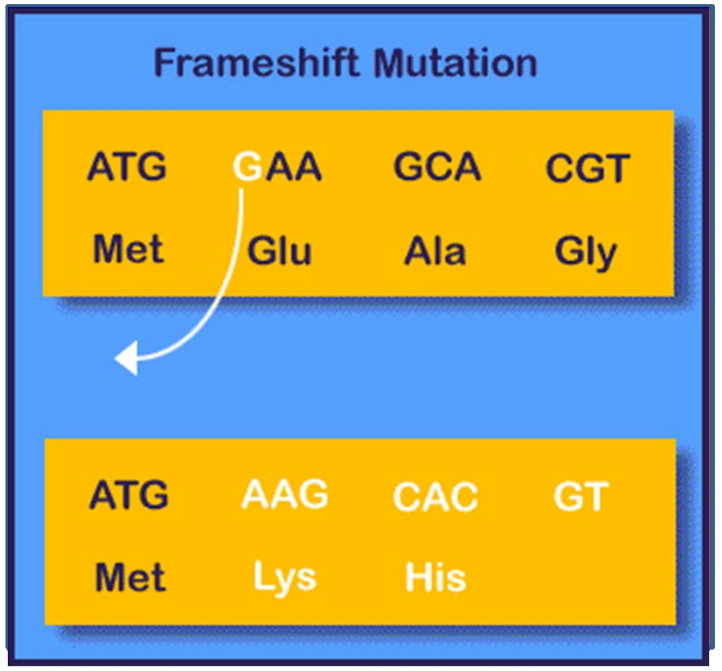


Mis-sense mutation

Non-sense

2. Frame shift mutation:

- One or more base are added or deleted
- Shift in the reading frame
- Corrupting the reading codons downstream mutations leading to inactive protein



post-translation modification of viral proteins

- Necessary for folding and 3 d structure formation
- Removal of initiation amino acid while the polypeptide is still attached to the ribosome.
- Glycosylation
- Covalent attachment of lipoic acid
- Addition of phosphate, sulphate and acyl groups
- Polyprotein splicing by proteolytic enzymes

Assembly, release & maturation

- Self assembly and genomic encapsidation may occur in the cytoplasm (Polio) or nucleus (Adenovirus)
- Release by lysis (polio), budding (Rota from ER; HIV, Influenza and measles from plasma membrane) or contiguous spread via pores/fusion (HIV, Herpes)
- Postrelease maturation: HIV and Influenza

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