بسم الله الرحمن الرحيم

Basic Principles and Perspectives in Medical Chemistry and Biochemistry

Nucleic Acids

Part 3

6th Medical and Biochemistry (BIQC-101) Lecture

Second Semester

by

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Mutation , Viruses

Learning Objectives

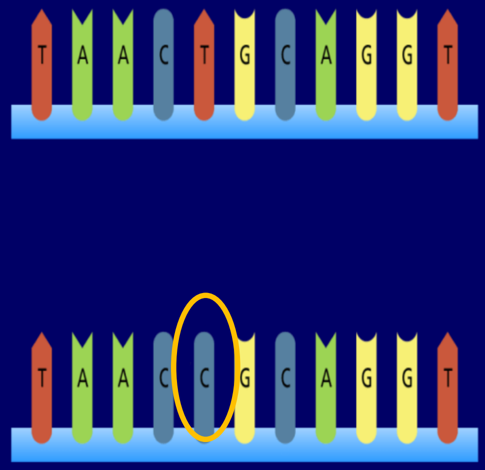
1. Define how errors by DNA polymerase create mutations
2. Identify the types of gene mutations.
3. Describe what occurs during each type of mutation.
4. Explain the structure and shape of viruses.
5. Know the viral replication, viral transaction and viral protein biosynthesis.
6. Discuss how to prevent viral transaction and viral protein biosynthesis

Gene Mutation

- **Genes** are segments of DNA located on chromosomes.
- **Gene mutation** is an alteration in the sequence of nucleotides in DNA. alteration can affect a single nucleotide pair or larger gene segments of a chromosome.
- During protein synthesis, DNA is transcribed into RNA and then translated to produce proteins.
- Altering nucleotide sequences most often results in nonfunctioning proteins.
- Mutations cause changes in the genetic code that lead to genetic variation and the potential to develop the disease.
- Gene mutations can be generally categorized into two types: point mutations and base-pair insertions or deletions.

1. Point Mutations

Point mutations are the most common type of gene mutation. Also called a base-pair substitution, this type of mutation changes a single nucleotide base pair. Point mutations can be categorized into three types:



1. **Silent Mutation:** Mutation does not change the protein that is to be produced because another multiple genetic codons can encode for the same amino acid. For example, the amino acid arginine is coded for by several DNA codons including CGT, CGC, CGA, and CGG If the DNA sequence CGC is changed to CGA, the amino acid arginine will still be produced.

2. **Missense Mutation:** Mutation alters the nucleotide sequence so that different amino acid is produced. This change alters the resulting protein. The change may not have much effect on the protein, may be beneficial to protein function, or may be dangerous. Using our previous example, if the codon for arginine CGC is changed to GGC, the amino acid glycine will be produced instead of arginine.
3. **Nonsense Mutation:** Mutation alters the nucleotide sequence so that a stop codon is coded for in place of amino acid. A stop codon signals the end of the translation process and stops protein production. If this process is ended too soon, the amino acid sequence is cut short and the resulting protein is most always nonfunctional.

2. Deletion and Insertion

1. **In-frame mutations :** Deleted or inserted base pairs is a multiple of three (one codon). This results in a change in only a few amino acids; it may still be possible for the protein to function.
2. **Frameshift mutations:** Deleted or inserted base pairs is NOT a multiple of three. for example, only one or two base pairs are deleted, then the way the DNA is read is shifted at the place of the deletion or insertion. After the place of the mutation, ALL of the amino acids that follow will be different. In this case, either an abnormal protein is made or no protein is made at all.

Original Sequence: CGA-CCA-ACG-GCG...

Amino Acids Produced: Arginine/Proline/Threonine/Alanine...

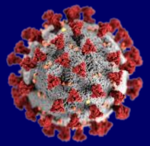
Inserted Base Pairs (GA): CGA-CCA-GAA-CGG-CG...

Amino Acids Produced: Arginine/Proline/Glutamic Acid/Arginine..

Causes of Gene Mutation

1. **External (environmental) factors:** such as chemicals, radiation, and ultraviolet light from the sun. These mutagens alter DNA by changing nucleotide bases and can even change the shape of DNA. These changes result in errors in DNA replication and transcription.
2. **Internal factors:** Errors made during mitosis. Mutations during cell division can lead to replication errors. Common errors can result in point mutations and frameshift mutations.

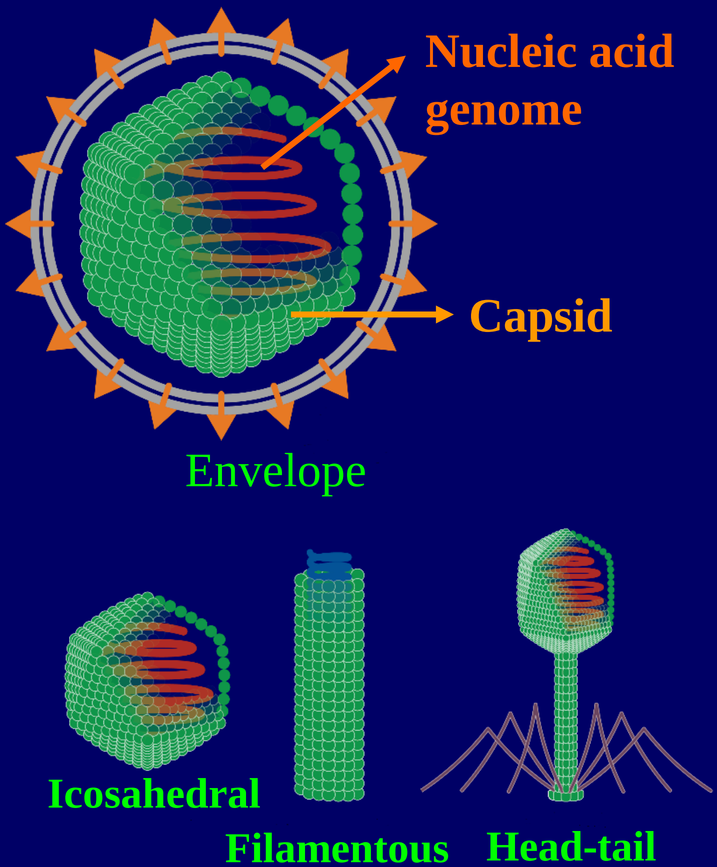
Viruses



- A virus is a tiny, infectious particle that can reproduce only by infecting a host cell.
- Viruses "commandeer" the host cell and use its resources to make more viruses, basically reprogramming it to become a virus factory. Because they can't reproduce by themselves (without a host).
- Viruses are not considered living. Nor do viruses have cells: they're very small, much smaller than the cells of living things, and are basically just packages of nucleic acid and protein.
- There are a lot of different viruses in the world. So, viruses vary a ton in their sizes, shapes, and life cycles.

❖ Viruses consist of the followings:

1. A protective protein shell, or capsid. The capsid, or protein shell, of a virus is made up of many protein molecules. The proteins join to make units called capsomers, which together make up the capsid. Capsid proteins are always encoded by the virus genome, meaning that it’s the virus (not the host cell) that provides instructions for making them.

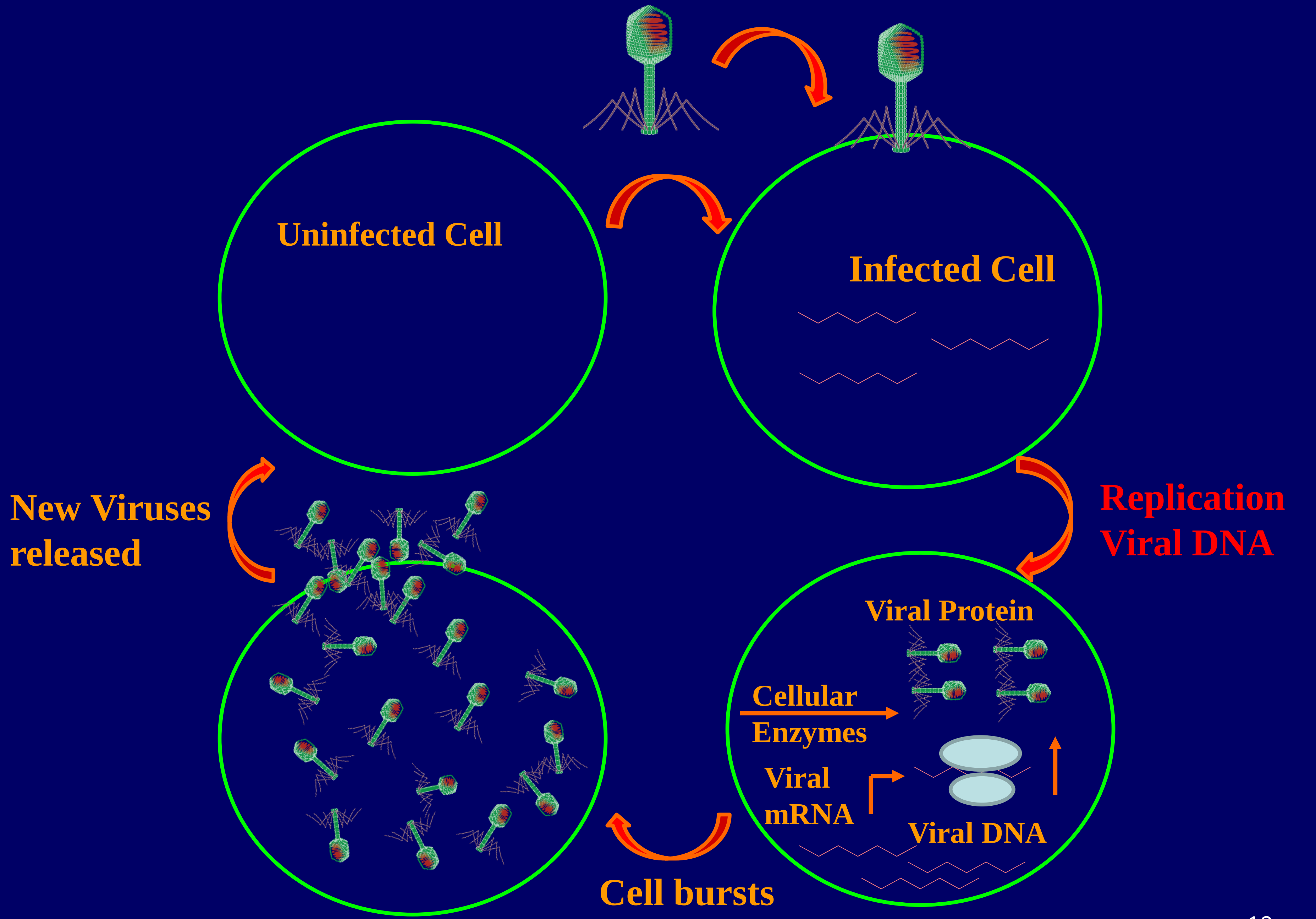


2. Some viruses also have an external lipid membrane known as an envelope, which surrounds the entire capsid. Envelopes contain proteins that are specified by the virus, which often help viral particles bind to host cells.
3. A nucleic acid genome made of DNA or RNA, tucked inside of the capsid. viruses can have all possible combos of strandedness and nucleic acid type (double-stranded DNA, double-stranded RNA, single-stranded DNA, or single-stranded RNA). Viral genomes are generally much smaller than the genomes of cellular organisms. DNA and RNA viruses always use the same genetic code as living

Viruses Life Cycle

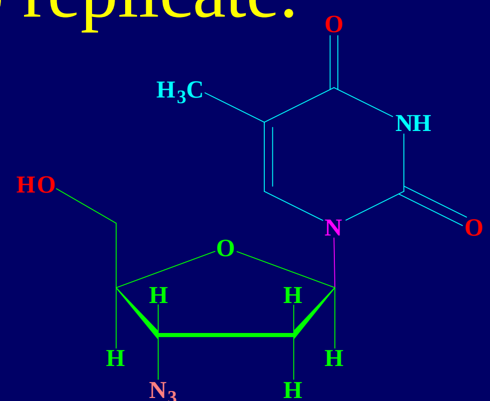
A general view of the life cycle of a virus. The life cycle can be explained in five steps:

1. Attachment of the virus to the host.
2. Penetration, where the genome (red) enters the host.
3. Biosynthesis of viral components, e.g. capsid proteins (green) and genome (red).
4. New virus particles are assembled.
5. The cell burst and releases the virus particles, which can infect other cells.

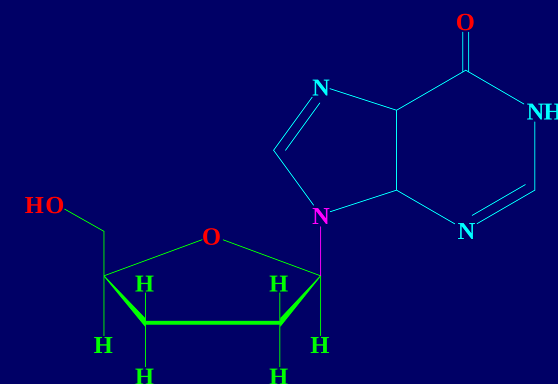

Uninfected Cell
Infected Cell
Replication
Viral DNA
Viral Protein
Cellular
Enzymes
Viral
mRNA
Viral DNA
Cell bursts
New Viruses
released

Prevents Reverse Biosynthesis Process

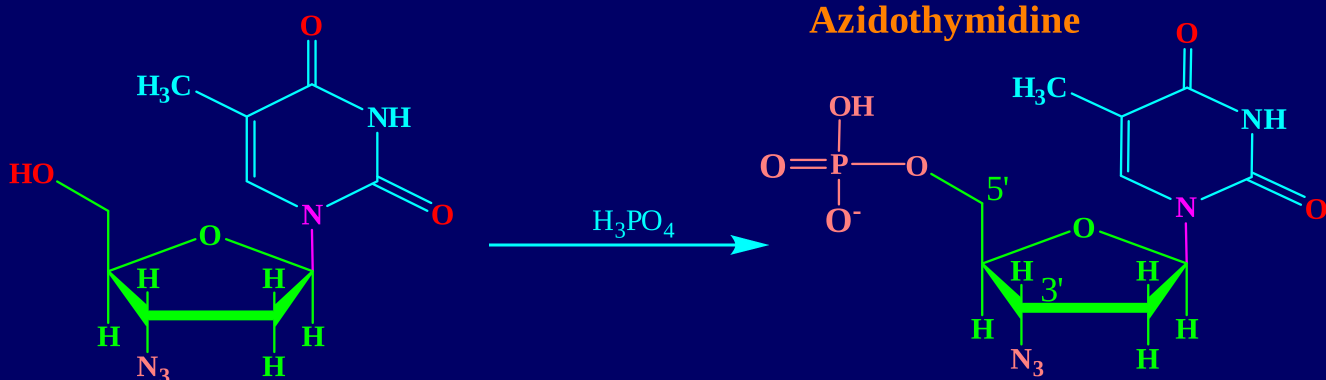
1. **By using chemicals :** one type of AIDS treatment prevents reverse transcription of the viral DNA. When altered nucleosides such as azidothymidine AZT and dideoxyyinosine ddI are incorporated into viral DNA, the virus is unable to replicate.

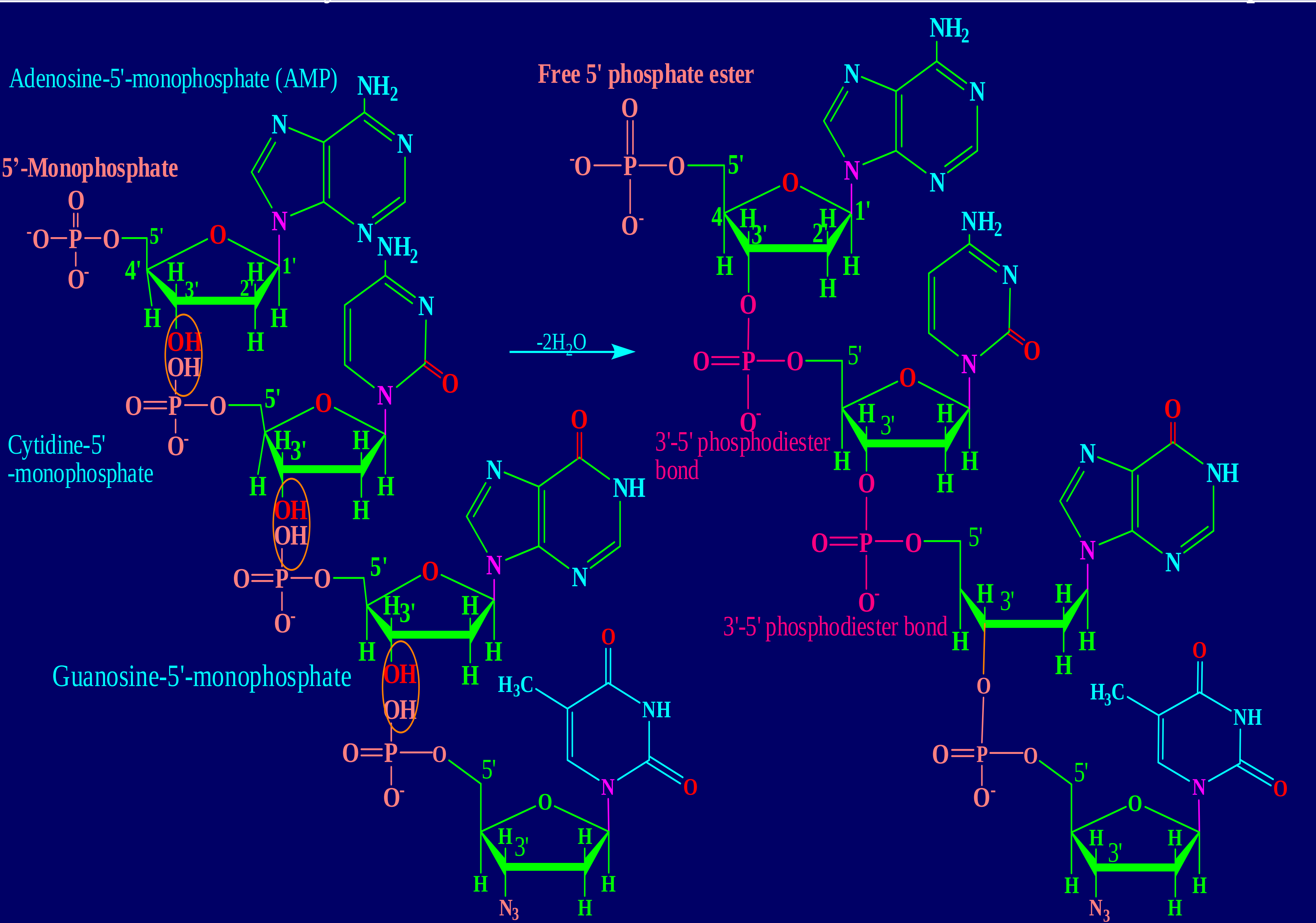


Azidothymidine



Dideoxyyinosine




Adenosine-5'-monophosphate (AMP)
5'-Monophosphate
Cytidine-5' -monophosphate
Guanosine-5'-monophosphate
-2H2O
Free 5' phosphate ester
3'-5' phosphodiester bond
3'-5' phosphodiester bond

2. By using enzymes inhibitors :

Protease is an enzyme in the body that's important for HIV replication.

A protease (also called a peptidase or proteinase) is an enzyme that catalyzes proteolysis, the breakdown of proteins into smaller polypeptides or single amino acids

Protease inhibitors are a class of antiviral drugs that are widely used to treat HIV/AIDS and hepatitis C. Protease inhibitors prevent viral replication by selectively binding to viral protease and blocking proteolytic cleavage of protein precursors that are necessary for the production of infectious viral protein.

Protease inhibitors that have been developed and are currently used in clinical practice include: saquinavir, indinavir, and ritonavir.

thank you!