

There are four phases of the human immune deficiency virus (HIV) life cycle. In binding and entry the virus binds to the CD4 receptor on CD4⁺ T-Cells via the viral glycoprotein, gp120. The binding results in the fusion of the viral and cellular membranes, followed by the entrance of the viral core in to the cell. After entry, synthesis and integration occur, during which viral RNA is transcribed in to double stranded DNA by reverse transcriptase. Viral DNA enters the nucleus and integrated in to the host genome. Following integration, expression of viral genes occurs. Finally, during assembly and release, viral structural proteins are synthesized and assemble into particles containing the viral enzymes and 2 copies of the viral RNA. The particles then bud from the cell. One of the most puzzling cytopathic effects of HIV is the depletion of T-cells, despite the fact that relatively few cells are actually infected. Four models that attempt to account for this effect are summarized below:

Hypothesis I: HIV particles that fail to integrate into the CD4⁺ T-cell genome produce a toxic factor that functionally impairs T-cells and eventually leads to cell death.

Hypothesis II: HIV integration promotes the synthesis of terminal maturation factors in CD4⁺ T-cells, increasing their susceptibility to the body's normal cell-destruction process.

Hypothesis III: Viral glycoproteins (gp 120 & gp 41) expressed on the surface of HIV infected T-cells fuse with CD4 receptors on healthy cells, forming a nonfunctional cell mass (syncytia formation).

Hypothesis IV: gp 120 molecules are released in to circulation by infected T-cells and bind to the CD4 receptors on healthy T-cells making the latter subject to an autoimmune attack by anti-gp 120 antibodies.

1. A researcher wanting to study the process by which viral mRNA is transcribed in an HIV infected CD4⁺ T-cell would add all of the following reagents to her cell culture EXCEPT:
 - a) Radiolabeled thymine
 - b) Radiolabeled guanine
 - c) Radiolabeled uracil
 - d) Radiolabeled adenine
2. If hypothesis I were true, which of the following pairs of processes would HIV have to undergo before a toxic factor could be produced.
 - a) Binding and entry; synthesis and integration
 - b) Reverse transcription and host cell death
 - c) Binding and entry
 - d) Reverse transcription, synthesis and integration
3. Which of the following supports hypothesis III.
 - a) Some CD4⁺ T-cell lines do not form syncytia, but are susceptible to the the cytopathic effect of HIV.
 - b) Syncytia formation is transient in some CD4⁺ T-cell lines.
 - c) Gp 120 and gp 41 bind almost irreversibly to CD4 receptor molecules in vitro.
 - d) Syncytia formation doesn't lead to cell death in some CD4⁺ T-cell lines.
4. If hypothesis III were true, which of the following cellular organelles would be responsible for directing the newly synthesized gp 120 & gp 41 molecules toward the plasma membrane on which they would eventually be expressed.
 - a) Centrioles
 - b) Golgi complex
 - c) Mitochondria
 - d) Lysosomes
5. HIV infection is detected by anti-HIV antibodies in the blood. This indicates that during infections:
 - a) helper T-cells are still able to activate cytotoxic T-cell proliferations.
 - b) B-lymphocytes are still able to produce antibodies in response to foreign antigens of HIV.
 - c) Anti-HIV antibodies are effective against the virus.
 - d) HIV has not infected host microphages.

Scientists have hypothesized that mitochondria evolved from aerobic heterotrophic bacteria that entered and established symbiotic relationships with primitive eukaryotic anaerobes. Many structural and functional similarities between mitochondria and present day bacteria support this hypothesis. They are approximately the same size, reproduce by similar means and contain non-histone-bound DNA. They contain the tRNAs, ribosomes, etc necessary for transcription and translation and they show some similarities in base sequences of rRNAs.

In addition, the inner membranes of mitochondria have enzymes and transport systems similar to those on the plasma membranes of bacteria. One similar system is the electron transport system. Electron transport in both mitochondria and bacteria is accomplished using three large protein complexes, each composed of multipolypeptides.

Hydrogen atoms and electrons donated from NADH are passed between components of the electron transport chain and eventually reduce oxygen to form water. This chain of events creates both a pH gradient and an electrical potential across the membrane. The protons are thought to move down the pH gradient, interacting with the enzyme ATP synthetase. This results in the production of ATP from ADP and phosphate.

6. According to the hypothesis discussed in the passage, the bacteria that entered the primitive eukaryotic cells were able to carry out which of the following functions that primitive eukaryotic cells could NOT.
 - a) Glycolysis
 - b) Krebs cycle and Electron transport
 - c) Cell division
 - d) Transcription and translation

7. According to the hypothesis in the passage, what is the most likely explanation for the origin(s) of the two mitochondria membranes.
 - a) Both inner and outer membranes were derived from folding of the prokaryotic plasma membrane.
 - b) Both inner and outer membranes were derived from invagination of the eukaryotic plasma membrane.
 - c) The inner membrane was derived from folding of the prokaryotic plasma membrane and the outer from invagination of the eukaryotic plasma membrane.
 - d) The inner membrane was derived from invagination of the eukaryotic plasma membrane and the outer from folding of the prokaryotic plasma membrane.

8. Which of the following pieces of evidence most strongly supports the hypothesis of mitochondrial origin described in the passage.
 - a) Mitochondria have fewer genes than typical bacterial cell have.
 - b) Mitochondria contain hundreds of different enzymes.
 - c) The diameter of mitochondria and typical present day bacteria are approximately equal.
 - d) Nitrogen fixing bacteria live symbiotically inside the cells of present day plants.

9. To support the symbiotic hypothesis presented in the passage, mitochondria should be similar to bacteria in which of the following ways.
 - a) They should use 80S ribosomes
 - b) They should be incapable of binary fission
 - c) They should have circular DNA
 - d) They should be capable of anaerobic respiration

The synthesis of proteins and nucleic acids is seen as being directed by a series of coded messages. The messages must be sent, received and decoded.

10. The primary source or repository of information concerning synthesis of nucleic acids and proteins is considered to be:
- Protein
 - DNA
 - RNA
 - Peptides
11. In the polymer that directs protein biosynthesis there is a requirement of _____ units (or monomers) to code for each amino acid.
- 1
 - 2
 - 3
 - 4
12. In a chromosome of higher animals there is (are) _____ strand(s) of DNA.
- 1
 - 2
 - 3
 - 4
13. If 100 somatic cells of higher animals are allowed to divide once in $^2\text{H}_2\text{O}$ (water containing only deuterium) _____ of the cells will have only DNA containing deuterium.
- none
 - $1/4$
 - $1/2$
 - all
14. The smallest unit possessing the capability to maintain life and to produce is
- an organ
 - a cell
 - DNA
 - RNA

Current theories of carcinogenesis are based on the concept of cellular and viral *oncogenes*. It is believed that the genome of any eukaryotic cell contains DNA segments, called proto-oncogenes, that normally code for cell growth-related proteins such as transcription factors, growth factor receptors, and tyrosine kinases (enzymes thought to regulate cell division). These cellular proto-oncogenes can be transformed into tumorigenic oncogenes (c-onc) by a number of mechanisms.

A common mechanism by which a cellular proto-oncogene is transformed into a c-onc is point mutation, which leads to formation of a defective protein. For example, one well-studied cellular proto-oncogene codes for the ras protein. Ras proteins have GTPase activity, and their activity is regulated by the presence of GTP or GDP. In the wild-type protein, growth factor receptors with tyrosine kinase activity stimulate ras to exchange GDP with GTP through an indirect process involving intermediate proteins. Ras then activates a cytosolic kinase (also an oncogene) c-raf. C-raf then activates MAP kinase-kinase, which in turn activates MAP-kinase. MAP-kinase appears capable of phosphorylating transcription factors in the nucleus. After the appropriate genes have been transcribed, ras GTPase activity hydrolyzes GTP converting ras to its inactive form. Mutant ras proteins are unable to hydrolyze GTP, and therefore remain in the active GTP-bound form.

Alternatively, a proto-oncogene may become an oncogene through a mutation that causes it to produce an excess of a normal protein. Such a mutation may place the gene under the control of a stronger promoter via either chromosomal translocation, or by the integration of a provirus with a strong promoter in the immediate proximity of the proto-oncogene. An excess of a normal protein may also be caused by gene amplification of the proto-oncogene.

Another mechanism of carcinogenesis that also depends on oncogenes is viral carcinogenesis, which is caused by transforming viruses. Transforming viruses, which occur widely in the avian and animal kingdoms, are retroviruses whose genomes contain oncogenes (called viral oncogenes, or v-onc) derived from their former eukaryotic hosts. Such viruses can later cause other host cells to become tumorigenic.

15. Which of the following activities would you expect to increase in a tumorigenic cell?

- I. mRNA synthesis
- II. Ribosomal assembly
- III. Cell division

- a) I only
- b) I and II only
- c) II and III only
- d) I, II and III

16. A c-onc activated by point mutation differs from the proto-oncogene from which it was derived by:

- a) a single base pair.
- b) two base pairs.
- c) a triplet insertion.
- d) a triplet insertion.

Passage IV *Continued*

17. Based on the information in the passage, cellular proto-oncogenes can become tumorigenic oncogenes by all of the following mechanisms EXCEPT:
- a) a mutation that results in the synthesis of a faulty protein.
 - b) a chromosomal translocation that produces an excess of a protein.
 - c) binding of complementary nucleic acid sequences to proto-oncogene transcripts.
 - d) a mutation that causes gene amplification of the proto-oncogene.
18. Comparison of a v-onc sequence with a corresponding c-onc sequence reveals that the organization of the viral gene corresponds to the mRNA of the c-onc gene, rather than to its own genomic organization. Which of the following best accounts for this observation?
- a) The v-onc gene contains only c-onc introns.
 - b) The v-onc gene has a greater level of expression than the corresponding c-onc gene.
 - c) The v-onc gene was captured from a host cell in the form of RNA during a retroviral infection.
 - d) Since retroviral DNA is incorporated into the cellular genome, the alternating exons and introns in the v-onc gene are spliced by cellular enzymes.
19. Which of the following processes function in an analogous way to ras activity?
- a) Formation of antibody-antigen complexes during an immune response.
 - b) Sodium-potassium pump in neurons.
 - c) Krebs cycle in mitochondria
 - d) Second messenger system involving cAMP.
20. The incorporation of a strong promoter near a proto-oncogene may lead to cancer because the stronger promoter most likely:
- a) increases the rate of translation.
 - b) increases the rate of transcription.
 - c) increases the rate of translocation.
 - d) increases the rate of point mutations.

Passage V: (AAMC. MCAT Practice Test III. 1991 pg. 67.)

According to the signal hypothesis, proteins destined for secretion are synthesized in the form of preproteins that consist of signal peptides (hydrophobic amino acids at the N-terminus) followed by the secretory proteins. The signal peptides and the secretory proteins are translated as a unit. Signal peptides function to help the secretory proteins cross the membrane of the endoplasmic reticulum (ER). Proteins that lack signal peptides cannot interact with the ER and thus remain inside the cell cytoplasm.

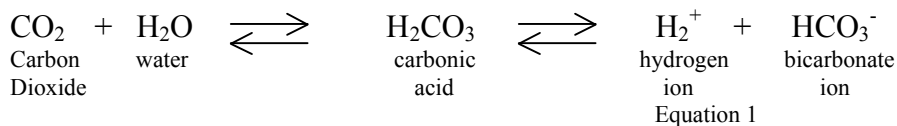
Before a preprotein is completely translated, the developing signal peptide forms an SRP complex by interacting with a signal recognition particle (SRP), which is composed of RNA and protein. Formation of this complex blocks the translation process until the SRP complex itself binds to an SRP receptor.

Once the SRP complex is bound to the SRP receptor, the signal peptide is able to interact with the ER. The developing preprotein penetrates the ER membrane, and ribosomes become anchored to the membrane to form rough ER. As translation proceeds, the preprotein elongates and extends into the cisterna of the ER, where the signal peptide is eventually cleaved enzymatically by a signal peptidase (present in the membrane or cisterna of the ER). The protein is then packaged for subsequent secretion.

21. If functional SRP for a given secretory protein was NOT available, which of the following processes could still be carried out by the cell?
- Translation of the preprotein
 - Formation of the SRP complex
 - Binding of the SRP complex to the SRP receptor
 - Cleaving of the signal peptide from the secretory protein
22. The SRP receptor is most likely located on the:
- signal peptide.
 - ribosome.
 - ER.
 - preprotein.
23. A cell has a point mutation in the gene coding for the SRP receptor, but the amount of protein secreted by the cell is the same as that of normal cells. This suggests that the point mutation:
- is not translated.
 - is repaired in the mRNA.
 - is cleaved by the peptidase.
 - does not affect the binding ability of the SRP receptor.
24. After the secretory proteins cross the ER, they will be processed further by the:
- Golgi apparatus.
 - Mitochondria.
 - lysosomes.
 - nucleus.
25. A secretory protein found in the blood has a molecular weight of 30,000 daltons, but when the same protein is translated from mRNA in a test tube, its MW is 32,000 daltons. This difference most likely results because the protein synthesized in the test tube:
- had random mutations during its synthesis.
 - still contained the signal peptide.
 - was not released from the ribosome/mRNA complex.
 - did not interact with ribosomes.

Passage VI: (AAMC. MCAT Practice Test III. 1991 pg. 55.)

Internal respiration is the exchange of O_2 and CO_2 between tissue cells and capillaries. As CO_2 is produced in the cells, it enters the capillaries, resulting in a blood partial pressure (P_{CO_2}) of approximately 45 mm Hg. In the capillaries, 70% of the CO_2 transported by the blood is converted to bicarbonate ions (HCO_3^-) by the following reaction that occurs within the red blood cells (RBCs).



Most of the bicarbonate ions leave the RBCs and enter the plasma. The resulting ionic imbalance in the RBCs is equalized by the rapid movement of chloride ions into the RBCs from the plasma.

Another 23% of the carbon dioxide is transported by the blood in the form of carbaminohemoglobin ($Hb \cdot CO_2$). Both carbon dioxide and hydrogen ion bind reversibly to the globin portion of the hemoglobin (Hb) molecules in the RBCs. The attachment of carbon dioxide to form $Hb \cdot CO_2$ also facilitates the dissociation of oxygen from Hb at low P_{O_2} levels in the tissue capillary beds. The final 7% of the carbon dioxide produced by respiring cells dissolves directly into the plasma.

All forms of carbon dioxide are transported from the tissue to the lungs, where they are returned to gaseous form and are exhaled during external respiration (the exchange of oxygen and carbon dioxide between the capillaries and the alveoli of the lungs).

26. Administration of a carbonic anhydrase inhibitor to the RBCs would most likely cause an increase in the concentration of:
- HCO_3^- in the RBCs.
 - H_2CO_3 in the RBCs.
 - Carbon dioxide in the tissues.
 - Water in the tissues.
27. Oxygen dissociates more readily from Hb in an acidic environment. This dissociation will therefore occur most readily when P_{CO_2} is:
- high, because Equation 1 will proceed to the right.
 - high because Equation 1 will proceed to the left.
 - low because Equation 1 will proceed to the right.
 - low, because Equation 1 will proceed to the left.
28. Lung capillaries are so narrow that RBCs must pass through them in a single file. This feature aids respiration by:
- increasing the production of carbon dioxide in the RBCs.
 - Allowing RBCs to have direct contact with alveoli.
 - Giving maximum exposure of each RBC to diffusing gases.
 - Making Hb available for carbon dioxide but not oxygen to bind.
29. The transport of carbon dioxide across biological membranes during cellular respiration is best accounted for by which of the following processes?
- osmosis
 - simple diffusion
 - facilitated diffusion
 - active transport

Bacteriophage (phage) lambda is a double-stranded DNA virus that infects the bacterium *Escherichia coli*. Lambda can reproduce either lytically (by intracellular reproduction with the release of its progeny by cell lysis) or lysogenically (by integration of its chromosome into the *E. coli* chromosome).

Just before divergence of the 2 growth pathways (Figure 1), phage and host proteins produce several copies of the phage chromosome, and 1 set of phage genes (called early genes) is expressed.

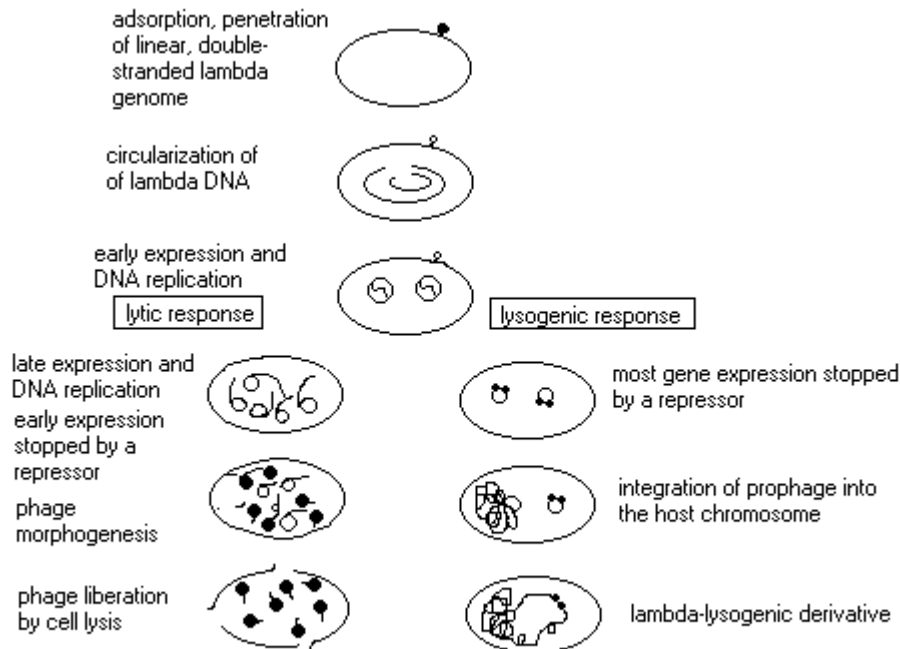


Figure 1

During lytic growth, expression of early genes is repressed by the binding of a phage-encoded protein to the phage DNA. The late genes are then expressed and begin to generate head and tail proteins. Multiple copies of the phage chromosome are made, the components form into complete phage progeny, and finally, phage-encoded proteins cause lysis of *E. coli*.

The lysogenic pathway begins with integration of the phage genome into the bacterial chromosome to form a prophage. Synthesis of most phage gene products is then stopped by the binding of a phage-encoded repressor protein to the phage DNA. The prophage remains dormant within the bacterium (now called a lysogen) until some event causes the repressor protein to be split off by a specific bacterial enzyme.

Excision, the process by which the phage chromosome leaves the bacterial chromosome, requires removal of the repressor and separation of the 2 DNA molecules by the bacteria and phage-encoded enzymes.

30. If *E. coli* cells are treated immediately prior to phage infection with an antibiotic that blocks initiation of protein synthesis, all of the following processes will be affected EXCEPT:
- Adsorption.
 - cell lysis.
 - integration.
 - replication of the phage chromosome.

Passage VII *Continued*

31. Lambda preferentially attaches to a specific region of the E. coli chromosome. If an E.coli lacks this site, which of the following processes is likely to be greatly decreased?
- a) Rate of DNA injection into E. coli.
 - b) Energy requirement for DNA injection into E. coli.
 - c) Frequency of integration of lambda into E. coli.
 - d) Number of phage progeny released from E. coli.
32. The presence in E. coli of a highly active exonuclease (an enzyme that removes nucleotides from the ends of nucleic acids) would directly block phage growth at which step in the infection process?
- a) Adsorption of the phage.
 - b) Circularization of the phage genome.
 - c) Expression of the early genes.
 - d) Replication of the phage DNA.
33. Which of the following mutations would most likely decrease the frequency of excision without blocking it completely?
- a) Deletion of phage genes encoding tail proteins.
 - b) Deletion of phage genes encoding excision proteins.
 - c) A mutation that causes the repressor to bind more tightly to DNA.
 - d) A mutation that increases the activity of the bacterial enzyme that attacks the repressor.
34. One phage-encoded enzyme that must be activated late in the lytic cycle but repressed in the lysogenic cycle is the enzyme that causes:
- a) integration of the phage DNA in to the bacterial chromosome.
 - b) splitting of the repressor from the phage DNA.
 - c) breakdown of the bacterial chromosome.
 - d) breakdown of the bacterial cell wall.

*The remaining questions on the exam do not pertain to the previous passage.
They stand alone.*

35. Marine and freshwater fish have different problems in maintaining their internal salt balances. Osmosis causes freshwater fish to gain water and marine fish to lose water. Based on this information which of the following must be true.
- a) Marine fish live in an environment hypertonic to their body fluids.
 - b) Marine fish live in an environment hypotonic to their body fluids.
 - c) Freshwater fish live in an environment hypertonic to their body fluids.
 - d) Freshwater fish live in an environment isotonic to their body fluids.

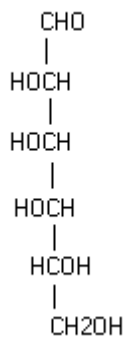
36. Which of the following observations would support the hypothesis that the movement of certain solutes into a cell is mediated by carrier proteins in the plasma membrane.

- a) The rate of solute influx increases proportionately with extracellular solute concentration.
- b) The rate of solute influx reaches a plateau, despite an increasing extracellular solute concentration.
- c) A cell bathed in an isotonic NaCl solution does not have a net uptake of Na^+ .
- d) A hypotonic cell bathed in a sugar solution takes up solutes.

37. The antibiotic penicillin has the effect of inhibiting the production of the chemical peptidoglycan. Therefore, penicillin is likely to be most effective in treating infections by:

- a) viruses
- b) bacteria
- c) fungi
- d) protozoa

38. The generic name for the carbohydrate below is:



- a) D-aldopentose
- b) D-ketohexose
- c) D-aldohexose
- d) L-ketohexose

39. The process by which a cell can move a substance from a point of lower concentration to a point of higher concentration (against the diffusion gradient) is called:

- a) osmosis
- b) plasmolysis
- c) turgor pressure
- d) active transport

40. The plasma membrane of animal cells:

- a) is usually rigid
- b) has selective channels made of protein
- c) is too thin to be seen by the use of any microscope
- d) is composed of only proteins and carbohydrates