Genetics of Viruses

1. [HCI Prelim 2010 H2 P2] Discuss whether viruses are living or non-living organisms and why viruses are obligate parasites. [9]

Viruses are considered as living organisms because

A1 They possess genetic material either in the form of DNA or RNA;
A2 They carry all the genes necessary to instruct the host cell to synthesise new viruses;
A3 E.g. Genes for synthesizing viral capsid OR Genes for regulating the actions of the host and for packaging the mature virus; (Any 1)
A4 They are able to reproduce within the host cell;
A5 They are capable of multiplying with same type of genetic material;
A6 They can react to environmental stimuli such as radiation, chemicals and heat;

Viruses are considered as non-living organisms because

B1 they are infectious particles that can be inactive OR are able to exist in a metabolically inert extracellular state for extended periods of time;
B2 They do not reproduce independently of the host cell;
B3 They do not have a method to obtain nutrition for growth;
B4 Cell wall and cell membranes/organelles are absent;
B5 Protoplasm is also absent;
B6 Where it does not carry out respiratory activities /unable to synthesise ATP/lack cell metabolism;
B7 They cannot synthesize proteins for survival/no ribosomes for translation or protein synthesis;

Hence, they are considered intracellular obligate parasites because

C1 they can only survive and reproduce in the host cell;
C2 using host cell machinery;
C3 at the expense of the host's life-sustaining functions;
C4 Isolated viruses are merely packaged sets of genes in transit from one host cell to another;
C5 They lack RNA polymerase and are unable to perform transcription;
C6 They cannot synthesise proteins because they lack ribosomes and must use the ribosomes of their host cells;
C7 to translate viral messenger RNA into viral proteins;
C8 Viruses cannot generate or store energy in the form of ATP;
C9 But need to derive their energy for all metabolic functions from the host cell;
C10 They also need to parasitize the host cell for basic building materials such as amino acids, nucleotides and lipids (fats); (Any 1 e.g. of basic building materials)

(HALF-MARK SYSTEM)

[Tutorial N2013/P2/Q10b] Explain why viruses may be regarded as non-living organisms. [7]

1. They do not show most of characteristics of living cells on their own, which include
2. They do not have cellular organization;
3. They are unable to acquire and use energy in order to maintain metabolic processes for survival on their own;
4. They do not grow and develop;
5. They are unable to reproduce on their own;
6. And therefore are unable to adapt to the environment without help of a host cell;
7. They do not have specialized receptors that detect environmental stimuli to allow their cells to adjust metabolism in response;
8. They are thus obligate parasites which may be regarded as non-living;

[SAJC 2010] Describe the general structure of a named animal virus, and explain why viruses are obligate parasites. [6]

1 example of animal viruses: influzena, HIV, herpes virus etc
2 animal viruses composed of phospholipids/glycoprotein envelope
3 similar in nature to cell surface membrane of animal cell
4 with glycoprotein spikes (for attachment to host cell membrane)
5 enclosed in the viral envelope is the capsid
6 which is composed of capsomeres / protein subunits
7 which contains the viral genome
8 either DNA or RNA, but never both
9 either single or segmented, linear or circular, single-stranded or double-stranded, etc
10 ref. viral enzymes (eg. reverse transcriptase in HIV)

11 acellular / absence of cytoplasm and cellular organelles
12 lacks ribosomes / protein-synthesising apparatus
13 hijacks host cell's host's protein synthesis machinery (transcription and translation machineries) to produce own viral proteins [REJECT 'metabolic machinery']
14 ref. replication of viral genome
15 metabolically inert / do not grow or divide on their own
16 can only multiply inside living cells, and not on inanimate media

2. Describe the role of the structural components of viruses. [5]

[NYJC 2010] Describe the structural components of viruses. [6]

1. Genome consists of DNA or RNA / linear or circular molecule of nucleic acid / single-stranded or double-stranded / one or more than one copy of the genome;

2. Capsid is a sheath / coat built from protein subunits / capsomeres, enclosing viral genome;

3. Capsids serve to protect viral genome / Has tail shaft with fibres attached to capsid that phages use to attach to bacterial cell wall;

4. Envelopes comprise of phospholipids derived from cell surface membrane of host cell;

5. Envelope surrounds capsid and embedded with glycoproteins;

6. Envelope protects virion from enzymes and other chemicals (optional: giving them advantage over capsid-only virions);

[Tutorial N2013/P2/Q10c] Outline the structure and function of viral nucleic acid. [7]

1. Viral nucleic acid can be in the form of DNA (bacteriophages) or RNA (influenza/HIV);
2. Either single-stranded (influenza/HIV) or double-stranded (bacteriophages);
3. If single-stranded RNA, can be positive sense, whereby sequence is the same as mRNA (HIV) or negative sense, whereby sequence is complementary to mRNA (influenza);
4. There can be one copy of the genome (influenza) or more (2 in HIV);
5. Genetic information can be contained in a single molecule (HIV) or segmented into more than one molecule (7 segments in influenza);
6. Codes for synthesis of viral components (capsid proteins, glycoproteins, enzymes) for assembly and synthesis of offspring;

3. Describe the reproductive cycle of T4 phage. [5]

[HCI 2010] Describe the lytic cycle of a bacteriophage. [7]

D1 During adsorption;
D2 Tail fibres bind to complementary receptors on the cell surface;
D3 Penetration takes place;

D4 The sheath of the tail contracts;
D5 thrusting a hollow core through the membrane of the cell;
D6 Phage DNA is then injected into the cytoplasm;
D7 The capsid is typically left behind;
D8 The viral DNA interacts with the host's machinery for transcribing mRNA/host cell RNA polymerase;
D9 And the viral mRNA is translated into viral proteins;
D10 by the host cell ribosomes;
D11 tRNA and translation factors;
D12 Expression of the phage's genetic information gives rise to proteins to seal the cell;
D13 Proteins that make up the capsid head and parts of the phage;
D14 Viral DNA can also undergo replication to produce daughter DNA molecules, which are used for the synthesis of new virus particles;
D15 using host cell DNA polymerase;
D16 Host cell DNA is degraded;
D17 The capsid proteins, sheath proteins and tail fibres assemble to form phage heads, tails and tail fibres/ new phages;
D18 Following which enzymes such as lysozyme;
D19 digest the bacterial cell wall;
D20 Osmosis will cause the cell to swell and burst;
D21 releasing phage by lysis;
D22 Each of these phages can infect a new prokaryotic cell;
(half-mark system)

[RI 2010] Relate the structure of the T4 bacteriophage to its function. [7]

Structure	Function
1. Icosahedral head/capsid composed of many copies of one or more different proteins	**Encapsulates the viral genome and acts as a protective covering.**
2. Viral genome composed of ds DNA	**Contains the genetic information necessary for the viral replication, assembly and its subsequent release.**
3. Tail fibres containing attachment sites (proteinaceous)	**Recognise and bind to complementary receptors on the host cell via weak bonds formed between attachment sites and receptors** **4. Attachment between receptor and attachment sites is specific → specific strains attach to specific hosts → confers viral specificity**
5. Tail pins (protein)	**Anchor the bacteriophage firmly onto the surface of the host cell.**
6. Base plate	**Interact with signals released from the host cell. Changes its shape to initiate the release of viral genome into the host cell.**
7. Contractile sheath (tail sheath) made up of protein subunits	**Rearrangement of protein subunits results in the spring-like contraction of the sheath, providing the driving force for the hollow core to move through the**

	host cell wall.
8. Hollow core – cylindrical and rigid	**Punctures a hole in the host cell wall** **9. Injects viral DNA into the host cell.** **10. Protects the viral DNA as it passes through the host cell wall.**

4. Describe the reproductive cycle of lambda phage. [5]
5. [Tutorial IJC/2/8c] Some bacteriophages undergo both lysogenic and lytic cycles. Suggest reasons why it may be advantageous for a bacteriophage to have a lysogenic cycle. [4]

1. Under unfavourable conditions (e.g. lack of nutrients), phage can remain dormant in host cell;
2. Phage genome is replicated each time the host cell replicates and bacteria is not killed;
3. allowing a large number of virions to be produced when induced to transit to lytic cell;
4. Survival of bacteriophages is ensured since host cell survives;
5. Bacteriophages are able to survive even in the presence of effective anti-viral drugs;

6. Describe the reproductive cycle of influenza virus. [6]
7. [VJC 2013] Discuss the importance of membranes in the reproductive cycle of the influenza virus. [6]

- Envelope/ cell membrane of viruses contains **hemagglutinin** (HA/H); which mediates the binding of the virus to **specific receptor sites containing sialic acid sugars** on the **cell surface membrane of epithelial cells;;** (especially in the nose, throat and lungs of mammals and intestines of birds);
- *Importance*: allows the virus to recognize and attach to specific host cells;
- The virus **enters by endocytosis** as the host cell membrane invaginates, forming a endocytic vesicle / endosome;
- *Importance of membrane*: fluid nature of the membrane allows formation of vesicles;
- Within the endosome, the acidic pH causes the hemagglutinin protein to undergo a conformational change;
- *Importance of membrane*: allow the setting up of an acidic medium within the endosome (with the help of proton pumps on endosome membrane);
- Resulting in the **fusion of the viral envelope with the endosome membrane**;
- releasing the **nucleocapsid** into the cytoplasm;

- (During synthesis of the new viruses) **glycoproteins(HA and NA)** are first synthesized in the **rER;** and then chemically modified in the **Golgi apparatus** (both are single membrane bound organelles in the host cells)**;;**
- The **glycoproteins** are then **transported to the cell membrane** via (secretory) **vesicles (pinched off the Golgi apparatus)**;
- These vesicles then fuse with the host cell membrane, thereby **incorporating/embedding the glycoproteins** into the (host) **cell surface membrane;**

- These sites then serve as **exit point for viral release**;

- New viruses leave the host cells through **budding**; thereby acquiring the host cell membrane (=envelope);
- **Neuraminidase** (NA/N), present on cell membrane helps in the release of new viruses by infected cells by cleaving off the sialic acids present on the host cells;;

8. [NYJC 2010] Suggest why the influenza virus displays high genetic diversity. [4]

Antigenic shift

1. antigenic shift / reassortment of RNA segments;;
2. occurs when different viral strains/subtypes infect the same cell;; REJCT different viruses
3. leads to viruses with new combinations of haemagglutinin and neuraminidase genes (genetic recombination);;
4. Production of new haemagglutinin / neuraminidase antigens on viral envelope;;

Antigenic drift

5. Spontaneous mutation occurring in the RNA genome;
6. Resulting in change in the specific three-dimensional conformation of viral proteins / glycoproteins;

Reject focus on different no of HA and NA antigens

[SAJC 2010] Outline how the influenza virus is able to bypass the human defense mechanism to cause disease. [4]

1 ref. antigenic drift
2 8 single-stranded RNA segments
3 spontaneous genetic mutation /mutation during replication
4 lack of proof-reading during RNA replication

5 ref. antigenic shift
6 genetic reassortment of the RNA segments between two strains of viruses
7 novel glycoproteins (spikes) produced on viral envelope /modified neuraminidase and haemaglutinin
8 cannot be recognized by previous antibodies

9. Describe the reproductive cycle of HIV. [6]

Stages of Reproductive Cycle of HIV:

- Attachment: Virus gp120 envelope protein binds to the CD4 glycoprotein plasma membrane receptor of host cell [T cells].

- Penetration: Viral envelope fuses with the plasma membrane and the virus releases its capsid into the cytoplasm.

- Uncoating: The capsid is degraded releasing integrase, protease and reverse transcriptase and RNA into the cytoplasm.

- Reverse transcription of the RNA genomes into a single-stranded DNA via reverse transcriptase and a complementary DNA strand is then synthesized to form a linear double-stranded DNA copy of the original RNA genome.

- A complex of double-stranded DNA and the integrase enzyme moves into the nucleus. The viral DNA is integrated into the cell's DNA through reactions catalyzed by integrase forming a provirus. The provirus can remain latent for many years and activate due to extracellular stimuli which forces the infected cell to produce more virions as outlined in the following steps.

- Transcription of the viral DNA, leading to the formation of viral mRNA and progeny viral RNA. Viral mRNA translated to form viral proteins such as envelope glycoproteins.

- Envelope glycoproteins are transported by vesicles to the cell membrane.

- Maturation: Capsid forms around the viral RNA and proteins. Nucleocapsid assembles at the cell membrane. HIV protease completes the maturation of the viruses by cutting viral polyproteins to form the structural and enzymatic proteins of the infective virus.

- Release: Host cell surface membrane surrounds the viral RNA and proteins. Budding of enveloped virions at the cytoplasmic membrane leading to release from cell. Reject: exocytosis of virions.

Pls also refer to NYJC 's comparison table on virus.

[HCI 2011] Explain how the structure of the Human Immunodeficiency Virus (HIV) is related to their functions in the viral reproductive cycle. [6]

- Glycoproteins binding to specific receptors CD4/ CXCR-4/ CCR-5
- during adsorption
- Enabling HIV to gain entry into the T-helper cell
- Viral genome consisting of two single stranded RNA molecules;
- The RNA is the viral genome that is used for template for new viral genomes
- Reverse transcriptase reverse transcribes viral RNA into a complementary DNA strand
- Integrase catalyses the integration of viral DNA into the host genome in the nucleus
- Protease cleaves the long chains of HIV proteins into smaller functional proteins

10. [TPJC 2013] Compare the mode of infection of Influenza Virus and Human Immunodeficiency Virus. [6]

3 Differences	**Influenza Virus**	**HIV**
Adsorption	With the use of HA	With the use of GP 120
Penetration	By Receptor mediated endocytosis	Fusion of Viral envelope with host cell membrane
Reverse transcription	No reverse transcription of Viral RNA genome	Reverse transcription of viral RNA genome to for Viral DNA
Integration	No integration of Viral genome into host cell genome	Integration of Viral DNA to host cell genome by integrase
Similarities (3 Similarities)		
• Nucleocapsid are both removed enzymatically		

- Both viruses involve embedding viral glycoproteins on the host cell membrane for the formation of viral envelope
- Host cell ribosomes are used for the translation of viral polypeptide for the formation of viral particles.

Pls also refer to NYJC 's comparison table on virus.

11. [NYJC 2010] Distinguish between the reproductive cycles of lambda phage and HIV. [5]

Feature	**Lambda phage**	**HIV**
Host cells	Bacteria/ *Escherichia coli*	T helper cells of immune system
Attachment / Adsorption;	**Tail fibres** recognise and bind to specific receptor sites on **outer surface of bacteria cell/** *Escherichia coli*	Glycoproteins **gp120** on viral envelope recognize / bind to specific receptor molecules ($CD4^+$)on cell surface membrane of T cell;
Entry / Penetration	Phage makes use of **specific pores** in the cell surface of E. coli to inject phage DNA into cell (and leaving empty capsid outside)	Viral envelope **fuses** with cell surface membrane, capsid degraded by host cell's enzymes;
Integration	Integrase is expressed soon after entry and inserts phage DNA into host cell's DNA, as a prophage	Viral RNA is reversed transcribed from a double-stranded DNA by reverse transcriptase. Integration of viral DNA, as a provirus, into host cell's DNA by integrase;
Synthesis of viral components	(prophage is excised when phage is induced to transit from lysogenic to lytic reproductive cycle) Phage DNA directs: - Synthesis of phage proteins - Replication of phage DNA in cytoplasm	Proviral genes are transcribed into RNA in nucleus RNA functions as: -Viral genomes -mRNAs which is translated into capsid proteins, viral proteins and glycoproteins in cytoplasm;
Viral Assembly/ Maturation	Phage DNA packaged inside the capsid	Capsid proteins enclose viral genome and viral proteins and assemble with glycoproteins during budding
Release	During lytic cycle, phage directs production of lysozyme that damages bacterial cell wall, allowing fluid to enter, which causes cell to swell and lyse	Each new virus buds from cell, surrounded by host cell surface membrane studded with viral glycoproteins;
Fate of host cell	Lysogenic cycle allows for replication of phage genome without destroying host	Provirus never leaves the host's genome, remaining permanently in the host cell, gradually killing host;

Uncoating	No uncoating required as capsid does not enter host cell (only dsDNA injected into host cell)	Uncoating of nucleocapsid to release genome and enzymes;

[SAJC 2010] Compare and contrast the reproductive cycles of the Lambda phage and the Human Immunodeficiency Virus (HIV). [10]

[1 mark per similarity] (max 4)

1 Life cycle of both viruses involves the stages attachment, penetration, replication, maturation, and release
2 Both attach to their host cell at receptor sites on the host cell's plasma membrane;
3 Both introduce their viral nucleic acids into their host cell
4 Both are obligate intracellular parasites/make use of their host cell's resources for synthesis of viral proteins and nucleic acids
5 Both integrate their viral DNA into host genome/viral DNA replicates as part of host's DNA every time the cell divides

[1 mark per difference] (max 6)

Feature of comparison	Lambda phage	HIV
Host cell	6 Infects bacterial cells	Infects human T-cells
Penetration / Entry	7 Phage does not undergo fusion with host cell's plasma membrane / contracts its tail sheath;	HIV envelope fuses with the host cell's plasma membrane;
	8 Phage injects only its ds DNA;	HIV releases its nucleocapsid (ssRNA and reverse transcriptase) into cytoplasm;
Uncoating	9 No uncoating required as capsid does not enter host cell;	Uncoating of nucleocapsid to release genome and enzymes;
Fate of viral nucleic acids	10 No reverse transcription / ds DNA is either immediately used as template for synthesis of viral proteins and nucleic acids (lytic cycle) or integrated into bacterial chromosome;	Its ssRNA is converted to dsDNA, using reverse transcriptase;
	11 Can enter lytic phase or lysogenic phrase (prophage);	Viral genome incorporated into host cell chromosomes (provirus);
	12 Prophage is excised from host cell's chromosome upon spontaneous induction;	Provirus is not excised as viral mRNA is transcribed from viral DNA together with host cell's genes;
Integration of viral glycoproteins into cell membrane	13 No integration of viral glycoproteins into host's cell membrane;	Integration of viral glycoproteins (gp120 and gp41) into host's cell membrane;
Release / Exit	14 Host cell is lysed to release the new viruses;	The new viruses bud off from host cell's plasma membrane;

Please study the following comparison table given to you earlier:

Compare the structure and reproduction cycles of T4 phage, Lambda phage, HIV and influenza. Use the following as features for comparison.

a) Genome
b) Capsid
c) Envelope
d) Host Cells
e) Attachment/adsorption
f) Entry/penetration
g) Integration
h) Synthesis of viral components
i) Viral assembly and maturation
j) Release

12. Describe how viral infections cause disease in animals, e.g. mammals (*Hint: relate HIV to T helper cells and influenza to epithelial cells*). [12]

[NYJC 2010] Explain how HIV infection causes disease in humans. [9]

1. HIV recognizes CD4 on T helper cells and infects them;
2. HIV causes **gp120 fragments** to be exhibited on the cell surface membrane of infected **helper T-cells** causing these helper T-cells to become targets for destruction by killer T-cells;
3. The loss of helper T-cells caused the immune system to fail and thus unable to mount a response against foreign particles;
4. Such that individual is susceptible to opportunistic infections;
5. AIDS (acquired immunodeficiency syndrome) results when infections become unmanageable;
6. Cancer may result if HIV integrates into middle of tumour suppressor gene to switch it off; / Cancer may result if HIV integrates into host cell genome disrupting the expression of TSGs and proto-oncogenes resulting in LOF and GF mutation respectively
7. **Inhibition of host cell's gene** / **inhibition of normal DNA, RNA or protein synthesis** result in altered cell functions;
8. **Depletion of host cell's cellular materials** essential for normal functioning of cell;

Rej HIV viral genome may be expressed in the host to produce toxins, disrupting the homeostatic mechanism in the host organism

Rej HIV triggers the release of hydrolytic enzymes in host cells, resulting in lysis of host cells.

Rej if only mention gof mutation of proto oncogene to oncogene induced by HIV, leads to increased amount of proto oncogene protein product. And lof mutation of tsg. Mention point 6.

OR

1. HIV causes Acquired Immune Deficiency Syndrome (AIDS);
2. Window period is the incubation period of HIV shortly after exposure to virus;
3. HIV replicates in blood cells of infected individual but infected person exhibits no detectable physiological response;
4. Acute primary infection phase takes place and patients can experience flu-like symptoms;
5. Caused by large numbers of free HIV particles and decreasing number of CD4 cells;

6. Number of HIV particles in blood declines and virus becomes localized in lymphatic system;
7. Asymptomatic phase occurs when infected person has gradual decline in number of helper T-cells;
8. gp120 exhibited on surface of helper T-cells, causing them to be destroyed by killer T-cells;
9. Immune system is still capable of managing the free viruses and infected cells;
10. Symptomatic phase occurs when population of helper T-cells diminishes;
11. Immune system subsequently wears down / fails to defend against pathogens and direct attack by virus on host's cells;
12. AIDS occurs when entire immune system fails and opportunistic infections occur, resulting in death;

[N2013/P2/Q7a] Describe how infection by HIV causes disease. [7]

[HCI 2011] Suggest how viruses can cause diseases other than cancer. [4]

- Influenza viruses infect cells of the respiratory tract;
- result in production of toxins
- and death of epithelial cells in the respiratory tract
- Human immunodeficiency virus (HIV) results in draining of host cell resources during its replication
- eventually killing of T-helper cells
- cause the person to enter an immunodeficient state