VICTORIA JUNIOR COLLEGE
BIOLOGY DEPARTMENT
JC2 PRELIMINARY EXAMINATIONS 2017
HIGHER 2 9744/3 Answers

Note: A: Accept; R: Reject

1 Huntington's disease (HD) is a rare neurodegenerative disease. Fig. 1.1 shows a pedigree of HD across three generations (**I** to **III**).

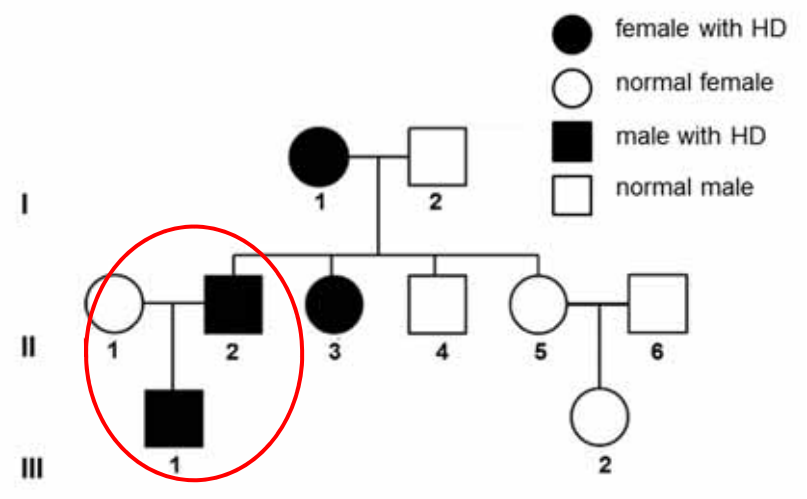

Fig. 1.1

(a) With reference to Fig. 1.1, account for the mode of inheritance of the disease. [3]

- HD is inherited in an **dominant** manner;
- every generation has affected offspring as long as one parent is affected (**I**1);;
- a single defective allele is sufficient for trait;

- Inherited in an **autosomal** manner;
- male and female offspring are similarly affected;
- an affected male parent (**II**2) can produce an affected son (**III**1);;

(b) (i) Explain the likely effect of the abnormal increase in CAG repeats on HTT protein structure and function. [3]

- Production of an abnormally **long polypeptide** / longer than the normal polypeptide (R! premature termination since length of CAG repeats is associated with disease); /
- Alters **primary structure** of polypeptide;
- disrupts the **R group interactions** such as hydrogen bonding, ionic, hydrophobic interactions and disulfide bridges;;
- essential for correct/ extensive folding into tertiary structure with specific 3D shape;;/ idea of 3D shape/conformation or tertiary structure is affected;;
- normal function of protein is lost/ abnormal protein is made; *Max 3m*

(ii) Suggest possible reasons why individuals having number of repeats ranging from 21-39 do not develop the disease. [2]

- Insertion mutation of multiples of 3 that code for chain of 20 glutamines (A! less than 40 glutamines) do not drastically affect 3D shape/ structure and thus function of the protein;;
- Slight effect on protein function but not drastic enough to develop disease;;
- A chain of more than 40 glutamines affect interactions between R groups that lead to folding into specific tertiary structure of the protein to affect normal function and cause HD;;

(c) **(i)** Explain why PCR can be used for the diagnosis of HD. [2]

- PCR makes use of specific primers that flank the region of the HTT gene/ exon 1 that contains the CAG repeats;;
- to **amplify** the **different fragment lengths** to allow for differentiating between normal and mutant allele;;

(ii) Explain how gel electrophoresis was used to detect the band patterns of the offspring in Fig.1.1. [4]

- During electrophoresis, negatively charged DNA fragments migrate through a gel towards the positive electrode;;
- under an electric field;
- agarose gel acts as a molecular sieve;
- Larger fragments (i.e. has more CAG triplets) move slower compared to shorter fragments;;
- Gel is stained with methylene blue and observed under white light;; / ethidium bromide and observed under uv light;;

(d) Based on this information, draw in the band patterns (in Fig. 1.2) for individuals #6, #10 and #11. [2]

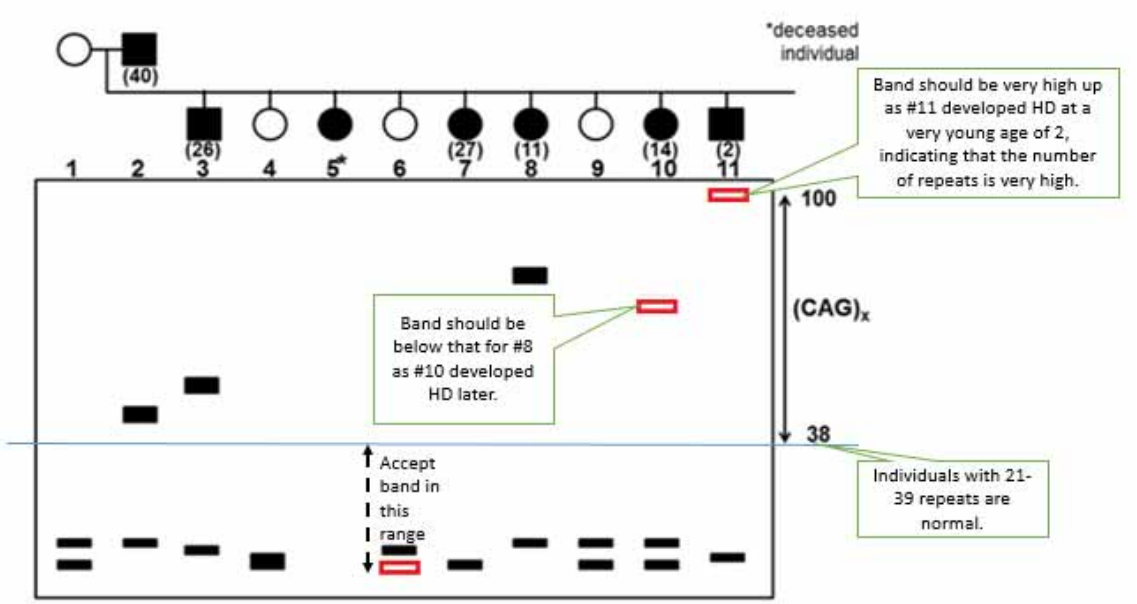

Fig. 1.2

(e) Individuals with 6-35 CAG repeats will be unaffected. Offspring of individuals with 36-39 repeats are at increased risk for HD.
Suggest how this increased risk can occur. [2]

- As the altered HTT gene is passed from one generation to the next, the size of the CAG trinucleotide repeat may increase in size due to **errors in DNA replication** of CAG repeat region **during formation of gametes**;;
- Since trait is dominant, they are at risk of having children who will develop HD when affected gamete with >40 repeats fuses with a healthy gamete;;

2 **(a)** Explain how the loss of control in the cell cycle can lead to cancer. [3]

- Loss of control means that the checkpoints regulating the stop and go signal of the cell cycle is lost;
- **Failure to halt cell cycle** /Cells continue to divide even if they have not properly completed the previous stage;

- **Even when** DNA is mutated (R: cells are damaged);
- Leads to an **accumulation of mutations**;
- Which includes **loss of function mutation** in **several TS genes**;;
- And **gain of function mutation** in *at least* **one proto-oncogene**;;
- causing cell to undergo uncontrolled cell division;
- cells cannot repair DNA damage; they evade apoptosis; grow in the absence of growth factor; loss of contact inhibition etc etc
- Ref to cancer development being a **multistep process**; [max 3m]

(b) Outline how such a mechanism is activated to be effective in its function. [4]

1) (cancer-derived) **peptides** presented **via MHC1** on surface of cancerous cells;
2) **Naïve cytotoxic T cells** with **receptors specific** to peptides recognize and bind; (idea of specific binding by cytotoxic T cells)
3) cancerous cells **recognized by macrophages / dendritic cells** (@ other examples of immune cells);
4) and **engulfed via phagocytosis;**
5) Presentation of peptides via **MHCII to naïve T helper cells;**
6) which **activates of T helper cells** (ref **clonal selection)**;
7) T helper cells **release cytokines**;
8) cause **activation of cytotoxic T cells (ref clonal selection)**;
9) Which target cancerous cells and perform **direct killing**;
10) Via release of **granzyme and perforin**;

(c) **(i)** Use the data in Fig. 2 to compare the effectiveness of the two drugs used to treat the tumours. [4]

- (similarity) Both drugs are effective for treatment of tumor A and B;
- total volume decreased compared to control;
- Vinblastine and T138067 are both equally effective against tumor A / T138067 is slightly more effective than Vinblastine against tumor A;
- QV;; eg. After 25 days, size of tumor A decreased from 600mm^3 to 220mm^3 when vinblastine was added; while size decreased from 600mm^3 to 160mm^3 when T138067 was added;
- T138067 is more effective for treatment against tumor B than Vin;
- QV;; eg. After 25 days, size of tumor B decreased from 620mm^3 to 360mm^3 when vinblastine was added; while size decreased from 600mm^3 to 120mm^3 when T138067 was added;
- Idea that Vinblastine is more effective against tumor A than tumor B;
- Idea that T138067 is more effective against tumor B than tumor A;

(ii) Both Vinblastine and T138067 were able to bind to tubulin.
Explain the effects of Vinblastine and T138067 as anti-cancer drugs. [3]

1) idea of preventing the polymerisation of tubulin / idea of tubulin being important component of spindle fibre;
2) thus prevent formation of spindle fibre
   Alternative: prevent shortening of spindle fibres;
3) spindle fibres cannot attach properly to chromosome during metaphase;
4) sister chromatids cannot be separated equally during anaphase; (reject if students describe as separation of chromosomes)
5) idea of **preventing mitosis** (nuclear division) **from occurring**;
6) idea of reduced number of cancer progeny cells formed / new cancer cells cannot be formed / new cancer cells are not viable;

(iii) Suggest why the same tumor cells may respond differently to these two drugs? [3]

- difference in uptake due to presence of different receptors to take in the drug;;
- difference in efflux of drug due to presence of different transporter proteins that can export the drug out of cell;;

- difference in stability of drug as it may be degraded to different extent (idea of susceptibility of drug to degradative enzymes);;
- different affinity of the drug to binding with tubulin leading to different extent of responses;;
- AVP;;

3 (a) With reference to the curve for Barley, explain the meaning of limiting factor. [3]

Definition of limiting factor: (Any one below)

- As a factor that is closest to its minimum value and changing the concentration (or idea of) of this factor will change the rate of reaction/ rate of CO2 uptake;; (A: if students make reference to either an increase ot decrease) **OR**
- as a factor that will directly affect the rate of reaction/ rate of CO2 uptake if its value is changed;;
- From CO2 concentration of <u>0 to 350ppm;</u>
  - increase [CO2], increases the rate of CO2 uptake;
  - CO2 is the limiting factor;
- From CO2 concentration of 350ppm onwards;
  - Increase in [CO2], does not bring about further increase in uptake/ rate remains constant;
  - CO2 is no longer limiting/ some other factors (or named factor) is limiting;

(b) Based on the morphological differences shown in Fig 3.2 and the K_m values for both enzymes, suggest reasons for the difference in rate of CO_2 uptake for Sugarcane (C4 plant) and Barley (C3 plant) shown in Fig 3.1. [5]

What are the differences?

- Much higher rate of CO2 uptake at low CO_2 concentrations
- QV/ quote gradient (steeper for sugarcane cf barley);
- Achieving a max of 35ugm^{-2}h^{-1} at very low CO2;
- At less than 100ppm of CO_2;
- Much higher than CO_2 uptake of 20ugm^{-2}h^{-1} in C3 plants;
- Higher enzyme saturation levels of PEPC compared to Rubisco;

Explanation:

- Presence of PEPC in C4 plants but not in C3;
- PEPC helps incorporate and concentrate CO_2 for use in Calvin cycle in bundle sheath cells;
- Lower Km value of PEPC implies that it has a higher affinity for carbon dioxide while Rubisco has a lower affinity since it has a higher Km 0f 12μM;;
- Presence of mesophyll cells that house PEPC, a morphological feature not observed in C3;
- Calvin cycle occurs deeper within cell, inside bundle sheath and away from Oxygen being exchanged near stomatal region;
- PEPC has no affinity for Oxygen, unlike Rubisco which can also bind to Oxygen other than just CO_2;
- Rubisco can bind to Oxygen and undergo photorespiration;
- Reduces contact with Oxygen by having Calvin cycle deeper inside cell layers; [5max]

(c) Suggest another structural difference in the leaf morphology between C3 and C4 plants. [1]

- C4 plants have thicker leaves;;

(d) In view of all the information that is given above, discuss the likely impact of predicted changes in carbon dioxide concentration, global temperatures and rainfall patterns on the distribution of C3 and C4 plants. [6]

- Climate change will raise global temperatures;
- Due to increased carbon dioxide levels serving as greenhouse gases;

- Rainfall patterns will be erratic with floods in some areas and drought in others;

Carbon dioxide rising:

- C4 plants can reach maximum photosynthetic capacity even at low carbon dioxide concentration;
- having higher levels will help them attain maximum capacity in shorter time compared to C3 plants;

OR

- C4 plants are more adapted to low carbon dioxide concentration than C3 plants ;
- C4 plants will, have reduced advantage / be at a disadvantage, over C3 plants with respect to higher atmospheric carbon dioxide concentration ;

Increased global temperatures:

- Increased enzyme activity due to raised temperatures possible to benefit both C3 and C4;
- Beyond optimal temperature however, both C3 and C4 plants will decline as enzymes become denatured;
- C4 plants will be better adapted to high temperatures as PEPCase might have a higher optimal temperature;
- Both C4 and C3 plants may spread to higher latitudes as temperatures are cooler up there;
- Increased temperature beyond optimum can also force the stomata to close more to reduce transpiration losses so water stress becomes a problem;

Water stress with changing rainfall patterns:

- C4 plants well adapted to, water stress / lack of water ;
- C4 absorb less water per gram of dry mass produced and so are better adapted to dry conditions;
- C4 plants likely to increase in hot dry areas;
- C4 crop plants will continue to be cultivated in places with high temperatures and low rainfall ;
- C4 crops will make more efficient use of irrigation ;
- higher rainfall will benefit C3 plants ;
- rising temperatures in some places will be linked to lower rainfall ;
- ref. to competition between C3 and C4 plants with respect to, water supply / [CO2]
- e.g. C4 plants thought to have evolved in (current) low carbon dioxide atmosphere
- and C3 plants when the carbon dioxide levels were higher (further back in the past);

[6 max]

Essay Questions

4(a) Discuss the effectiveness of a live, attenuated vaccine against an RNA virus. [13]

1. Define live attenuated vaccine in the context of natural acquired immunity @1m max
   - Live attenuated vaccine is the preparation of a ***weakened form/ less or non-pathogenic variants** of the disease-causing pathogen will stimulate the body's immune system (idea of active immunisation) / recognise it as foreign;;
   - to destroy the attenuated version, and "remember" it so that the immune system will more rapidly recognise and destroy the natural pathogens that it encounters later;;
2. Define purpose of using live attenuated type and its link to effectiveness @2m max
   - as attenuated virus are able to replicate in host cell and not degrade, it can induce lifelong immunity as it continues to thrive in the body;;
   - replication of the weakened pathogen does not cause symptoms/ disease yet is able to stimulate natural immune response in vaccinated person; (award only once);
   - no need for booster shots will be required in order to revive immunity in the individual;;
3. Explain primary and secondary immune response to vaccination @3m max

- in *first exposure to the vaccine or primary response, there is a lag phase and a low amount of antibody produced against the vaccine;;
- Mainly IgM antibodies are secreted with low potency;;
- in *secondary response when the body encounters the natural virus pathogen that the vaccine is intended to protect against, the pool of memory B cells remaining from primary response will be activated to divide and differentiate more rapidly and potently;;
- To develop into plasma cells that produce high levels of antibodies of different classes due to class switching that has started in primary response;;
- Together with somatic hypermutation and affinity maturation will produce plasma cells that secrete antibodies with higher specificity and affinity for the natural virus pathogen;;

4. Explain sequence of events activated by vaccine: (i) innate, (ii) humoral and cell-mediated arms of adaptive immunity, and (iii) immunological memory @3m max
   - Antigen presenting cells (APCs) in the body will engulf extracellular virus in the blood stream or infected body cells;; (students were not penalised for missing out infected cells)
   - *APCs will present the processed antigenic protein to the helper T cells via MHC class II molecules;;
   - *Activated $CD4^+$ Helper T cells will produce cytokines that activate naive B cells to develop into plasma cells which will secrete antibodies specific to the antigen;;
   - *$CD8^+$ Cytotoxic T cells to perform direct killing of virus-infected cells after altered infected cells present processed antigen peptide through MHC class I molecule;;
   - *Memory B cells and T cells remain in the body for future encounter of the same pathogen;;
5. RNA viruses and high rate of mutation (ref lack of proof reading capacity of virus RNA polymerase or reverse transcriptase of retroviruses) @2m max
   - *Errors in genome replication by virus RNA-dependent RNA polymerase are not corrected (name at least one virus enzyme responsible for this);;
   - missense mutations result in changes in codons in mRNA;;
   - changes in primary structure of virus proteins, including virus surface proteins;;
6. Structural change in **viral surface glycoproteins** that act as antigens @1m max
   - *altered primary structure leads to altered folding into tertiary structure with alteration of 3D shape; (award once as it overlaps with point 9)
   - *change in epitopes/ antigenic determinants that are no longer recognised by antigen binding site of antibody raised in immune response to vaccine;;
7. Link to challenge of vaccine design due to constant change in RNA viral antigens @2m max (check with point 10)
   - constant mutations in virus surface proteins lead to continuous change in epitopes/ antigenic determinants;;
   - antibody raised in immune response to vaccine now have antigen binding site that is specific to original epitope can no longer bind altered epitope;;
   - unable to eliminate new strains of RNA virus that evolve from the original strain, so there is loss of immunity;;

AVP wrt effectiveness of live attenuated vaccine (capped at 4m max in total);;

- live attenuated virus mutates within the body into virulent / pathogenic form to cause full-blown disease;;
- weakened virus causing full-blown disease in people with weak immune systems;;
- reference to herd immunity awarded ½ m as this applies to vaccination in general;
- reference to antigenic shift in influenza virus leading to new subtypes;;

***essential points**

4b Discuss the various ways in which the concentration of an enzyme in a cell can be regulated. [12]

Overview:

1 Enzymes are proteins and their concentration in a cell is regulated by controlling/regulating gene expression;;

Regulation of enzyme production in Eukaryotes [9 max]

2 *Presence or absence of enzyme*: [3m max]

- Chromatin remodelling - level link to accessibility of promoter of gene to transcription factors and RNA polymerase, formation of transcription initiation complex (TIC);;
- Via histone acetylation (description) – idea of gene expression: eg. decrease binding of negatively charged DNA to positively charged histones, resulting in DNA being more loosely coiled around histones)
- DNA methylation;; (gene silencing: CpG rich regions required for binding of TF and recruiting of histone deacetylases)

3 *Increase concentration of enzyme or Up regulation*: [2m]

- Enhancer and activator; with idea of stabilising transcription initiation complex to increase transcription; (R: RNA pol)

4. *Decrease concentration of enzyme or Down regulation*:

- Silencer and repressor with idea of blocks assembly of TIC/ prevents release of RNA polymerase from TIC to decrease transcription/ blocks assembly of RNA pol;;

5 Translational level: controlling the Half-life of mRNA [3m max]

- The longer the half-life of an mRNA, the more stable it is and hence the more times it can serve as a template for the translation of the enzyme;; (idea of :The mRNA can allow the synthesis of more proteins if it remains in the cytoplasm for a longer period of time)
- This is done by
  - Presence of 5' cap and 3' poly A tail prevents digestion from 5' and 3' exonucleases respectively;;
  - Longer poly A tail, longer half life; (offers more resistance to 3' exonuclease)
  - Specific proteins that bind to the 3' UTR to mark the mRNA for rapid degradation;;
  - Certain hormones can stimulate or retard the rate of degradation of mRNA, thereby decreasing or increasing its availability for translation to protein;

6 Initiation of translation [1m]

- Masking of mRNA by specific proteins to 5"UTR of mRNA prevents ribosome binding;;

7 Biochemical modification to make functional enzyme; [2m max]

- Enzymes may have to undergo certain post-translational modification to form functional enzymes through the addition of any of a number of these biochemical: [any 2, 1 max]
  - Glycosylation - Addition of carbohydrates;
  - Phosphorylation – Addition of phosphate groups;
  - Acetylation / Methylation – Addition of acetate or methyl group;
  - Proteolytic cleavage;

8 Enzyme degradation [decrease enzyme concentration] [1m]

- Ubiquitinylation involves the addition of ubiquitin which marks the enzyme for degradation by proteasome;;

9 Presence of growth factor/ signalling molecule that

- cause the activation of transcription via cell signalling pathway;; [1m]

Regulation of enzyme production in Prokaryotes [4 max]

9 via operons;

10 Presence of **substrate/ inducible operon** (eg. lactose for lac operon); [3m]

- In the absence of lactose: active repressor binds to operator to prevent binding of RNA

pol to promoter, no transcription;;
- Presence of lactose: repressor inactivated (or description) by allolactose binding to active repressor, hence transcription of structural genes or named example;;
- Upregulation: by the binding of cAMP-CAP complex to the CAP binding site upstream of promoter;;

11 Presence of **end product/ repressible operon** (eg. tryptophan for trp operon) [2m]
- In the absence of tryptophan: inactive repressor cannot bind to operator to prevent binding of RNA pol to promoter, transcription;;
- Presence of tryptophan: tryptophan active inactive repressor, binding to promoter, hence transcription of structural genes or named example;;

12 AVP

Activity: Note: here the reference is about **functional** enzyme [2m max]
- End product inhibition/ allosterism explained;;
- Optimal condition: pH eg. lysosome;;
- Enzyme inactivation at high temperatures eg. Himalayan rabbits

QWC (Quality of Witten Expression)
To be awarded if students write on regulation in both prokaryotes and eukaryotes.

5a Describe the functions of various components found in the plasma membrane and explain, using named examples, why there is a different composition of these components in membranes of different cells and organelles. [13]

Components of membrane and their functions:

(1) Phospholipids
- Forms bilayer due to amphipathic nature
- Barrier to water-soluble substances
- Provides fluidity to membrane;
- compartmentalisation;

(2) Cholesterol
- Regulates fluidity of membrane
- Maintain mechanical stability of membrane
- Reduces uncontrolled leakage of polar molecules / ions

(3) Proteins
- transport proteins - Allow water-soluble ions, glucose, amino acids etc to be transported in and out of cell
- enzymes – catalyse chemical reactions on the membrane eg. adenylyl cyclase
- receptor – allows for specific binding of signalling ligand
- structural support – proteins attached to cytoskeleton to provide framework to cell
- energy transducers eg. ATP synthase

(4) Carbohydrates (@glycoproteins or glycolipids)
- Form H bonds with water and stabilizes membrane
- Cell-cell recognition / cell communication
- Cell-cell adhesion

Significance of different components:

<u>In different organelles</u>
- Eg mitochondrion and chloroplast;
- Require proteins (electron carriers) to be arranged in order;
- To facilitate electron transfer along electron transport chain;
- Idea of carrying out chemiosmosis;
- Eg. nucleus

- Require opening such as nuclear pores to be present in the membrane;
- Eg. rER; more protein channels for newly synthesized proteins to enter lumen;
- Eg. chloroplasts; photosynthetic pigments on thylakoid membrane for absorption of light;
- Eg. lysosome; more proton pumps to maintain acidic internal environments;

In different cells

- Ref different cell types contains different amount and types of glycoproteins and glycolipids;
- idea of similar cell types can adhere together to form tissues;
- Ref cells receiving signalling ligand / specific example of effector cells etc;
- Require specific protein receptors to be present on cell membrane;
- To allow specific signalling ligand to recognize and bind;
- For signal to be received and transmitted;
- Ref cells that produces / synthesized proteins for extracellular use / cells that perform secretory functions etc;
- Contains more transporter proteins on the plasma membrane;
- Ref immune cells eg. B cell/macrophage/ T helper cell etc
- To contain specific receptor eg. BCR with specific antigen binding sites;
- That enable it to bind to specific antigen;
- Ref cells in organisms living in areas of higher temp (accept reverse)
- Higher % of saturated fatty acids in phospholipids;
- For greater stability of the membrane;
- AVP

5b Hyperglucagonemia is a condition where there is excess glucagon secretion. Using your knowledge of how glucagon works and how HIV infects a cell, explain how drugs can be used to target the different stages in each condition. Highlight in your answer, similarities in the mechanism of the drugs. [12]

Similarities: (3max)

- Bind to **specific receptors** on **cell surface membrane**;;
- Due to **complementary** binding/fitting to relevant **receptors** on specific **target** cells;;
- Drug can also act as **competitive inhibitor**/ structural analog to relevant receptors on target cells;
- **Block the binding** of glucagon or HIV and hence limit the propagation of the diseases;
- Drug can also enter the cell and work by inhibiting **intracellular** cell processes;
- Eg. involving **enzymes**;
- Drug can be steroid based to facilitate entry into cell;
- Drug can be administered in liposomes to ensure quick delivery to target cells via bloodstream;

Examiner's comments:
Despite prompting from the question, this part was barely discussed. Many offered only a sweeping statement about the two drugs to be similar in action of targeting receptors as some sort of competitive inhibitor. Some mentioned the common target of intracellular enzymes but most never mentioned about the common mode of drug entry into the cell.

Differences: (9 max)
Other targets

	Glucagon	**HIV**
Target Receptor	G-protein linked receptors	CD4 /CCR5 receptors
Target Cell Type	liver cells	T helper cells

Molecular shape specificity	Similar to glucagon	Can be similar to T helper cell surface receptors or bind directly to gp120 /41 on HIV
Target other cellular pathways Eg. enzymes	**GTPase enzyme** activity used to hydrolyze its bound GTP to back GDP, inactivating the G-protein once again	Drug that inhibits HIV **reverse transcriptase** activity will prevent viral DNA transcription from RNA
Target other cellular pathways Eg. enzymes	**Phosphodiesterase** which inactivates cAMP by converting it to AMP can be used to reduce the number of second messengers.	Drug that inhibits HIV **DNA polymerase** activity will prevent doubled stranded HIV DNA from being made
Target other cellular pathways Eg. enzymes	Inhibitor to cellular responses preventing the breakdown of glycogen polymers to glucose -1-phosphate by **glycogen phosphorylase**	Drug that works against **HIV integrase** will prevent incorporation of viral DNA into host cell
Target other cellular pathways Eg. enzymes	--	**HIV protease** inhibitors prevent the assembly of the capsid coat around the viral RNA and enzymes to form nucleocapsids.
Target other cellular pathways	--	Drugs can be co-receptor analogs deployed to reduce the efficiency of co-receptor binding
Target other cellular pathways	--	Drugs designed to prevent uncoating, by preventing the fusion of the membranes via steric hinderance of the hairpin formation
Regulation of release	Glucagon release can be inhibited at the (α cells) of pancreas	Prevent release of HIV by blocking the formation of new virions so that they cannot bud off to infect new T cells