# Likely Essay Questions

Explain how one named factor can increase the chances of a cancerous growth/Why is development of cancer a multi-step process

1. (For first question) State one of the first 3 factors ⇒ Causative agent increases the chance of DNA damage and mutations in the genes which control regulatory checkpoints of the cell cycle in a single cell.
2. Development of cancer requires the accumulation of mutations in the genes which control **regulatory checkpoints** of the cell cycle in a single cell
3. Mutations disrupt normal cell cycle ⇒ Uncontrolled cell division ⇒ Excessive cell growth and proliferation
4. Loss-of-function mutation of **tumour suppressor genes** ⇒ Inability to inhibit cell cycle, repair damaged DNA and promote apoptosis
5. Gain-in-function mutation of **proto-oncogenes** to form **oncogenes** ⇒ Over-expression of proteins OR production of hyperactive/degradation resistant proteins
6. Upregulation/Activation of genes coding for **telomerase** ⇒ Telomeres lengthened and cell can divide indefinitely as chromosomes are prevented from shortening with each round of DNA replication
7. Loss of contact inhibition enables cells to grow into a tumour
8. **Angiogenesis** → Blood vessels formed can transport oxygen and nutrients for its growth
9. Tumour must be malignant where cells can **metastasise** to spread to other parts of the body via the blood stream to form secondary tumours
10. Takes years to accumulate these mutations ⇒ Multi-step process

Why is the population the smallest unit that can evolve? (possible essay)

- Define population: A **population** is a group of interbreeding individuals of the same species and sharing a common geographic area
- Define evolution: **Evolution** is a measure of changes in allele frequencies in a population over time
- **Variation** must exist in a population for natural selection to take place
- **Natural selection** acts on individuals in a population and results in individuals being selected for or against
- Individuals cannot evolve/don't change in their lifetimes
- Individuals can only **pass on their favourable alleles** to the next generation
- And introduce new alleles through **mutation** during the formation of gametes
- Over many generations, allele frequencies of favourable characteristics increase over time, leading to evolution

Preservation of recessive alleles (possible essay)

- **Heterozygote protection**
    - Occurs in diploid organisms with 2 copies of each gene
    - Heterozygous = 2 different alleles at 1 gene locus where dominant alleles can mask the effect of recessive alleles
    - Homozygous recessive genotype has disadvantageous phenotype which is selected against but does not manifest in heterozygotes ⇒ Heterozygotes survive
    - Heterozygotes able to pass on recessive allele to their offspring when they interbreed, maintaining recessive allele in the population
- Balancing selection = Natural selection maintains 2 or more alleles at a gene locus
    - **Heterozygote advantage**
        - Heterozygotes may have greater fitness than both types of homozygotes
        - e.g. Heterozygote individuals selected for
            - In malaria prone areas → Do not develop sickle cell anaemia + less chance of contracting malaria
        - e.g. Both homozygotes selected against as
            - HbAHbA ⇒ Normal haemoglobin ⇒ Susceptible to malaria
            - HbSHbS ⇒ Sickle cell anaemia ⇒ Early death
        - Heterozygotes able to pass on recessive allele to their offspring when they interbreed, maintaining recessive allele in the population
    - **Frequency dependent selection**
        - Selective advantage of the phenotype depends on the relative frequency of the particular phenotype
        - Frequency of each phenotype oscillates over time but is kept close to 50%, maintaining both alleles
        - e.g. Left-mouthed and Right-mouthed scale eating fish in Lake Taganyika
            - Prey guards against attack from the more common phenotype of the scale-eating fish in the lake
        - Selection favours whichever phenotype is least common
- Neutral mutations = mutations that are selectively neutral
    - Silent mutations = Mutated sequence still codes for the same amino acid
    - Conservative mutations = Mutated sequence codes for chemically similar amino acid
    - Mutations in non-regulatory, non-coding regions
    - Thus, no change in protein structure and function + no change in quantity of protein produced

Advantages of molecular methods to determine phylogeny

1. Can compare all organisms which share common genes
2. Can compare morphologically indistinguishable organisms due to convergent evolution or are very closely related
3. Objective as molecular character states are unambiguous (A, C, G, T)
4. Quantitative as it can easily be converted to a numerical form for statistical analysis
    - Degree of relatedness can be inferred and quantified by calculating nucleotide differences

between species

5. Changes in nucleotide sequences accumulate over time with clockwork regularity, allowing it to estimate the time of speciation of a particular species
    - Forms basis of the molecular clock
6. Does not underestimate/exaggerate differences unlike morphological analysis
    - Some molecular differences may not be reflected as differences in morphological character, some small genetic differences may result in major phenotypic differences
7. Both living and dead tissue can be used + Not necessary to have an entire specimen
8. Large set of characters can be studied relatively quickly
9. Sequences can be accessed electronically for easy comparisons and classification

Explain the small yield of ATP from anaerobic respiration (possible essay)

1. Only 2 net ATP is generated per glucose molecule during anaerobic respiration as compared to 38 ATP for aerobic respiration
2. In the absence of oxygen, there is no final electron acceptor to remove electrons from the ETC, hence no ATP is produced by the substrate level phosphorylation in the mitochondria (link reaction, Krebs cycle)
3. Proton gradient cannot be maintained to drive the synthesis of ATP in the ATP synthase complex without flow of electrons down the ETC hence no ATP generated from chemiosmosis
    - Reactions in the mitochondria produce the bulk of ATP
4. Glycolysis alone continues to produce only 2 ATP per glucose molecule
5. As glycolysis proceeds, NADH accumulates because it is unable to donate its electrons to the ETC. However, $NAD^{\pm}$ needs to be regenerated in order for glycolysis to continue.
6. Therefore, pyruvate acts as the final electron acceptor and is reduced to lactic acid by NADH
7. In the process, $NAD^{+}$ is regenerated so that it may return to take part in glycolysis to continue to produce ATP
8. However, no extra ATP is produced during the regeneration of $NAD^{+}$ under anaerobic respiration

What is the role of NAD in cells?

1. Organic molecules are oxidised during glycolysis, link reaction and Krebs cycle and the high energy electrons and protons produced are transferred to the coenzyme $NAD^{+}$ to form NADH
2. $NAD^{+}$ serves as a mobile electron carrier to carry high energy electrons and protons from organic molecules to the energy transport chain on the cristae of mitochondria
3. High energy electrons in NADH are used to reduce the electron carriers of the electron transport chain while NADH gets re-oxidised
4. As electrons pass down the chain, the release of energy in a series of redox reactions is coupled to the phosphorylation of ADP to form ATP
5. The protons liberated in the oxidation of NADH is used to establish the proton motive

force necessary for ATP synthesis
6. Reoxidation of NADH allows the regeneration of the coenzyme $NAD^+$, allowing it to pick up more protons and electrons from the Krebs cycle, link reaction and glycolysis so that these reactions can continue
7. Each NADH in the matrix yields 3 ATP through oxidative phosphorylation

Genetic Variation

1. **Crossing over** between non-sister chromatids of homologous chromosomes during prophase 1
    - Homologous chromosomes pair up via synapsis to form bivalents
    - Corresponding segments exchange genetic material to form non-identical sister chromatids
    - Results in new combinations of alleles on chromosomes of gametes
2. **Independent assortment of homologous chromosomes** during metaphase 1 and their subsequent separation during anaphase 1
    - Orientation of chromosomes of each bivalent completely independent of the orientation of the other bivalents
    - Results in $2^n$ different combinations of maternal and paternal chromosomes in daughter cells where n is the number of chromosome pairs
3. **Random orientation of non-genetically identical sister chromatids** during metaphase 2 and subsequent separation during anaphase 2
    - Results in gametes with new combinations of alleles that differ from parental combination of allele with $2^n$ possible combinations
4. **Random fusion** of large number of genetically different gametes during fertilisation
    - Results in greater number of genotypic combinations of a zygote

Mechanism of Action
Interaction/Binding

- Enzyme has specific active site with **specific 3D conformation** that is **complementary in shape and charge** to the substrate that is held by R group interactions between structural residues
- Effective collisions between enzyme and substrate form a temporary **enzyme-substrate complex** held together by weak interactions such as hydrogen bonds, ionic bonds and hydrophobic interactions between the contact residues and the substrate
- Based on induced fit hypothesis, binding of substrate induces a change in shape in the enzyme active site so that the active site is a more precise fit for substrate for effective catalysis
- Based on lock and key model, substrate is the key and enzyme is the lock

Catalysis

- R groups of catalytic residues help to catalyse the reaction

- Enzyme lowers the activation energy by:
    1. Proximity effects = By aligning substrates next to each other in **close proximity** in the active site, increasing chance of the reaction occurring
    2. Strain effects = By **applying strain on the bonds** to be broken/By distorting the substrates hence reducing the activation energy required to achieve transition state
    3. Orientation effects = By holding the substrates in the correct orientation such that its **bonds are exposed to chemical attack**
    4. Microenvironment effects = By providing a **favorable microenvironment**
    5. Acid-base catalysis = Where the R-groups of catalytic acidic and basic amino acid residues in active site participate in direct catalysis
- More of the substrate molecules will possess energy exceeding activation energy, allowing the reaction to proceed at a higher rate

Release

- Products are no longer complementary in shape and charge to the enzyme active site and hence, are released. The enzyme remains unchanged and can be used again.

Sickle-Cell Anaemia
Mutation:

- Point substitution mutation
- T → A in the 6th triplet codon in the template DNA strand of gene coding for the β-globin chain
- Amino acid glutamate → valine
- Valine is a non-polar, hydrophobic amino acid whereas glutamate is a charged, hydrophilic amino acid

Effect of mutation:

- Normal haemoglobin (HbA) → Sickle cell haemoglobin (HbS)
- Low [$O_2$] ⇒ Hydrophobic areas on different HbS stick together causing HbS to polymerise into abnormal rigid rod-like fibres that distort the shape of red blood cells ⇒ Sickling of RBC

Type of disease: Autosomal recessive disease → Requires 2 copies of HbS for symptoms to occur

Effect of disease

- Sickle RBC more fragile and have shorter life span ⇒ Shortage of RBC + Poor oxygen transport ⇒ Anaemia + Lack of energy + Heart failure

- Sickle-shaped RBC may get lodged in small blood vessels ⇒ Interfere with blood circulation ⇒ Organ damage

Prevalence in malaria stricken areas of Africa

- HbAHbA ⇒ Individuals have normal haemoglobin ⇒ Susceptible to malaria
- HbSHbS ⇒ Individuals have sickle cell anaemia ⇒ Early death
- HbAHbS ⇒ Individuals do not develop sickle cell anaemia + Less chance of contracting malaria
    - Maintains both HbA and HbS recessive allele in the population
    - Sickle shape of RBC ⇒ Lower oxygen carrying capacity ⇒ Malaria parasite cannot survive
    - Heterozygotes have selective advantage in regions of endemic malaria over homozygotes