GAT B Biotechnology & Life Sciences

Sample Paper – 10

Duration: 180 Minutes **Maximum Marks: 200**

Instructions

- This paper contains **65** Multiple Choice Questions (Single Correct Answer), modelled on the full **GAT B** (Graduate Aptitude Test – Biotechnology) entrance exam.
- **Section A** (Questions 1–15, General Aptitude): Each correct answer carries **+2 marks**. A deduction of $\frac{1}{3}$ **mark** for each incorrect answer. Unattempted questions carry zero marks.
- **Section B** (Questions 16–65, Biotechnology & Life Sciences): Each correct answer carries **+3.4 marks**. A deduction of $\frac{1}{3}$ **mark** for each incorrect answer. Unattempted questions carry zero marks.
- Only **one** option is correct per question. Choose carefully.
- The exam is a **Computer Based Test (CBT)** conducted in **English only**. Personal calculators, log tables, and mobile phones are strictly prohibited. Rough sheets are provided at the test centre.
- Maximum marks: **200** (Section A: 30 marks | Section B: 170 marks).

Section A — General Aptitude (Questions 1–15)

Q1. A figure skater spinning on ice has a moment of inertia $I_1 = 4\,\text{kg}\cdot\text{m}^2$ and an initial angular velocity $\omega_1 = 5\,\text{rad/s}$. She pulls her arms inward so that her moment of inertia decreases to $I_2 = 2\,\text{kg}\cdot\text{m}^2$. Assuming no external torque acts, what is her new angular velocity ω_2?

(A) $10\,\text{rad/s}$

(B) $5\,\text{rad/s}$

(C) $2.5\,\text{rad/s}$

(D) $20\,\text{rad/s}$

Q2. A chemist treats *butan-2-ol* (a secondary alcohol) with excess acidified potassium dichromate ($K_2Cr_2O_7/H^+$). Which of the following best describes the **organic product** obtained under these conditions?

(A) Butanal (an aldehyde)

(B) Butanone (a ketone)

(C) Butanoic acid (a carboxylic acid)

(D) No oxidation occurs; the alcohol is recovered unchanged

Q3. A diagnostic test for a rare disease has sensitivity $= 0.95$ (true positive rate) and specificity $= 0.90$ (true negative rate). The disease prevalence in the population is 1%. A randomly chosen patient tests **positive**. Using Bayes' theorem, which of the following is the approximate **positive predictive value (PPV)**—the probability that the patient actually has the disease?

(A) $\approx 50\%$

(B) $\approx 85\%$

(C) $\approx 8.7\%$

(D) $\approx 95\%$

Q4. The van der Waals equation for a real gas is $\left(P + \dfrac{a}{V^2}\right)(V - b) = nRT$. Which of the following gases would you expect to have the **highest value of the parameter** a, which corrects for intermolecular attractive forces?

(A) He (helium)

(B) H_2 (hydrogen)

(C) N_2 (nitrogen)

(D) H_2O (water vapour)

Q5. Find the perpendicular distance from the point $(3,\ 4)$ to the straight line $3x + 4y - 10 = 0$.

(A) 3

(B) 5

(C) $\dfrac{15}{\sqrt{7}}$

(D) $\dfrac{3}{5}$

Q6. EDTA (ethylenediaminetetraacetic acid) is described as a hexadentate ligand and forms extraordinarily stable metal complexes. The unusually large stability constants of EDTA complexes (e.g. $\log K \approx 10.7$ for Ca^{2+}–EDTA) are primarily due to the:

(A) High charge density of EDTA's carboxylate groups

(B) Chelate effect: the large positive entropy gain when one EDTA replaces six individual monodentate ligands

(C) Strong π-back-bonding from the metal d-orbitals to EDTA

(D) Covalent character of the metal–nitrogen bonds in the EDTA complex

Q7. The number of Barr bodies (condensed, inactivated X chromosomes) visible in interphase cells equals $n - 1$, where n is the number of X chromosomes present. How many Barr bodies would be found in the somatic cells of an individual with a **47, XXY** (Klinefelter syndrome) karyotype?

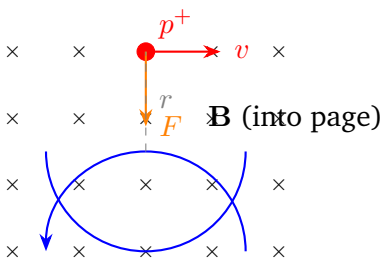
(A) 0

(B) 2

(C) 1

(D) 3

Q8. A proton (charge $+e$, mass m_p) moves with velocity v perpendicular to a uniform magnetic field $\mathbf{B}$ directed into the page. The proton undergoes uniform circular motion. Which diagram best represents the trajectory and the direction of the magnetic force at the instant shown?



Given this setup, which expression correctly gives the radius r of the circular path?

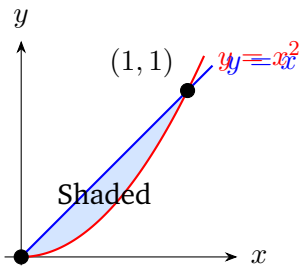
(A) $r = \dfrac{qB}{m_p v}$

(B) $r = \dfrac{qBv}{m_p}$

(C) $r = \dfrac{m_p B}{qv}$

(D) $r = \dfrac{m_p v}{qB}$

Q9. The diagram below shows the curves $y = x$ (straight line) and $y = x^2$ (parabola) intersecting at $x = 0$ and $x = 1$. What is the area of the shaded region enclosed between the two curves?



(A) $\dfrac{1}{6}$

(B) $\dfrac{1}{3}$

(C) $\dfrac{1}{2}$

(D) $\dfrac{1}{12}$

Q10. The industrial synthesis of ammonia proceeds by the Haber process:

$$\mathrm{N_2(g) + 3\,H_2(g) \rightleftharpoons 2\,NH_3(g), \quad \Delta H = -92\,kJ\,mol^{-1}}$$

Which of the following correctly describes the effect of **simultaneously increasing both temperature and pressure** on the **equilibrium yield** of $\mathrm{NH_3}$?

(A) Both increase the equilibrium yield of $\mathrm{NH_3}$

(B) Increasing pressure increases yield; increasing temperature decreases yield (shifts equilibrium left)

(C) Both decrease the equilibrium yield of NH_3

(D) Increasing temperature increases yield; increasing pressure has no effect on an ideal-gas equilibrium

Q11. Using molecular orbital (MO) theory, the ground-state electronic configuration of O_2 includes two electrons in the degenerate π^*_{2p} antibonding orbitals. Which of the following statements about O_2 is **correct**?

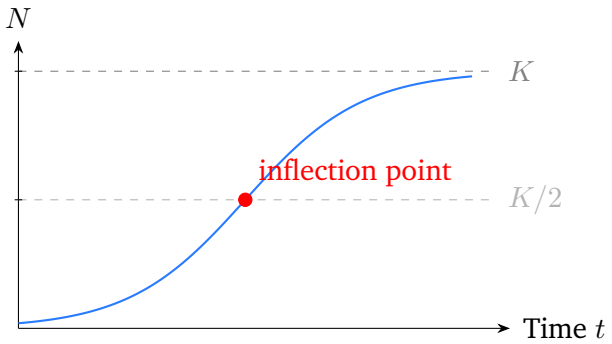
(A) O_2 is diamagnetic with a bond order of 3

(B) O_2 is paramagnetic with a bond order of 3

(C) O_2 is paramagnetic with a bond order of 2

(D) O_2 is diamagnetic with a bond order of 2

Q12. The logistic growth equation $\dfrac{dN}{dt} = rN\left(1 - \dfrac{N}{K}\right)$ produces the S-shaped (sigmoidal) curve shown below. At which value of N is the **instantaneous growth rate** dN/dt at its **maximum**?



(A) $N = K$ (carrying capacity)

(B) $N = 0$ (initial inoculation)

(C) $N = K/4$

(D) $N = K/2$ (inflection point)

Q13. The half-life of carbon-14 (^{14}C) is approximately 5730 years. An archaeologist analyses a piece of charcoal from an ancient fire and finds that it retains only **25%** of its original ^{14}C activity. How old is the sample?

(A) $11{,}460$ years

(B) $5{,}730$ years

(C) $17{,}190$ years

(D) $22{,}920$ years

Q14. An unknown organic compound shows two prominent features in its IR spectrum: a strong carbonyl stretch at $\approx 1715\,\mathrm{cm^{-1}}$ and a broad, strong O–H stretch in the region 2500–$3300\,\mathrm{cm^{-1}}$. Which functional group is most consistent with **both** absorptions?

(A) Ketone ($\mathrm{C{=}O}$ only, no O–H)

(B) Carboxylic acid ($\mathrm{C{=}O}$ + broad O–H due to hydrogen bonding)

(C) Primary alcohol (O–H at $\sim 3350\,\mathrm{cm^{-1}}$ only, no carbonyl)

(D) Ester ($\mathrm{C{=}O}$ at $\sim 1735\,\mathrm{cm^{-1}}$, no O–H)

Q15. In the Gram staining procedure, a mixed bacterial smear is treated sequentially with: (1) crystal violet, (2) iodine (mordant), (3) acetone/ethanol decoloriser, (4) safranin counterstain. After step (3) only, a gram-positive organism appears **purple** while a gram-negative organism appears **colourless**. What is the structural reason for this difference?

(A) Gram-positive cells lack a cell wall and therefore cannot retain any stain

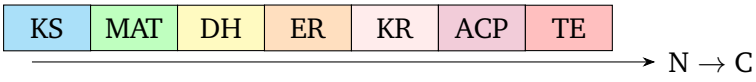
(B) Gram-negative cells have a thicker peptidoglycan layer that holds the crystal violet–iodine complex

(C) Gram-positive cells have a thick peptidoglycan layer that traps the crystal violet–iodine complex; gram-negative cells have a thin peptidoglycan layer plus an outer membrane that is disrupted by decoloriser, releasing the complex

(D) Gram-negative cells have more lipopolysaccharide (LPS), which irreversibly binds crystal violet

Section B — Biotechnology & Life Sciences (Questions 16–65)

Q16. The mammalian fatty acid synthase (FAS) is a type I multifunctional enzyme consisting of a homodimer. The catalytic domains are arranged in a specific order along the polypeptide. Which of the following correctly lists the domain order from the N-terminus to C-terminus of a single FAS subunit?



(A) TE – ACP – KR – ER – DH – MAT – KS (C to N, reversed)

(B) KS – MAT – DH – ER – KR – ACP – TE

(C) ACP – KS – MAT – TE – DH – KR – ER

(D) MAT – KS – ER – DH – KR – ACP – TE

Q17. Acetyl-CoA carboxylase (ACC) catalyses the committed (rate-limiting) step in fatty acid synthesis. Which of the following statements about the **allosteric and hormonal regulation** of ACC is **correct**?

(A) Palmitoyl-CoA activates ACC; citrate inhibits ACC

(B) AMPK activates ACC by phosphorylating Ser79; this increases malonyl-CoA production

(C) Citrate allosterically activates ACC; palmitoyl-CoA (product) inhibits ACC; glucagon/AMPK-mediated phosphorylation inactivates ACC

(D) Insulin phosphorylates ACC directly via PKA, activating fatty acid synthesis in the fed state

Q18. The de novo synthesis of one molecule of **palmitate** ($C_{16:0}$) from acetyl-CoA and malonyl-CoA requires 7 elongation cycles, each consuming 2 NADPH. In addition to the pentose phosphate pathway (oxidative branch), which of the following enzymes can supply cytoplasmic NADPH for fatty acid synthesis in the liver?

(A) Pyruvate kinase and phosphoglucose isomerase

(B) Succinate dehydrogenase and fumarase (TCA cycle enzymes)

(C) NADH dehydrogenase (Complex I) and cytochrome bc_1 (Complex III)

(D) Malic enzyme (malate $\rightarrow$ pyruvate + CO_2 + NADPH) and $NADP^+$-isocitrate dehydrogenase

Q19. Humans cannot synthesise linoleic acid ($C18:2$, $\Delta^{9,12}$, ω-6) or α-linolenic acid ($C18:3$, $\Delta^{9,12,15}$, ω-3) de novo because they lack specific desaturase enzymes. Which desaturases are absent in humans that make these fatty acids **nutritionally essential**?

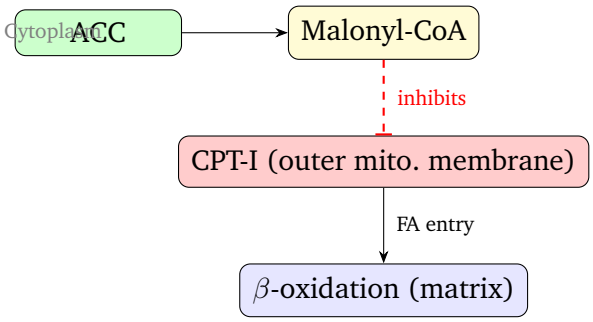
(A) Δ^{12}-desaturase and Δ^{15}-desaturase

(B) Δ^{9}-desaturase (SCD) and Δ^{6}-desaturase

(C) Δ^{4}-desaturase and Δ^{5}-desaturase only

(D) Δ^{9}-desaturase and Δ^{11}-desaturase

Q20. In the fed state, high cytoplasmic malonyl-CoA coordinates the suppression of fatty acid β-oxidation. The diagram below illustrates this cross-regulation. Which protein does malonyl-CoA **directly inhibit** to prevent fatty acid entry into the mitochondria?



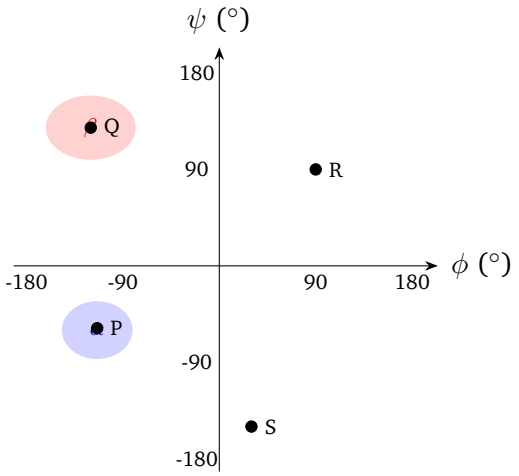
(A) Carnitine acetyltransferase (CrAT) in the mitochondrial matrix

(B) Carnitine palmitoyltransferase I (CPT-I) on the outer mitochondrial membrane

(C) Acyl-CoA synthetase (FACS) on the cytoplasmic face

(D) Carnitine palmitoyltransferase II (CPT-II) on the inner mitochondrial membrane

Q21. The Ramachandran plot maps the backbone dihedral angles ϕ (phi, rotation about N–Cα) and ψ (psi, rotation about Cα–C) for each residue in a protein. The plot below shows allowed regions. Which point correctly represents the backbone angles of a residue in an α-**helix**?



(A) Point Q ($\phi \approx -120°$, $\psi \approx +130°$)

(B) Point R ($\phi \approx +90°$, $\psi \approx +90°$)

(C) Point P ($\phi \approx -57°$, $\psi \approx -47°$)

(D) Point S ($\phi \approx +30°$, $\psi \approx -150°$)

Q22. Many metazoan signalling proteins are modular, being composed of multiple independently folding domains. The SH2, SH3, and PH domains are found in numerous signalling proteins. Which of the following correctly matches a domain with its **binding target**?

(A) SH2 domain binds proline-rich PXXP peptide sequences

(B) SH3 domain binds phosphotyrosine-containing peptides

(C) PH domain binds phosphoserine/phosphothreonine motifs on target proteins

(D) SH2 domain binds phosphotyrosine-containing peptides; SH3 domain binds proline-rich PXXP motifs; PH domain binds PIP_3 (phosphoinositide) at the membrane

Q23. The Monod–Wyman–Changeux (MWC) model of allostery proposes that a multimeric protein exists in two states: the T (tense, low-affinity) state and the R (relaxed, high-affinity) state, which are in equilibrium. An allosteric **activator** exerts its effect by:

(A) Preferentially binding to and stabilising the R state, thereby shifting the T $\rightleftharpoons$ R equilibrium toward R and increasing apparent substrate

affinity cooperatively

(B) Inducing a sequential conformational change in each individual subunit upon substrate binding (the KNF model)

(C) Covalently modifying the active-site residues of the T state to convert it permanently to R

(D) Increasing the Michaelis constant K_m without changing $V_{\max}$ (competitive inhibition pattern)

Q24. High concentrations of urea (8 M) and guanidinium hydrochloride (GdnHCl, 6 M) are commonly used to unfold proteins in vitro. The **primary mechanism** by which these chaotropic agents destabilise protein native structure is:

(A) Hydrolysis of peptide bonds at high chaotrope concentration

(B) Disruption of intramolecular hydrogen bonds and hydrophobic interactions by competing with protein groups for water H-bonding and disordering the hydration shell

(C) Chelation of structural metal ions (e.g. zinc in zinc-finger proteins) leading to unfolding

(D) Covalent modification of cysteine residues, breaking disulfide bonds

Q25. Thermophilic microorganisms produce proteins that retain full activity at temperatures $> 70^{\circ}\mathrm{C}$. Which of the following structural features **collectively** contribute to the enhanced thermal stability of thermophilic proteins compared to their mesophilic counterparts?

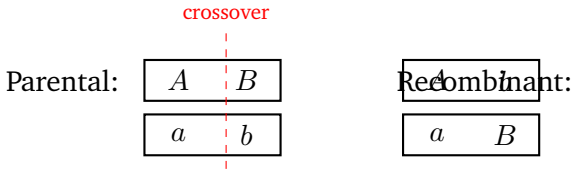
(A) Fewer salt bridges, longer surface loops, and more glycine residues in helices

(B) Increased number of asparagine and glutamine residues exposed on the surface

(C) More salt bridges (ion pairs), proline substitutions in loop regions, tighter hydrophobic core packing, and additional disulfide bonds

(D) Replacement of all α-helical secondary structure with β-sheet to minimise solvent exposure

Q26. Two genes A and B are located on the same chromosome (i.e. they are linked). In a test cross of a double heterozygote AB/ab with ab/ab, the following offspring are observed: $AB = 432$, $ab = 428$, $Ab = 68$, $aB = 72$. The diagram below illustrates the parental and recombinant chromosome configurations.



What is the **recombination frequency** (map distance) between genes A and B?

(A) $50\,\text{cM}$ (genes are unlinked)

(B) $10\,\text{cM}$

(C) $7\,\text{cM}$

(D) $14\,\text{cM}$

Q27. In a three-point cross in Drosophila, the map distances between genes P–Q and Q–R are determined to be $12\,\text{cM}$ and $8\,\text{cM}$ respectively. Out of 5000 total progeny, only 32 double-crossover (DCO) offspring are observed. What is the **coefficient of coincidence (CoC)** and the **interference (I)**?

(A) CoC $= 0.667$; $I = 0.333$ (positive interference: observed DCO is $\frac{2}{3}$ of expected)

(B) CoC $= 1.333$; $I = -0.333$ (negative interference: more DCOs than expected)

(C) CoC $= 1.0$; $I = 0$ (no interference)

(D) CoC $= 0.333$; $I = 0.667$ (strong positive interference)

Q28. A geneticist isolates six eye-colour mutants in *Drosophila*, all showing recessive white-eye phenotypes. To determine how many genes are involved, she performs pairwise complementation tests. In a cross between mutant 1 (m_1/m_1) and mutant 4 (m_4/m_4), the F_1 trans-heterozygotes

$(m_1/+; +/m_4)$ have **wild-type (red) eyes**. What does this result indicate?

(A) Mutants 1 and 4 are alleles of the same gene (same complementation group); they fail to complement

(B) Mutants 1 and 4 are in **different genes** (different complementation groups); each mutant allele is complemented by the wild-type allele of the other gene

(C) Mutant 1 is dominant to mutant 4; the cross simply produces the dominant phenotype

(D) The result is ambiguous because both mutations could be in the same gene but show intragenic complementation

Q29. In human genetics, linkage between a disease locus and a marker is assessed using LOD scores. The LOD score is defined as:

$$Z(\theta) = \log_{10}\left[\frac{P(\text{data} \mid \theta)}{P(\text{data} \mid \theta = 0.5)}\right]$$

where θ is the recombination fraction. Which of the following correctly states the conventional **threshold for declaring significant linkage**?

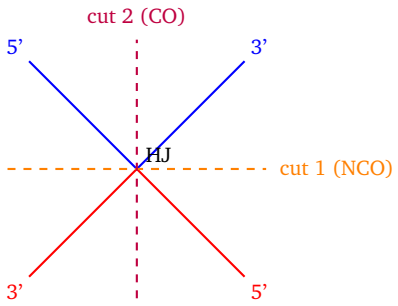
(A) LOD ≥ 1.0 (10:1 odds in favour of linkage)

(B) LOD ≥ 2.0 (100:1 odds in favour of linkage)

(C) LOD ≥ 3.0 (1000:1 odds in favour of linkage)

(D) LOD ≥ 5.0 (required for genome-wide significance with dense SNP arrays)

Q30. During homologous recombination, a double Holliday junction (DHJ) is formed. The DHJ can be resolved by nucleases (resolvases) in two orientations, yielding different genetic outcomes. The diagram below shows an X-shaped Holliday junction.



Which statement correctly describes the two resolution outcomes?

(A) Both orientations of cutting always produce crossover (CO) products with flanking-marker exchange

(B) Both orientations always produce noncrossover (NCO) products

(C) Cut 1 (horizontal, orange) produces crossover products; cut 2 (vertical, purple) produces noncrossover products

(D) Cut 1 (horizontal, orange) produces noncrossover products; cut 2 (vertical, purple) produces crossover products with flanking-marker exchange

Q31. Which of the following ELISA formats provides the **highest sensitivity** for detecting a protein antigen in a complex biological matrix (e.g. serum), and what is its fundamental principle?

(A) Sandwich ELISA: capture antibody on plate binds antigen; a second, enzyme-conjugated detection antibody recognises a non-overlapping epitope; the two-antibody sandwich provides high specificity and signal amplification

(B) Direct ELISA: antigen bound to plate is detected by a single enzyme-labelled antibody; fewest steps give highest sensitivity

(C) Competitive ELISA: labelled and unlabelled antigen compete for limited antibody; signal is directly proportional to antigen concentration

(D) Indirect ELISA: antigen is labelled directly before being captured by plate-bound antibody

Q32. The ELISpot (enzyme-linked immunospot) assay is used to enumerate antigen-specific cells at the single-cell level. Which of the following best

describes the **principle** of ELISpot and a key **application**?

(A) Cells are lysed, and total secreted cytokine is measured in the supernatant by standard ELISA; used for measuring bulk cytokine production

(B) Cells are fixed and permeabilised; intracellular cytokine is stained with fluorescent antibody and quantified by flow cytometry

(C) PVDF membrane coated with capture antibody captures cytokines/antibodies secreted locally by individual cells; each cell's secretion produces one spot; used to count antigen-specific T cells or antibody-secreting B cells

(D) Proximity-based ligation of DNA oligonucleotides on two antibodies detects cytokine receptor dimerisation on the cell surface

Q33. The proximity ligation assay (PLA) is used to detect **protein–protein interactions** directly in fixed cells or tissue sections. What is the key mechanistic step that converts a proximity event into a detectable signal?

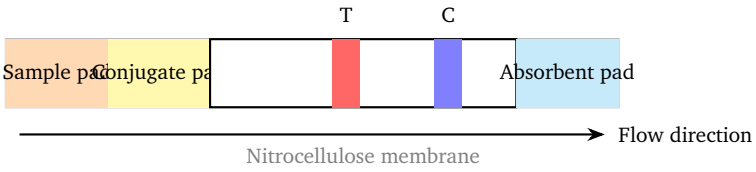
(A) FRET between two fluorophore-labelled antibodies when they are within 10 nm of each other

(B) Two secondary antibodies each carry a DNA oligonucleotide probe; when the two target proteins are within $\sim$40 nm, the DNA probes are ligated by connector oligonucleotides and amplified by rolling-circle amplification, producing a localised fluorescent punctum

(C) Bioluminescence resonance energy transfer (BRET) from a luciferase-tagged antibody to a fluorophore-tagged antibody

(D) Split-GFP complementation triggered when two antibodies bring their respective GFP fragments into proximity

Q34. The lateral flow immunoassay (LFA) is a point-of-care rapid test. The diagram below shows the strip components. In a **positive result** for the analyte, what is observed at the test line (T) and control line (C)?



(A) Only the control line (C) is visible; test line (T) is absent

(B) Only the test line (T) is visible; control line (C) is absent

(C) Neither T nor C line is visible (invalid test)

(D) Both the test line (T) **and** the control line (C) are visible (positive result confirmed)

Q35. Time-resolved fluoroimmunoassay (TRFIA) uses lanthanide chelates (e.g. Eu^{3+}) as labels instead of enzymes or conventional fluorophores. The key analytical advantage of lanthanide labels over conventional fluorescent labels is:

(A) Lanthanide chelates have extremely long fluorescence lifetimes (100 μs–1 ms) compared to background autofluorescence ($<$10 ns); time-gating completely eliminates background signal, giving detection limits of 10^{-13}–10^{-15} mol/L

(B) Lanthanide labels are far cheaper than enzyme conjugates (HRP, AP), reducing the cost per assay

(C) Lanthanide ions amplify the signal by acting as enzymatic catalysts similar to HRP

(D) Lanthanide chelates emit at UV wavelengths ($<$300 nm), avoiding interference from visible-range sample components

Q36. β-Lactam antibiotics (penicillins, cephalosporins, carbapenems) kill bacteria by inhibiting cell-wall synthesis. Which of the following correctly describes both the **mechanism of action** and a major **resistance mechanism**?

(A) β-Lactams inhibit the 30S ribosomal subunit; resistance occurs through ribosomal methylation (erm genes)

(B) β-Lactams acylate the active-site serine of penicillin-binding proteins (PBPs/transpeptidases), blocking peptidoglycan cross-linking; resistance occurs via β-lactamase hydrolysis of the β-lactam ring or acquisition of low-affinity PBP2a (mecA – MRSA)

(C) β-Lactams chelate magnesium ions required for DNA gyrase; resistance is via gyrase mutations

(D) β-Lactams disrupt the cytoplasmic membrane; resistance occurs through lipid A modification reducing membrane permeability

Q37. Azole antifungals (fluconazole, voriconazole, itraconazole) are widely used to treat Candida and Aspergillus infections. Their **primary molecular target** in fungal cells is:

(A) β-1,3-glucan synthase (the target of echinocandins, not azoles)

(B) Ergosterol itself (direct membrane disruption, the mechanism of polyene antifungals such as amphotericin B)

(C) Lanosterol 14α-demethylase (CYP51), a cytochrome P450 enzyme in the ergosterol biosynthesis pathway; azole nitrogen coordinates the heme iron, depleting ergosterol and causing accumulation of toxic sterol intermediates

(D) Dihydropteroate synthase in the fungal folate synthesis pathway (the target of sulfonamides)

Q38. Acyclovir (ACV) is highly effective against herpes simplex virus (HSV) and varicella-zoster virus (VZV) but has minimal toxicity to uninfected host cells. This selective toxicity depends critically on which **initial activation step**?

(A) Phosphorylation of ACV by host cellular kinases, which are present at higher levels in virally infected cells

(B) Spontaneous chemical activation of ACV's acyclic sugar moiety in the acidic environment of the HSV replication compartment

(C) ACV is directly inserted into viral DNA without activation; its selectivity arises because viral DNA polymerase has a higher affinity for ACV

than host DNA polymerase

(D) Phosphorylation of ACV to ACV-monophosphate by the **viral thymidine kinase (TK)**, which is encoded by HSV/VZV and absent in uninfected cells; subsequent phosphorylation to the triphosphate by host kinases yields the active chain-terminating form

Q39. Nucleoside reverse transcriptase inhibitors (NRTIs) such as zidovudine (AZT) act as chain terminators of HIV reverse transcription. What structural feature of AZT is responsible for chain termination, and what cellular step is required before AZT becomes pharmacologically active?

(A) AZT has a 3'-azido ($-N_3$) group replacing the normal 3'-OH; this prevents formation of the 3'$\rightarrow$5' phosphodiester bond needed for chain elongation; cellular kinases must first phosphorylate AZT to AZT-triphosphate

(B) AZT intercalates into double-stranded DNA, blocking the RT polymerase; no activation is required

(C) AZT covalently alkylates the active-site cysteine of RT, irreversibly inactivating it; no phosphorylation is needed

(D) AZT binds the RNA primer/template junction of RT and prevents $tRNA^{Lys3}$ from priming; phosphorylation by viral protease activates AZT

Q40. HIV aspartyl protease cleaves the Gag and Gag-Pol polyproteins during virion maturation. HIV protease inhibitors prevent this cleavage. Which of the following describes the **consequence** of protease inhibition during HIV infection?

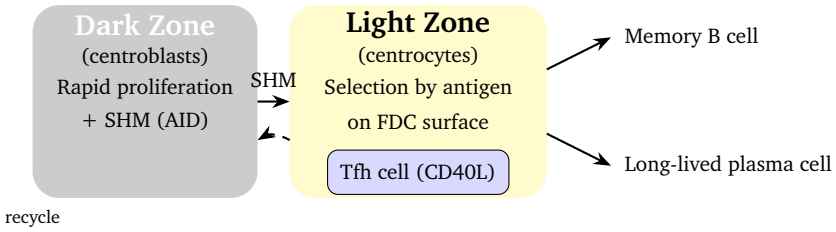
(A) Viral RNA cannot be reverse transcribed; no proviral DNA is formed

(B) The gp120/gp41 envelope glycoproteins are not processed; virions cannot fuse with new target cells

(C) Immature, non-infectious virus particles are produced because Gag-Pol polyprotein is not cleaved into functional structural proteins (capsid, matrix, nucleocapsid) and enzymes (RT, integrase, protease)

(D) Viral integrase is inactivated; the proviral DNA cannot integrate into the host chromosome

Q41. The germinal centre (GC) reaction is the site of affinity maturation of B cells. The GC has two functional zones. The diagram below schematises the GC.



Which of the following correctly describes the **fate of centrocytes with high-affinity BCR** in the light zone?

(A) High-affinity centrocytes immediately undergo apoptosis to remove the highest-affinity clones (negative selection)

(B) High-affinity centrocytes downregulate all surface receptors and re-enter the dark zone unconditionally for further SHM

(C) High-affinity centrocytes home to the bone marrow to become short-lived plasma cells that provide immediate but transient antibody

(D) High-affinity centrocytes receive survival signals (CD40L from Tfh, antigen from FDC) and either exit as memory B cells/long-lived plasma cells or recycle to the dark zone for additional SHM rounds

Q42. Activation-induced cytidine deaminase (AID) is essential for both somatic hypermutation (SHM) and class switch recombination (CSR). The **biochemical activity** of AID and its **primary substrate** are:

(A) AID deaminates cytosine to uracil in single-stranded DNA exposed by transcription at immunoglobulin V-region loci (SHM) and switch regions (CSR)

(B) AID is an endonuclease that introduces double-strand breaks directly at consensus recombination signal sequences (RSS) flanking V_H, D, and J_H gene segments

(C) AID methylates CpG dinucleotides in the immunoglobulin locus to increase transcription and accessibility

(D) AID is a helicase that unwinds G-quadruplex structures in switch regions to facilitate CSR

Q43. Cytokine signals provided by T helper cells instruct B cells which immunoglobulin isotype to switch to. Which of the following cytokine–isotype switch relationships is **correct** in humans?

(A) IFN-γ drives switching to IgE; IL-4 drives switching to IgG1/IgG3

(B) IL-4 (together with CD40L) drives switching to IgE and IgG4 (Th2 response); TGF-β drives switching to IgA (mucosal immunity); IFN-γ drives switching to IgG1/IgG3 (Th1)

(C) TGF-β exclusively drives switching to IgE; IL-4 exclusively drives switching to IgA

(D) IL-12 drives switching to IgE; IL-10 drives switching to IgG4; IFN-α drives switching to IgA

Q44. Long-lasting humoral immunity after vaccination depends on two distinct B cell compartments. Which of the following correctly distinguishes **memory B cells** from **long-lived plasma cells (LLPCs)**?

(A) Memory B cells continuously secrete high-affinity IgG; LLPCs do not secrete antibody but are poised for rapid proliferation on re-exposure

(B) Both memory B cells and LLPCs secrete antibody continuously; they are distinguished only by anatomical location (spleen vs. bone marrow)

(C) Memory B cells are long-lived, express surface BCR ($CD27^{+}$), do **not** secrete antibody constitutively, and rapidly proliferate/differentiate on re-exposure; LLPCs are terminally differentiated, lack surface BCR, and constitutively secrete antibody (maintained by APRIL/BAFF in bone marrow niches)

(D) Memory B cells are short-lived ($<$1 month); LLPCs divide approximately once per week to maintain antibody levels

Q45. Somatic hypermutation (SHM) produces point mutations at the immunoglobulin V-region at a rate $\sim 10^6$-fold above background. AID deaminates C→U in the V-region DNA. If the resulting U is processed by the mismatch repair pathway (MSH2/MSH6 recognising the U:G mispair) followed by error-prone polymerase η, what types of mutations are preferentially generated?

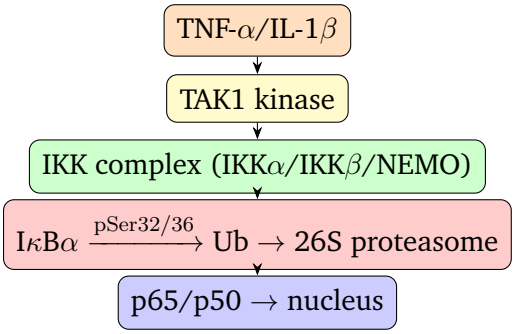
(A) Only C→T transitions, because uracil is simply read as thymine during the next replication cycle

(B) Only G→C transversions at GC base pairs, because MSH2 exclusively removes G from G:U mispairs

(C) Only insertions and deletions (indels) at WRCY hotspot motifs, because Pol η introduces frameshift mutations

(D) Mutations at A:T base pairs as well as C:G pairs in AGCT (WRC) hotspot motifs, because Pol η performs error-prone synthesis across the MMR-generated patch surrounding the original AID deamination site

Q46. The canonical NF-κB pathway is activated by pro-inflammatory stimuli such as TNF-α, IL-1β, and LPS. The key regulatory step controlling NF-κB nuclear translocation is shown in the simplified diagram below.



Which of the following statements about this pathway is **correct**?

(A) IKKβ phosphorylates p65 directly in the nucleus to enhance DNA binding

(B) IKKβ (the catalytic subunit) phosphorylates IκBα at Ser32/Ser36, targeting it for K48-linked polyubiquitination and proteasomal degradation, thereby releasing p65/p50 for nuclear translocation

(C) NEMO (IKKγ) is the catalytic kinase subunit that directly phosphorylates IκBα

(D) p65/p50 is retained in the cytoplasm by direct association with TAK1; TNF signalling dissociates this complex

Q47. NF-κB is a master transcription factor for inflammation. Constitutive (inappropriate) NF-κB activation drives the growth and survival of several B cell malignancies. Which of the following correctly identifies a **direct NF-κB target gene** and explains its role in oncogenesis?

(A) PTEN: NF-κB directly activates the PTEN tumour suppressor, leading to PI3K pathway suppression

(B) p53: NF-κB transcribes p53, which induces apoptosis; constitutive NF-κB therefore promotes cell death

(C) Bcl-2/Bcl-xL/XIAP: NF-κB drives transcription of anti-apoptotic genes, conferring survival advantage to tumour cells; and IKKα/IKKβ mutations or upstream activators (e.g. MyD88 L265P in DLBCL) that constitutively activate NF-κB are found in many B cell lymphomas

(D) Rb (retinoblastoma protein): NF-κB transcribes Rb, blocking cell cycle entry at the G1/S checkpoint

Q48. The non-canonical NF-κB pathway is activated by BAFF, LTβ, and CD40L, and is important for B cell survival and lymphoid organogenesis. A key difference from the canonical pathway is:

(A) The non-canonical pathway requires NEMO (IKKγ) and IKKβ for signal transmission, identical to the canonical pathway

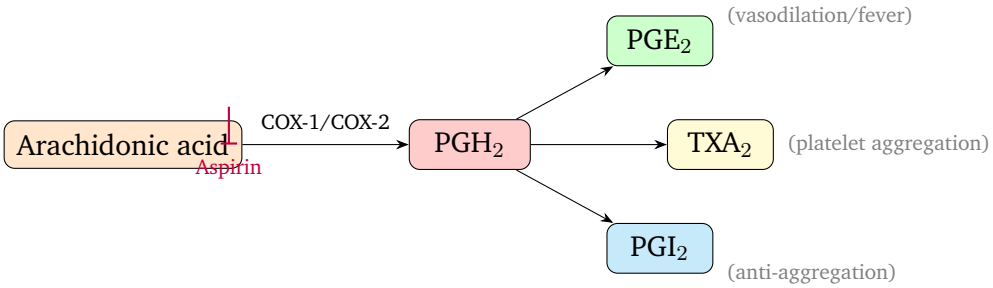
(B) The non-canonical pathway activates p65/p50 heterodimers via IKKβ-mediated IκBα degradation, identical to the canonical pathway

(C) The non-canonical pathway is activated exclusively by viral infections (EBV, HTLV-1) and uses a completely distinct set of adapter proteins

(D) In the non-canonical pathway, NF-κB-inducing kinase (NIK) accumulates and activates an IKKα homodimer, which phosphorylates p100 (not IκBα); p100 is then partially processed by the proteasome to

p52; the p52/RelB dimer translocates to the nucleus

Q49. Cyclooxygenase (COX) enzymes catalyse the committed step in prostaglandin/thron synthesis from arachidonic acid. The pathway is shown below.



Which statement about COX-1 and COX-2 inhibition is **correct**?

(A) Aspirin irreversibly acetylates both COX-1 and COX-2; selective inhibition of COX-2 (e.g. rofecoxib) reduces prostaglandin-mediated inflammation without eliminating platelet TXA_2 (COX-1-derived), but may increase cardiovascular risk by leaving endothelial PGI_2 synthesis (also COX-2-dependent) unopposed

(B) COX-2 is constitutively expressed in all cells (including platelets) and is the primary source of TXA_2 for platelet aggregation

(C) Aspirin reversibly inhibits both COX enzymes by competitive blockade of the arachidonate binding channel

(D) COX-1 selective inhibitors (e.g. SC-560) are used clinically as the safest NSAIDs with fewest GI side effects

Q50. The NLRP3 inflammasome is a multi-protein complex that activates caspase-1. Assembly of NLRP3 inflammasome requires a **two-signal model**. Which of the following correctly describes both signals and the downstream consequences of NLRP3 activation?

(A) Signal 1: potassium efflux (direct NLRP3 activation); Signal 2: NF-κB activation and NLRP3 transcription; downstream: caspase-8 activation and extrinsic apoptosis only

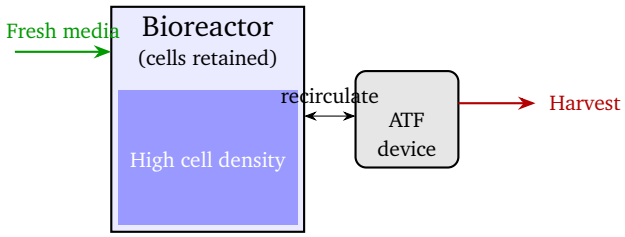
(B) Signal 1 (priming): NF-κB-mediated transcription of pro-IL-1β and NLRP3; Signal 2 (activation): danger signals (K^+ efflux, ATP, uric acid

crystals, cholesterol) trigger NLRP3 oligomerisation $\rightarrow$ ASC speck $\rightarrow$ caspase-1 activation $\rightarrow$ IL-1β/IL-18 maturation + GSDMD cleavage $\rightarrow$ pyroptotic pores $\rightarrow$ inflammatory cell death

(C) Signal 1: GSDMD cleavage by caspase-3; Signal 2: IL-1β secretion activates NLRP3 from outside the cell; downstream: apoptosis with membrane blebbing

(D) Signal 1: RIG-I sensing of viral dsRNA; Signal 2: NLRP3 is activated by interferon-stimulated genes; downstream: interferon-β secretion and antiviral state

Q51. Perfusion cell culture enables very high cell densities for monoclonal antibody (mAb) manufacturing. The diagram below shows the principle of an alternating tangential flow (ATF) perfusion system. Compared to standard fed-batch culture, a key **advantage** of perfusion is:



(A) Lower media consumption compared to fed-batch (perfusion always uses less media per litre of product)

(B) Simpler process control because cell density is self-limiting in perfusion (no fouling risk)

(C) Achieves 10$\times$ or higher viable cell densities (10^7–10^8 cells/mL) compared to fed-batch; smaller bioreactor footprint for equivalent volumetric productivity; continuous product harvest minimises product degradation

(D) Perfusion is suitable for all products including intracellular proteins, since cell lysis occurs at the ATF membrane

Q52. In an intensified biopharmaceutical manufacturing process, the N-1 bioreactor is the **final inoculum culture** immediately preceding the production (N) bioreactor. What is the primary **benefit** of running the N-1 bioreactor

in high-density perfusion mode and using it to inoculate the production bioreactor at a high seeding density?

(A) It eliminates the need for a production bioreactor entirely, because the N-1 perfusion culture IS the production culture

(B) It reduces the number of seed train steps because each cell doubles faster in perfusion mode

(C) It allows use of animal-derived media components that are normally prohibited in the production bioreactor

(D) A high-density N-1 inoculum seeds the production bioreactor at $\geq 5 \times 10^6$ cells/mL, shortening the time to peak cell density, increasing productivity, and reducing the number of overall seed train steps needed

Q53. The Quality by Design (QbD) framework (ICH Q8/Q9/Q10) applied to biopharmaceutical cell culture involves identifying Critical Quality Attributes (CQAs) and Critical Process Parameters (CPPs). Which of the following correctly defines these two concepts and their relationship?

(A) CQAs are product attributes (e.g. glycan profile, aggregation level, potency) important to safety and efficacy; CPPs are process inputs (e.g. pH, temperature, feeding rate) whose variation impacts CQAs when outside their acceptable range; Design of Experiments (DoE) maps CPP–CQA relationships to define the Design Space

(B) CQAs are real-time process measurements (online sensors); CPPs are the product quality targets defined in the regulatory submission

(C) CQAs and CPPs are synonymous terms for any parameter monitored in a bioreactor run

(D) CPPs are determined by the final drug product clinical trials; CQAs are set by the equipment manufacturer

Q54. The N-glycan profile of a monoclonal antibody is a Critical Quality Attribute (CQA) because glycosylation affects Fc effector function and pharmacokinetics. Which cell culture parameter manipulation can **increase the galactosylation** of an IgG1 mAb?

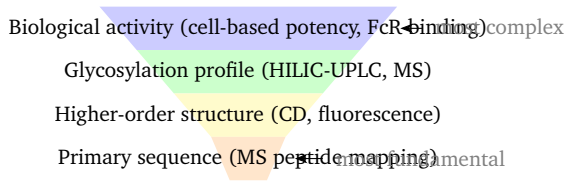
(A) Increasing dissolved CO_2 (pCO_2) above 150 mmHg in the production bioreactor

(B) Supplementation of the cell culture medium with manganese (Mn^{2+}), which is a cofactor for β-1,4-galactosyltransferase in the Golgi

(C) Increasing the ammonia concentration by reducing glutamine feeding; ammonia shifts Golgi pH and promotes galactosylation

(D) Running the bioreactor at reduced temperature (29°C) to decrease metabolic activity and increase galactosylation

Q55. Biopharmaceutical product characterisation requires multiple analytical techniques at different levels of structural complexity. A funnel diagram summarises these layers.



The ICH Q6B guideline requires demonstration of comparability after a manufacturing change. Which analytical combination is most appropriate to assess **higher-order structure (HOS)** comparability?

(A) SDS-PAGE under reducing conditions (to check primary sequence integrity) and ELISA (to check binding)

(B) SEC-HPLC (size-exclusion chromatography) to assess charge variants and IEX-HPLC to assess aggregates

(C) Circular dichroism (CD) spectroscopy (secondary structure content) and intrinsic tryptophan fluorescence (tertiary fold); supported by hydrogen-deuterium exchange MS (HDX-MS) or NMR for detailed HOS mapping

(D) Capillary isoelectric focusing (cIEF) alone is sufficient for full HOS characterisation

Q56. During poly(A)-selected RNA-seq library preparation, after mRNA fragmentation and reverse transcription, the cDNA molecules must be pre-

pared for adaptor ligation. Which of the following is the **correct sequence** of enzymatic steps between double-stranded cDNA synthesis and final PCR amplification?

(A) Adaptor ligation $\rightarrow$ end repair + A-tailing $\rightarrow$ size selection $\rightarrow$ PCR

(B) End repair (blunt ends) $\rightarrow$ 3′-A overhang addition $\rightarrow$ adaptor ligation $\rightarrow$ AMPure bead size selection $\rightarrow$ PCR amplification

(C) Size selection $\rightarrow$ end repair $\rightarrow$ PCR amplification $\rightarrow$ adaptor ligation

(D) A-tailing $\rightarrow$ size selection $\rightarrow$ adaptor ligation $\rightarrow$ end repair $\rightarrow$ PCR

Q57. When aligning RNA-seq reads to a reference genome, reads that originate from spliced mRNAs span exon–exon junctions and cannot be aligned as a continuous block to the genome. Which aligner is specifically designed as a **splice-aware aligner** for this purpose, and what is an alternative pseudoalignment approach?

(A) BWA-MEM and Bowtie2 (both splice-aware); pseudoalignment alternative is STAR

(B) TopHat2 (splice-aware); pseudoalignment is BLAST

(C) STAR (Spliced Transcripts Alignment to a Reference) and HISAT2 (splice-aware genome aligners); pseudoalignment alternatives are kallisto and salmon (align reads to a transcriptome index using quasi-mapping, faster but require a known transcriptome)

(D) STAR (splice-aware); the only pseudoalignment alternative is featureCounts

Q58. Normalisation of RNA-seq count data is essential for valid comparisons between samples. Which of the following statements about **TPM (transcripts per million)** is **correct** and why is it preferred over RPKM/FPKM for between-sample comparisons?

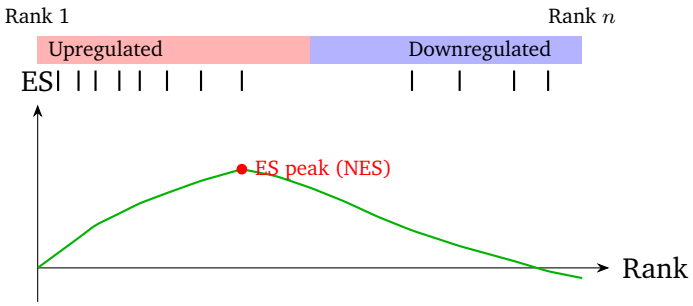
(A) TPM normalises only by library size (total mapped reads), ignoring gene length; it is preferred because gene length effects are negligible for short-read RNA-seq

(B) TPM and RPKM are mathematically identical; the difference is only in the name used by different tools

(C) TPM is calculated by first normalising for library size (RPM), then for gene length; this is identical to FPKM and both can be used interchangeably across samples

(D) TPM is calculated by first normalising each gene's count by its length (reads per kilobase, RPK), then dividing by the sum of all RPK values in the sample $\times 10^6$; this ensures that the sum of all TPM values is always 10^6, making all samples directly comparable, unlike RPKM/FPKM whose sum varies across samples

Q59. Gene Set Enrichment Analysis (GSEA) tests whether predefined gene sets (pathways, GO terms) are enriched at the top or bottom of a ranked gene list. The key diagram produced by GSEA is the **enrichment plot**, shown schematically below.



Which of the following best describes a key **advantage** of GSEA over traditional over-representation analysis (ORA)?

(A) GSEA does not require a pre-ranked gene list and can analyse raw count data directly without normalisation

(B) ORA uses all genes in the ranked list without any significance cutoff; GSEA requires an arbitrary fold-change cutoff to define the foreground gene set

(C) GSEA requires an arbitrary fold-change cutoff identical to ORA and its advantage is purely computational speed

(D) GSEA uses all genes ranked by a continuous score (fold change, signal-to-noise ratio) without requiring an arbitrary significance cutoff, mak-

ing it more sensitive to coordinated moderate changes across all genes in a pathway compared to ORA, which analyses only a foreground list defined by an arbitrary threshold

Q60. RNA velocity analysis (La Manno et al.; Bergen et al.) can infer the **future transcriptional state** of individual cells in a scRNA-seq dataset. On which molecular measurement is RNA velocity based?

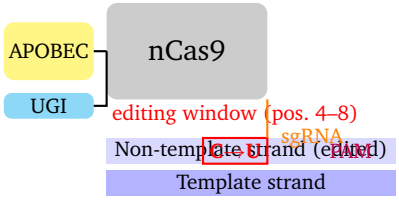
(A) The ratio of protein abundance (measured by CITE-seq antibody tags) to mRNA abundance for each gene

(B) The ratio of **unspliced pre-mRNA** to **spliced mRNA** for each gene: a high unspliced:spliced ratio indicates that transcription is currently *active* and the cell is likely to express more of that gene in the future; a low ratio indicates transcriptional silencing and declining expression, providing directional arrows on a UMAP/embedding

(C) The correlation between spliced mRNA levels and chromatin accessibility (ATAC-seq) at each gene's promoter

(D) The difference between nuclear mRNA abundance and cytoplasmic mRNA abundance, measured by nuclear-cytoplasmic RNA fractionation followed by sequencing

Q61. Cytosine base editors (CBEs) enable precise C→T (or G→A on the complementary strand) conversions without double-strand DNA breaks. The schematic below shows the CBE complex.



Which of the following correctly describes the **role of UGI** (uracil DNA glycosylase inhibitor) in the CBE system?

(A) UGI enhances the deaminase activity of APOBEC, increasing the rate of C→U conversion in the editing window

(B) UGI recruits the base excision repair machinery to efficiently correct the U:G mismatch back to C:G (i.e. it promotes faithful repair, reducing indels)

(C) UGI inhibits uracil DNA glycosylase (UNG), preventing removal of the uracil intermediate before DNA replication; this allows U to be read as T during replication, completing the C→T conversion without generating an abasic site and minimising indels

(D) UGI serves as the structural linker between APOBEC and nCas9 and has no enzymatic function

Q62. Adenine base editors (ABEs) convert A·T to G·C base pairs at targeted genomic loci. The adenosine deaminase component of ABEs (evolved TadA) deaminates adenine to inosine (I) in ssDNA within the editing window. Why is inosine functionally equivalent to guanine in this context, and which mutation types can ABEs correct?

(A) Inosine is read as adenine during replication, converting A·T to T·A (transversion); ABEs are used to correct G→T mutations

(B) Inosine is recognised and removed by inosine-specific glycosylases, generating a strand break that initiates HDR-mediated correction using a supplied donor template

(C) Inosine pairs with adenine (I:A), so after replication one daughter cell retains A:T and the other gains A:T as well; no net change occurs without a donor template

(D) Inosine is read as guanine (G) by DNA polymerases during replication; after replication, the original A·T pair becomes G·C; ABEs can therefore correct pathogenic A→G (on sense strand) or T→C (on antisense strand) point mutations, covering a large fraction of known disease-causing SNVs

Q63. Prime editing (Anzalone et al., 2019) can introduce all 12 types of point mutations, small insertions, and small deletions without requiring double-strand breaks or donor DNA templates. The key component unique to prime editing (beyond nCas9) is the **pegRNA**. What does the 3′ extension

of a pegRNA encode?

(A) A primer binding site (PBS) complementary to the nicked strand, and a reverse transcriptase template (RTT) encoding the desired edit; together they allow the engineered RT (fused to nCas9) to synthesise new DNA with the intended sequence at the cut site

(B) A polyadenylation signal that stabilises the pegRNA in the nucleus and prevents its degradation by the RNA exosome

(C) An aptamer sequence that recruits endogenous HDR factors (RAD51, BRCA2) to the cut site to stimulate template-directed repair

(D) A guide sequence targeting a second genomic locus (dual-guide strategy) used to nick the complementary strand, which is required for converting the 3′ flap to a 5′ flap

Q64. CRISPR-based transcriptional regulation uses a catalytically dead Cas9 (dCas9) fused to transcriptional effector domains. Which of the following correctly describes **CRISPRi (interference)** and its mechanism of gene silencing?

(A) CRISPRi uses dCas9 fused to VP64-p65-Rta (VPR) transcriptional activators targeted to the promoter of the gene to be silenced

(B) CRISPRi uses dCas9 fused to the KRAB (Krüppel-associated box) repressor domain; when targeted to a gene's promoter or TSS, KRAB recruits KAP1/TRIM28, which then deposits H3K9me3 repressive histone marks, leading to heterochromatin formation and transcriptional silencing of up to 1000-fold; the silencing is reversible because no permanent DNA change is made

(C) CRISPRi directly cleaves the target gene's mRNA using the Cas9 nuclease activity retained in the dCas9 fusion

(D) CRISPRi uses dCas9 fused to TET1 (DNA demethylase) to remove CpG methylation from the target promoter, activating (not silencing) gene expression

Q65. Epigenome editing tools fuse dCas9 to chromatin-modifying enzymes to

alter gene expression without changing the DNA sequence. Researchers want to **reactivate a silenced tumour suppressor gene** whose promoter CpGs are hypermethylated. Which dCas9 fusion protein would be most appropriate?

(A) dCas9–DNMT3A (DNA methyltransferase): adds CpG methylation, which would further silence the already hypermethylated tumour suppressor

(B) dCas9–EZH2 (histone methyltransferase): deposits H3K27me3 repressive marks, maintaining silencing

(C) dCas9–TET1 (catalytic domain): catalyses oxidation of 5-methylcytosine (5mC) $\rightarrow$ 5-hydroxymethylcytosine (5hmC) $\rightarrow$ ultimately unmethylated C; targeted CpG demethylation at the hypermethylated promoter reactivates the tumour suppressor gene

(D) dCas9–LSD1 (KDM1A, histone H3K4 demethylase): removes active enhancer marks H3K4me1/me2, which would inactivate nearby enhancers and potentially reduce (not increase) expression

Detailed Solutions

Sol. 1.

Solution

Concept — Angular Momentum Conservation | Chapter: Rotational Motion: In the absence of external torques, the total angular momentum $L = I\omega$ is conserved. When a spinning skater pulls her arms inward, her moment of inertia decreases, so her angular velocity must increase proportionally.

Step 1 — Apply conservation of angular momentum:

$$L_1 = L_2 \implies I_1\omega_1 = I_2\omega_2$$

$$\omega_2 = \frac{I_1\omega_1}{I_2} = \frac{4 \times 5}{2} = \frac{20}{2} = 10\,\text{rad/s}$$

Why other options are wrong:

- Option A: Correct — $\omega_2 = 10\,\text{rad/s}$.
- Option B: $5\,\text{rad/s}$ would mean no change; this would only be true if I were unchanged.
- Option C: $2.5\,\text{rad/s}$ would imply ω decreased, violating conservation when I decreases.
- Option D: $20\,\text{rad/s}$ would require $I_2 = 1\,\text{kg}\cdot\text{m}^2$, not the stated value.

Final Answer: $\omega_2 = 10\,\text{rad/s} \Rightarrow \boxed{\text{A}}$

Answer: (A) Go Back to Q 1

Sol. 2.

Solution

Concept — Oxidation of Alcohols | Chapter: Organic Chemistry — Alcohols: Primary alcohols are oxidised to aldehydes (mild conditions) or carboxylic acids (excess oxidant); secondary alcohols are oxidised to ketones; tertiary alcohols resist oxidation. Butan-2-ol is a secondary alcohol (OH on C2).

Step 1 — Identify the substrate: Butan-2-ol: $CH_3CH(OH)CH_2CH_3$ — secondary alcohol.

Step 2 — Determine product with $K_2Cr_2O_7/H^+$: Secondary alcohol + Cr(VI) $\rightarrow$ ketone; cannot be further oxidised to carboxylic acid (no C–H on the carbonyl carbon). Product: butanone ($CH_3COCH_2CH_3$).

Why other options are wrong:

- Option A: Butanal would arise from oxidation of a primary alcohol (butan-1-ol), not a secondary alcohol.
- Option B: Correct — butanone (ketone) is the product from a secondary alcohol.
- Option C: Carboxylic acid cannot be obtained from a secondary alcohol; it requires a primary alcohol.
- Option D: Tertiary alcohols resist oxidation; butan-2-ol is secondary and does react.

Final Answer: Butanone (ketone) $\Rightarrow$ B

Answer: (B) Go Back to Q 2

Sol. 3.

Solution

Concept — Bayes' Theorem / Positive Predictive Value | Chapter: Probability & Statistics: PPV is the probability that a positive test truly indicates disease. At low disease prevalence, PPV is dominated by the false-positive rate even when sensitivity is high (base-rate fallacy).

Step 1 — Set up the values: Sensitivity $= P(+|D) = 0.95$; Specificity $= P(-|\bar{D}) = 0.90$; Prevalence $= P(D) = 0.01$.

Step 2 — Calculate PPV using Bayes' theorem:

$$P(D|+) = \frac{0.95 \times 0.01}{(0.95 \times 0.01) + (0.10 \times 0.99)} = \frac{0.0095}{0.0095 + 0.099} = \frac{0.0095}{0.1085} \approx 8.7\%$$

Why other options are wrong:

- Option A: 50% ignores the very low prevalence; this intuitive guess is far too high.
- Option B: 85% is close to the sensitivity value but ignores the base rate.
- Option C: Correct — PPV $\approx 8.7\%$; most positives are false positives at 1% prevalence.
- Option D: 95% equals the sensitivity value; this confuses sensitivity with PPV.

Final Answer: PPV $\approx 8.7\% \Rightarrow$ C

Answer: (C) Go Back to Q 3

Sol. 4.

Solution

Concept — Van der Waals Parameter a | Chapter: States of Matter / Real Gases: The parameter a in $(P + a/V^2)(V - b) = nRT$ corrects for intermolecular attractive forces. Gases with stronger intermolecular attractions (dispersion, dipole–dipole, hydrogen bonding) have larger a values.

Step 1 — Compare intermolecular forces: He: noble gas, negligible dispersion forces ($a = 0.034\,\mathrm{L^2 \cdot atm \cdot mol^{-2}}$); H_2: nonpolar diatomic, very small ($a = 0.244$); N_2: larger nonpolar molecule ($a = 1.39$); H_2O: strong hydrogen bonding AND dipole–dipole AND dispersion ($a = 5.54$, the highest among common gases).

Why other options are wrong:

- Option A: He has the smallest a value; virtually no intermolecular forces.
- Option B: H_2 has only weak dispersion forces; a is very small.
- Option C: N_2 has moderate dispersion forces; a is intermediate.
- Option D: Correct — H_2O has the largest a due to extensive hydrogen bonding and permanent dipole.

Final Answer: H_2O has the highest a value $\Rightarrow$ D

Answer: (D) Go Back to Q 4

Sol. 5.

Solution

Concept — Distance from a Point to a Line | Chapter: Coordinate Geometry: The perpendicular distance from point (x_1, y_1) to line $ax + by + c = 0$ is $d = |ax_1 + by_1 + c|/\sqrt{a^2 + b^2}$.

Step 1 — Identify parameters: Point $(3, 4)$; line $3x + 4y - 10 = 0$; so $a = 3$, $b = 4$, $c = -10$.

Step 2 — Substitute:

$$d = \frac{|3(3) + 4(4) - 10|}{\sqrt{3^2 + 4^2}} = \frac{|9 + 16 - 10|}{\sqrt{9 + 16}} = \frac{|15|}{\sqrt{25}} = \frac{15}{5} = 3$$

Why other options are wrong:

- Option A: Correct — $d = 3$.
- Option B: $5 = \sqrt{a^2 + b^2}$; this is the denominator, not the distance.
- Option C: $15/\sqrt{7}$ uses an incorrect denominator $\sqrt{7}$ instead of $\sqrt{25} = 5$.
- Option D: $3/5$ inverts the numerator and denominator in the formula.

Final Answer: Distance $= 3 \Rightarrow$ A

Answer: (A) Go Back to Q 5

Sol. 6.

Solution

Concept — Chelate Effect and EDTA Stability | Chapter: Coordination Chemistry: The chelate effect explains why polydentate ligands form far more stable complexes than the equivalent number of monodentate ligands. The dominant thermodynamic contribution is entropy.

Step 1 — Entropy argument: One EDTA molecule (hexadentate) replaces 6 individual water molecules (or monodentate ligands) bound to the metal. This releases 6 molecules into solution for each 1 EDTA molecule that binds, giving a large positive ΔS and thus a more negative $\Delta G = \Delta H - T\Delta S$, dramatically increasing $K_{stability}$.

Why other options are wrong:

- Option A: Charge density is relevant but does not specifically explain why EDTA is so much more stable than six acetate ions.
- Option B: Correct — the large positive entropy gain from releasing 6 individual ligands drives the chelate effect.
- Option C: π-back-bonding requires low-oxidation-state metals and involves d-orbitals; EDTA forms complexes with main-group and high-valent transition metals where this does not apply.
- Option D: EDTA complexes are coordinate (dative) bonds, not truly covalent; this does not explain the differential stability.

Final Answer: The chelate effect (entropy-driven) $\Rightarrow$ B

Answer: (B) Go Back to Q 6

Sol. 7.

Solution

Concept — Barr Bodies and X-Inactivation | Chapter: Human Genetics: In female mammals, all X chromosomes beyond one are inactivated (Lyon hypothesis). The number of Barr bodies $= n(X) - 1$.

Step 1 — Apply the rule to 47, XXY (Klinefelter syndrome): $n(X) = 2$; Barr bodies $= 2 - 1 = 1$.

Why other options are wrong:

- Option A: 0 Barr bodies is seen in normal males (46, XY) and Turner syndrome (45, X0).
- Option B: 2 Barr bodies would be seen in 47, XXX females ($n(X) = 3$).
- Option C: Correct — 47, XXY has 2 X chromosomes, so $2 - 1 = 1$ Barr body.
- Option D: 3 Barr bodies would require 4 X chromosomes (e.g. 48, XXXX).

Final Answer: 1 Barr body $\Rightarrow$ C

Answer: (C) Go Back to Q 7

Sol. 8.

Solution

Concept — Circular Motion of a Charged Particle in a Magnetic Field | Chapter: Electromagnetism / Magnetism: When a charged particle moves perpendicular to a uniform magnetic field, the Lorentz force $F = qvB$ acts as centripetal force.

Step 1 — Equate Lorentz force and centripetal force:

$$qvB = \frac{m_p v^2}{r} \implies r = \frac{m_p v}{qB}$$

Why other options are wrong:

- Option A: $r = qB/(m_p v)$ inverts the relationship; r would decrease with increasing mass.
- Option B: $r = qBv/m_p$ is dimensionally incorrect (gives acceleration $\times$ charge/mass).
- Option C: $r = m_p B/(qv)$ has v in the denominator; radius would decrease as velocity increases (wrong).

- Option D: Correct — $r = m_p v/(qB)$; radius increases with momentum and decreases with field strength.

Final Answer: $r = m_p v/(qB) \Rightarrow$ D

Answer: (D) Go Back to Q 8

Sol. 9.

Solution

Concept — Area Between Two Curves | Chapter: Integral Calculus: The area between $y = f(x)$ (upper curve) and $y = g(x)$ (lower curve) from $x = a$ to $x = b$ is $\int_a^b [f(x) - g(x)]\,dx$.

Step 1 — Identify limits and upper/lower curves: Curves $y = x$ and $y = x^2$ intersect at $x = 0$ and $x = 1$. On $[0, 1]$, $x \geq x^2$, so upper curve is $y = x$.

Step 2 — Evaluate the integral:

$$A = \int_0^1 (x - x^2)\,dx = \left[\frac{x^2}{2} - \frac{x^3}{3}\right]_0^1 = \frac{1}{2} - \frac{1}{3} = \frac{3-2}{6} = \frac{1}{6}$$

Why other options are wrong:

- Option A: Correct — Area $= 1/6$.
- Option B: $1/3$ would result from integrating $y = x$ alone from 0 to 1 ($[x^2/2]_0^1 = 1/2$) or from an arithmetic error.
- Option C: $1/2 = \int_0^1 x\,dx$ is the area under $y = x$ alone, not between the two curves.
- Option D: $1/12$ is half the correct answer, arising from incorrectly halving the integral.

Final Answer: Area $= 1/6 \Rightarrow$ A

Answer: (A) Go Back to Q 9

Sol. 10.

Solution

Concept — Le Chatelier's Principle Applied to the Haber Process | Chapter: Chemical Equilibrium: The Haber process equilibrium $N_2 + 3H_2 \rightleftharpoons 2NH_3$ ($\Delta H = -92\,\text{kJ/mol}$) responds to changes in temperature and pressure as predicted by Le Chatelier's principle.

Step 1 — Effect of pressure: The forward reaction produces 2 moles of gas from 4 moles (4 reactant molecules $\rightarrow$ 2 product molecules). Increasing pressure shifts equilibrium toward fewer gas moles (right), increasing NH_3 yield.

Step 2 — Effect of temperature: The forward reaction is exothermic ($\Delta H < 0$). Increasing temperature shifts equilibrium left (endothermic direction), decreasing NH_3 equilibrium yield. Industrially, a compromise temperature ($\sim$450°C) balances yield and reaction rate.

Why other options are wrong:

- Option A: Increasing temperature does NOT increase equilibrium yield; it decreases it.
- Option B: Correct — increased pressure increases yield; increased temperature decreases yield.
- Option C: Increased pressure does not decrease NH_3 yield; it increases it.
- Option D: Temperature does affect gas-phase equilibria; the ideal gas approximation does not negate Le Chatelier.

Final Answer: Pressure increases yield; temperature decreases yield $\Rightarrow$ $\boxed{\text{B}}$

Answer: (B) Go Back to Q 10

Sol. 11.

Solution

Concept — MO Theory: Bond Order and Magnetic Properties of O_2 | Chapter: Chemical Bonding / MO Theory: Molecular orbital theory assigns electrons to bonding and antibonding MOs. Bond order = (bonding – antibonding)/2. Unpaired electrons confer paramagnetism.

Step 1 — Electron configuration of O_2 (16 electrons): $(\sigma_{1s})^2(\sigma^*_{1s})^2(\sigma_{2s})^2(\sigma^*_{2s})^2(\sigma_{2p})^2(\pi_{2p})^4(\pi^*_{2p})^2$

Step 2 — Calculate bond order: Bonding electrons $= 2 + 2 + 2 + 4 = 10$; antibonding $= 2 + 2 + 2 = 6$. Bond order $= (10 - 6)/2 = 2$.

Step 3 — Determine magnetism: The two π^*_{2p} electrons occupy the degenerate pair of antibonding π^* orbitals with one electron each (Hund's rule) $\rightarrow$ 2 unpaired electrons $\rightarrow$ paramagnetic.

Why other options are wrong:

- Option A: Bond order of 3 belongs to N_2; O_2 has bond order 2.
- Option B: Bond order of 3 is incorrect for O_2.
- Option C: Correct — O_2 is paramagnetic with bond order 2.
- Option D: O_2 is paramagnetic, not diamagnetic, due to two unpaired π^* electrons.

Final Answer: O_2 is paramagnetic, bond order $= 2 \Rightarrow$ C

Answer: (C) Go Back to Q 11

Sol. 12.

Solution

Concept — Logistic Growth and Maximum Growth Rate | Chapter: Population Ecology: In the logistic equation $dN/dt = rN(1 - N/K)$, the instantaneous growth rate is a product of rN (increasing with N) and $(1 - N/K)$ (decreasing with N). The maximum occurs at the inflection point of the S-curve.

Step 1 — Maximise dN/dt: Let $f(N) = rN(1 - N/K) = rN - rN^2/K$. Differentiate: $df/dN = r - 2rN/K = 0 \implies N = K/2$.

Step 2 — Verify: At $N = K/2$: $dN/dt = r(K/2)(1/2) = rK/4$ (maximum). At $N = K$: $dN/dt = 0$. At $N = 0$: $dN/dt = 0$.

Why other options are wrong:

- Option A: At $N = K$, $(1 - N/K) = 0$, so $dN/dt = 0$ (minimum, not maximum).
- Option B: At $N = 0$, there are no organisms to grow; $dN/dt = 0$.
- Option C: $N = K/4$ gives $dN/dt = r(K/4)(3/4) = 3rK/16 < rK/4$; not the maximum.
- Option D: Correct — maximum growth rate at $N = K/2$.

Final Answer: Maximum dN/dt at $N = K/2 \Rightarrow$ D

Answer: (D) Go Back to Q 12

Sol. 13.

Solution

Concept — Radiocarbon Dating | Chapter: Nuclear Chemistry / Radioactivity: ^{14}C decays with $t_{1/2} = 5730$ years. Remaining activity $N/N_0 = (1/2)^{t/t_{1/2}}$. If 25% remains, $N/N_0 = 0.25 = (1/2)^2$, so $t = 2 \times t_{1/2}$.

Step 1 — Count half-lives: $0.25 = (1/2)^n \implies n = 2$ half-lives.

Step 2 — Calculate age:

$$t = 2 \times 5730\,\text{years} = 11{,}460\,\text{years}$$

Why other options are wrong:

- Option A: Correct — two half-lives = 11,460 years.
- Option B: 5,730 years $= 1$ half-life; at that point 50% remains, not 25%.
- Option C: 17,190 years $= 3$ half-lives; at that point 12.5% remains.
- Option D: 22,920 years $= 4$ half-lives; at that point 6.25% remains.

Final Answer: Age $= 11{,}460$ years $\Rightarrow$ $\boxed{\text{A}}$

Answer: (A) Go Back to Q 13

Sol. 14.

Solution

Concept — IR Spectroscopy | Chapter: Spectroscopy (Organic Chemistry): Each functional group has characteristic IR absorption bands. A combination of diagnostic peaks identifies the compound's functional groups.

Step 1 — Interpret the two peaks: (a) Strong absorption at $\sim$1715 cm^{-1}: carbonyl ($\text{C}=\text{O}$) stretch of a carboxylic acid (ketone $\sim$1715, ester $\sim$1735, acid $\sim$1710–1725 cm^{-1}). (b) Broad absorption at 2500–3300 cm^{-1}: characteristic broad O–H stretch of a **carboxylic acid**, due to strong hydrogen-bonded O–H.

Why other options are wrong:

- Option A: Ketone has a $\text{C}=\text{O}$ at $\sim$1715 cm^{-1} but NO broad O–H stretch; the 2500–3300 band rules out a simple ketone.
- Option B: Correct — carboxylic acid has both the carbonyl and the characteristic broad hydrogen-bonded O–H stretch.
- Option C: A primary alcohol shows a sharp O–H at $\sim$3350 cm^{-1} (not broad

2500–3300) and no carbonyl.
- Option D: Ester has $C=O$ at $\sim$1735 cm^{-1} (higher than observed) and no O–H stretch.

Final Answer: Carboxylic acid $\Rightarrow$ B

Answer: (B) Go Back to Q 14

Sol. 15.

Solution

Concept — Gram Staining Mechanism | Chapter: Microbiology: The differential staining result reflects differences in cell wall structure between gram-positive and gram-negative bacteria.

Step 1 — Crystal violet–iodine complex formation: Both cell types initially stain purple. The CV–iodine complex is large.

Step 2 — Decolorisation step (the critical differential step): Gram-positive cells: thick peptidoglycan (20–80 nm) dehydrates and shrinks on alcohol treatment, trapping the CV–iodine complex $\rightarrow$ remains purple. Gram-negative cells: thin peptidoglycan (2–7 nm) plus an outer membrane (phospholipid + LPS); alcohol dissolves the outer membrane lipids and the thin PG cannot retain the complex $\rightarrow$ decolorised.

Why other options are wrong:

- Option A: Gram-positive cells do have a cell wall; in fact their thick peptidoglycan IS the wall.
- Option B: Reverses the relationship; gram-positive, not gram-negative, has the thicker PG.
- Option C: Correct — thick PG (gram-positive) retains the complex; thin PG + outer membrane (gram-negative) loses it.
- Option D: LPS is a gram-negative feature, but it does not "irreversibly bind" crystal violet; the outer membrane is what is dissolved by decoloriser.

Final Answer: Gram-positive thick PG retains complex; gram-negative thin PG + OM loses it $\Rightarrow$ C

Answer: (C) Go Back to Q 15

Sol. 16.

Solution

Concept — Mammalian FAS Domain Architecture | Chapter: Lipid Metabolism / Fatty Acid Synthesis: Type I mammalian FAS is a multifunctional single polypeptide. The domains are arranged in the order required for the sequential biochemical reactions of each elongation cycle.

Step 1 — Domain order (N→C): KS (ketoacyl synthase, condensation) → MAT (malonyl/acetyl transferase, loading) → DH (dehydratase, dehydration) → ER (enoyl reductase, reduction) → KR (ketoreductase, reduction) → ACP (acyl carrier protein, tethering) → TE (thioesterase, product release).

Why other options are wrong:

- Option A: Lists the domains in reverse order (C to N).
- Option B: Correct — KS–MAT–DH–ER–KR–ACP–TE is the canonical N→C domain map.
- Option C: Places ACP at the N-terminus; ACP is near the C-terminus as the acyl-tether for all reactions.
- Option D: Swaps KS and MAT positions and misplaces ER.

Final Answer: KS–MAT–DH–ER–KR–ACP–TE ⇒ B

Answer: (B) Go Back to Q 16

Sol. 17.

Solution

Concept — ACC Regulation | Chapter: Lipid Metabolism / Fatty Acid Synthesis: Acetyl-CoA carboxylase (ACC) is the committed, rate-limiting enzyme of fatty acid synthesis. It is regulated by multiple mechanisms to coordinate synthesis with energy status.

Step 1 — Allosteric regulation: Citrate (exported from mitochondria when acetyl-CoA is abundant) allosterically activates ACC by promoting polymerisation into active filaments. Palmitoyl-CoA (the end product) allosterically inhibits ACC (product feedback).

Step 2 — Hormonal/covalent regulation: Glucagon/epinephrine → PKA; AMPK (activated by low energy) both phosphorylate ACC at Ser79 → inactive. Insulin → protein phosphatase 2A → dephosphorylates ACC → active.

Why other options are wrong:

- Option A: Reverses the roles; citrate activates (not inhibits) ACC, and palmitoyl-CoA inhibits (not activates).
- Option B: AMPK phosphorylates ACC to *inactivate* it, reducing malonyl-CoA production (not increasing it).
- Option C: Correct statement of both allosteric and hormonal regulation.
- Option D: Insulin does not act through PKA; PKA is activated by glucagon/epinephrine and inactivates ACC.

Final Answer: Citrate activates, palmitoyl-CoA inhibits, phosphorylation inactivates ACC $\Rightarrow$ C

Answer: (C) Go Back to Q 17

Sol. 18.

Solution

Concept — Cytoplasmic NADPH Sources for FAS | Chapter: Lipid Metabolism / Fatty Acid Synthesis: Each elongation cycle of fatty acid synthesis requires 2 NADPH (one for KR reaction, one for ER reaction). Palmitate synthesis uses 14 NADPH total.

Step 1 — Cytoplasmic NADPH-generating enzymes in liver: (1) Oxidative PPP: glucose-6-phosphate dehydrogenase + 6-phosphogluconate dehydrogenase (main source). (2) Malic enzyme: malate $\rightarrow$ pyruvate + CO_2 + NADPH (cytoplasmic isoform). (3) $NADP^+$-isocitrate dehydrogenase (cytoplasmic isoform). (4) 10-formyl-THF dehydrogenase (minor).

Why other options are wrong:

- Option A: Pyruvate kinase produces ATP/pyruvate; phosphoglucose isomerase is a glycolytic isomerase; neither generates NADPH.
- Option B: Succinate dehydrogenase and fumarase are mitochondrial TCA enzymes; they use FAD and water, not $NADP^+$.
- Option C: Complex I reduces NAD^+ to NADH (not NADPH) in the mitochondrial inner membrane; these are mitochondrial enzymes.
- Option D: Correct — malic enzyme and $NADP^+$-isocitrate dehydrogenase are both cytoplasmic NADPH suppliers.

Final Answer: Malic enzyme and $NADP^+$-isocitrate dehydrogenase $\Rightarrow$ D

Answer: (D) Go Back to Q 18

Sol. 19.

Solution

Concept — Essential Fatty Acids and Desaturase Gaps | Chapter: Lipid Metabolism / Essential Fatty Acids: Humans can introduce double bonds at Δ^9 (SCD), Δ^5, and Δ^6 positions but cannot introduce double bonds beyond Δ^9 toward the methyl end (ω-end). Linoleic acid requires a Δ^{12} double bond; α-linolenic acid requires Δ^{12} and Δ^{15}.

Step 1 — Identify missing desaturases: Humans lack Δ^{12}-desaturase (cannot insert double bond at carbon 12, counted from carboxyl end) and Δ^{15}-desaturase. Plants possess both. Therefore linoleic (C18:2,$\Delta^{9,12}$) and α-linolenic (C18:3,$\Delta^{9,12,15}$) acids must come from the diet.

Why other options are wrong:

- Option A: Correct — humans lack Δ^{12}- and Δ^{15}-desaturases.
- Option B: Humans DO possess Δ^9-desaturase (SCD, stearoyl-CoA desaturase) and Δ^6-desaturase; these are not the missing enzymes.
- Option C: Δ^4- and Δ^5-desaturases are used by humans to synthesise EPA and DHA from EFA precursors; they are not absent.
- Option D: Δ^{11}-desaturase is relevant to insect pheromone synthesis; Δ^9-desaturase is present in humans.

Final Answer: Δ^{12}- and Δ^{15}-desaturases are absent in humans $\Rightarrow$ A

Answer: (A) Go Back to Q 19

Sol. 20.

Solution

Concept — Malonyl-CoA as a Metabolic Fuel Sensor | Chapter: Lipid Metabolism / Beta-Oxidation Regulation: Malonyl-CoA, the product of ACC and substrate for FAS, directly inhibits CPT-I, the gate-keeper for fatty acid entry into mitochondria. This ensures that synthesis and oxidation are not simultaneously active.

Step 1 — Identify the target: CPT-I (carnitine palmitoyltransferase I) resides on the outer mitochondrial membrane and catalyses transfer of long-chain acyl groups from acyl-CoA to carnitine, enabling transport into the matrix for β-oxidation. Malonyl-CoA binds CPT-I at a site distinct from the substrate site and allosterically inhibits it with high affinity ($K_i \sim \mu$M range).

Why other options are wrong:

- Option A: CrAT (carnitine acetyltransferase) handles short-chain acyl groups in the matrix; it is not the primary malonyl-CoA target.
- Option B: Correct — CPT-I on the outer mitochondrial membrane is directly inhibited by malonyl-CoA.
- Option C: Acyl-CoA synthetase activates fatty acids in the cytoplasm; it is not directly inhibited by malonyl-CoA.
- Option D: CPT-II is on the inner mitochondrial membrane (matrix side) and catalyses the reverse reaction (acyl-carnitine $\rightarrow$ acyl-CoA); it is not the malonyl-CoA target.

Final Answer: CPT-I is inhibited by malonyl-CoA $\Rightarrow$ $\boxed{\text{B}}$

Answer: (B) Go Back to Q 20

Sol. 21.

Solution

Concept — Ramachandran Plot and Secondary Structure | Chapter: Protein Structure: Each secondary structure occupies a characteristic region of ϕ/ψ space. The α-helix occupies the region $\phi \approx -57°$, $\psi \approx -47°$ (lower left of the allowed area).

Step 1 — Match points to regions: Point P ($\phi \approx -57°$, $\psi \approx -47°$) falls in the α-helix region. Point Q ($\phi \approx -120°$, $\psi \approx +130°$) falls in the β-sheet region. Points R and S are in disallowed regions.

Why other options are wrong:

- Option A: Point Q is in the β-sheet allowed region, not α-helix.
- Option B: Point R is in a disallowed (forbidden) region of the Ramachandran plot.
- Option C: Correct — Point P ($\phi \approx -57°$, $\psi \approx -47°$) is the α-helix region.
- Option D: Point S is in a disallowed region; no common secondary structure is found there.

Final Answer: Point P in the α-helix region $\Rightarrow$ $\boxed{\text{C}}$

Answer: (C) Go Back to Q 21

Sol. 22.

Solution

Concept — Modular Signalling Domains and Their Binding Targets | Chapter: Protein Structure & Cell Signalling: Protein modules such as SH2, SH3, and PH domains mediate specific protein–protein or protein–lipid interactions and are key to assembling signalling complexes.

Step 1 — Domain–ligand assignments: SH2 (Src Homology 2) domain: binds peptides containing phosphotyrosine (pTyr). SH3 domain: binds proline-rich peptides containing PXXP core motifs. PH (Pleckstrin Homology) domain: binds phosphoinositides, especially PIP_3 or PIP_2, at the inner leaflet of the plasma membrane.

Why other options are wrong:

- Option A: Reverses SH2 and SH3; SH2 binds pTyr, not PXXP.
- Option B: Reverses SH3 and SH2; SH3 binds PXXP, not pTyr.
- Option C: PH domains bind phosphoinositides (lipids), not phospho-Ser/Thr on proteins.
- Option D: Correct — complete and accurate description of all three domain binding specificities.

Final Answer: SH2 binds pTyr; SH3 binds PXXP; PH binds $PIP_3 \Rightarrow \boxed{D}$

Answer: (D) Go Back to Q 22

Sol. 23.

Solution

Concept — MWC Concerted Allostery | Chapter: Enzyme Regulation / Allostery: In the Monod–Wyman–Changeux model, all subunits of a protein switch concertedly between the low-affinity T state and high-affinity R state. Allosteric activators shift this equilibrium toward R.

Step 1 — Mechanism of an allosteric activator in MWC: An activator has higher affinity for the R state than the T state. By binding preferentially to R, it stabilises R and shifts the $T \rightleftharpoons R$ equilibrium rightward (toward R). This manifests as increased apparent substrate affinity and cooperative (sigmoidal) binding.

Why other options are wrong:

- Option A: Correct — activator stabilises R state, shifting T⇌R equilibrium.
- Option B: Describes the KNF (sequential/induced-fit) model, not MWC.

- Option C: MWC allosteric regulation is non-covalent; covalent modification is a different regulatory mechanism.
- Option D: Increasing K_m without changing $V_{\max}$ describes competitive inhibition, not allosteric activation.

Final Answer: Activator stabilises R state $\Rightarrow$ A

Answer: (A) Go Back to Q 23

Sol. 24.

Solution

Concept — Chaotropic Denaturation | Chapter: Protein Folding & Stability: Chaotropic agents (urea, GdnHCl) unfold proteins primarily by disrupting the non-covalent interactions that stabilise the native fold.

Step 1 — Primary mechanism: At high concentrations, chaotropes (a) directly form H-bonds with protein backbone and side chains, replacing intraprotein H-bonds, and (b) disorder the hydration shell of hydrophobic residues, destabilising the hydrophobic effect. Together, these eliminate the two main non-covalent stabilising forces.

Why other options are wrong:

- Option A: Urea and GdnHCl do not hydrolyse peptide bonds; that requires acid/base/proteases.
- Option B: Correct — disruption of H-bonds and hydrophobic interactions is the primary mechanism.
- Option C: Chelation of metal ions is the mechanism of EDTA treatment, not general protein denaturation by urea/GdnHCl.
- Option D: Covalent modification of Cys (reducing disulfides) is done by DTT/BME, not urea/GdnHCl; urea can unfold proteins with intact disulfides.

Final Answer: Disruption of H-bonds and hydrophobic interactions $\Rightarrow$ B

Answer: (B) Go Back to Q 24

Sol. 25.

Solution

Concept — Thermophilic Protein Stability | Chapter: Protein Folding & Stability: Thermophilic enzymes have higher T_m values due to specific structural features that reduce the entropy of unfolding or increase the enthalpy of the folded state.

Step 1 — Identified stabilising features: (a) Increased salt bridges (ion pairs) at the protein surface stabilise the native conformation electrostatically. (b) Proline substitutions in loop regions reduce the conformational entropy of the unfolded state, disfavouring unfolding (ΔS_{unfold} smaller). (c) Tighter hydrophobic core packing maximises van der Waals contacts. (d) Additional disulfide bonds covalently constrain the fold (in extracellular or secreted thermophilic proteins).

Why other options are wrong:

- Option A: Fewer salt bridges and more glycine (increased flexibility) would destabilise the protein.
- Option B: Increased Asn/Gln are problematic at high temperatures (deamidation); these do not enhance thermostability.
- Option C: Correct — increased salt bridges, Pro substitutions, tighter packing, and extra disulfides are the canonical thermostability features.
- Option D: Replacing all α-helices with β-sheet is not a general thermostability strategy and would likely be destabilising.

Final Answer: Salt bridges, Pro substitutions, tight core, disulfide bonds $\Rightarrow$ $\boxed{\text{C}}$

Answer: (C) Go Back to Q 25

Sol. 26.

Solution

Concept — Recombination Frequency (Map Distance) | Chapter: Genetics / Genetic Mapping: RF is the fraction of offspring that are recombinant (have undergone crossover between the two loci). RF (in %) = cM (centimorgans).

Step 1 — Identify parental vs recombinant classes: Parental: $AB = 432$ and $ab = 428$. Recombinant: $Ab = 68$ and $aB = 72$.

Step 2 — Calculate RF:

$$\text{RF} = \frac{68 + 72}{432 + 428 + 68 + 72} \times 100 = \frac{140}{1000} \times 100 = 14\,\text{cM}$$

Why other options are wrong:

- Option A: 50 cM would indicate genes are unlinked (independent assortment); recombinants would equal parentals.
- Option B: 10 cM would result from only 100 recombinant offspring out of 1000; the actual recombinant count is 140.
- Option C: 7 cM would result from only 70 recombinant offspring out of 1000.
- Option D: Correct — 14 cM is the calculated recombination frequency.

Final Answer: RF $= 14\,\text{cM} \Rightarrow$ D

Answer: (D) Go Back to Q 26

Sol. 27.

Solution

Concept — Coefficient of Coincidence and Interference | Chapter: Genetics / Genetic Mapping: These statistics quantify whether double crossovers occur more or less frequently than expected if crossovers were independent.

Step 1 — Calculate expected DCO: Expected DCO $= 0.12 \times 0.08 \times 5000 = 0.0096 \times 5000 = 48$.

Step 2 — Calculate CoC and I:

$$\text{CoC} = \frac{\text{observed DCO}}{\text{expected DCO}} = \frac{32}{48} = 0.667$$

$$I = 1 - \text{CoC} = 1 - 0.667 = 0.333$$

Positive interference ($I > 0$): one crossover reduces the probability of a nearby second crossover.

Why other options are wrong:

- Option A: Correct — CoC $= 0.667$; $I = 0.333$.
- Option B: CoC > 1 would indicate negative interference (more DCOs than expected); observed DCO (32) $<$ expected (48), so CoC < 1.
- Option C: CoC $= 1$ means no interference; the data show fewer DCOs than expected.
- Option D: CoC $= 0.333$ would require only 16 observed DCOs, not 32.

Final Answer: CoC $= 0.667$; $I = 0.333 \Rightarrow$ A

Answer: (A) Go Back to Q 27

Sol. 28.

Solution

Concept — Complementation Test (cis-trans Test) | Chapter: Genetics / Gene Function: Complementation tests determine whether two recessive mutations affect the same gene (fail to complement) or different genes (complement each other, restoring wild-type phenotype).

Step 1 — Interpret trans-heterozygote result: The F_1 offspring have genotype $m_1/+ \quad +/m_4$ (in trans configuration). Each chromosome carries a wild-type allele of the other gene. If the F_1 has wild-type (red) eyes, each mutant allele is complemented by the wild-type copy on the other chromosome $\rightarrow$ the two mutations are in **different genes** (different complementation groups).

Why other options are wrong:

- Option A: Failure to complement (same gene) would result in a mutant (white-eye) F_1, not wild-type.
- Option B: Correct — wild-type F_1 indicates complementation, meaning different genes.
- Option C: Both mutations are recessive; dominance is not the explanation for wild-type F_1.
- Option D: Intragenic complementation is rare and usually observed as partial restoration, not full wild-type; the standard interpretation is different complementation groups.

Final Answer: Mutations are in different genes (complement) $\Rightarrow \boxed{\text{B}}$

Answer: (B) Go Back to Q 28

Sol. 29.

Solution

Concept — LOD Score Significance Threshold | Chapter: Human Genetics / Linkage Analysis: The LOD score is a likelihood ratio (log base 10). The conventional threshold of LOD ≥ 3.0 was established by Morton (1955) as a balance between type I error (false positive linkage) and the prior probability that any two loci in the genome are linked.

Step 1 — Interpret LOD $= 3.0$: LOD $= \log_{10}(1000/1) = 3.0$ means the data are 1000 times more likely if the loci are linked at θ than if they assort independently. This is conventionally accepted as statistically significant linkage in two-point analysis.

Why other options are wrong:

- Option A: LOD ≥ 1.0 (10:1 odds) is far too lenient; it would produce many false positives.
- Option B: LOD ≥ 2.0 (100:1 odds) is used as a threshold for "suggestive" linkage, not definitive.
- Option C: Correct — LOD ≥ 3.0 (1000:1 odds) is the conventional genome-wide significance threshold for two-point linkage.
- Option D: LOD ≥ 5.0 is occasionally used for dense SNP-based linkage analyses, but the classical threshold remains 3.0.

Final Answer: LOD ≥ 3.0 (1000:1 odds) $\Rightarrow$ C

Answer: (C) Go Back to Q 29

Sol. 30.

Solution

Concept — Holliday Junction Resolution | Chapter: Molecular Biology / Homologous Recombination: A Holliday junction (HJ) is an X-shaped intermediate of homologous recombination. Resolution by structure-specific nucleases (resolvases) in two orientations gives different genetic outcomes.

Step 1 — Determine the outcomes: The HJ is formed between two homologous duplexes. Cut 1 (horizontal cuts, orange in diagram): cuts the two strands that *did not* exchange — flanking markers are maintained on their original chromosomes $\rightarrow$ **noncrossover (NCO)** product. Cut 2 (vertical cuts, purple in diagram): cuts the two strands that *exchanged* — flanking sequences are exchanged between the two duplexes $\rightarrow$ **crossover (CO)** product.

Why other options are wrong:

- Option A: Not both orientations give CO; one orientation gives NCO.
- Option B: Not both give NCO; one orientation gives CO.
- Option C: Reverses the outcomes of the two cuts.
- Option D: Correct — horizontal cuts $\rightarrow$ NCO; vertical cuts $\rightarrow$ CO with flanking-marker exchange.

Final Answer: Horizontal cuts → NCO; vertical cuts → CO ⇒ D

Answer: (D) Go Back to Q 30

Sol. 31.

Solution

Concept — ELISA Formats and Sensitivity | Chapter: Immunology / Immunoassays: Different ELISA configurations offer varying levels of sensitivity, specificity, and complexity.

Step 1 — Compare ELISA formats: Sandwich ELISA uses two antibodies recognising non-overlapping epitopes; the antigen is captured by one and detected by another (enzyme-labelled). This provides both high specificity (two-antibody requirement) and high sensitivity (signal amplification via enzyme). It is the format of choice for complex matrices like serum.

Why other options are wrong:

- Option A: Correct — sandwich ELISA with capture + detection antibodies gives highest sensitivity and specificity.
- Option B: Direct ELISA uses one labelled antibody, giving lowest signal amplification and sensitivity.
- Option C: In competitive ELISA, signal is *inversely* proportional to antigen concentration; it is typically less sensitive than sandwich format for large proteins.
- Option D: Indirect ELISA uses an unlabelled primary and enzyme-labelled secondary antibody; it is flexible but generally not as sensitive as sandwich for complex samples.

Final Answer: Sandwich ELISA has highest sensitivity ⇒ A

Answer: (A) Go Back to Q 31

Sol. 32.

Solution

Concept — ELISpot Assay Principle | Chapter: Immunology / Immunoassays: ELISpot measures secretion by individual cells, enabling enumeration of rare antigen-specific cells without requiring cell lysis.

Step 1 — Mechanism: A PVDF membrane plate is coated with capture antibody. Living cells are seeded and stimulated with antigen. Cytokines/antibodies secreted by individual cells are captured locally by the antibody directly beneath each secreting cell. After cell removal, a detection antibody and enzyme-substrate system produces a coloured precipitate at each secretion site (one spot = one secreting cell).

Why other options are wrong:

- Option A: Describes a standard ELISA measuring bulk cytokine in supernatant; does not measure individual cells.
- Option B: Describes intracellular cytokine staining (ICS) by flow cytometry; requires cell permeabilisation and a different platform.
- Option C: Correct — PVDF membrane captures locally secreted molecules; spots are counted per secreting cell.
- Option D: Describes a proximity ligation assay (PLA); does not involve cytokine secretion measurement.

Final Answer: Each spot on PVDF membrane = one secreting cell $\Rightarrow \boxed{\text{C}}$

Answer: (C) Go Back to Q 32

Sol. 33.

Solution

Concept — Proximity Ligation Assay (PLA) | Chapter: Immunology / Immunoassays: PLA uniquely converts a protein–protein proximity event (interaction) into a nucleic acid amplification signal detectable as a fluorescent punctum, providing single-molecule sensitivity in intact cells.

Step 1 — Key mechanistic steps: Two primary antibodies (one per protein of interest) are bound by secondary antibodies each carrying a unique DNA oligonucleotide probe. When the two target proteins are within ~40 nm, the oligonucleotide probes are close enough to be ligated by two connector oligonucleotides → a circular DNA template is formed → phi29 DNA polymerase amplifies it by rolling-circle amplification (RCA) → the long amplicon is detected by fluorescent

complementary probes → one bright fluorescent punctum per interaction event.

Why other options are wrong:

- Option A: FRET requires fluorophores within <10 nm and does not use DNA ligation; PLA works at <40 nm via a DNA-based mechanism.
- Option B: Correct — DNA oligo probes on secondary antibodies are ligated then amplified by RCA when proteins are in proximity.
- Option C: BRET uses a luciferase–fluorophore pair and is used in live cells, not fixed tissue; it does not involve DNA ligation.
- Option D: Split-GFP complementation is used in live cells to detect protein interactions in real time; it does not involve rolling-circle amplification.

Final Answer: Ligation of oligo probes + rolling-circle amplification ⇒ B

Answer: (B) Go Back to Q 33

Sol. 34.

Solution

Concept — Lateral Flow Immunoassay (LFA) | Chapter: Immunology / Immunoassays: LFA is a membrane-based point-of-care test. The test line (T) is specific for the analyte; the control line (C) confirms that the test functioned correctly.

Step 1 — Positive result interpretation: When the analyte (e.g. antigen) is present in the sample: (1) analyte–colloidal-gold-antibody complexes form in the conjugate pad; (2) these complexes flow to the test line where a capture antibody binds the analyte in a sandwich format → coloured T line appears; (3) excess colloidal gold antibody (not bound at T line) continues to the control line (C) where anti-species or anti-IgG antibody captures it → C line always appears if test functioned. Positive = both T and C lines visible.

Why other options are wrong:

- Option A: Only C line visible = negative result (no analyte to bind at T line).
- Option B: Only T line visible (no C) = invalid test (flow was incomplete or incorrect).
- Option C: Neither line = invalid test (flow failure or kit malfunction).
- Option D: Correct — both T and C lines visible = positive result.

Final Answer: Both T and C lines visible = positive result ⇒ D

Answer: (D) Go Back to Q 34

Sol. 35.

Solution

Concept — TRFIA and Lanthanide Labels | Chapter: Immunology / Immunoassays: The key advantage of TRFIA over conventional fluoroimmunoassay is the ability to time-gate the signal, completely eliminating autofluorescence background.

Step 1 — Physical basis: Lanthanide chelates (Eu^{3+}, Tb^{3+}, Sm^{3+}) have fluorescence lifetimes of $\sim$0.1–1 ms, which is 10^4–10^5 times longer than biological autofluorescence ($<$10 ns). A time-gate delay of a few microseconds after the excitation pulse allows all short-lived background fluorescence to decay. The lanthanide signal is then measured in the near-silence, giving a signal-to-background ratio many orders of magnitude better than conventional fluorescence assays.

Why other options are wrong:

- Option A: Correct — long lifetime $\rightarrow$ time-gating eliminates background; detection limit 10^{-13}–10^{-15} mol/L.
- Option B: Lanthanide reagents are expensive specialty chelates, not cheaper than HRP conjugates.
- Option C: Lanthanides do not act as enzymes; they are spectroscopic labels only.
- Option D: Lanthanide chelates typically emit in the visible range (Eu^{3+} at $\sim$615 nm, Tb^{3+} at $\sim$545 nm), not UV.

Final Answer: Long-lifetime time-gating eliminates autofluorescence background $\Rightarrow$ A

Answer: (A) Go Back to Q 35

Sol. 36.

Solution

Concept — β-Lactam Mechanism and Resistance | Chapter: Pharmacology / Antimicrobials: β-Lactams kill bacteria by mimicking the D-Ala-D-Ala terminus of PBP substrate and irreversibly acylating the PBP active site, blocking cell wall cross-linking.

Step 1 — Mechanism of action: The β-lactam ring is a structural analogue of the D-Ala-D-Ala terminus of the pentapeptide PBP substrate. It acylates the catalytic serine of transpeptidase (PBP), forming a stable acyl-enzyme intermediate that cannot turn over $\rightarrow$ no cross-linking $\rightarrow$ weakened cell wall $\rightarrow$ osmotic lysis.

Step 2 — Resistance mechanisms: (a) β-Lactamases: serine (class A, C, D) or metallo (class B) enzymes that hydrolyse the β-lactam ring before it can reach PBP. (b) Altered PBPs: MRSA acquires PBP2a (mecA gene) with very low affinity for β-lactams.

Why other options are wrong:

- Option A: β-Lactams do not target ribosomes; that is the mechanism of aminoglycosides, tetracyclines.
- Option B: Correct — PBP acylation + β-lactamase / PBP2a resistance.
- Option C: β-Lactams do not chelate Mg^{2+}; fluoroquinolones target DNA gyrase.
- Option D: β-Lactams do not disrupt the cytoplasmic membrane; that is the mechanism of polymyxins/daptomycin.

Final Answer: PBP acylation; resistance via β-lactamase or PBP2a (mecA) $\Rightarrow$ $\boxed{\text{B}}$

Answer: (B) Go Back to Q 36

Sol. 37.

Solution

Concept — Azole Antifungal Target | Chapter: Pharmacology / Antifungals: Azoles exploit the difference between fungal ergosterol and mammalian cholesterol biosynthesis pathways. Their target (CYP51) is a fungal cytochrome P450 enzyme.

Step 1 — Mechanism: The azole nitrogen atom (N3 of imidazole or N4 of triazole) coordinates the haem iron of CYP51 (lanosterol 14α-demethylase), blocking the active site. CYP51 normally demethylates lanosterol at C14 in the ergosterol

pathway. Inhibition causes lanosterol and toxic methylated sterol intermediates to accumulate, depleting ergosterol from the fungal membrane $\rightarrow$ altered membrane permeability and function.

Why other options are wrong:

- Option A: β-1,3-glucan synthase (FKS1) is the target of echinocandins (caspofungin, micafungin, anidulafungin), not azoles.
- Option B: Direct ergosterol binding and membrane disruption is the mechanism of polyene antifungals (amphotericin B, nystatin), not azoles.
- Option C: Correct — azoles inhibit CYP51 (lanosterol 14α-demethylase) in the ergosterol biosynthesis pathway.
- Option D: Dihydropteroate synthase is the bacterial target of sulfonamides; fungi synthesise folate differently and this is not the azole target.

Final Answer: Lanosterol 14α-demethylase (CYP51) $\Rightarrow$ C

Answer: (C) Go Back to Q 37

Sol. 38.

Solution

Concept — Acyclovir Selective Toxicity | Chapter: Pharmacology / Antivirals: Acyclovir is a prodrug whose selectivity depends entirely on the first phosphorylation step being performed by a virally-encoded enzyme absent from uninfected cells.

Step 1 — Activation pathway: HSV and VZV encode a viral thymidine kinase (TK) that has much broader substrate specificity than cellular TK. Viral TK phosphorylates ACV to ACV-monophosphate. Host cellular kinases then convert ACV-MP $\rightarrow$ ACV-DP $\rightarrow$ ACV-TP (the active form). Uninfected cells have negligible viral TK $\rightarrow$ ACV is not phosphorylated $\rightarrow$ no toxic triphosphate accumulates.

Step 2 — ACV-TP mechanism: ACV-TP lacks a 3′-OH group (acyclic sugar), so after incorporation into viral DNA it terminates chain elongation. It also competitively inhibits viral DNA polymerase with $>100\times$ selectivity over host DNA Pol δ.

Why other options are wrong:

- Option A: Host cellular TK does not efficiently phosphorylate ACV (it has narrow substrate specificity for thymidine).

- Option B: There is no spontaneous chemical activation; enzymatic phosphorylation is required.
- Option C: ACV must be phosphorylated to the triphosphate form before incorporation; unactivated ACV is not recognised by viral DNA polymerase.
- Option D: Correct — viral TK performs the critical first phosphorylation step, conferring cell-selective activation.

Final Answer: Viral TK phosphorylates ACV to ACV-MP (selective activation) $\Rightarrow$ D

Answer: (D) Go Back to Q 38

Sol. 39.

Solution

Concept — NRTIs as Chain Terminators | Chapter: Pharmacology / Antivirals (HIV): NRTIs lack the 3′-OH group essential for the 3′$\rightarrow$5′ phosphodiester bond extension. They must first be phosphorylated to the triphosphate by cellular kinases.

Step 1 — Structural basis of chain termination: AZT (3′-azidothymidine) has an azido group ($-N_3$) at the 3′ position instead of the normal $-$OH. After incorporation into the nascent DNA chain by HIV RT, the 3′-azido group cannot form the next phosphodiester bond $\rightarrow$ chain elongation halts.

Step 2 — Cellular activation requirement: AZT is a prodrug. Cellular thymidine kinase (and subsequently thymidylate kinase and nucleoside diphosphate kinase) convert AZT $\rightarrow$ AZT-MP $\rightarrow$ AZT-DP $\rightarrow$ AZT-TP, the active form incorporated by RT.

Why other options are wrong:

- Option A: Correct — 3′-azido group prevents chain extension; cellular kinases generate AZT-TP.
- Option B: AZT does not intercalate into DNA; it is incorporated as a substrate analogue.
- Option C: AZT does not covalently alkylate cysteine; it acts as a substrate/chain terminator, not an irreversible covalent inhibitor.
- Option D: AZT is not activated by viral protease; it is activated by host cellular kinases.

Final Answer: 3′-azido group $\rightarrow$ chain termination; activated by cellular kinases to AZT-TP $\Rightarrow$ A

Answer: (A) Go Back to Q 39

Sol. 40.

Solution

Concept — HIV Protease and Virion Maturation | Chapter: Virology / HIV: HIV aspartyl protease cleaves the Gag-Pol polyprotein during or just after budding. Without processing, the virion cannot mature into an infectious particle.

Step 1 — Consequence of protease inhibition: If the HIV protease is inhibited, the Gag (p55) and Gag-Pol (p160) polyproteins cannot be cleaved into functional subunits: matrix (p17), capsid (p24), nucleocapsid (p7), protease, reverse transcriptase, and integrase. The budding virions appear morphologically as "doughnut-shaped" (immature) by EM and are completely non-infectious.

Why other options are wrong:

- Option A: Reverse transcription is blocked by NRTIs and NNRTIs, not protease inhibitors.
- Option B: Envelope glycoprotein (gp120/gp41) processing is performed by cellular furin, not HIV protease.
- Option C: Correct — immature, non-infectious particles result from failure to cleave Gag-Pol.
- Option D: Integrase strand-transfer inhibitors (e.g. raltegravir) block integration; this is not the protease inhibitor mechanism.

Final Answer: Immature non-infectious particles due to unprocessed Gag-Pol $\Rightarrow$ C

Answer: (C) Go Back to Q 40

Sol. 41.

Solution

Concept — Germinal Centre Selection | Chapter: Immunology / Humoral Immunity: The GC is a Darwinian selection environment. High-affinity BCR variants are positively selected; low-affinity variants die by apoptosis.

Step 1 — Fate of high-affinity centrocytes in the light zone: High-affinity centrocytes can efficiently capture antigen displayed on follicular dendritic cells (FDCs) $\rightarrow$ process and present peptides to follicular T helper (Tfh) cells $\rightarrow$ receive

CD40L and cytokine survival signals. Rescued centrocytes: (a) exit the GC as long-lived plasma cells (secrete high-affinity antibody for years in bone marrow niches) or memory B cells (circulate, ready for rapid secondary response), or (b) re-enter the dark zone for further rounds of SHM.

Why other options are wrong:

- Option A: The opposite is true; it is low-affinity centrocytes that undergo apoptosis (negative selection by default).
- Option B: High-affinity cells can recycle to DZ, but they also exit as memory/plasma cells; the statement "unconditionally" is incorrect.
- Option C: GC output cells seed bone marrow as long-lived plasma cells providing durable protection, not short-lived ones.
- Option D: Correct — high-affinity centrocytes receive survival signals and differentiate into memory B cells / LLPCs or recycle.

Final Answer: High-affinity centrocytes are rescued and exit or recycle $\Rightarrow$ $\boxed{\text{D}}$

Answer: (D) Go Back to Q 41

Sol. 42.

Solution

Concept — AID Biochemical Activity | Chapter: Immunology / Antibody Diversity: AID is a B cell-specific DNA mutase that is the master regulator of antibody diversification. It acts on single-stranded DNA exposed during transcription.

Step 1 — AID's catalytic activity: AID is a cytidine deaminase that converts cytosine (C) to uracil (U) in single-stranded DNA. In SHM, AID deaminates Cs in the V-region coding sequence. In CSR, AID acts on transcription-induced R-loops or single-stranded DNA at switch (S) regions, generating staggered nicks that are converted to double-strand breaks initiating end-joining.

Why other options are wrong:

- Option A: Correct — AID deaminates C$\rightarrow$U in ssDNA; this is its mechanism for both SHM and CSR.
- Option B: AID is not an endonuclease and does not directly cleave at RSS sequences; V(D)J recombination uses RAG1/RAG2 at RSS.
- Option C: AID has no methyltransferase activity; it is a deaminase.
- Option D: AID has no helicase activity; it requires pre-existing ssDNA generated by transcription.

Final Answer: AID deaminates C→U in ssDNA (SHM and CSR) ⇒ A

Answer: (A) Go Back to Q 42

Sol. 43.

Solution

Concept — Class Switch Recombination Cytokine Signals | Chapter: Immunology / Class Switch Recombination: Distinct cytokines from Th1 and Th2 cells direct B cells to switch to specific IgG subclasses, IgE, or IgA. This tailors the antibody effector function to the nature of the pathogen.

Step 1 — Key cytokine–isotype pairs: IL-4 (Th2) → IgE and **IgG4** in humans (allergic/anti-parasitic responses; note: IL-4 drives IgG1 in mice, but IgG4 in humans). IFN-γ (Th1) → IgG1/IgG3 in humans (opsonising, complement-activating). TGF-β (regulatory T cells, mucosal DCs) → IgA (mucosal immunity in gut and respiratory tract); retinoic acid co-signals IgA CSR in Peyer's patches. CD40L co-stimulation is required alongside cytokine signals.

Why other options are wrong:

- Option A: Reverses IL-4 and IFN-γ roles; IFN-γ does not drive IgE, and IL-4 does not drive IgG3.
- Option B: Correct — IL-4 drives IgE/IgG4 in humans; TGF-β drives IgA; IFN-γ drives IgG1/IgG3.
- Option C: TGF-β drives IgA, not IgE; IL-4 drives IgE, not IgA — these are reversed.
- Option D: IL-12 activates Th1 cells but does not directly instruct B cell CSR to IgE; these pairings are incorrect.

Final Answer: IL-4 → IgE/IgG4 (humans); TGF-β → IgA; IFN-γ → IgG1/IgG3 ⇒ B

Answer: (B) Go Back to Q 43

Sol. 44.

Solution

Concept — Memory B Cells vs Long-lived Plasma Cells | Chapter: Immunology / Humoral Memory: These two GC output populations provide durable immunological memory through fundamentally different mechanisms.

Step 1 — Distinguishing features: Memory B cells are long-lived, surface BCR^+ (IgG^+), $CD27^+$, $CD80/CD86^+$; they do NOT constitutively secrete antibody. They survive for decades in secondary lymphoid organs and bone marrow niches. Upon re-encounter with antigen, they rapidly proliferate and differentiate into secondary plasma cells within days (secondary immune response: faster, higher titre, more class-switched, higher affinity). LLPCs are terminally differentiated, have extinguished BCR surface expression, and constitutively secrete IgG; they reside in bone marrow survival niches (sustained by APRIL, BAFF, CXCL12) and maintain serum antibody titres for years without antigen re-exposure.

Why other options are wrong:

- Option A: Reverses the functions; memory B cells do not secrete; LLPCs secrete continuously.
- Option B: Both populations are at different maturational stages; they are not functionally equivalent.
- Option C: Correct — memory B cells do not secrete; LLPCs constitutively secrete antibody.
- Option D: Memory B cells are long-lived (can persist for life); LLPCs do not divide regularly.

Final Answer: Memory B: no secretion, BCR^+; LLPC: constitutive secretion, $BCR^- \Rightarrow \boxed{C}$

Answer: (C) Go Back to Q 44

Sol. 45.

Solution

Concept — SHM Mutation Spectrum | Chapter: Immunology / Somatic Hypermutation: The molecular pathway of U processing after AID deamination determines whether only transitions at C:G or also mutations at A:T are introduced.

Step 1 — MMR pathway + Pol η: MSH2/MSH6 recognise the U:G mismatch. Instead of faithful repair, MSH2/MSH6 recruit Rev1 and the error-prone transle-

sion synthesis polymerase η (eta). Pol η is notorious for introducing mutations at A:T pairs as well as extending beyond the original deamination site. The patch-synthesis typically covers WRC hotspot motifs (W=A/T, R=purine), which is why A:T mutations are clustered at these positions. This distinguishes SHM from simple mutation (C→T only) and explains the broad spectrum of mutations observed in CDRs.

Why other options are wrong:

- Option A: C→T only (direct replication of U as T) is the outcome when U is simply replicated without repair. MMR + Pol η generates the broader mutation spectrum.
- Option B: MMR does not exclusively remove G; and the mutations generated are not exclusively G→C transversions.
- Option C: Pol η does not exclusively produce frameshifts; it generates point mutations at both G:C and A:T positions.
- Option D: Correct — Pol η error-prone synthesis generates mutations at A:T as well as C:G pairs, particularly at AGCT/WRC hotspots.

Final Answer: MMR + Pol η generates A:T and C:G mutations at WRC hotspots ⇒ D

Answer: (D) Go Back to Q 45

Sol. 46.

Solution

Concept — Canonical NF-κB Pathway | Chapter: Cell Signalling / NF-κB: The key regulatory event is the phosphorylation and proteasomal degradation of IκBα, which normally sequesters p65/p50 in the cytoplasm.

Step 1 — IKK complex and IκBα: IKKβ is the catalytic serine/threonine kinase subunit of the trimeric IKK complex (IKKα + IKKβ + NEMO/IKKγ). NEMO serves as the regulatory/scaffold subunit that recruits the IKK complex to activated receptors. IKKβ phosphorylates IκBα at Ser32 and Ser36, creating a phosphodegron recognised by the SCF$^{\beta\text{-TrCP}}$ E3 ubiquitin ligase → K48-linked polyubiquitination → 26S proteasome degrades IκBα → p65/p50 released and translocates to nucleus → transcription of κB target genes.

Why other options are wrong:

- Option A: IKKβ acts in the cytoplasm on IκBα; p65 phosphorylation by IKKβ in the nucleus is a different (minor) event.

- Option B: Correct — IKKβ phosphorylates IκBα at Ser32/36 $\rightarrow$ ubiquitination $\rightarrow$ degradation $\rightarrow$ p65/p50 nuclear translocation.
- Option C: NEMO is the regulatory scaffold, not the catalytic kinase; IKKβ (and to a lesser extent IKKα) perform the kinase activity.
- Option D: p65/p50 is retained by IκBα (not TAK1); TAK1 is upstream of the IKK complex.

Final Answer: IKKβ phosphorylates IκBα $\rightarrow$ proteasomal degradation $\rightarrow$ p65/p50 nuclear translocation $\Rightarrow$ B

Answer: (B) Go Back to Q 46

Sol. 47.

Solution

Concept — NF-κB Target Genes and Oncogenesis | Chapter: Cell Signalling / NF-κB & Oncogenesis: NF-κB activates a suite of genes governing inflammation, immune activation, cell survival, and proliferation. Constitutive NF-κB activation provides tumour cells with an anti-apoptotic survival advantage.

Step 1 — Anti-apoptotic NF-κB targets: Key NF-κB-driven pro-survival genes include Bcl-2, Bcl-xL, XIAP, and c-FLIP. These proteins block both intrinsic (Bcl-2/Bcl-xL: inhibit cytochrome c release) and extrinsic (c-FLIP: blocks caspase-8 activation; XIAP: inhibits executioner caspases) apoptosis pathways. In diffuse large B cell lymphoma (DLBCL), MyD88 L265P mutation constitutively activates NF-κB, driving expression of these survival genes.

Why other options are wrong:

- Option A: PTEN is a tumour suppressor; NF-κB does not activate it. NF-κB can actually suppress PTEN expression in some contexts.
- Option B: p53 is not a direct NF-κB target; its induction would oppose oncogenesis, not promote it.
- Option C: Correct — Bcl-2/Bcl-xL/XIAP are NF-κB targets conferring survival advantage; constitutive NF-κB activators (MyD88 L265P) drive lymphomagenesis.
- Option D: Rb is a tumour suppressor; NF-κB does not transcribe Rb.

Final Answer: Bcl-2/Bcl-xL/XIAP are anti-apoptotic NF-κB targets; constitutive NF-κB $\rightarrow$ B cell lymphoma $\Rightarrow$ C

Answer: (C) Go Back to Q 47

Sol. 48.

Solution

Concept — Non-canonical NF-κB Pathway | Chapter: Cell Signalling / NF-κB: The non-canonical pathway is a distinct signalling axis with different key kinases, adapter proteins, and transcription factor subunits compared to the canonical pathway.

Step 1 — Non-canonical pathway mechanism: Normally, NIK (NF-κB-inducing kinase) is constitutively degraded by a TRAF2–TRAF3–cIAP1/2 E3 ligase complex. When BAFF, LTβ, or CD40L engage their receptors, TRAF2/TRAF3 are degraded, allowing NIK to accumulate. NIK activates an IKKα homodimer (no IKKβ, no NEMO). Active IKKα phosphorylates p100 (which has ankyrin repeats functioning like IκB at its C-terminus). Phospho-p100 is ubiquitinated and partially processed by the proteasome to p52. The p52/RelB heterodimer translocates to the nucleus and regulates a distinct set of genes (e.g. BAFF, BLyS, chemokines for lymphoid organogenesis).

Why other options are wrong:

- Option A: The non-canonical pathway uses IKKα homodimer (no NEMO, no IKKβ); these are canonical components.
- Option B: Describes the canonical pathway, not the non-canonical.
- Option C: Non-canonical NF-κB is activated by TNFR family ligands (BAFF, CD40L, LTβ), not exclusively viral infections.
- Option D: Correct — NIK accumulates $\rightarrow$ activates IKKα homodimer $\rightarrow$ p100 processing to p52 $\rightarrow$ p52/RelB nuclear translocation.

Final Answer: NIK $\rightarrow$ IKKα $\rightarrow$ p100 $\rightarrow$ p52/RelB nuclear translocation $\Rightarrow$ $\boxed{\text{D}}$

Answer: (D) Go Back to Q 48

Sol. 49.

Solution

Concept — COX Enzymes and NSAIDs | Chapter: Biochemistry / Eicosanoid Metabolism: COX-1 (constitutive) and COX-2 (inducible by NF-κB) have overlapping but distinct functions. Selective COX-2 inhibitors were developed to reduce GI side effects but were later found to increase cardiovascular risk.

Step 1 — Aspirin mechanism: Aspirin irreversibly acetylates Ser530 in the COX active site channel, blocking access of arachidonate. It inhibits both COX-1 and COX-2 (COX-1 preferentially at low doses). Platelets cannot synthesise new COX

(anucleate) → life-long loss of TXA_2 production per platelet.

Step 2 — Selective COX-2 inhibition cardiovascular risk: Endothelial cells use COX-2 to synthesise prostacyclin (PGI_2), which inhibits platelet aggregation and causes vasodilation. Selective COX-2 inhibitors suppress PGI_2 without suppressing platelet COX-1-derived TXA_2 → prothrombotic imbalance → increased MI and stroke risk.

Why other options are wrong:

- Option A: Correct — selective COX-2 inhibition spares platelet TXA_2 (COX-1) but removes endothelial PGI_2 (COX-2), increasing cardiovascular risk.
- Option B: COX-1, not COX-2, is the constitutive platelet isoform supplying TXA_2.
- Option C: Aspirin inhibits COX irreversibly by covalent acetylation, not reversibly.
- Option D: SC-560 is a research tool; COX-1-selective NSAIDs would increase GI side effects, not reduce them (COX-1 protects gastric mucosa).

Final Answer: Aspirin irreversibly acetylates both COX isoforms; selective COX-2 inhibitors increase CV risk by sparing TXA_2 ⇒ A

Answer: (A) Go Back to Q 49

Sol. 50.

Solution

Concept — NLRP3 Inflammasome Two-Signal Model | Chapter: Immunology / Innate Immunity & Inflammasome: NLRP3 inflammasome activation requires two sequential signals to prevent inadvertent inflammation. Its activation leads to a form of inflammatory cell death called pyroptosis.

Step 1 — Two signals: Signal 1 (priming): Pattern recognition (NF-κB activation by TLRs, TNF receptor, etc.) → transcription of pro-IL-1β, pro-IL-18, and NLRP3. Signal 2 (activation): Danger/damage signals (K^+ efflux from ATP via P2X7, cholesterol crystals, MSU crystals, silica, lysosomal rupture) → NLRP3 oligomerises → recruits ASC (pyrin domain PYD–CARD) → ASC speck forms → pro-caspase-1 recruitment → autocatalytic caspase-1 activation.

Step 2 — Downstream consequences: Active caspase-1 cleaves pro-IL-1β and pro-IL-18 → mature cytokines secreted. Caspase-1 also cleaves gasdermin D (GSDMD) → N-terminal GSDMD inserts into plasma membrane forming 20–30 nm

pores → pyroptotic cell death with membrane rupture and cytokine/HMGB1 release.

Why other options are wrong:

- Option A: Reverses the signals; K^+ efflux activates (signal 2), not primes (signal 1).
- Option B: Correct — NF-κB priming (signal 1) then danger signals trigger NLRP3 oligomerisation → caspase-1 → IL-1β/IL-18 + GSDMD → pyroptosis.
- Option C: Caspase-3 cleaves GSDME (not GSDMD) and causes secondary necrosis; GSDMD is cleaved by caspase-1/4/5/11.
- Option D: NLRP3 senses sterile danger signals, not viral dsRNA (sensed by RIG-I/MDA5 for IFN induction).

Final Answer: Two signals → NLRP3 → caspase-1 → IL-1β/IL-18 + GSDMD pores → pyroptosis ⇒ $\boxed{\text{B}}$

Answer: (B) Go Back to Q 50

Sol. 51.

Solution

Concept — Perfusion Culture vs Fed-Batch | Chapter: Bioprocess Engineering / Cell Culture: Perfusion enables continuous removal of inhibitory metabolites and continuous supply of fresh nutrients while retaining cells, enabling much higher cell densities than achievable in fed-batch.

Step 1 — Cell density advantage: Fed-batch cultures typically reach 5–10×10^6 viable cells/mL with viability declining as lactate and ammonia accumulate. Perfusion cultures routinely achieve 50–100×10^6 cells/mL (i.e. 10–$20\times$ higher) because inhibitory metabolites are washed away and nutrients are continuously replenished.

Step 2 — Additional benefits: Smaller bioreactor volume is needed for the same total cell mass. Continuous product harvest reduces time in the bioreactor, limiting product degradation (glycosylation, oxidation, deamidation). This is particularly valuable for labile proteins.

Why other options are wrong:

- Option A: Perfusion consumes far more media than fed-batch (continuous flow); media cost is higher.

- Option B: Perfusion process control is more complex (ATF fouling risk, bleed rate, perfusion rate); it is not simpler.
- Option C: Correct — 10–100$\times$ higher cell densities; smaller footprint; continuous harvest.
- Option D: Perfusion retains intact cells; products are extracellular secreted proteins (mAbs), not intracellular proteins requiring lysis.

Final Answer: $\sim$10$\times$ higher viable cell density; smaller footprint; continuous harvest $\Rightarrow$ C

Answer: (C) Go Back to Q 51

Sol. 52.

Solution

Concept — N-1 High-Density Seeding Strategy | Chapter: Bioprocess Engineering / Seed Train: The N-1 bioreactor is the last step in the seed train before the production vessel. Running it in high-density perfusion mode intensifies the seed train and improves the production run.

Step 1 — Benefits of high-density N-1 seeding: Traditional seeding density into a production bioreactor is $\sim$0.3–0.5 $\times 10^6$ cells/mL. High-density N-1 perfusion can provide $\geq$5–20 $\times 10^6$ cells/mL seeding density. This shortens the lag phase and time to peak viable cell density in the production bioreactor, increases overall volumetric productivity (shorter batch cycle), and can reduce the number of seed train expansion steps required (fewer bioreactors in the seed train = lower risk of contamination, less facility capacity needed).

Why other options are wrong:

- Option A: The N-1 is an inoculum vessel; the production bioreactor is separate and required.
- Option B: Cell doubling time is a biological constant; perfusion does not speed up cell division per se.
- Option C: Regulatory regulations (ICH Q5A) restrict animal-derived components; this is not a benefit of N-1 perfusion.
- Option D: Correct — high-density N-1 $\rightarrow$ high seeding density $\rightarrow$ faster ramp-up, higher productivity, fewer seed train steps.

Final Answer: High-density N-1 $\rightarrow$ high seeding density $\rightarrow$ shortened production cycle, higher productivity $\Rightarrow$ D

Answer: (D) Go Back to Q 52

Sol. 53.

Solution

Concept — QbD Framework (ICH Q8/Q9/Q10) | Chapter: Bioprocess Engineering / Quality by Design: QbD shifts biopharmaceutical manufacturing from a "test-and-fix" to a "design-in-quality" approach by understanding how process parameters affect product quality attributes.

Step 1 — CQA and CPP definitions: A CQA is a physical, chemical, biological, or microbiological property or characteristic of the final drug product (or intermediate) that should be within an appropriate limit, range, or distribution to ensure the desired product quality. Examples: glycan profile (affects immunogenicity/ADCC), aggregation (immunogenicity risk), potency (efficacy). A CPP is a process parameter whose variability has an impact on a CQA; it should be monitored and controlled to ensure the process produces the desired quality.

Step 2 — Design Space: The proven acceptable ranges (PARs) of CPP combinations that produce conforming CQAs constitute the Design Space, derived from DoE studies.

Why other options are wrong:

- Option A: Correct — CQAs are product quality attributes; CPPs are process inputs impacting CQAs; DoE defines Design Space.
- Option B: Reverses CQA and CPP; real-time sensor readings are process data (CPP-related), not CQAs.
- Option C: CQAs and CPPs are distinct; CQAs are product properties, CPPs are process inputs.
- Option D: Neither CQAs nor CPPs are defined by equipment manufacturers; they are defined through regulatory and scientific risk assessment.

Final Answer: CQAs = product quality attributes; CPPs = process inputs impacting CQAs; DoE maps Design Space $\Rightarrow$ $\boxed{\text{A}}$

Answer: (A) Go Back to Q 53

Sol. 54.

Solution

Concept — Glycosylation Control in Cell Culture | Chapter: Bioprocess Engineering / Glycosylation: N-glycan processing in the Golgi requires metal cofactors for glycosyltransferases. Manganese is the critical cofactor for β-1,4-galactosyltransferase.

Step 1 — Manganese supplementation: β-1,4-Galactosyltransferase (B4GalT) transfers galactose from UDP-Gal onto the terminal GlcNAc of complex N-glycans. This enzyme requires Mn^{2+} as a cofactor. Mn^{2+} supplementation to the cell culture medium at low μM concentrations ($\sim$0.5–2 μM) increases B4GalT activity in the Golgi $\rightarrow$ higher galactosylation of the mAb Fc glycan, which modulates complement activation and ADCC.

Why other options are wrong:

- Option A: High pCO_2 (above $\sim$150 mmHg) decreases Golgi pH, reducing sialyltransferase and galactosyltransferase activity $\rightarrow$ lower galactosylation.
- Option B: Correct — Mn^{2+} is the cofactor for β-1,4-galactosyltransferase; supplementation increases galactosylation.
- Option C: Ammonia accumulation impairs glycosylation by altering Golgi pH and inhibiting glycosyltransferases; it does not increase galactosylation.
- Option D: Reduced temperature (29°C) generally slows metabolic activity and can reduce glycan site occupancy; it does not specifically increase galactosylation.

Final Answer: Mn^{2+} supplementation activates β-1,4-galactosyltransferase $\rightarrow$ increased galactosylation $\Rightarrow$ $\boxed{\text{B}}$

Answer: (B) Go Back to Q 54

Sol. 55.

Solution

Concept — Higher-Order Structure (HOS) Characterisation | Chapter: Analytical Methods / Biopharmaceutical Characterisation: HOS encompasses secondary structure (α-helix/β-sheet), tertiary fold, and quaternary assembly. ICH Q6B requires HOS comparability to be demonstrated after manufacturing changes.

Step 1 — Appropriate techniques for HOS: (a) Circular dichroism (CD) spectroscopy: far-UV CD (190–260 nm) probes secondary structure (α-helix at

222/208 nm; β-sheet at 218 nm); near-UV CD (260–320 nm) probes tertiary environment of aromatic residues. (b) Intrinsic tryptophan fluorescence (λ_{em} shift reports on burial/solvent exposure of Trp residues) $\rightarrow$ tertiary fold integrity. (c) HDX-MS (hydrogen–deuterium exchange mass spectrometry) provides residue-level HOS information. (d) NMR provides atomic-level HOS but is limited to small proteins.

Why other options are wrong:

- Option A: SDS-PAGE under reducing conditions measures primary sequence integrity (MW) and ELISA measures binding; neither probes HOS.
- Option B: SEC-HPLC measures aggregation; IEX-HPLC measures charge variants; neither directly measures secondary or tertiary structure.
- Option C: Correct — CD spectroscopy + intrinsic fluorescence are the standard HOS tools; HDX-MS/NMR provide additional depth.
- Option D: cIEF measures charge heterogeneity (charge variants); it does not probe secondary or tertiary structure.

Final Answer: CD spectroscopy + Trp fluorescence (+ HDX-MS) for HOS comparability $\Rightarrow$ C

Answer: (C) Go Back to Q 55

Sol. 56.

Solution

Concept — RNA-seq Library Preparation Steps | Chapter: Genomics / RNA-seq: After dscDNA synthesis from fragmented mRNA, the cDNA must be end-repaired, A-tailed, ligated with adaptors, size-selected, and PCR-amplified before sequencing.

Step 1 — Correct order of enzymatic steps: Double-stranded cDNA has irregular ends from second-strand synthesis. (1) **End repair**: T4 DNA polymerase + Klenow fill in 5′ recesses and chew back 3′ overhangs $\rightarrow$ blunt ends + 5′ phosphorylation. (2) **3′-A overhang addition**: Klenow exo$^-$ + dATP adds a single A to 3′ ends for T-A ligation with adaptors. (3) **Adaptor ligation**: T4 DNA ligase joins Y-shaped adaptors (containing P5/P7 Illumina sequences + sample index). (4) **Size selection**: AMPure XP beads select insert size (typically 200–400 bp). (5) **PCR amplification**: enriches ligated fragments.

Why other options are wrong:

- Option A: Ligation before end repair is impossible; blunt/A-tailed ends are required for efficient adaptor ligation.
- Option B: Correct — end repair → A-tailing → adaptor ligation → size selection → PCR.
- Option C: Size selection before end repair is non-standard and inefficient; PCR before adaptor ligation would amplify unmodified fragments.
- Option D: A-tailing before end repair would give non-blunt ends that cannot be efficiently A-tailed; ordering is incorrect.

Final Answer: End repair → A-tailing → adaptor ligation → size selection → PCR ⇒ B

Answer: (B) Go Back to Q 56

Sol. 57.

Solution

Concept — Splice-Aware RNA-seq Alignment | Chapter: Genomics / RNA-seq: RNA-seq reads from spliced mRNAs must be aligned to the genome with awareness of exon–intron boundaries. Standard DNA aligners (BWA, Bowtie2) cannot handle long intronic gaps and will discard or misalign junction-spanning reads.

Step 1 — Splice-aware aligners: STAR (Spliced Transcripts Alignment to a Reference) uses a two-pass approach with a genome index. HISAT2 uses a graph-based FM-index incorporating known splice sites. Both output BAM files that can be used for downstream count-based DEA.

Step 2 — Pseudoalignment alternatives: kallisto and salmon use quasi-mapping to a transcriptome index (not the genome), making them faster but requiring a complete transcriptome annotation. They cannot discover novel junctions.

Why other options are wrong:

- Option A: BWA-MEM and Bowtie2 are not splice-aware and will fail to map junction reads; STAR is a genome aligner, not a pseudoaligner.
- Option B: TopHat2 was an earlier splice-aware aligner; BLAST is a general sequence alignment tool, not an RNA-seq pseudoaligner.
- Option C: Correct — STAR and HISAT2 are splice-aware genome aligners; kallisto and salmon are pseudoalignment tools for transcriptome quantification.

- Option D: featureCounts is a read-counting tool (counts reads overlapping gene features in a BAM file), not an aligner or pseudoaligner.

Final Answer: STAR and HISAT2 (splice-aware); kallisto and salmon (pseudoalignment) $\Rightarrow$ C

Answer: (C) Go Back to Q 57

Sol. 58.

Solution

Concept — RNA-seq Normalisation: TPM vs RPKM/FPKM | Chapter: Genomics / RNA-seq Normalisation: Normalisation is required to account for (1) different gene lengths (longer genes produce more fragments) and (2) different library sizes (more deeply sequenced samples have more reads).

Step 1 — TPM calculation:

$$\mathrm{RPK}_i = \frac{\text{counts}_i}{\text{gene length}_i \text{ (kb)}} \quad ; \quad \mathrm{TPM}_i = \frac{\mathrm{RPK}_i}{\sum_j \mathrm{RPK}_j} \times 10^6$$

Because each sample is normalised by its own sum of RPK values, the denominator scales with library size. Crucially, $\sum_i \mathrm{TPM}_i = 10^6$ for every sample, making samples directly comparable.

Step 2 — RPKM/FPKM problem: RPKM normalises by library size first, then gene length. The sum of RPKM values differs between samples (a gene contributing much to the total can shift all other values). This means RPKM values are not directly comparable across samples.

Why other options are wrong:

- Option A: TPM does correct for gene length (via the RPK step); the claim that length is ignored is wrong.
- Option B: TPM and RPKM are mathematically different in the order of normalisation steps; they are NOT identical.
- Option C: TPM and RPKM are NOT interchangeable; the order of division steps differs and FPKM $\neq$ TPM for between-sample comparisons.
- Option D: Correct — length normalisation first (RPK), then scale to 10^6; constant sum across samples ensures comparability.

Final Answer: TPM length-normalises first then scales; sum always 10^6, enabling between-sample comparison $\Rightarrow$ D

Answer: (D) Go Back to Q 58

Sol. 59.

Solution

Concept — GSEA vs Over-Representation Analysis | Chapter: Bioinformatics / Gene Set Analysis: Traditional ORA requires researchers to define a "foreground" gene set using an arbitrary significance cutoff (e.g. $p < 0.05$ and $|\log_2 \text{FC}| > 1$), then tests if any pathways are over-represented. GSEA avoids this by testing the entire ranked list.

Step 1 — GSEA advantage: GSEA ranks *all* expressed genes by a continuous statistic (e.g. signal-to-noise ratio, fold change, $-\log_{10} p \times \text{sign}$) and then assesses whether each gene set is enriched at the top or bottom of the ranked list using a running-sum Kolmogorov–Smirnov-like statistic. This detects sets of genes that are coordinately upregulated or downregulated even if no single gene passes a fold-change threshold.

Why other options are wrong:

- Option A: GSEA *does* require a pre-ranked gene list; it is ORA that requires a defined foreground list.
- Option B: Reverses the descriptions of GSEA and ORA; it is ORA that requires a foreground list.
- Option C: GSEA does NOT require an arbitrary fold-change cutoff; this is the property of ORA.
- Option D: Correct — GSEA uses the full ranked gene list without arbitrary cutoffs, capturing coordinated moderate changes in a pathway.

Final Answer: GSEA ranks all genes; no arbitrary cutoff needed; more sensitive for pathway-level changes $\Rightarrow$ D

Answer: (D) Go Back to Q 59

Sol. 60.

Solution

Concept — RNA Velocity | Chapter: Bioinformatics / Single-Cell Transcriptomics: RNA velocity (La Manno et al. 2018; Bergen et al. 2020) exploits the kinetic relationship between unspliced and spliced mRNA counts to infer the direction and speed of gene expression changes at the single-cell level.

Step 1 — Molecular basis: For each gene, intronic reads in a scRNA-seq dataset represent nascent unspliced pre-mRNA (actively being transcribed), while exonic reads represent the steady-state spliced mRNA. The ratio of unspliced to spliced mRNA reveals whether a gene's expression level is increasing (high unspliced:spliced $\rightarrow$ more mRNA is being produced than degraded) or decreasing (low ratio $\rightarrow$ transcription has slowed and existing spliced mRNA is being degraded). RNA velocity vectors on a UMAP projection show the inferred future transcriptional state of each cell as arrows.

Why other options are wrong:

- Option A: Protein:mRNA ratios require CITE-seq or proteomics; RNA velocity is an mRNA-only measurement.
- Option B: Correct — unspliced:spliced pre-mRNA ratio infers direction of transcriptional change.
- Option C: Chromatin accessibility (ATAC-seq) is a separate assay; multiomic approaches (SHARE-seq) combine it with RNA, but standard RNA velocity uses RNA reads alone.
- Option D: Nuclear–cytoplasmic RNA fractionation is a traditional approach; modern RNA velocity uses standard $10\times$ scRNA-seq reads covering introns.

Final Answer: Unspliced:spliced mRNA ratio infers direction of transcriptional change (RNA velocity) $\Rightarrow$ $\boxed{\text{B}}$

Answer: (B) Go Back to Q 60

Sol. 61.

Solution

Concept — Cytosine Base Editor (CBE) and UGI | Chapter: Genome Editing / Base Editing: In the CBE system, AID/APOBEC converts C to U within the editing window. Without UGI, cellular uracil DNA glycosylase (UNG) would excise the uracil, creating an abasic site that leads to indels rather than the desired C$\rightarrow$T conversion.

Step 1 — UGI mechanism: UGI is a bacteriophage PBS2-encoded protein that stoichiometrically inhibits UNG. By inhibiting UNG, UGI allows the uracil generated by APOBEC to persist until DNA replication. During replication, DNA polymerase reads U as T → C:G pair becomes T:A pair → desired C→T base edit achieved. Without UGI, the abasic site left after UNG excision would be bypassed by error-prone polymerases → indels.

Why other options are wrong:

- Option A: UGI does not directly enhance APOBEC deaminase activity; it blocks UNG.
- Option B: UGI does the opposite of promoting faithful repair; it blocks the repair enzyme (UNG) to allow U→T conversion.
- Option C: Correct — UGI inhibits UNG → U persists → read as T during replication → C→T conversion without abasic site or indels.
- Option D: UGI has an enzymatic function (UNG inhibitor); it is a functional protein, not merely a structural linker.

Final Answer: UGI inhibits UNG → U persists → read as T during replication ⇒ C

Answer: (C) Go Back to Q 61

Sol. 62.

Solution

Concept — Adenine Base Editors and the Role of Inosine | Chapter: Genome Editing / Base Editing: ABEs use an evolved TadA (tRNA adenosine deaminase) that deaminates A→I in ssDNA within the editing window. The key is that inosine is recognised as guanine by replicative DNA polymerases.

Step 1 — Why I is equivalent to G: Inosine lacks the 2-amino group of guanine but retains the keto group at O6 and N1-H. Hydrogen-bonding geometry of inosine matches cytosine, not thymine → C is incorporated opposite I during replication → after one replication cycle: original A:T → I:T → I:C → G:C (in progeny). Net result: A:T → G:C base pair conversion.

Step 2 — Therapeutic applications: ABEs can correct any mutation that is A→G (on the sense strand) or T→C (on the antisense strand, viewing the opposite strand A→G). This covers a large fraction of known pathogenic point mutations.

Why other options are wrong:

- Option A: Inosine is read as G, not A; the conversion is A:T → G:C (transition), not a transversion.
- Option B: Inosine is not removed by glycosylases in the context of ABE editing (TadA-evolved ABE generates inosine in ssDNA which is then replicated before repair).
- Option C: Inosine pairs with C (like G), not A; the outcome is G:C, not A:T.
- Option D: Correct — inosine is read as G → A:T becomes G:C; ABEs correct A→G or T→C pathogenic SNVs.

Final Answer: Inosine read as G → A:T → G:C; corrects A→G or T→C mutations ⇒ D

Answer: (D) Go Back to Q 62

Sol. 63.

Solution

Concept — Prime Editing and the pegRNA | Chapter: Genome Editing / Prime Editing: Prime editing uses a pegRNA (prime editing guide RNA) that is an extended sgRNA with additional 3′ sequences encoding the edit. The pegRNA directs both target recognition and reverse transcription.

Step 1 — 3′ extension of the pegRNA: The 3′ extension beyond the sgRNA scaffold consists of two functional elements: (a) **PBS (primer binding site)**: a sequence complementary to the 3′ end of the nicked strand (the PAM-containing strand is nicked by nCas9); the PBS base-pairs with the nicked 3′-OH overhang to prime reverse transcription. (b) **RTT (reverse transcriptase template)**: encodes the desired edited sequence; the engineered MMLV RT copies the RTT using the 3′-OH of the nicked strand as primer → 3′ DNA flap containing the desired edit is synthesised and incorporated.

Why other options are wrong:

- Option A: Correct — PBS + RTT are the functional 3′ extension elements of the pegRNA.
- Option B: A polyadenylation signal would destabilise the pegRNA (cause premature transcription termination in Pol II); prime editing uses Pol III for short pegRNA or modified pegRNAs (epegRNAs) to enhance stability.
- Option C: HDR factors are not recruited by pegRNA aptamers; prime editing works independently of HDR.
- Option D: A second guide targeting a separate locus is used in PE3/PE3b strategies to nick the complementary strand, but this is a separate sgRNA,

not part of the pegRNA 3′ extension.

Final Answer: pegRNA 3′ extension = PBS (primer binding site) + RTT (reverse transcriptase template encoding the edit) ⇒ A

Answer: (A) Go Back to Q 63

Sol. 64.

Solution

Concept — CRISPRi Mechanism | Chapter: Genome Editing / CRISPR Transcriptional Regulation: CRISPRi uses dCas9 (no nuclease activity) fused to the KRAB domain to achieve targeted, reversible transcriptional silencing without altering the DNA sequence.

Step 1 — KRAB–KAP1 silencing mechanism: The KRAB domain is a transcriptional repressor module found in many mammalian zinc-finger proteins. When dCas9-KRAB is guided to a gene's promoter or TSS: (1) KRAB recruits KAP1 (TRIM28/TIF1β). (2) KAP1 recruits the NuRD histone deacetylase complex and SETDB1 (H3K9 methyltransferase). (3) SETDB1 deposits H3K9me3, a repressive histone mark recognised by HP1 → heterochromatin spreading → transcriptional silencing. Silencing is reversible; withdraw dCas9-KRAB and the chromatin reverts.

Why other options are wrong:

- Option A: VPR (VP64-p65-Rta) is used for CRISPRa (activation), not CRISPRi.
- Option B: Correct — dCas9-KRAB recruits KAP1 → H3K9me3 → heterochromatin → reversible silencing.
- Option C: dCas9 has no nuclease activity; it cannot cleave mRNA.
- Option D: TET1 is a DNA demethylase and is used for CRISPRa (reactivation by removing repressive methylation), not CRISPRi.

Final Answer: dCas9-KRAB → KAP1 → H3K9me3 → reversible silencing ⇒ B

Answer: (B) Go Back to Q 64

Sol. 65.

Solution

Concept — Epigenome Editing with dCas9–TET1 | Chapter: Genome Editing / Epigenome Editing: To reactivate a gene silenced by CpG hypermethylation, the appropriate tool is a DNA demethylase fused to dCas9.

Step 1 — dCas9–TET1 mechanism: TET1 (ten-eleven translocation 1) is an iron(II)/2-oxoglutarate-dependent dioxygenase that sequentially oxidises 5-methylcytosine (5mC) $\rightarrow$ 5-hydroxymethylcytosine (5hmC) $\rightarrow$ 5-formylcytosine (5fC) $\rightarrow$ 5-carboxylcytosine (5caC). 5fC and 5caC are excised by thymine DNA glycosylase (TDG) and replaced by unmodified cytosine via base-excision repair $\rightarrow$ net CpG demethylation. Targeted to a hypermethylated tumour suppressor promoter by dCas9, TET1 removes the silencing methylation marks $\rightarrow$ gene reactivation.

Why other options are wrong:

- Option A: dCas9-DNMT3A adds CpG methylation; this would further silence an already hypermethylated gene.
- Option B: dCas9-EZH2 deposits H3K27me3 (repressive); it would maintain or enhance silencing.
- Option C: Correct — dCas9-TET1 oxidises 5mC $\rightarrow$ 5hmC $\rightarrow$ unmethylated C, reactivating the hypermethylated tumour suppressor.
- Option D: dCas9-LSD1 removes H3K4me1/me2 from enhancers, inactivating them; it does not demethylate CpGs and would not reactivate a promoter-methylated gene.

Final Answer: dCas9–TET1 demethylates CpGs $\rightarrow$ reactivates silenced tumour suppressor $\Rightarrow$ $\boxed{\text{C}}$

Answer: (C) Go Back to Q 65

Answer Key

Q	Ans	Q	Ans	Q	Ans	Q	Ans	Q	Ans
1	A	2	B	3	C	4	D	5	A
6	B	7	C	8	D	9	A	10	B
11	C	12	D	13	A	14	B	15	C
16	B	17	C	18	D	19	A	20	B
21	C	22	D	23	A	24	B	25	C
26	D	27	A	28	B	29	C	30	D
31	A	32	C	33	B	34	D	35	A
36	B	37	C	38	D	39	A	40	C
41	D	42	A	43	B	44	C	45	D
46	B	47	C	48	D	49	A	50	B
51	C	52	D	53	A	54	B	55	C
56	B	57	C	58	D	59	D	60	B
61	C	62	D	63	A	64	B	65	C