FMGE Biochemistry Sample Paper – 4

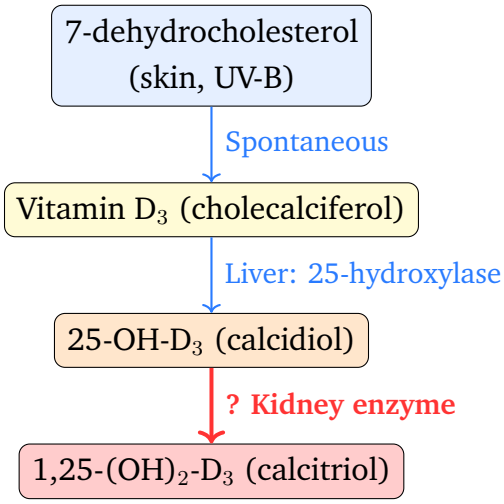
Duration: 60 Minutes **Maximum Marks: 40**

Instructions

- This paper contains **40 Multiple Choice Questions** modelled on the **Biochemistry** section of FMGE (Part A – Pre-clinical).
- Each correct answer carries **+1 mark**. There is **no negative marking** – attempt all questions.
- Questions follow the clinically integrated pattern of FMGE examination.
- Click a question number in the answer key to navigate to its solution.

FMGE Biochemistry – Q1 to Q40

Q1. A 65-year-old man with chronic renal failure on dialysis complains of bone pain and muscle weakness. Despite adequate sunlight exposure, his serum 1,25-$(OH)_2$-D_3 (calcitriol) is very low. Which enzyme, primarily expressed in the kidney, is responsible for the final activation step of vitamin D to calcitriol, and is deficient in this patient?



(A) 1α-hydroxylase (CYP27B1) – stimulated by PTH

(B) 24-hydroxylase – produces inactive 24,25-$(OH)_2$-D_3

(C) 25-hydroxylase (CYP2R1) – liver enzyme

(D) 7-dehydroreductase – skin enzyme

Q2. A biochemist classifies an enzyme based on the International Union of Biochemistry and Molecular Biology (IUBMB) system. The enzyme she is studying catalyses the transfer of a phosphate group from ATP to glucose (forming glucose-6-phosphate). According to the IUBMB enzyme classification, this enzyme belongs to which class (EC number)?

(A) EC 1 – Oxidoreductases

(B) EC 2 – Transferases

(C) EC 3 – Hydrolases

(D) EC 4 – Lyases

Q3. A 6-month-old infant presents with hypotonia (floppy baby), cardiomegaly, hepatomegaly, and severe respiratory distress. Muscle biopsy shows massive lysosomal glycogen accumulation. Acid α-glucosidase (acid maltase) activity is absent. These findings are most consistent with:

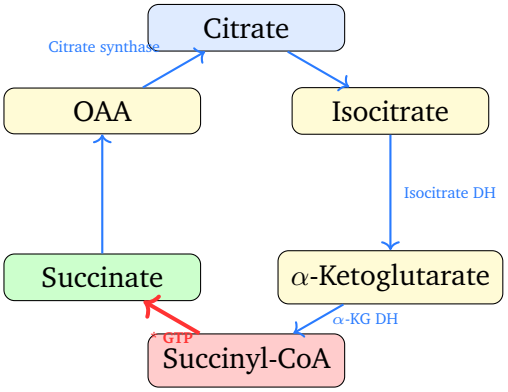
(A) Von Gierke disease (GSD type I)

(B) Pompe disease (GSD type II)

(C) Cori disease (GSD type III)

(D) McArdle disease (GSD type V)

Q4. In the TCA cycle shown below, only one enzyme reaction generates GTP (or ATP) directly by substrate-level phosphorylation. This enzyme, succinyl-CoA synthetase, catalyses the conversion of succinyl-CoA to succinate. Which reaction is indicated by the asterisk?



(A) Isocitrate dehydrogenase (isocitrate $\rightarrow$ α-ketoglutarate)

(B) Citrate synthase (OAA + acetyl-CoA $\rightarrow$ citrate)

(C) Succinyl-CoA synthetase (succinyl-CoA $\rightarrow$ succinate) – generates GTP

(D) Malate dehydrogenase (malate $\rightarrow$ OAA)

Q5. A premature neonate of 28 weeks gestation develops haemolytic anaemia with red cell fragility and echinocytes on blood smear. Serum vitamin E level is undetectable. This presentation is consistent with deficiency of which fat-soluble vitamin, which acts as a membrane-protecting lipid-soluble antioxidant?

(A) Vitamin A (α-tocopherol)

(B) Vitamin D (calcitriol)

(C) Vitamin K (phylloquinone)

(D) Vitamin E (α-tocopherol)

Q6. A patient with a urea cycle disorder has markedly elevated plasma ammonia. The enzyme carbamoyl phosphate synthetase I (CPS-I) is the mitochondrial enzyme that initiates urea cycle metabolism. Which molecule serves as the obligatory allosteric activator of CPS-I, without which the enzyme is essentially inactive?

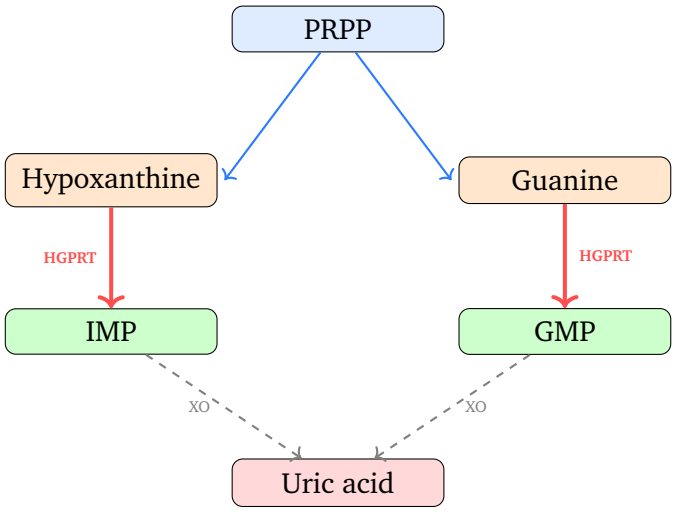
(A) Ornithine

(B) Citrulline

(C) N-acetylglutamate (NAG)

(D) Arginine

Q7. A patient with gout overproduces uric acid due to de novo purine synthesis. In the purine salvage pathway shown below, hypoxanthine and guanine are recycled back to IMP and GMP respectively, conserving energy. Which enzyme catalyses both these reactions?



(A) Adenine phosphoribosyltransferase (APRT)

(B) Xanthine oxidase (XO)

(C) Hypoxanthine-guanine phosphoribosyltransferase (HGPRT)

(D) Adenosine deaminase (ADA)

Q8. After ingestion of a fatty meal, chylomicrons are assembled in intestinal enterocytes and secreted into lymph. In the circulation, triglycerides are hydrolysed from chylomicrons by lipoprotein lipase (LPL). The resulting chylomicron remnants are taken up by the liver. Which apolipoprotein on the remnant surface serves as the ligand recognised by the hepatic LRP1 (LDL receptor-related protein) receptor?

(A) ApoE

(B) ApoB-48

(C) ApoC-II

(D) ApoA-I

Q9. In the TCA cycle, the first step condenses acetyl-CoA with oxaloacetate (OAA) to form citrate. The enzyme catalysing this step is the rate-

limiting enzyme of the cycle. This enzyme is allosterically inhibited by ATP, NADH, and succinyl-CoA. Identify this enzyme.

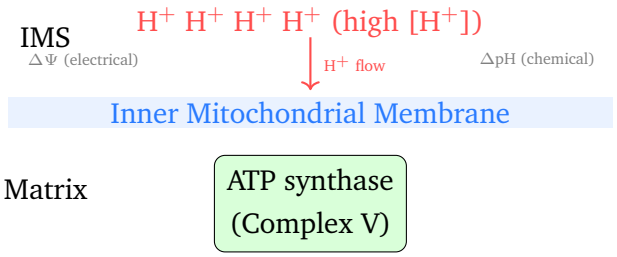
(A) Citrate synthase

(B) Isocitrate dehydrogenase

(C) α-Ketoglutarate dehydrogenase

(D) Malate dehydrogenase

Q10. The chemiosmotic hypothesis (Peter Mitchell) explains how ATP is synthesised in mitochondria. The proton gradient across the inner mitochondrial membrane has two components. Which equation correctly represents the proton motive force (Δp) that drives Complex V (F_0F_1-ATPase)?



(A) $\Delta p = \Delta\Psi$ only (electrical gradient alone)

(B) $\Delta p = \Delta\text{pH}$ only (chemical gradient alone)

(C) $\Delta p = \Delta\Psi - \Delta\text{pH}$ (electrical minus chemical)

(D) $\Delta p = \Delta\Psi + \Delta\text{pH}$ (electrical potential plus pH gradient – both components)

Q11. A 25-year-old woman presents with pallor, jaundice, and dark urine following an upper respiratory tract infection. Blood film shows spherocytes. Direct Coombs test is positive. Serum haptoglobin is markedly decreased. What is the significance of decreased serum haptoglobin in this clinical context?

(A) It confirms intravascular haemolysis – haptoglobin binds free Hb released into plasma and is consumed

(B) It indicates liver failure causing reduced haptoglobin synthesis

(C) It reflects extravascular haemolysis in the spleen only

(D) It indicates increased haptoglobin renal excretion

Q12. A young boy presents with self-mutilating behaviour (biting fingers and lips), spasticity, choreoathetosis, intellectual disability, and markedly elevated serum uric acid. Urine shows orange sandy deposits (urate crystals). HGPRT activity in red blood cells is absent. Why does HGPRT deficiency cause hyperuricaemia in Lesch-Nyhan syndrome?

(A) HGPRT directly produces uric acid from hypoxanthine

(B) Failure to salvage purines leads to accumulation of PRPP, which drives overactive de novo purine synthesis and excess uric acid production

(C) HGPRT deficiency impairs urate excretion by the kidney

(D) HGPRT normally converts uric acid back to xanthine

Q13. A molecular biology student labels the strands of a DNA duplex to study replication direction. DNA synthesis by DNA polymerase always proceeds in the 5'→3' direction on the newly synthesised strand, reading the template 3'→5'. Which statement about the leading and lagging strands is correct?

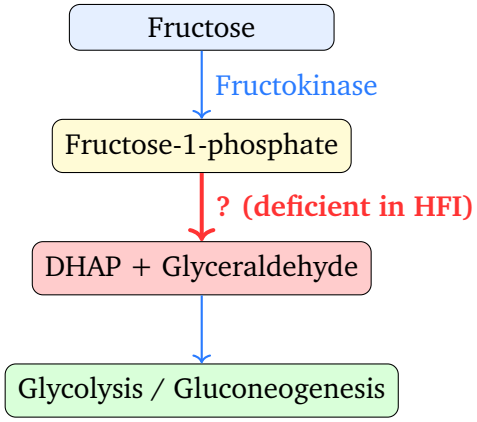
(A) Both strands are synthesised continuously in the same direction

(B) The lagging strand is synthesised continuously; the leading strand uses Okazaki fragments

(C) Both strands require Okazaki fragments

(D) The leading strand is synthesised continuously; the lagging strand uses discontinuous Okazaki fragments synthesised 5'→3'

Q14. A 2-year-old child presents with vomiting, hypoglycaemia, and liver enlargement after ingesting fruit juice. Investigations reveal fructosuria, elevated fructose-1-phosphate in liver, and depleted hepatic ATP. The diagram below outlines hepatic fructose metabolism. Which enzyme deficiency is responsible for hereditary fructose intolerance (HFI)?



(A) Fructokinase (leads to essential fructosuria – benign)

(B) Glucose-6-phosphatase

(C) Fructose-1,6-bisphosphatase

(D) Aldolase B (liver isoform)

Q15. A 10-month-old infant develops jaundice, vomiting, and hepatomegaly immediately after being given fruit puree containing apple juice. Blood glucose drops to 1.8 mmol/L. Liver biopsy shows fructose-1-phosphate accumulation. Phosphate depletion in the hepatocyte leads to impaired glycogenolysis and gluconeogenesis. This condition, hereditary fructose intolerance, is caused by deficiency of:

(A) Fructokinase – causing fructosaemia (benign)

(B) Aldolase B – leading to fructose-1-phosphate accumulation and hypoglycaemia

(C) Phosphoglucose isomerase

(D) Fructose-2,6-bisphosphatase

Q16. A patient with familial lipoprotein lipase (LPL) deficiency presents with eruptive xanthomas, recurrent pancreatitis, and a plasma triglyceride level of 4800 mg/dL (chylomicronaemia). LPL on capillary endothelium normally hydrolyses triglycerides from circulating chylomicrons and VLDL. Which apolipoprotein is the essential cofactor that activates LPL?

(A) ApoC-II

(B) ApoB-48

(C) ApoA-I

(D) ApoE

Q17. A chronic alcoholic undergoes liver biopsy showing Mallory-Denk bodies (cytokeratin aggregates), mitochondrial swelling, and perisinusoidal fibrosis. Biochemically, which property of acetaldehyde – the first metabolic product of ethanol oxidation – is primarily responsible for protein adduct formation and cellular toxicity?

(A) It is a ketone and reacts with polar amino acid residues

(B) It is a stable molecule that competes with NADH

(C) It raises intracellular pH directly

(D) It is a highly reactive aldehyde that forms covalent adducts with proteins, impairing microtubule function and stimulating collagen synthesis

Q18. Many biosynthetic reactions (e.g., aminoacyl-tRNA synthesis, fatty acid activation) consume ATP and release inorganic pyrophosphate (PP_i). An enzyme immediately hydrolyses PP_i to 2 P_i, with a strongly negative ΔG. What is the biochemical significance of this inorganic pyrophosphatase reaction?

(A) It drives the biosynthetic reaction forward by removing PP_i, making the overall reaction irreversible and thermodynamically favourable

(B) It regenerates ATP from AMP

(C) It provides inorganic phosphate for oxidative phosphorylation

(D) It inhibits further protein synthesis at the ribosome

Q19. A patient with iron-deficiency anaemia is found to have elevated serum transferrin receptor (TfR1) levels. At the molecular level, iron deficiency activates iron regulatory proteins (IRPs) that bind to iron responsive elements (IREs) in mRNA. What is the effect of IRP binding to the 3' IRE of TfR1 mRNA in iron-deficient cells?

(A) It promotes TfR1 mRNA degradation, reducing iron uptake

(B) It inhibits TfR1 mRNA translation without affecting mRNA stability

(C) It promotes ferritin translation to store excess iron

(D) It stabilises TfR1 mRNA, preventing its degradation and increasing TfR1 expression to enhance iron uptake

Q20. Arachidonic acid (AA) is released from membrane phospholipids to serve as the precursor for eicosanoid synthesis (prostaglandins, leukotrienes, thromboxanes). Which enzyme cleaves the fatty acid at the *sn*-2 position of glycerophospholipid to release AA, and is inhibited by corticosteroids (via induction of annexin-1/lipocortin)?

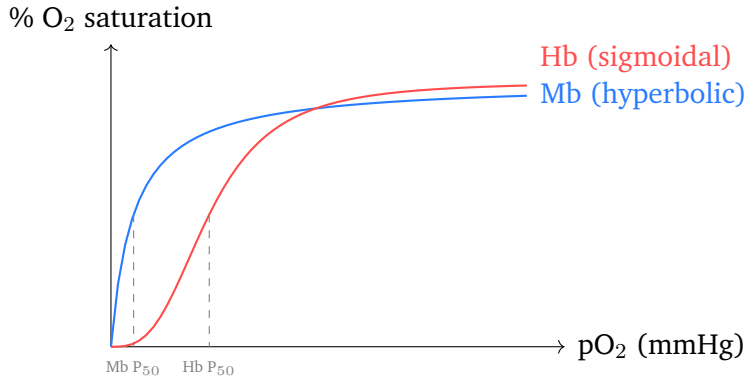
(A) Cyclooxygenase (COX-1/COX-2)

(B) Lipoxygenase (5-LOX)

(C) Phospholipase A_2 (PLA_2)

(D) Phospholipase C (PLC)

Q21. The oxygen dissociation curves for myoglobin (Mb) and haemoglobin (Hb) are compared below. Which statement correctly describes myoglobin's oxygen-binding behaviour?



(A) Myoglobin has a hyperbolic dissociation curve, a lower P_{50} than Hb, higher O_2 affinity, and releases O_2 only at very low pO_2 in exercising muscle

(B) Myoglobin has a sigmoidal dissociation curve due to cooperativity between four subunits

(C) Myoglobin's P_{50} is higher than haemoglobin's, meaning it releases O_2 more readily

(D) Myoglobin is the major O_2 carrier in blood

Q22. A 35-year-old woman of Northern European descent reports bloating, flatulence, and diarrhoea after consuming milk and dairy products since childhood. She tolerates yoghurt and hard cheese. Genetic testing reveals the common European lactase persistence allele (LCT-13910*T) in homozygous ancestral form (CC). What is the underlying mechanism of her symptoms?

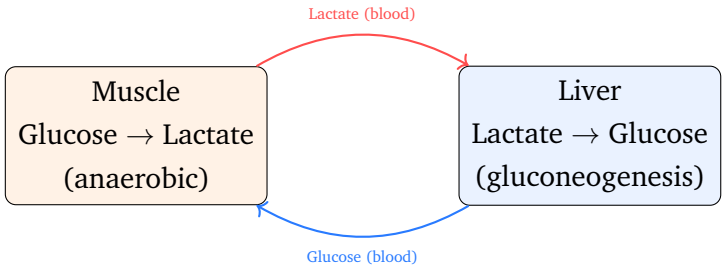
(A) Absence of lactase (lactase non-persistence) means intestinal brush-border lactase activity declines after weaning; undigested lactose is fermented by colonic bacteria producing gas and osmotic diarrhoea

(B) She has sucrase-isomaltase deficiency

(C) Lactose is absorbed intact and excreted unchanged in urine

(D) She has an allergy to casein (milk protein)

Q23. A marathon runner's muscles produce lactate during exercise. After the race, the lactate is transported to the liver via the bloodstream. The Cori cycle (lactic acid cycle) converts this lactate back to glucose. Which of the following correctly describes the Cori cycle?



(A) The Cori cycle generates net ATP in both muscle and liver

(B) The Cori cycle converts lactate to glucose in muscle

(C) Lactate is converted to acetyl-CoA in the liver and enters the TCA cycle

(D) Muscle produces lactate by anaerobic glycolysis; liver converts lactate to glucose by gluconeogenesis, consuming 6 ATP per glucose; net energy transfer from liver to muscle

Q24. Transamination reactions are the primary mechanism by which amino groups are transferred between amino acids and α-keto acids. The coenzyme that accepts the amino group in transamination reactions, forming a Schiff base intermediate, is derived from which vitamin?

(A) Thiamine (B1) – TPP

(B) Niacin (B3) – NAD^+

(C) Pyridoxine (B6) – pyridoxal phosphate (PLP)

(D) Riboflavin (B2) – FAD

Q25. A 55-year-old patient with type 2 diabetes mellitus has a significantly elevated fasting LDL and is at high cardiovascular risk. Genetic testing reveals an ApoE4/E4 genotype. ApoE4 is associated with impaired clearance of which lipoprotein particles, and what additional disease risk does ApoE4 confer?

(A) ApoE4 impairs HDL clearance; associated with reduced risk of Alzheimer disease

(B) ApoE4 reduces the clearance of chylomicron remnants and IDL (via LDL receptor / LRP1) compared to ApoE3; associated with increased atherosclerosis risk and Alzheimer disease risk

(C) ApoE4 increases LPL activity; associated with hypertriglyceridaemia only

(D) ApoE4 is the most protective allele for cardiovascular disease

Q26. A 26-year-old pregnant woman undergoes second-trimester triple screen. Her maternal serum alpha-fetoprotein (AFP) is markedly elevated. Ultrasound reveals an open neural tube defect (spina bifida aperta). AFP is produced by which fetal structures, and what does elevated maternal AFP indicate?

(A) AFP is produced by fetal liver and yolk sac; elevated maternal serum AFP indicates open neural tube defects (spina bifida, anencephaly) or abdominal wall defects; LOW AFP is seen in Down syndrome

(B) AFP is produced by the placenta; elevated AFP indicates Down syndrome

(C) AFP is produced only by the fetal kidney; elevated AFP is a normal finding

(D) AFP is produced by maternal liver; elevated levels indicate hepatitis B infection

Q27. A genetic counsellor explains to a family that the affected child has a mutation in the CFTR gene caused by deletion of 3 nucleotides (F508del). This in-frame deletion removes one amino acid. A different patient has an insertion of 1 nucleotide in the BRCA1 gene, causing a premature stop codon 15 codons downstream. The BRCA1 mutation is classified as a frameshift mutation. Why are frameshift mutations generally more severe than in-frame mutations?

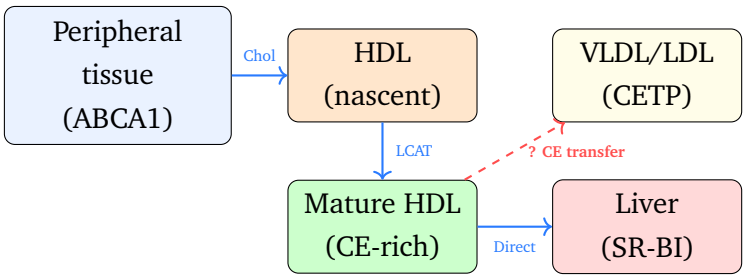
(A) Frameshift mutations affect only one amino acid

(B) Insertion or deletion of a non-multiple of 3 nucleotides shifts the reading frame, altering every subsequent codon and usually producing a premature stop codon, resulting in a truncated, non-functional protein

(C) In-frame deletions always produce non-functional protein

(D) Frameshift mutations only affect the 3' UTR of the gene

Q28. HDL particles are responsible for reverse cholesterol transport (RCT) – carrying cholesterol from peripheral tissues back to the liver. The diagram below summarises key steps of RCT. Which protein transfers cholesterol esters from HDL to VLDL/LDL in exchange for triglycerides?



(A) LCAT (lecithin-cholesterol acyltransferase) – esterifies free cholesterol in HDL

(B) ApoA-I – activates LCAT

(C) SR-BI (scavenger receptor class B type I) – hepatic HDL receptor

(D) CETP (cholesteryl ester transfer protein) – transfers CE from HDL to VLDL/LDL in exchange for TG

Q29. During intense aerobic exercise, heart and liver cells rely on the malate-aspartate shuttle to transfer cytosolic NADH equivalents into the mitochondria for oxidative phosphorylation. Which of the following correctly describes the net outcome of the malate-aspartate shuttle?

(A) Cytosolic NADH is transferred as reducing equivalents into the mitochondrial matrix (as mitochondrial NADH), yielding 2.5 ATP per NADH; this is the most efficient NADH shuttle

(B) Cytosolic NADH is converted to $FADH_2$ inside the mitochondria

(C) The shuttle operates in skeletal muscle, yielding 1.5 ATP per NADH

(D) The shuttle uses glycerol-3-phosphate as the primary carrier of reducing equivalents

Q30. A patient on erythromycin develops elevated levels of a co-administered drug (cyclosporin) causing toxicity. Erythromycin is a well-known inhibitor of CYP3A4. Which of the following statements about hepatic CYP450 enzymes is most accurate?

(A) CYP450 enzymes are located in the mitochondrial matrix and use $FADH_2$ as electron donor

(B) CYP450 enzymes perform phase II (conjugation) reactions only

(C) CYP450 enzymes are liver microsomal mixed-function oxidases requiring NADPH and O_2 for phase I drug metabolism; CYP3A4 is inhibited by erythromycin and grapefruit juice, and induced by rifampicin

(D) CYP450 enzymes are induced by substrate-level phosphorylation

Q31. In prokaryotic transcription termination, the Rho protein recognises specific sequences on nascent mRNA and uses ATP-dependent helicase activity to disrupt the RNA-DNA hybrid in the transcription bubble. This mechanism is called:

(A) Intrinsic (Rho-independent) termination – occurs at GC-rich hairpin + poly-U sequence

(B) Sigma factor release

(C) Rho-dependent transcription termination

(D) Anti-termination by N protein (lambda phage)

Q32. A newly synthesised protein destined for secretion contains multiple cysteine residues. In the endoplasmic reticulum, pairs of cysteine thiols are oxidised to form disulfide bonds essential for proper protein folding and extracellular stability. Which enzyme catalyses disulfide bond formation (and isomerisation) in the ER lumen?

(A) Peptidyl prolyl isomerase (PPI) – isomerises proline bonds

(B) Protein disulfide isomerase (PDI) – catalyses formation and isomerisation of disulfide bonds in the oxidising ER lumen

(C) Transglutaminase – cross-links glutamine and lysine in extracellular matrix

(D) BiP/GRP78 (Hsp70) – ATP-dependent chaperone recognising unfolded proteins

Q33. A patient is started on propylthiouracil (PTU) for Graves' disease. PTU blocks thyroid hormone synthesis. In normal thyroid hormone synthesis, thyroid peroxidase (TPO) catalyses the iodination of tyrosine residues

on thyroglobulin to produce MIT and DIT, and then couples them. What is the product of coupling one MIT (monoiodotyrosine) with one DIT (diiodotyrosine)?

(A) T4 (thyroxine) – two DIT residues coupled

(B) T3 (triiodothyronine) – one MIT + one DIT coupled

(C) rT3 (reverse T3) – produced by peripheral 5-deiodination of T4

(D) Thyroglobulin precursor (Tg) – before iodination

Q34. An athlete's muscle is stimulated by a single sprint. For the first few seconds before glycolysis is activated, ATP regeneration depends entirely on phosphocreatine (creatine phosphate). The reaction catalysed by creatine kinase (CK) is: creatine phosphate + ADP $\rightleftharpoons$ creatine + ATP. Which statement about phosphocreatine as an ATP buffer is most accurate?

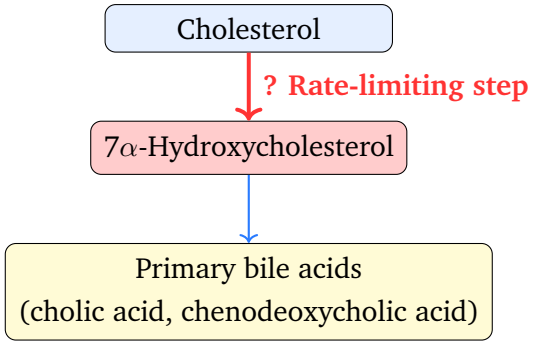
(A) Phosphocreatine is the primary ATP source during sustained aerobic exercise (hours)

(B) Phosphocreatine generates ATP only in cardiac muscle, not skeletal muscle

(C) Phosphocreatine is the fastest mechanism for ATP regeneration in muscle, depleted within seconds of intense exercise before glycolysis accelerates

(D) Phosphocreatine synthesis requires GTP as phosphate donor

Q35. A patient on cholestyramine (bile acid sequestrant) has reduced enterohepatic circulation of bile acids. The rate-limiting enzyme of bile acid synthesis from cholesterol is upregulated. Which enzyme is this, and what reaction does it catalyse?



(A) HMG-CoA reductase – rate-limiting step of cholesterol synthesis

(B) 24-hydroxylase (CYP46A1) – brain-specific cholesterol catabolism

(C) 7α-hydroxylase (CYP7A1) – rate-limiting step of bile acid synthesis, inhibited by bile acids (feedback), induced by cholesterol

(D) 12α-hydroxylase – determines cholic acid vs chenodeoxycholic acid ratio

Q36. A 35-year-old man is told he has Gilbert syndrome after a routine blood test reveals mild unconjugated hyperbilirubinaemia (total bilirubin 2.8 mg/dL). He is asymptomatic but notices jaundice during fasting or illness. Which molecular defect underlies Gilbert syndrome?

(A) Deficiency of haem oxygenase causing impaired bilirubin production

(B) Promoter polymorphism in UGT1A1 [$(TA)_7$ instead of $(TA)_6$] reducing UDP-glucuronosyltransferase expression and bilirubin conjugation capacity

(C) Complete absence of UGT1A1 activity – as seen in Crigler-Najjar type I

(D) Conjugated hyperbilirubinaemia from impaired canalicular bilirubin excretion (as in Dubin-Johnson syndrome)

Q37. A patient with I-cell disease (mucolipidosis type II) has elevated lysosomal hydrolases in serum but deficient activity within lysosomes. Fibroblasts show large cytoplasmic inclusions. The underlying defect is failure to tag lysosomal hydrolases with mannose-6-phosphate (M6P). The enzyme deficient in I-cell disease is:

(A) α-Mannosidase – a lysosomal hydrolase

(B) M6P receptor – on the Golgi membrane

(C) GlcNAc phosphotransferase – adds GlcNAc-phosphate to mannose residues of lysosomal enzymes in the Golgi; deficiency prevents M6P tagging and reroutes enzymes to secretion

(D) Sialyltransferase – adds sialic acid to glycoproteins

Q38. A 45-year-old male with a history of heavy alcohol binge over 3 days followed by vomiting presents with metabolic acidosis and elevated ketones. Blood glucose is 68 mg/dL (low-normal). Urine dipstick shows 3+ ketones. He has no history of diabetes. How does alcoholic ketoacidosis differ biochemically from diabetic ketoacidosis?

(A) Alcoholic KA has high blood glucose; diabetic KA has normal or low blood glucose

(B) Alcoholic KA presents with low or normal blood glucose and high NADH/NAD^+ ratio (from ethanol metabolism) driving ketogenesis; diabetic KA presents with high blood glucose from insulin deficiency; both have elevated ketones

(C) Alcoholic KA is characterised by metabolic alkalosis

(D) Alcoholic KA is caused by excess insulin secretion

Q39. A glycoprotein is being assembled in the rough ER. N-linked glycosylation involves en bloc transfer of a 14-sugar oligosaccharide core to asparagine residues within the sequon Asn-X-Ser/Thr. Before transfer, this oligosaccharide is assembled on a lipid carrier embedded in the ER membrane. What is this lipid carrier?

(A) Ceramide (sphingolipid backbone)

(B) Phosphatidylinositol (PI)

(C) GPI anchor precursor

(D) Dolichol phosphate – a polyisoprenol lipid carrier on which the Glc_3Man_9GlcNA oligosaccharide is assembled before en bloc transfer to protein

Q40. A tumour suppressor gene is found to be silenced in colorectal cancer cells. Sequencing shows no mutation in the coding sequence, but the CpG island in the promoter is heavily methylated. Methylation of cytosine at CpG sites to form 5-methylcytosine is an epigenetic mechanism of gene regulation. Which of the following statements about DNA methylation in cancer is most accurate?

(A) Hypermethylation of CpG islands in oncogene promoters activates oncogenes

(B) DNA methylation is carried out by histone acetyltransferases (HATs)

(C) Global hypermethylation of all CpG sites activates all genes simultaneously

(D) Hypermethylation of CpG islands in tumour suppressor gene promoters silences those genes; global genomic hypomethylation can activate proto-oncogenes; DNMT1/3a/3b catalyse DNA methylation; this is an epigenetic (heritable, non-sequence) change

Detailed Solutions

Q1.

Solution

Concept – Vitamin D hydroxylation steps: Vitamin D_3 (cholecalciferol) undergoes two sequential hydroxylations to become active. **Step 1**: In the liver, 25-hydroxylase (CYP2R1) converts D_3 to 25-OH-D_3 (calcidiol) – this is the major circulating storage form and measured in serum to assess vitamin D status. **Step 2**: In the kidney, **1α-hydroxylase (CYP27B1)** converts 25-OH-D_3 to the active hormone **1,25-(OH)$_2$-D$_3$ (calcitriol)**. PTH stimulates renal 1α-hydroxylation; hyperphosphataemia and high calcitriol inhibit it. In chronic renal failure, loss of renal CYP27B1 activity causes deficient calcitriol production $\rightarrow$ renal osteodystrophy.

Distractors: 24-hydroxylase produces the inactive 24,25-(OH)$_2$-D$_3$. 25-hydroxylase is the liver enzyme (Step 1, not the deficient one in renal failure). 7-dehydroreductase is not a vitamin D activation enzyme.

Final Answer: 1α-hydroxylase (CYP27B1) in kidney. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q1

Q2.

Solution

Concept – IUBMB Enzyme Classification: The IUBMB system divides enzymes into six main classes: EC 1 Oxidoreductases (redox reactions), **EC 2 Transferases** (transfer functional groups – including phosphate, amino, methyl, acyl groups), EC 3 Hydrolases (hydrolysis), EC 4 Lyases (addition/removal across double bonds), EC 5 Isomerases (isomerisation), EC 6 Ligases (bond formation using ATP). Hexokinase/glucokinase transfers a phosphate group from ATP to glucose – classifying it as a **transferase (EC 2.7.1.1 for hexokinase)**.

Distractors: Oxidoreductases catalyse redox (e.g., LDH, G6PD). Hydrolases cleave bonds with water (e.g., lipase, protease). Lyases eliminate groups to form double bonds (e.g., aldolase, carbonic anhydrase).

Final Answer: EC 2 – Transferases. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q2

Q3.

Solution

Concept – Pompe disease (GSD type II): Pompe disease is caused by deficiency of **acid α-glucosidase (acid maltase)** – a lysosomal enzyme. Glycogen accumulates within lysosomes in all tissues, but most severely in muscle and heart. The infantile-onset form presents with **cardiomegaly, profound hypotonia** ("floppy infant"), hepatomegaly, and respiratory failure leading to death within the first year without treatment. It is unique among GSDs because it is a **lysosomal storage disease**. Enzyme replacement therapy (alglucosidase alfa) is available.

Distractors: GSD type I (Von Gierke) causes hepatomegaly and hypoglycaemia but NOT cardiomegaly. GSD type III (Cori) is a debranching enzyme defect. GSD type V (McArdle) affects skeletal muscle phosphorylase with exercise intolerance, not cardiomegaly.

Final Answer: Pompe disease (GSD type II). $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q3

Q4.

Solution

Concept – Succinyl-CoA synthetase and substrate-level phosphorylation in TCA cycle: Among all TCA cycle enzymes, **succinyl-CoA synthetase** is the only one that generates a high-energy phosphate bond directly (substrate-level phosphorylation). The reaction: Succinyl-CoA + GDP + P_i $\rightarrow$ Succinate + GTP + CoA. GTP is freely interconvertible with ATP via nucleoside diphosphate kinase. One turn of the TCA cycle generates **1 GTP** by substrate-level phosphorylation (plus 3 NADH and 1 $FADH_2$).

Distractors: Isocitrate dehydrogenase generates NADH. Citrate synthase starts the cycle but generates no high-energy phosphate directly. Malate dehydrogenase generates NADH (regenerates OAA).

Final Answer: Succinyl-CoA synthetase (succinyl-CoA $\rightarrow$ succinate) – generates GTP. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q4

Q5.

Solution

Concept – Vitamin E (α-tocopherol) deficiency: Vitamin E (tocopherols and tocotrienols) is the major fat-soluble, chain-breaking antioxidant in cell membranes.

It donates a hydrogen atom to lipid peroxyl radicals, terminating lipid peroxidation chain reactions. α-Tocopherol is the most biologically active form. **Deficiency in premature neonates** – who have limited adipose stores and immature antioxidant defences – causes **haemolytic anaemia** due to oxidative damage to erythrocyte membranes. In adults, prolonged deficiency causes spinocerebellar ataxia and peripheral neuropathy.

Distractors: Vitamin A deficiency causes night blindness and xerophthalmia. Vitamin D deficiency causes rickets. Vitamin K deficiency causes bleeding diathesis (impaired coagulation factor γ-carboxylation). "Vitamin A (α-tocopherol)" is a deliberate distractor testing knowledge that α-tocopherol is vitamin E, not A.

Final Answer: Vitamin E (α-tocopherol). $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q5

Q6.

Solution

Concept – CPS-I and N-acetylglutamate (NAG) activation: Carbamoyl phosphate synthetase I (CPS-I) is a mitochondrial enzyme that catalyses: NH_3 + CO_2 + 2 ATP $\rightarrow$ carbamoyl phosphate. It is the **first and rate-limiting step of urea synthesis** (strictly, the step immediately preceding the urea cycle proper). CPS-I is **obligatorily activated by N-acetylglutamate (NAG)**, synthesised by NAG synthase from glutamate + acetyl-CoA, stimulated by arginine. Without NAG, CPS-I is essentially inactive. This is clinically important: NAG synthase deficiency or valproate-induced NAG depletion can cause hyperammonaemia.

Distractors: Ornithine is a substrate for the next step (OTC). Citrulline is the product of the OTC reaction. Arginine stimulates NAG synthase (indirect activation of CPS-I, not a direct allosteric activator of CPS-I itself).

Final Answer: N-acetylglutamate (NAG). $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q6

Q7.

Solution

Concept – Purine salvage pathway and HGPRT: Purines can be synthesised de novo (PRPP $\rightarrow$ IMP $\rightarrow$ AMP/GMP, requiring 10 steps and substantial energy) or recovered by the **salvage pathway**. **Hypoxanthine-guanine phosphoribosyltransferase (HGPRT)** catalyses both: (i) Hypoxanthine + PRPP $\rightarrow$ IMP + PP_i and (ii) Guanine + PRPP $\rightarrow$ GMP + PP_i. Adenine is salvaged by APRT (adenine phos-

phoribosyltransferase). Salvage is far more energy-efficient than de novo synthesis. HGPRT deficiency (X-linked) causes Lesch-Nyhan syndrome: hyperuricaemia (purines not salvaged, fed to xanthine oxidase → uric acid) and neurological features.

Distractors: APRT salvages adenine only. Xanthine oxidase converts hypoxanthine → xanthine → uric acid (catabolism, NOT salvage). Adenosine deaminase deaminates adenosine → inosine.

Final Answer: HGPRT (Hypoxanthine-guanine phosphoribosyltransferase). ⇒ $\boxed{C}$

Answer: (C) Go Back to Q7

Q8.

Solution

Concept – Chylomicron remnant clearance by ApoE: After LPL-mediated triglyceride hydrolysis in peripheral capillaries, chylomicrons shrink to **chylomicron remnants**. During this process, ApoC-II and ApoA-I are transferred to HDL, but **ApoE** and ApoB-48 remain on the remnant. The liver has LRP1 (LDL receptor-related protein) and LDL receptors, both of which recognise **ApoE** as the hepatic uptake ligand. ApoE binds these receptors with high affinity, mediating receptor-mediated endocytosis of remnants. ApoB-48 (the truncated intestinal ApoB) does NOT bind the LDL receptor.

Distractors: ApoB-48 is on the remnant but is not the ligand for hepatic clearance. ApoC-II activates LPL (transferred away by the time the remnant is formed). ApoA-I is the main HDL apolipoprotein, activates LCAT.

Final Answer: ApoE. ⇒ $\boxed{A}$

Answer: (A) Go Back to Q8

Q9.

Solution

Concept – Citrate synthase as the rate-limiting enzyme of the TCA cycle: Citrate synthase catalyses the condensation of acetyl-CoA (2C) with oxaloacetate (4C) to form citrate (6C) – the first step and rate-limiting step of the TCA cycle. It is inhibited by: (i) **ATP** (energy sufficiency), (ii) **NADH** (reflecting reduced state), and (iii) **succinyl-CoA** (product inhibition downstream in the cycle). It is activated by ADP and Ca^{2+} (during muscle contraction). While isocitrate dehydrogenase is also a major regulatory point, citrate synthase controls the initial entry

of acetyl-CoA into the cycle.

Distractors: Isocitrate dehydrogenase is a major regulatory enzyme but not the first step. α-KG dehydrogenase is regulated similarly to PDC. Malate dehydrogenase has a very unfavourable equilibrium towards malate (not the rate-limiting step).

Final Answer: Citrate synthase. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q9

Q10.

Solution

Concept – Chemiosmosis and the proton motive force: Peter Mitchell's chemiosmotic hypothesis (Nobel Prize 1978) proposes that the proton gradient across the inner mitochondrial membrane drives ATP synthesis. The proton motive force (Δp) has two components: (i) **electrical potential ($\Delta\Psi$)**: the inside of the mitochondrial matrix is negative relative to the IMS, because protons (positive charges) are pumped out; (ii) **chemical gradient (ΔpH)**: the matrix is more alkaline (fewer H^+) than the IMS. Both drive H^+ back into the matrix through Complex V. Therefore: $\Delta p = \Delta\Psi + \Delta\text{pH}$ (both components additive, both drive proton re-entry).

Distractors: $\Delta\Psi$ alone underestimates the driving force. ΔpH alone ignores the electrical component. $\Delta\Psi - \Delta\text{pH}$ would subtract a component, which is incorrect.

Final Answer: $\Delta p = \Delta\Psi + \Delta\text{pH}$ (both components). $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q10

Q11.

Solution

Concept – Haptoglobin and intravascular haemolysis: Haptoglobin is a serum α_2-glycoprotein that binds free haemoglobin released into plasma during intravascular haemolysis. The haptoglobin-Hb complex is rapidly taken up by liver macrophages (Kupffer cells) via CD163 receptors, preventing haem-iron loss in urine and renal tubular damage. In intravascular haemolysis, serum haptoglobin is **decreased** (consumed/depleted). Other markers of intravascular haemolysis: elevated serum LDH, elevated indirect bilirubin, haemoglobinaemia, haemoglobinuria, haemosiderinuria. The clinical scenario (warm AIHA: spherocytes, positive Coombs, jaundice, dark urine) confirms intravascular haemolysis.

Distractors: Liver failure can reduce haptoglobin synthesis, but the context here

is haemolysis. Extravascular haemolysis in spleen does NOT cause haemoglobinaemia or haemoglobinuria. Haptoglobin is not renally excreted.

Final Answer: Confirms intravascular haemolysis – haptoglobin binds free Hb and is consumed. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q11

Q12.

Solution

Concept – Lesch-Nyhan syndrome and hyperuricaemia mechanism: When **HGPRT is absent**, hypoxanthine and guanine cannot be salvaged back to IMP and GMP. Consequently: (i) PRPP (the "currency" of purine synthesis) is not consumed by the salvage pathway and **accumulates**, providing an excess substrate for de novo purine synthesis; (ii) De novo synthesis is overactive, producing excess AMP and GMP, which are catabolised to uric acid via xanthine oxidase. The net result is massive overproduction of uric acid. Allopurinol (xanthine oxidase inhibitor) reduces uric acid but does NOT correct the neurological features.

Distractors: HGPRT does not directly produce uric acid. Kidney urate excretion may actually be elevated (overproduction). HGPRT does not interconvert uric acid and xanthine.

Final Answer: Failure of purine salvage $\rightarrow$ PRPP accumulation $\rightarrow$ overactive de novo synthesis $\rightarrow$ excess uric acid. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q12

Q13.

Solution

Concept – DNA polarity and leading/lagging strand synthesis: DNA polymerases can only synthesise DNA **5'$\rightarrow$3'** (adding nucleotides to the 3'-OH end). The replication fork has two template strands with opposite polarity. **Leading strand**: template runs 3'$\rightarrow$5' in the direction of the fork, so synthesis is continuous in the same direction as fork movement. **Lagging strand**: template runs 5'$\rightarrow$3' in the direction of fork movement, so synthesis must be **discontinuous**, producing **Okazaki fragments** each primed by a short RNA primer, each synthesised 5'$\rightarrow$3'. RNA primers are removed by DNA pol I (prokaryotes) or RNase H + FEN1 (eukaryotes) and replaced with DNA.

Distractors: Both strands cannot be continuous in the same direction (opposite template polarities). The lagging strand (not leading) is discontinuous.

Final Answer: Leading strand continuous; lagging strand discontinuous (Okazaki fragments, synthesised 5'→3'). ⇒ $\boxed{D}$

Answer: (D) Go Back to Q13

Q14.

Solution

Concept – Fructose metabolism in liver and HFI: In the liver, fructose is phosphorylated by **fructokinase** to fructose-1-phosphate (F1P). F1P is then cleaved by **aldolase B** into DHAP and glyceraldehyde. In **hereditary fructose intolerance (HFI)**, **aldolase B** is deficient. F1P accumulates, causing: (i) sequestration of inorganic phosphate → ATP depletion (impairs glycogenolysis and gluconeogenesis → hypoglycaemia); (ii) direct hepatotoxicity. Benign fructosuria (fructokinase deficiency) is asymptomatic – fructose is not phosphorylated, so F1P does not accumulate.

Distractors: Fructokinase deficiency causes benign essential fructosuria. Glucose-6-phosphatase deficiency causes Von Gierke disease. Fructose-1,6-bisphosphatase deficiency impairs gluconeogenesis but does not accumulate F1P.

Final Answer: Aldolase B (liver isoform). ⇒ $\boxed{D}$

Answer: (D) Go Back to Q14

Q15.

Solution

Concept – Hereditary Fructose Intolerance (HFI) – Aldolase B deficiency: This question reinforces Q14. The critical point is that **aldolase B** (liver-specific isoform) cleaves fructose-1-phosphate. Its deficiency leads to **fructose-1-phosphate accumulation**. F1P is a competitive inhibitor of phosphorylase and aldolase A, and sequesters inorganic phosphate, causing hepatic ATP depletion → impaired gluconeogenesis and glycogenolysis → **severe hypoglycaemia**. Symptoms appear when sucrose or fructose is introduced into the diet. Treatment: eliminate fructose, sucrose, and sorbitol from the diet.

Distractors: Fructokinase deficiency (essential fructosuria) is completely benign. Phosphoglucose isomerase is a glycolytic enzyme, not involved in fructose catabolism. Fructose-2,6-bisphosphatase regulates PFK-1 activity.

Final Answer: Aldolase B deficiency. ⇒ $\boxed{B}$

Answer: (B) Go Back to Q15

Q16.

Solution

Concept – Lipoprotein lipase (LPL) and ApoC-II activation: LPL is anchored on the luminal surface of capillary endothelium by heparan sulfate proteoglycans. It hydrolyses triglycerides from chylomicrons and VLDL into free fatty acids and glycerol. LPL requires **ApoC-II** as an obligatory activating cofactor – without ApoC-II, LPL activity is negligible. ApoC-III inhibits LPL. Familial LPL deficiency (also called type I hyperlipoproteinaemia) presents with massive chylomicronaemia, eruptive xanthomas, and recurrent pancreatitis. It is autosomal recessive.

Distractors: ApoB-48 is structural (does not activate LPL). ApoA-I activates LCAT (lecithin-cholesterol acyltransferase) on HDL. ApoE is the hepatic clearance ligand for remnant particles.

Final Answer: ApoC-II. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q16

Q17.

Solution

Concept – Acetaldehyde toxicity in alcoholic liver disease: Ethanol $\overset{\text{ADH}}{\rightarrow}$ **acetaldehyde** $\overset{\text{ALDH}}{\rightarrow}$ acetate. Acetaldehyde is a **highly reactive aldehyde** that: (i) Forms covalent adducts with protein amino groups (acetaldehyde-protein adducts) – altering protein structure and function; (ii) Damages mitochondria (impairs oxidative phosphorylation); (iii) Disrupts microtubule polymerisation, causing **Mallory-Denk bodies** (cytokeratin aggregates); (iv) Stimulates hepatic stellate cells to produce collagen $\rightarrow$ fibrosis $\rightarrow$ cirrhosis. ALDH2*2 (Asian flush) variant has reduced ALDH activity, causing acetaldehyde accumulation.

Distractors: Acetaldehyde is an aldehyde, not a ketone. It does not raise pH. It does not compete with NADH directly.

Final Answer: Highly reactive aldehyde forming covalent protein adducts, impairing microtubule function, stimulating collagen synthesis. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q17

Q18.

Solution

Concept – Inorganic pyrophosphate (PP_i) hydrolysis drives biosynthesis: Many ligase reactions (aminoacyl-tRNA synthetase, fatty acyl-CoA synthetase, DNA/RNA ligase) consume ATP and release PP_i:

R + ATP $\rightarrow$ R-AMP + PP_i. The reaction has a relatively small ΔG, so it might be reversible. However, **inorganic pyrophosphatase** immediately hydrolyses PP_i $\rightarrow$ 2 P_i ($\Delta G^{0'} = -7.3$ kcal/mol), making the overall reaction **thermodynamically irreversible** (total ΔG very negative). This "coupled hydrolysis" principle – harnessing the hydrolysis of PP_i to drive unfavourable reactions – is a fundamental thermodynamic strategy in biosynthesis.

Distractors: PP_i hydrolysis does not regenerate ATP from AMP (that requires adenylate kinase: 2 ADP $\rightarrow$ ATP + AMP). It does not provide phosphate specifically for oxidative phosphorylation. It has no direct effect on ribosomes.

Final Answer: Drives biosynthetic reactions irreversibly forward by removing PP_i. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q18

Q19.

Solution

Concept – IRP/IRE system and transferrin receptor regulation: Iron homeostasis is regulated post-transcriptionally by **Iron Regulatory Proteins (IRP-1 and IRP-2)**. In iron-deficient cells, IRPs are active and bind **Iron Responsive Elements (IREs)**: (i) **3' IRE of TfR1 mRNA**: IRP binding protects mRNA from endonuclease degradation $\rightarrow$ **mRNA stabilised** $\rightarrow$ more TfR1 protein $\rightarrow$ increased cellular iron uptake; (ii) **5' IRE of ferritin mRNA**: IRP binding **blocks translation** $\rightarrow$ less ferritin (storage reduced when iron is scarce). When iron is replete, IRPs are inactivated (IRP-1 assembles Fe-S cluster; IRP-2 is degraded) $\rightarrow$ TfR1 mRNA destabilised, ferritin translated.

Distractors: IRP binding to TfR1 mRNA STABILISES (not degrades) the mRNA. It affects mRNA stability (not just translation). Ferritin translation is REPRESSED (not promoted) by IRP in iron deficiency.

Final Answer: Stabilises TfR1 mRNA $\rightarrow$ increased TfR1 $\rightarrow$ enhanced iron uptake. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q19

Q20.

Solution

Concept – Phospholipase A_2 (PLA_2) and eicosanoid synthesis: The committed step in eicosanoid biosynthesis is release of **arachidonic acid (AA, 20:4$\Delta^{5,8,11,14}$)** from the *sn-2* position of membrane glycerophospholipids by **phospholipase A_2**

(PLA_2). AA is then converted to prostaglandins/thromboxanes by COX (cyclooxygenase) or to leukotrienes by lipoxygenase. **Corticosteroids** (glucocorticoids) inhibit PLA_2 by inducing **annexin-1 (lipocortin)**, which blocks PLA_2 substrate access. This is the mechanism by which steroids suppress inflammation more broadly than NSAIDs (which block only COX).

Distractors: COX-1/COX-2 converts AA to prostaglandins/thromboxanes (inhibited by NSAIDs/aspirin). 5-LOX converts AA to leukotrienes. PLC cleaves phosphatidylinositol-4,5-bisphosphate to IP_3 + DAG (second messenger pathway).

Final Answer: Phospholipase A_2 (PLA_2). $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q20

Q21.

Solution

Concept – Myoglobin oxygen dissociation curve: Myoglobin (Mb) is a **monomeric** protein with a single haem group and **no cooperativity**. Its O_2 dissociation curve is **hyperbolic**. Key features: (i) **$P_{50} \approx$ 2.75 mmHg** – much lower than Hb's P_{50} (≈26 mmHg), meaning Mb has **higher O_2 affinity** than Hb; (ii) Mb is almost fully saturated at the pO_2 found in resting muscle and releases O_2 only when pO_2 falls to very low levels (as occurs in vigorously contracting muscle); (iii) Mb serves as an O_2 **storage** molecule in muscle, not a transport molecule in blood. Haemoglobin's sigmoidal curve reflects cooperative binding among its four subunits.

Distractors: Mb is monomeric (no cooperativity, no sigmoidal curve). Mb's P_{50} is LOWER than Hb's (higher affinity). Mb is not a blood O_2 carrier.

Final Answer: Hyperbolic curve, lower P_{50} than Hb, higher O_2 affinity, releases O_2 only at very low pO_2. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q21

Q22.

Solution

Concept – Lactase non-persistence (lactose intolerance): Lactase (LCT gene) expression is regulated by an enhancer element. The ancestral genotype (CC at -13910) results in **lactase non-persistence**: lactase activity declines after weaning (≈2–5 years). **Lactose**, the disaccharide in milk (glucose-β1,4-galactose), is NOT hydrolysed by brush-border lactase $\rightarrow$ passes undigested to the colon $\rightarrow$ fermented by bacteria producing H_2, CO_2, CH_4 (bloating, flatulence) and short-chain

fatty acids that osmotically retain water (osmotic diarrhoea). Yoghurt is tolerated because bacterial lactase pre-digests much of the lactose; hard cheeses contain little lactose.

Distractors: Sucrase-isomaltase deficiency causes intolerance to sucrose/starch, not milk. Lactose is not absorbed intact. Casein allergy is an immune (IgE-mediated) reaction, not an enzyme deficiency.

Final Answer: Lactase non-persistence – absence of brush-border lactase $\rightarrow$ colonic fermentation of lactose. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q22

Q23.

Solution

Concept – Cori cycle (lactic acid cycle): Named after Carl and Gerty Cori. The cycle involves: **Muscle**: glucose $\xrightarrow{\text{anaerobic glycolysis}}$ 2 lactate + 2 ATP (net); **Liver**: 2 lactate $\xrightarrow{\text{gluconeogenesis}}$ glucose (consumes 6 ATP). Net energy cost: 4 ATP equivalents per cycle (liver subsidises muscle). The cycle does NOT generate net ATP overall – it distributes the metabolic burden. The liver, with its mitochondria and gluconeogenic enzymes, uses aerobic metabolism to regenerate glucose from lactate, while muscle performs anaerobic glycolysis.

Distractors: The Cori cycle does NOT generate net ATP in both organs – liver consumes 6 ATP. Muscle does not convert lactate to glucose (no gluconeogenesis in muscle). Lactate is not converted to acetyl-CoA in liver for TCA (it is gluconeogenic substrate, going through pyruvate $\rightarrow$ OAA/PEP pathway).

Final Answer: Muscle: anaerobic glycolysis $\rightarrow$ lactate; liver: lactate $\rightarrow$ glucose (gluconeogenesis, 6 ATP consumed); net energy transfer from liver to muscle. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q23

Q24.

Solution

Concept – Pyridoxal phosphate (PLP) as transamination cofactor: Pyridoxal phosphate (PLP), the active form of **vitamin B6 (pyridoxine)**, is the coenzyme for **all aminotransferases (transaminases)** including ALT and AST. Mechanism: (i) PLP is covalently bound to an active-site lysine of the enzyme as a Schiff base (aldimine); (ii) The incoming amino acid displaces lysine, forming an external Schiff base; (iii) PLP accepts the amino group, forming **pyridoxamine phosphate**

(PMP); (iv) PMP transfers the amino group to an α-keto acid, regenerating PLP. Example: Alanine + α-KG $\overset{\text{ALT/PLP}}{\rightleftharpoons}$ Pyruvate + Glutamate.

Distractors: TPP (thiamine) is the cofactor for pyruvate dehydrogenase and transketolase. NAD^+ is the cofactor for oxidation-reduction reactions (LDH, malate DH). FAD is for flavoenzymes (succinate DH, acyl-CoA DH).

Final Answer: Pyridoxine (B6) – pyridoxal phosphate (PLP). $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q24

Q25.

Solution

Concept – Apolipoprotein E (ApoE) alleles and lipoprotein clearance: ApoE has three common isoforms: ApoE2, ApoE3 (most common), ApoE4. ApoE is found on chylomicron remnants, IDL, and HDL and serves as the ligand for hepatic LDL receptor (LDLR) and LRP1. **ApoE4** binds LDL receptor with **lower affinity** than ApoE3 $\rightarrow$ **impaired clearance of chylomicron remnants and IDL** $\rightarrow$ elevated remnant lipoproteins and LDL $\rightarrow$ increased atherosclerosis risk. ApoE4 is also the strongest genetic risk factor for **late-onset Alzheimer disease** (mechanism: impaired amyloid clearance, synaptic dysfunction). ApoE2 is associated with type III hyperlipoproteinaemia (dysbetalipoproteinaemia) due to even poorer receptor binding.

Distractors: ApoE4 does not impair HDL clearance (HDL is cleared by SR-BI). ApoE4 does NOT increase LPL activity. ApoE2 (not E4) is the "protective" cardiovascular allele relative to E4.

Final Answer: ApoE4 reduces clearance of chylomicron remnants and IDL; associated with atherosclerosis and Alzheimer disease risk. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q25

Q26.

Solution

Concept – Alpha-fetoprotein (AFP): AFP is the fetal equivalent of albumin, synthesised by the **fetal liver and yolk sac**. It is the major serum protein in the fetus. Normal AFP levels decline after birth. **Elevated maternal serum AFP (MSAFP)** at 15–20 weeks indicates: (i) **Open neural tube defects** (anencephaly, spina bifida aperta) – AFP leaks from exposed neural tissue into amniotic fluid and then into maternal blood; (ii) Abdominal wall defects (gastroschisis, omphalocele); (iii) Multiple gestation; (iv) Underestimated gestational age. **LOW MSAFP** is associ-

ated with Down syndrome (trisomy 21) – the triple/quadruple screen pattern for Down syndrome is LOW AFP, LOW uE_3, HIGH hCG ($\pm$ LOW inhibin A).

Distractors: AFP is made by fetal liver/yolk sac, NOT the placenta. Elevated AFP does not indicate Down syndrome (LOW AFP does). AFP is not produced by maternal liver.

Final Answer: AFP from fetal liver/yolk sac; elevated $\rightarrow$ open NTD; low $\rightarrow$ Down syndrome. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q26

Q27.

Solution

Concept – Frameshift mutations: A **frameshift mutation** results from insertion or deletion of a number of nucleotides that is **not a multiple of 3**. Since the genetic code is read in non-overlapping triplet codons, shifting the reading frame alters every codon downstream of the mutation. This typically: (i) Changes multiple amino acids (altered protein sequence); (ii) Usually creates a **premature stop codon (nonsense)** within a short distance $\rightarrow$ truncated, non-functional protein; (iii) Triggers **nonsense-mediated mRNA decay (NMD)**. In-frame mutations (multiple of 3 insertions/deletions) affect only one or a few amino acids (as in CF F508del) and may still produce a partially functional protein.

Distractors: Frameshift mutations alter ALL downstream codons, not one amino acid. In-frame deletions do not always cause complete protein dysfunction. Frameshift mutations affect the coding sequence, not the 3' UTR.

Final Answer: Non-multiple of 3 insertion/deletion shifts the reading frame $\rightarrow$ altered downstream codons $\rightarrow$ premature stop $\rightarrow$ truncated non-functional protein. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q27

Q28.

Solution

Concept – HDL reverse cholesterol transport and CETP: The steps of reverse cholesterol transport (RCT): (1) Peripheral cells export cholesterol to nascent HDL via **ABCA1** transporter (ApoA-I is the major HDL apolipoprotein that accepts this cholesterol); (2) **LCAT** (lecithin-cholesterol acyltransferase, activated by ApoA-I) esterifies free cholesterol in HDL $\rightarrow$ cholesterol esters (CE) $\rightarrow$ HDL becomes CE-rich and spherical; (3a) HDL delivers CE directly to liver via **SR-BI** (scavenger

receptor class B type I); (3b) **CETP** (cholesteryl ester transfer protein) transfers CE from HDL to VLDL/LDL in exchange for triglycerides. CETP inhibitors (anacetrapib, torcetrapib) raise HDL-CE.

Distractors: LCAT esterifies cholesterol (not transfer to VLDL). ApoA-I activates LCAT. SR-BI is the hepatic receptor for direct HDL-CE uptake.

Final Answer: CETP (cholesteryl ester transfer protein). $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q28

Q29.

Solution

Concept – Malate-aspartate shuttle: NADH generated in the cytosol (by glycolysis) cannot directly cross the inner mitochondrial membrane. The **malate-aspartate shuttle** (main shuttle in heart and liver) transfers reducing equivalents: (1) Cytosolic OAA is reduced to malate by cytosolic malate dehydrogenase (using NADH $\rightarrow$ NAD^+); (2) Malate enters the mitochondria via the malate-α-KG carrier; (3) Mitochondrial malate DH oxidises malate $\rightarrow$ OAA (generating mitochondrial NADH); (4) OAA is transaminated to aspartate, which exits via aspartate-glutamate carrier. Net result: 1 cytosolic NADH $\rightarrow$ 1 mitochondrial NADH $\rightarrow$ **2.5 ATP** (most efficient shuttle). The glycerol-3-phosphate shuttle (used in skeletal muscle/brain) yields only 1.5 ATP per cytosolic NADH (as $FADH_2$).

Distractors: Cytosolic NADH is not converted to $FADH_2$ by malate-aspartate shuttle (that is glycerol-3-phosphate shuttle). The shuttle operates mainly in heart and liver, NOT skeletal muscle. Glycerol-3-phosphate shuttle uses glycerol-3-phosphate, not malate-aspartate shuttle.

Final Answer: Cytosolic NADH $\rightarrow$ mitochondrial NADH, yielding 2.5 ATP; most efficient NADH shuttle. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q29

Q30.

Solution

Concept – Hepatic CYP450 enzymes: Cytochrome P450 (CYP450) enzymes are **liver microsomal** (smooth ER) **mixed-function oxidases**. Reaction: Drug + NADPH + O_2 $\rightarrow$ Drug-OH + $NADP^+$ + H_2O. They catalyse **phase I** drug metabolism (oxidation, reduction, hydrolysis – adding or unmasking polar groups). The electron donor is **NADPH** (via NADPH-cytochrome P450 reductase). **CYP3A4** (most abundant, $\approx$50% of hepatic CYPs): inhibited by erythromycin,

ketoconazole, grapefruit juice (furanocoumarins) → drug toxicity; induced by rifampicin, phenytoin, carbamazepine, St John's wort → reduced drug levels.

Distractors: CYP450 enzymes are in ER (not mitochondrial matrix) and use NADPH (not $FADH_2$). Phase II reactions are conjugation reactions (glucuronidation, sulfation – different enzymes). Substrate-level phosphorylation is unrelated to CYP450 induction.

Final Answer: CYP450 = liver microsomal mixed-function oxidases, NADPH + O_2, phase I metabolism; CYP3A4 inhibited by erythromycin/grapefruit, induced by rifampicin. ⇒ $\boxed{C}$

Answer: (C) Go Back to Q30

Q31.

Solution

Concept – Rho-dependent transcription termination (prokaryotes): Two mechanisms terminate transcription in bacteria: (1) **Intrinsic (Rho-independent)**: GC-rich hairpin (stem-loop) forms in the nascent RNA followed by a poly-U run → destabilises RNA-DNA hybrid → transcript release – no protein factors needed. (2) **Rho-dependent**: **Rho protein** (hexameric ATP-dependent RNA/DNA helicase) binds *rut* sites (Rho utilisation sites) on the nascent mRNA → translocates 5'→3' along the RNA using ATP hydrolysis → catches the paused RNA polymerase → unwinds the RNA-DNA hybrid → releases the transcript.

Distractors: Intrinsic termination requires hairpin + poly-U, not Rho protein. Sigma factor is released early after initiation (not termination). Anti-termination by N protein occurs in lambda phage (blocks Rho-dependent termination of early genes).

Final Answer: Rho-dependent transcription termination. ⇒ $\boxed{C}$

Answer: (C) Go Back to Q31

Q32.

Solution

Concept – Disulfide bond formation by Protein Disulfide Isomerase (PDI): Disulfide bonds form between two cysteine residues when their **thiol groups (–SH)** are oxidised to form a **disulfide bridge (–S–S–)** . This occurs in the **ER lumen**, which is **oxidising** (unlike the reducing cytosol). **Protein disulfide isomerase (PDI)** catalyses both: (i) **Formation** of disulfide bonds (oxidising two –SH groups); (ii) **Isomerisation** (rearranging incorrect disulfide bonds to correct

ones). PDI is regenerated by Ero1 (ER oxidoreductin 1) using FAD/O_2. Disulfide bonds provide covalent stabilisation to extracellular proteins (e.g., insulin, immunoglobulins, albumin) that would otherwise be denatured in the extracellular environment.

Distractors: Peptidyl prolyl isomerase (PPI) catalyses *cis-trans* isomerisation of peptide bonds at proline (aids folding, not disulfide formation). Transglutaminase cross-links Gln-Lys in fibrin and extracellular matrix. BiP/GRP78 is an HSP70 chaperone that binds unfolded proteins (does not form disulfide bonds).

Final Answer: Protein disulfide isomerase (PDI). $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q32

Q33.

Solution

Concept – Thyroid hormone synthesis – MIT + DIT coupling: Thyroid hormone synthesis occurs on thyroglobulin (Tg) within the thyroid follicle. **Thyroid peroxidase (TPO)** catalyses: (i) Iodide oxidation; (ii) Iodination of tyrosine residues on Tg (organification): Tyr $\rightarrow$ MIT (monoiodotyrosine) $\rightarrow$ DIT (diiodotyrosine); (iii) Coupling of iodotyrosines: **MIT + DIT** $\rightarrow$ **T3** (triiodothyronine, 3 iodines); DIT + DIT $\rightarrow$ T4 (thyroxine, 4 iodines). PTU and methimazole block TPO, inhibiting both organification and coupling. T3 is more active than T4; peripheral conversion of T4$\rightarrow$T3 by deiodinase (5'-deiodinase) is the main source of circulating T3.

Distractors: T4 = DIT + DIT (not MIT + DIT). rT3 is from peripheral 5-deiodination (different iodine position) of T4 in non-thyroidal illness. Thyroglobulin is the scaffold protein before iodination.

Final Answer: MIT + DIT $\rightarrow$ T3 (triiodothyronine). $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q33

Q34.

Solution

Concept – Phosphocreatine (creatine phosphate) as immediate ATP buffer: During sudden, intense muscular activity, ATP demand exceeds the rate at which glycolysis and oxidative phosphorylation can supply it. **Phosphocreatine** serves as an immediate, high-energy phosphate reservoir: Creatine-P + ADP $\overset{\text{CK}}{\rightleftharpoons}$ Creatine + ATP. This reaction is catalysed by **creatine kinase (CK)** and regenerates ATP **within milliseconds** – the fastest ATP-replenishing mechanism. Phosphocreatine stores are depleted within **5–10 seconds** of maximal exercise. After deple-

tion, anaerobic glycolysis takes over (seconds to minutes), followed by aerobic metabolism (minutes onwards). Synthesis of creatine in liver uses glycine, arginine, and methionine (SAM as methyl donor).

Distractors: Phosphocreatine sustains only the first few seconds (not hours) of exercise. It is present in both cardiac and skeletal muscle. Creatine phosphate synthesis uses ATP as phosphate donor (from creatine kinase running in reverse direction, i.e., ATP + creatine $\rightarrow$ creatine-P + ADP, during recovery).

Final Answer: Phosphocreatine is the fastest ATP regeneration mechanism in muscle, depleted within seconds before glycolysis accelerates. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q34

Q35.

Solution

Concept – Bile acid synthesis and CYP7A1 (7α-hydroxylase): Bile acids are synthesised in the liver from cholesterol. The **rate-limiting step** is **7α-hydroxylation of cholesterol** by **CYP7A1 (cholesterol 7α-hydroxylase)**, a microsomal enzyme. Regulation: (i) Inhibited by bile acids (returning via enterohepatic circulation $\rightarrow$ feedback inhibition via FXR $\rightarrow$ induces SHP $\rightarrow$ represses CYP7A1); (ii) Induced by excess cholesterol (via LXR); (iii) Fibrates upregulate CYP7A1. When bile acid sequestrants (cholestyramine, colestipol) interrupt enterohepatic circulation, negative feedback is relieved $\rightarrow$ CYP7A1 upregulated $\rightarrow$ more cholesterol converted to bile acids $\rightarrow$ hepatocytes upregulate LDLR to import more cholesterol $\rightarrow$ serum LDL falls.

Distractors: HMG-CoA reductase is the rate-limiting enzyme of cholesterol synthesis (not bile acid synthesis). CYP46A1 is brain cholesterol catabolism (neurosteroid pathway). 12α-Hydroxylase determines whether cholic vs chenodeoxycholic acid is made.

Final Answer: 7α-Hydroxylase (CYP7A1) – rate-limiting step of bile acid synthesis. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q35

Q36.

Solution

Concept – Gilbert syndrome (UGT1A1 promoter polymorphism): Gilbert syndrome is the most common hereditary cause of mild unconjugated hyperbilirubinaemia (≈3–10% of the population). It is caused by a **TA repeat polymor-**

phism in the UGT1A1 gene promoter: the normal sequence has $(TA)_6$ TATA box; the Gilbert variant has **$(TA)_7$** (extra TA insertion), which reduces UGT1A1 (UDP-glucuronosyltransferase 1A1) transcription by ≈30–80%, reducing bilirubin conjugating capacity. Bilirubin rises mildly, especially with fasting, illness, or haemolysis. Liver histology and liver function tests are otherwise normal. Benign condition – no treatment required.

Distractors: Haem oxygenase produces biliverdin (deficiency would reduce, not increase, bilirubin). Complete absence of UGT1A1 is Crigler-Najjar type I (life-threatening unconjugated hyperbilirubinaemia). Dubin-Johnson syndrome has **conjugated** hyperbilirubinaemia (impaired canalicular excretion via MRP2).

Final Answer: UGT1A1 promoter $(TA)_7$ polymorphism $\rightarrow$ reduced bilirubin conjugation $\rightarrow$ mild unconjugated hyperbilirubinaemia. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q36

Q37.

Solution

Concept – Mannose-6-phosphate (M6P) targeting and I-cell disease: Lysosomal hydrolases (acid phosphatase, cathepsins, etc.) are distinguished from secretory glycoproteins in the Golgi by being tagged with **mannose-6-phosphate (M6P)**. The enzyme that adds M6P is **GlcNAc phosphotransferase** (UDP-GlcNAc:lysosomal enzyme N-acetylglucosamine-1-phosphotransferase). It adds GlcNAc-phosphate to mannose residues of lysosomal hydrolases. Then a phosphodiesterase removes GlcNAc, exposing M6P. M6P is recognised by M6P receptors in the trans-Golgi network, diverting the enzyme to lysosomes. In **I-cell disease (mucolipidosis type II)**, GlcNAc phosphotransferase is **deficient** $\rightarrow$ lysosomal enzymes lack M6P $\rightarrow$ secreted extracellularly instead of going to lysosomes $\rightarrow$ elevated serum lysosomal enzymes + dense cytoplasmic inclusions.

Distractors: α-Mannosidase deficiency causes mannosidosis (a different lysosomal storage disease). M6P receptor deficiency is not I-cell disease. Sialyltransferase adds sialic acid (for secretory glycoprotein routing, not lysosomal targeting).

Final Answer: GlcNAc phosphotransferase deficiency. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q37

Q38.

Solution

Concept – Alcoholic ketoacidosis vs. diabetic ketoacidosis: Both conditions feature elevated ketones (acetoacetate + β-hydroxybutyrate), but differ in blood glucose: **Diabetic KA**: Insulin deficiency $\rightarrow$ unrestrained glucagon $\rightarrow$ hyperglycaemia (>250 mg/dL) + ketogenesis + metabolic acidosis. **Alcoholic KA**: Binge drinking + vomiting + starvation $\rightarrow$ high **NADH/NAD$^+$** ratio from ethanol oxidation $\rightarrow$ (i) Gluconeogenesis inhibited (pyruvate $\rightarrow$ lactate, OAA $\rightarrow$ malate); (ii) Blood glucose is **low-normal or low**; (iii) High NADH drives β-hydroxybutyrate $\gg$ acetoacetate; (iv) Urine dipstick (nitroprusside) may underestimate ketones (detects acetoacetate only, not β-OHB). Treatment: IV dextrose + thiamine.

Distractors: Alcoholic KA has LOW (not high) blood glucose. Alcoholic KA causes metabolic acidosis, not alkalosis. Alcoholic KA is not caused by excess insulin.

Final Answer: Alcoholic KA: low/normal glucose + high NADH/NAD$^+$; Diabetic KA: high glucose from insulin deficiency; both have elevated ketones. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q38

Q39.

Solution

Concept – Dolichol phosphate in N-linked glycosylation: N-linked glycosylation begins in the rough ER. The oligosaccharide core ($Glc_3Man_9GlcNAc_2$, 14 sugars) is assembled stepwise on a **dolichol phosphate** lipid carrier embedded in the ER membrane. Dolichol is a long-chain polyisoprenol alcohol (55–95 carbons). Once the 14-sugar core is complete on dolichol-PP, it is transferred en bloc by oligosaccharyltransferase (OST) to an Asn residue within the sequon **Asn-X-Ser/Thr** (where X $\neq$ Pro). Subsequent processing in the ER and Golgi (trimming and addition of specific sugars) produces the final complex, hybrid, or high-mannose N-glycan.

Distractors: Ceramide is the backbone of sphingolipids (O-linked or glycolipid synthesis). Phosphatidylinositol is used in GPI anchor synthesis, not N-linked glycosylation. GPI anchor precursor is assembled on PI for GPI-anchored proteins (distinct mechanism from N-glycosylation).

Final Answer: Dolichol phosphate – polyisoprenol lipid carrier for N-glycan core assembly. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q39

Q40.

Solution

Concept – DNA methylation in cancer (epigenetics): **DNA methylation** is the addition of a methyl group to the C5 position of cytosine in CpG dinucleotides (5-methylcytosine), catalysed by **DNA methyltransferases (DNMT1, DNMT3a, DNMT3b)**. Effects on gene expression: **Hypermethylation of CpG islands in promoters** $\rightarrow$ gene silencing (chromatin compaction, blocks transcription factor binding). In cancer: (i) **Tumour suppressor genes** (e.g., RB1, MLH1, CDKN2A/p16) are silenced by promoter hypermethylation; (ii) **Global genomic hypomethylation** (loss of methylation at non-CpG-island regions) can **activate proto-oncogenes** (e.g., RAS). Importantly, these are epigenetic changes – heritable through cell divisions without altering the DNA sequence.

Distractors: Hypermethylation silences (not activates) genes. Histone acetyltransferases (HATs) modify histones (different mechanism). Global hypermethylation of ALL sites would silence all genes (not activate).

Final Answer: Hypermethylation of CpG islands silences tumour suppressors; global hypomethylation activates oncogenes; DNMT1/3a/3b are the enzymes; epigenetic (non-sequence) inheritance. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q40

Answer Key – FMGE Biochemistry Sample Paper 4

1	A	2	B	3	B	4	C	5	D
6	C	7	C	8	A	9	A	10	D
11	A	12	B	13	D	14	D	15	B
16	A	17	D	18	A	19	D	20	C
21	A	22	A	23	D	24	C	25	B
26	A	27	B	28	D	29	A	30	C
31	C	32	B	33	B	34	C	35	C
36	B	37	C	38	B	39	D	40	D