FMGE Biochemistry Sample Paper – 10

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 45-year-old man with chronic liver disease (hepatitis C cirrhosis) undergoes liver biopsy. Electron microscopy reveals that a specific non-parenchymal cell type has lost its characteristic lipid droplets and has transformed into an activated myofibroblast, contributing to hepatic fibrosis. These cells are also the primary storage site for vitamin A in the liver. These cells are:

(A) Hepatic stellate cells (Ito cells / perisinusoidal cells)

(B) Kupffer cells (resident hepatic macrophages)

(C) Endothelial cells lining the sinusoids

(D) Hepatocytes (parenchymal cells)

Q2. A biochemist performs Michaelis-Menten kinetics experiments on an enzyme at two different enzyme concentrations: $[\mathrm{E}]_1$ and $[\mathrm{E}]_2 = 2[\mathrm{E}]_1$. All other conditions (substrate concentrations, pH, temperature) are kept identical. Which of the following best describes the effect of doubling the enzyme concentration?

(A) Both V_{max} and K_m are doubled

(B) V_{max} is doubled but K_m remains unchanged

(C) K_m is halved and V_{max} remains unchanged

(D) Both V_{max} and K_m are halved

Q3. A 5-day-old neonate presents with vomiting, poor feeding, extreme irritability, and a distinctive "sweaty feet" body odour. Plasma acylcarnitine profile shows elevated isovalerylcarnitine (C5). The metabolic block in this condition involves which enzyme and which amino acid's catabolism?

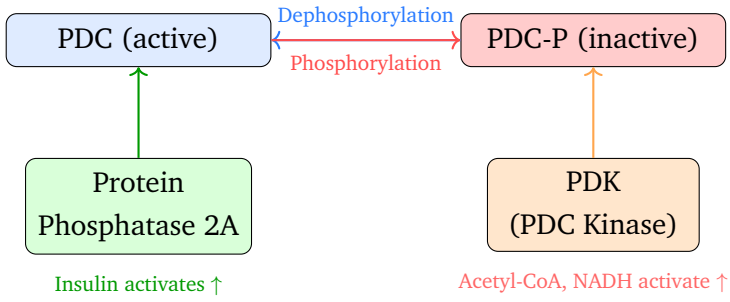
(A) Propionyl-CoA carboxylase; valine catabolism

(B) Isovaleryl-CoA dehydrogenase; leucine catabolism

(C) Methylmalonyl-CoA mutase; isoleucine catabolism

(D) Glutaryl-CoA dehydrogenase; lysine catabolism

Q4. Pyruvate dehydrogenase complex (PDC) is a key regulatory enzyme at the entry point of glycolytic carbon into the TCA cycle. The diagram below shows its regulatory signals. Which of the following correctly describes how **insulin** activates PDC?



(A) Insulin directly phosphorylates PDC at the E1α subunit

(B) Insulin activates PDC kinase (PDK), which phosphorylates and activates PDC

(C) Insulin activates protein phosphatase 2A, which dephosphorylates and activates PDC

(D) Insulin increases intracellular NAD^+/NADH ratio, indirectly activating PDC

Q5. A nutritional biochemist studying fat-soluble vitamins differentiates between tocopherols and tocotrienols. Which of the following correctly distinguishes these two subclasses of vitamin E?

(A) Tocopherols have an unsaturated phytyl tail with three double bonds; tocotrienols have a saturated phytyl tail

(B) Tocopherols have a saturated phytyl tail; tocotrienols have an unsaturated isoprenoid tail with three double bonds

(C) Both tocopherols and tocotrienols have identical phytyl tails; they differ only in the number of methyl groups on the chromanol ring

(D) Tocotrienols are water-soluble while tocopherols are fat-soluble

Q6. A medical student studying pyrimidine biosynthesis notes that the first committed step involves carbamoyl phosphate synthetase. Which statement correctly differentiates the cytoplasmic CPS-II (pyrimidine synthesis) from the mitochondrial CPS-I (urea cycle)?

(A) CPS-II uses glutamine as nitrogen donor and does not require N-acetylglutamate; CPS-I uses ammonia and requires N-acetylglutamate

(B) CPS-II uses ammonia as nitrogen donor and requires N-acetylglutamate; CPS-I uses glutamine and does not require N-acetylglutamate

(C) Both CPS-I and CPS-II use glutamine and require N-acetylglutamate as an allosteric activator

(D) CPS-II is mitochondrial; CPS-I is cytoplasmic

Q7. During eukaryotic translation, the initiator AUG codon is decoded by the ribosome and methionine is incorporated as the first amino acid. A post-translational processing enzyme then removes this initiator methionine from a large proportion of newly synthesised proteins. This co-translational or post-translational removal occurs when which condition is met?

(A) The residue adjacent to the initiator methionine (position 2) is small and uncharged (e.g., Gly, Ala, Ser, Cys, Thr, Pro, Val)

(B) The protein is destined for secretion (signal peptide present)

(C) The initiator methionine is formylated (fMet)

(D) The protein is targeted for proteasomal degradation

Q8. A 62-year-old woman with documented coronary artery disease has a fasting HDL-cholesterol of 28 mg/dL. Her physician explains the HDL subclasses: the "mature" cardioprotective form that is large, cholesterol ester-rich, and less dense is formed as nascent HDL matures by accepting cholesterol from peripheral tissues. This mature form is:

(A) HDL3 (small, dense, protein-rich)

(B) Nascent HDL (pre-β HDL, discoidal)

(C) HDL2 (large, cholesterol ester-rich, less dense)

(D) VLDL remnant (IDL)

Q9. In bioenergetics, ATP synthesis can occur via two distinct mechanisms. A metabolic exam question asks a student to identify which of the following correctly contrasts substrate-level phosphorylation from oxidative phosphorylation. Which answer is correct?

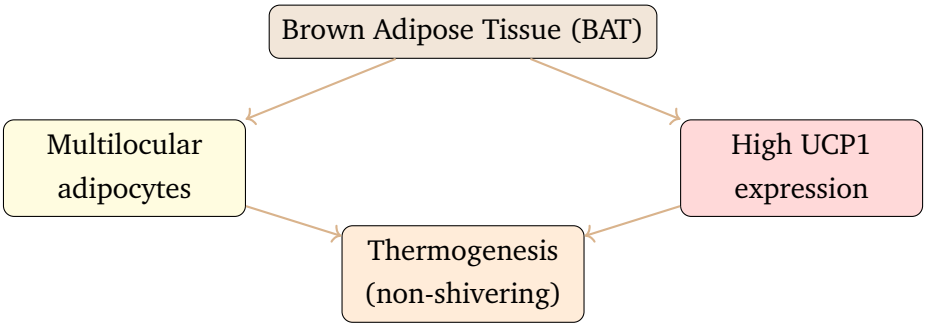
(A) Substrate-level phosphorylation requires the electron transport chain and a proton gradient; oxidative phosphorylation does not require oxygen

(B) Both substrate-level and oxidative phosphorylation require an intact inner mitochondrial membrane

(C) Substrate-level phosphorylation directly couples high-energy intermediate hydrolysis to ATP synthesis without a membrane gradient; oxidative phosphorylation requires the ETC and proton gradient driven by ATP synthase

(D) Oxidative phosphorylation does not require oxygen; substrate-level phosphorylation is the only anaerobic ATP-generating mechanism

Q10. A pathologist examining adipose tissue from a 2-week-old newborn's interscapular region notes that the adipocytes are multilocular (containing multiple small lipid droplets) and contain an exceptionally high density of mitochondria. Immunohistochemistry reveals high expression of a key uncoupling protein. Which of the following best describes this tissue?



(A) White adipose tissue (WAT) – unilocular, energy storage function

(B) Beige (brite) adipocytes – induced by cold in adult WAT depots

(C) Ectopic fat – lipid accumulation in non-adipose organ

(D) Brown adipose tissue (BAT) – multilocular, thermogenic, UCP1-rich

Q11. During fetal life, haemoglobin F (HbF, $\alpha_2\gamma_2$) is the predominant haemoglobin. After birth, a developmental switch occurs resulting in replacement by haemoglobin A (HbA, $\alpha_2\beta_2$) in normal adults. When is this switch to predominantly HbA typically complete?

(A) Within the first week of life

(B) By approximately 6 months of age

(C) By 2 years of age

(D) At puberty, when adult haemoglobin synthesis is fully established

Q12. A 4-month-old exclusively breast-fed infant is brought to the clinic. The mother's breast milk is her primary nutritional source. Lactoferrin, abundant in human milk, serves dual roles for the infant. Which of the following correctly describes both functions of lactoferrin?

(A) Lactoferrin is a digestive enzyme that cleaves lipids AND provides passive immunity via IgG transfer

(B) Lactoferrin catalyses lactose synthesis in the mammary gland AND inhibits intestinal flora

(C) Lactoferrin binds ferric iron (Fe^{3+}) providing bioavailable iron to the infant AND exerts antimicrobial activity by sequestering iron from bacteria

(D) Lactoferrin activates complement AND neutralises rotavirus by direct binding

Q13. A forensic laboratory uses a molecular technique to identify individuals from crime scene blood samples. The technique detects variations in DNA sequence at specific restriction enzyme recognition sites between individuals. Different individuals produce different-sized DNA fragments after restriction enzyme digestion, detected by Southern blotting. This technique is:

(A) PCR amplification of microsatellite (STR) loci

(B) Single nucleotide polymorphism (SNP) genotyping array

(C) Whole-genome sequencing (WGS)

(D) Restriction fragment length polymorphism (RFLP) analysis

Q14. A 38-year-old man undergoes a routine health check. His fasting blood glucose (8-hour fast) is reported as 92 mg/dL. How should this value be interpreted according to current diagnostic criteria?

(A) Diabetes mellitus (fasting glucose $\geq$126 mg/dL meets diagnostic threshold)

(B) Impaired fasting glucose / pre-diabetes (100–125 mg/dL range)

(C) Hypoglycaemia (below normal reference range)

(D) Normal fasting plasma glucose (reference range 70–100 mg/dL)

Q15. A biochemistry student studying sphingolipid metabolism draws the structure of ceramide. Which of the following correctly identifies the components and linkage that define ceramide?

(A) Sphingosine + long-chain fatty acid via an ester bond + one phosphate group

(B) Sphingosine + glucose via a glycosidic bond, forming the simplest glycosphingolipid

(C) Sphingosine + long-chain fatty acid via an amide bond (no phosphate group); the universal backbone of all sphingolipids

(D) Glycerol + two fatty acids + sphingomyelin via phosphodiester linkage

Q16. A patient with scurvy is found to have impaired adrenal function. Biochemically, which of the following best explains the high concentration of ascorbic acid (vitamin C) in the adrenal gland and its role in steroidogenesis?

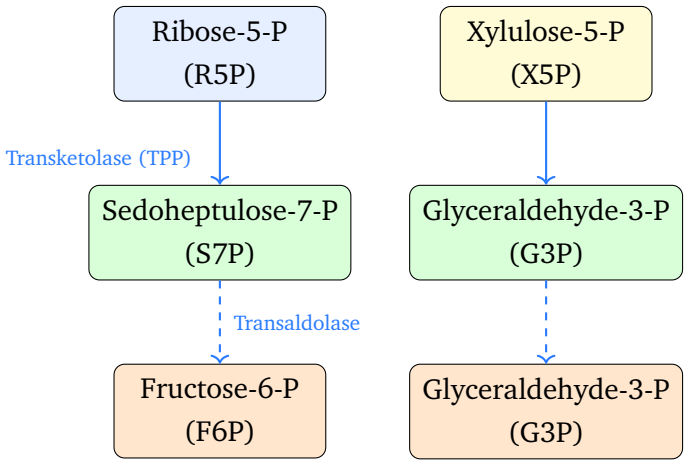
(A) Ascorbic acid supports cytochrome P450 enzyme activity (including CYP11B1) required for glucocorticoid biosynthesis; ACTH stimulates ascorbic acid release from the adrenal cortex

(B) Ascorbic acid is the rate-limiting substrate for StAR protein, which transports cholesterol into mitochondria for steroidogenesis

(C) Ascorbic acid directly activates PKA in the adrenal cortex, bypassing ACTH signalling

(D) Ascorbic acid inhibits cortisol catabolism in peripheral tissues, increasing circulating cortisol

Q17. During the non-oxidative phase of the pentose phosphate pathway (PPP), two enzymes interconvert sugar phosphates to allow pentose phosphates to enter glycolysis when NADPH – not ribose-5-phosphate – is the primary cellular need. The diagram below summarises these reactions. Which pair of enzymes catalyse these interconversions?



(A) Transketolase (transfers 2-carbon units, requires TPP/Vitamin B1) and transaldolase (transfers 3-carbon units)

(B) Phosphoglucose isomerase and phosphofructokinase-1

(C) Glucose-6-phosphate dehydrogenase and 6-phosphogluconate dehydrogenase

(D) Glucokinase and phosphoglucomutase

Q18. Iron within haem can exist in different oxidation states, each with different physiological consequences. A clinical scenario involving methemoglobinaemia presents a patient with cyanosis and a PaO_2 that is normal but oxygen saturation measured by co-oximetry is low. Which oxidation state of haem iron is found in methaemoglobin and why can it not transport oxygen?

(A) Fe^{2+} (ferrous) – methaemoglobin has ferrous iron that binds O_2 too tightly

(B) Fe^{4+} (ferryl) – hyperoxidised iron formed during peroxide exposure

(C) Fe^{3+} (ferric) – oxidised iron cannot reversibly bind O_2 and gives blood a chocolate-brown colour

(D) Fe^{0} (elemental) – reduced iron found in deoxyhaemoglobin

Q19. A 3-year-old boy presents with acute encephalopathy, hyperammonaemia, and orotic aciduria following a high-protein meal. His mother had a history of unexplained episodic confusion. Plasma amino acid analysis

shows no increase in citrulline. The most likely diagnosis involves which enzyme deficiency and by what mechanism does orotic acid appear in the urine?

(A) Ornithine transcarbamylase (OTC) deficiency – carbamoyl phosphate that cannot enter the urea cycle leaks to the cytoplasm and enters the pyrimidine synthesis pathway, producing orotic acid

(B) Carbamoyl phosphate synthetase I (CPS-I) deficiency – absence of CPS-I diverts carbamoyl phosphate to pyrimidine synthesis

(C) Argininosuccinate synthetase deficiency – citrulline accumulates and is converted to orotic acid

(D) N-acetylglutamate synthase (NAGS) deficiency – elevated glutamate is directly converted to orotic acid

Q20. A patient undergoing a surgical procedure under general anaesthesia receives a bolus of ACTH (cosyntropin) for adrenal stimulation testing. At the cellular level, ACTH binds the MC2R receptor on adrenocortical cells. Which intracellular event is the immediate first step in ACTH-stimulated steroidogenesis?

(A) ACTH directly enters the cell and binds the nucleus, activating CYP11A1 gene transcription

(B) ACTH binds MC2R (Gs-coupled GPCR) $\rightarrow$ cAMP $\rightarrow$ PKA $\rightarrow$ phosphorylates StAR protein, facilitating cholesterol transport from the outer to inner mitochondrial membrane

(C) ACTH activates phospholipase C $\rightarrow$ IP_3/DAG $\rightarrow$ calcium release $\rightarrow$ steroidogenesis

(D) ACTH inhibits ACTH-responsive element binding, reducing StAR mRNA levels

Q21. A 4-year-old child presents with recurrent episodes of rhabdomyolysis triggered by febrile illness or prolonged fasting. Between attacks she appears normal. Muscle biopsy shows lipid vacuoles. Plasma acylcarnitine

profile shows elevated palmitoyl- and stearoyl-carnitines (C16, C18). Fibroblast studies show deficiency of phosphatidate phosphatase (lipin-1). Mutations in the *LPIN1* gene cause:

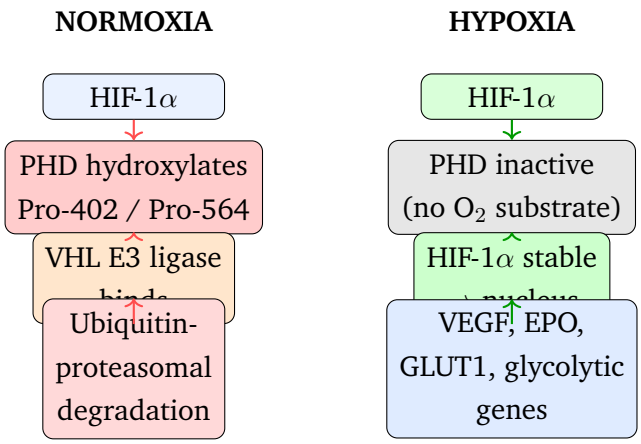
(A) Carnitine palmitoyltransferase I (CPT-I) deficiency with hepatic presentation

(B) Medium-chain acyl-CoA dehydrogenase (MCAD) deficiency

(C) Primary carnitine deficiency (OCTN2 transporter mutation)

(D) Lipin-1 deficiency with acute childhood rhabdomyolysis and partial lipodystrophy

Q22. A tumour pathologist studying renal cell carcinoma finds that the tumour cells show constitutive activation of HIF-1α even under normoxic conditions, due to loss-of-function mutations in the VHL gene. The diagram below illustrates HIF-1α regulation. Under normal (normoxic) conditions, what prevents HIF-1α accumulation?



(A) PHD (prolyl hydroxylase domain) enzymes hydroxylate HIF-1α proline residues $\rightarrow$ VHL E3 ubiquitin ligase binds $\rightarrow$ ubiquitin-proteasomal degradation

(B) HIF-1α is sequestered in the cytoplasm by HSP90, preventing nuclear entry

(C) ARNT (HIF-1β) is degraded in normoxia, preventing heterodimer formation

(D) Asparaginyl hydroxylase (FIH) acetylates HIF-1α, targeting it for mitochondrial import

Q23. A structural biologist examines the right-handed α-helix in a protein. A student asks about the pattern of hydrogen bonding that stabilises this secondary structure. Which description is correct?

(A) H-bond between the carbonyl oxygen (C=O) of residue n and the amide hydrogen (N-H) of residue $n+3$; approximately 3.0 residues per turn

(B) H-bond between the R-groups (side chains) of adjacent residues stabilises the helix backbone

(C) H-bond between the carbonyl oxygen (C=O) of residue n and the amide hydrogen (N-H) of residue $n+4$; approximately 3.6 residues per turn; side chains project outward

(D) H-bond between the carbonyl oxygen of residue n and the amide hydrogen of residue $n+2$; 3-10 helix pattern

Q24. A 3-year-old child whose parents have been giving large supplemental doses of a fat-soluble vitamin presents with anorexia, vomiting, irritability, and hypercalcaemia. Serum 25-OH-vitamin D level is markedly elevated at 420 nmol/L. Renal ultrasound reveals nephrocalcinosis. Which of the following best explains the mechanism of toxicity?

(A) Excess vitamin D inhibits calcitonin release, directly reducing calcium excretion from kidneys

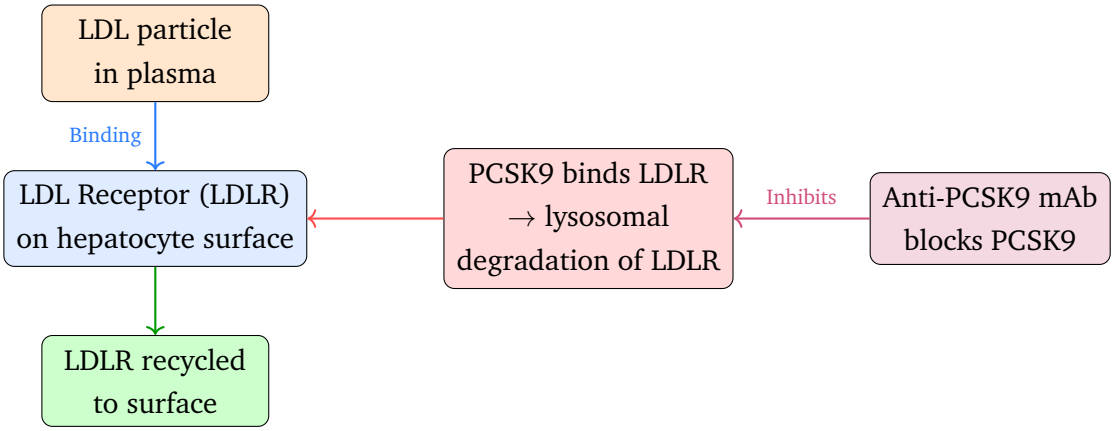
(B) Excess vitamin D competes with parathyroid hormone at renal tubular receptors, causing hypercalciuria followed by hypercalcaemia

(C) Vitamin D toxicity causes intravascular haemolysis, releasing calcium from erythrocytes

(D) Excess 1,25-$(OH)_2$-vitamin D (calcitriol) massively increases intestinal calcium absorption and bone calcium resorption, causing hypercalcaemia and soft tissue/renal calcification

Q25. A 58-year-old man with heterozygous familial hypercholesterolaemia has LDL-C of 210 mg/dL despite maximum-dose statin plus ezetimibe therapy. His cardiologist adds a novel injectable agent (subcutaneous, every

2 weeks). This drug is a fully human monoclonal antibody that targets and inhibits a serine protease that normally degrades LDL receptors in the liver. Which drug mechanism is being described?



(A) It inhibits HMG-CoA reductase, blocking de novo cholesterol synthesis in hepatocytes

(B) It blocks intestinal NPC1L1, reducing cholesterol absorption from the gut

(C) It upregulates ABCA1 transporter in macrophages, promoting reverse cholesterol transport

(D) It inhibits PCSK9, preventing LDLR degradation and increasing LDL receptor recycling to the hepatocyte surface

Q26. A pharmacologist studying neuropeptides reviews the structure of oxytocin. Oxytocin is a nonapeptide hormone synthesised in the hypothalamus. Which of the following correctly describes its structural features?

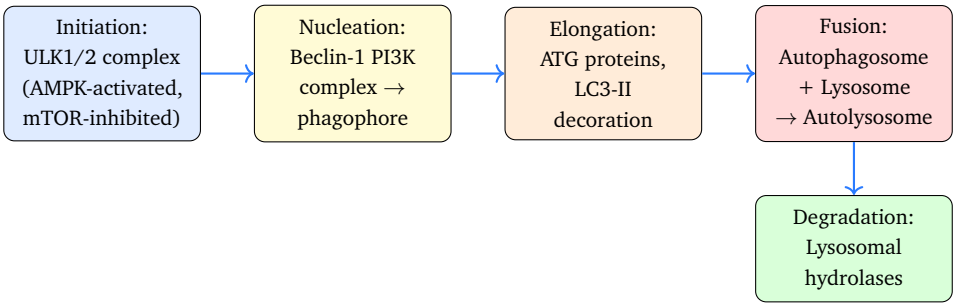
(A) Linear nonapeptide with no disulfide bridge; C-terminus is free carboxyl group; contains arginine at position 8

(B) Cyclic nonapeptide (9 amino acids); disulfide bridge between Cys1 and Cys6 forms a ring; C-terminus is amidated glycine; contains isoleucine at position 3

(C) Cyclic decapeptide; two disulfide bridges; contains phenylalanine at position 3 like vasopressin

(D) Linear octapeptide; no ring structure; synthesised exclusively in the posterior pituitary

Q27. A researcher studying protein quality control investigates macroautophagy – a process by which cells degrade and recycle cytoplasmic components, including damaged organelles. Which sequence of events correctly describes the stages of macroautophagy?



(A) Lysosome → phagophore formation → autophagosome → cargo sequestration → mTOR activation

(B) mTOR activation → ULK1 activation → beclin-1 PI3K complex → phagophore → autophagosome fusion with lysosome

(C) Proteasome activation → ubiquitin tagging of cargo → lysosomal import via LAMP2A

(D) ULK1/2 initiation → beclin-1-PI3K phagophore nucleation → ATG/LC3-II elongation → autophagosome-lysosome fusion → lysosomal hydrolysis

Q28. A medical student is studying the insulin signalling cascade and its downstream metabolic effects. Starting from insulin receptor activation, which of the following correctly lists the key sequential steps of the PI3K-Akt pathway and its metabolic outcomes?

(A) Insulin receptor → IRS proteins → PI3K → PIP3 → PDK1 → Akt (PKB) activation → GLUT4 translocation, GSK-3 inhibition (glycogen synthesis), FOXO inhibition (suppress gluconeogenesis), mTOR activation (protein synthesis)

(B) Insulin receptor → MAPK pathway → ERK1/2 → GLUT4 translocation

(C) Insulin receptor → adenylyl cyclase → cAMP → PKA → glycogen synthesis

(D) Insulin receptor $\rightarrow$ PLCβ $\rightarrow$ IP_3/DAG $\rightarrow$ calcium release $\rightarrow$ GLUT4 translocation

Q29. A 62-year-old man with decompensated liver cirrhosis (Child-Pugh C) develops confusion and asterixis after eating a high-protein meal. Serum ammonia is 220 μmol/L (normal $<$50). Brain MRI shows diffuse astrocyte swelling (Alzheimer type II astrocytosis). The **primary** mechanism for ammonia detoxification in the brain involves which reaction and which cells?

(A) Carbamoyl phosphate synthetase in hepatocytes; ammonia is converted to carbamoyl phosphate

(B) Glutamate dehydrogenase in neurons; reductive amination of α-ketoglutarate to glutamate

(C) Glutamine synthetase in astrocytes; glutamate + NH_3 + ATP $\rightarrow$ glutamine; excess glutamine accumulation causes astrocyte osmotic swelling

(D) Arginase in brain microglia; arginine + H_2O $\rightarrow$ ornithine + urea

Q30. A cell biology lecture describes a large glycoprotein of the extracellular matrix that plays essential roles in cell adhesion, migration, and wound healing. It contains the integrin-binding tripeptide sequence RGD (Arg-Gly-Asp) and also binds collagen, fibrin, and heparan sulfate proteoglycans. The plasma form acts as an opsonin in wound healing. This protein is:

(A) Laminin – cross-shaped glycoprotein of basement membranes

(B) Vitronectin – serum glycoprotein that binds plasminogen activator inhibitor-1

(C) Fibronectin – large dimeric ECM glycoprotein with RGD motif recognised by $\alpha_5\beta_1$ integrins

(D) Tenascin – ECM glycoprotein with anti-adhesive properties

Q31. A molecular oncologist is studying a lung cancer cell line and finds that the cells express very high levels of telomerase (hTERT). Normal somatic lung cells do not express telomerase. Which of the following best explains the significance of telomere biology in cancer?

(A) Telomere shortening in cancer cells activates p53, promoting continued proliferation

(B) Telomerase in normal somatic cells maintains telomere length, allowing unlimited replication

(C) Telomere elongation in normal cells triggers the Hayflick limit (replicative senescence) after ∼50 doublings

(D) Normal somatic cells undergo progressive telomere shortening (∼50–200 bp/division) leading to replicative senescence; cancer cells reactivate telomerase (TERT) to maintain telomeres and achieve unlimited proliferative potential

Q32. A 45-year-old strict vegan (no B12 supplementation for 3 years) presents with macrocytic anaemia and a serum B12 level of 98 pg/mL (normal 200–900 pg/mL). Serum folate is normal. The "folate trap" hypothesis explains the megaloblastic changes in B12 deficiency. Which of the following best explains this hypothesis?

(A) B12 deficiency impairs dihydrofolate reductase (DHFR) activity, blocking all folate reduction steps

(B) B12 deficiency directly inhibits thymidylate synthase, reducing dTMP synthesis independent of folate status

(C) B12 deficiency traps folate as 5-methyl-THF (the circulating form); without B12, methionine synthase cannot transfer the methyl group to homocysteine, so THF is not regenerated – causing functional folate deficiency despite normal serum folate

(D) B12 deficiency increases intracellular folate degradation by lysosomal enzymes

Q33. Hartnup disorder is an autosomal recessive condition affecting neutral amino acid transport. A patient presents with intermittent cerebellar ataxia, pellagra-like photosensitive rash, and psychiatric symptoms. Urine amino acid analysis shows marked neutral aminoaciduria (tryptophan, alanine, serine, histidine). The defective transporter in Hartnup disorder is:

(A) SLC7A9 ($b^{0,+}AT$) – cationic amino acid transporter; defective in cystinuria

(B) SLC6A19 (B^0AT1) – sodium-dependent neutral amino acid transporter in intestine and kidney proximal tubule

(C) SLC3A1 + SLC7A9 heterodimer – responsible for dibasic amino acid transport

(D) ABCB1 (P-glycoprotein) – ATP-binding cassette multidrug transporter

Q34. A marathon runner exhausts his phosphocreatine stores within the first 10–15 seconds of an explosive sprint. Phosphocreatine serves as an immediate ATP buffer in muscle and brain. The enzyme that catalyses this reaction and the clinical significance of its serum elevation are:

(A) Adenylate kinase (myokinase): $2ADP \rightarrow ATP + AMP$; elevated in renal failure

(B) Creatine kinase (CK): creatine phosphate + ADP $\rightleftharpoons$ creatine + ATP; serum CK elevated in myocardial infarction, myopathy, and rhabdomyolysis

(C) Phosphoglycerate kinase (PGK): substrate-level phosphorylation step in glycolysis; not elevated in MI

(D) Pyruvate kinase (PK): PEP + ADP $\rightarrow$ pyruvate + ATP; isoform PK-M2 elevated in cancer

Q35. A liver biopsy from a 52-year-old man with alcoholic hepatitis shows Mallory-Denk bodies on haematoxylin-eosin staining. The pathogenesis of these inclusion bodies and the key role of acetaldehyde in alcoholic liver injury involves which of the following mechanisms?

(A) Acetaldehyde activates PPAR-α, promoting fatty acid oxidation and reducing hepatic lipid accumulation

(B) Acetaldehyde inhibits cytochrome P450 2E1 (CYP2E1), reducing reactive oxygen species generation in hepatocytes

(C) Acetaldehyde upregulates collagen type IV synthesis by hepatocytes, directly remodelling the space of Disse

(D) Acetaldehyde forms covalent adducts with proteins (cytokeratin-acetaldehyde adducts $\rightarrow$ Mallory-Denk bodies) and DNA; these adducts impair protein function, trigger immune responses, and activate stellate cells to produce collagen, promoting fibrosis

Q36. A biochemist studying fatty acid oxidation notes that very-long-chain fatty acids (VLCFAs, carbon chain length $>$22) are not substrates for carnitine-mediated mitochondrial import. Zellweger syndrome (cerebrohepatorenal syndrome) is caused by absent functional peroxisomes. Which of the following correctly describes the unique features of peroxisomal β-oxidation compared to mitochondrial β-oxidation?

(A) Peroxisomal β-oxidation is the exclusive site for oxidation of medium-chain fatty acids; it generates ATP via substrate-level phosphorylation

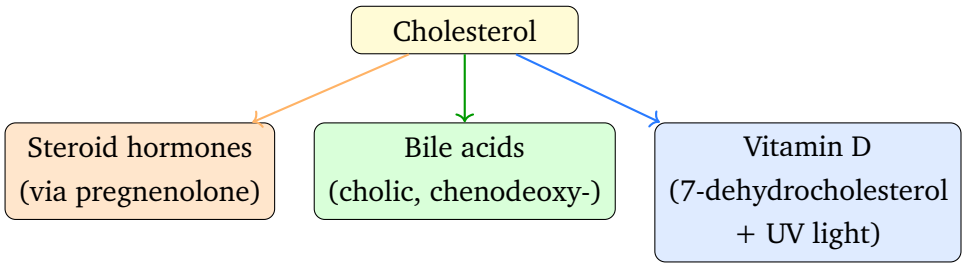
(B) Peroxisomal β-oxidation handles VLCFAs and branched-chain fatty acids; produces H_2O_2 (detoxified by catalase) rather than $FADH_2$-linked ATP; short/medium-chain products are transferred to mitochondria for complete oxidation

(C) Peroxisomal β-oxidation is coupled to the electron transport chain via a specific flavoprotein; it generates the same ATP yield per carbon as mitochondrial β-oxidation

(D) Peroxisomal β-oxidation is activated by insulin and suppressed by glucagon, unlike mitochondrial β-oxidation

Q37. Cholesterol is a metabolic precursor to multiple classes of bioactive molecules. The diagram below summarises the major biosynthetic pathways diverg-

ing from cholesterol. Which statement correctly describes all three major biosynthetic products of cholesterol?



(A) Cholesterol is the precursor for steroid hormones (via pregnenolone), bile acids (cholic and chenodeoxycholic acid), and vitamin D (via 7-dehydrocholesterol, which is UV-converted in skin); rate-limiting: StAR for substrate supply, CYP11A1 for first reaction in steroidogenesis

(B) Cholesterol is converted to catecholamines (dopamine, adrenaline, noradrenaline) in the adrenal medulla and to eicosanoids in platelets

(C) Cholesterol is the precursor only for bile acids; steroid hormones are derived from mevalonate directly

(D) Cholesterol is converted to retinol (vitamin A) in the liver via a series of hydroxylation reactions

Q38. A patient with X-linked chronic granulomatous disease (CGD) presents with recurrent Staphylococcal and Aspergillus abscesses. The defective protein in the most common form of CGD is a component of the NADPH oxidase (NOX2) complex in neutrophils. Which of the following correctly describes the biochemical role of NOX2 and why catalase-positive organisms are most problematic in CGD?

(A) NOX2 ($gp91^{phox}$) uses NADPH + O_2 $\rightarrow$ superoxide ($O_2^{\bullet -}$) $\rightarrow$ H_2O_2 $\rightarrow$ HOCl (via myeloperoxidase); catalase-positive organisms (Staphylococcus, Aspergillus) decompose H_2O_2 they generate, depriving the CGD neutrophil of the oxidative burst substrate; CGD patients can only kill catalase-negative organisms whose own H_2O_2 fuels the MPO pathway

(B) NOX2 uses NADH to generate nitric oxide (NO) for bactericidal activity; CGD is due to iNOS deficiency

(C) NOX2 generates reactive nitrogen species that degrade bacterial cell walls; CGD patients cannot produce these species

(D) NOX2 is a mitochondrial enzyme; CGD affects mitochondrial oxidative phosphorylation in neutrophils

Q39. Ubiquitin is a highly conserved 76-amino acid protein that tags proteins for proteasomal degradation or signalling functions. A biochemistry student is asked to identify the biochemical linkage through which ubiquitin is attached to a target protein and the three-enzyme cascade required. Which of the following is correct?

(A) Ubiquitin's Lys48 is linked to the α-amino group (N-terminus) of the target protein via a peptide bond; attachment requires only E1 (ubiquitin-activating enzyme)

(B) Ubiquitin Gly76 is linked to the γ-carboxyl of glutamate residues on the target protein; E2 (conjugating enzyme) confers substrate specificity

(C) Ubiquitin Lys63 of the first ubiquitin is always used for polyubiquitin chain formation leading to proteasomal degradation; K48-linked chains are exclusively used for signalling

(D) Ubiquitin Gly76 (C-terminus) forms an isopeptide bond with the ε-amino group of a lysine residue on the target protein; three enzymes required: E1 (activating), E2 (conjugating), E3 (ligase, confers specificity); K48-linked chains $\rightarrow$ proteasomal degradation; K63-linked chains $\rightarrow$ signalling

Q40. A 72-year-old woman presents with profound fatigue, macrocytic anaemia (MCV 118 fL), and a smooth, beefy red tongue (glossitis). Her serum vitamin B12 is 68 pg/mL. She has a history of autoimmune thyroid disease. Anti-parietal cell and anti-intrinsic factor antibodies are positive. Serum gastrin is markedly elevated. She requires intramuscular vitamin B12

injections because oral supplementation in standard doses is ineffective. The pathophysiology of her condition is:

(A) Terminal ileal resection causing failure of IF-B12 complex absorption at cubilin receptor

(B) Autoimmune destruction of gastric parietal cells $\rightarrow$ loss of intrinsic factor (IF) AND gastric acid $\rightarrow$ B12 malabsorption; anti-parietal cell (anti-H^+/K^+-ATPase) and anti-IF antibodies; secondary hypergastrinaemia from achlorhydria

(C) Dietary B12 deficiency due to strict veganism with adequate gastric intrinsic factor production

(D) Pancreatic exocrine insufficiency impairing R-protein cleavage in the duodenum, preventing IF-B12 complex formation

Detailed Solutions

Q1.

Solution

Concept – Vitamin A storage in hepatic stellate cells (Ito cells): The liver contains two major cell types relevant here: hepatocytes (parenchymal cells, 70–80% of liver mass) and non-parenchymal cells including hepatic stellate cells (HSCs), Kupffer cells, and sinusoidal endothelial cells. **Hepatic stellate cells (Ito cells / perisinusoidal cells)** are the primary storage site for vitamin A in the body, storing it as retinyl esters in their characteristic cytoplasmic lipid droplets (80–90% of the body's retinol reserves). In liver disease or chronic injury, HSCs become activated, lose their lipid droplets (retinyl ester reserves fall), and transdifferentiate into myofibroblasts that synthesise collagen type I and III, causing hepatic fibrosis and ultimately cirrhosis. Kupffer cells are hepatic macrophages (innate immunity); sinusoidal endothelial cells form the fenestrated lining; hepatocytes are the primary metabolic cells.

Distractors: Kupffer cells store degraded red blood cell iron (haemosiderin) not vitamin A. Hepatocytes synthesise retinol-binding protein (RBP) for vitamin A transport but are not the primary storage depot.

Final Answer: Hepatic stellate cells (Ito cells). $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q1

Q2.

Solution

Concept – Effect of enzyme concentration on kinetic parameters: V_{max} is defined as $k_{cat} \times [\mathrm{E}]_{total}$. Therefore V_{max} is directly proportional to enzyme concentration – doubling $[\mathrm{E}]$ doubles V_{max} because there are now twice as many active sites catalysing the reaction per unit time. In contrast, K_m (Michaelis constant) is an intrinsic thermodynamic property of the enzyme-substrate interaction (related to k_{cat}/k_{-1}) and is **independent of enzyme concentration**. K_m reflects the substrate concentration needed to half-saturate the enzyme's active sites – this is determined solely by the affinity of the enzyme for its substrate, not by how many enzyme molecules are present.

Distractors: Option A (both doubled) is wrong – K_m cannot be changed by enzyme amount. Option C (K_m halved) is wrong for the same reason. Option D (both halved) reverses the correct relationship.

Final Answer: V_{max} doubled, K_m unchanged. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q2

Q3.

Solution

Concept – Isovaleric acidaemia (IVA): IVA is caused by deficiency of **isovaleryl-CoA dehydrogenase (IVD)**, which catalyses the third step in **leucine catabolism** (the oxidative decarboxylation of isovaleryl-CoA to 3-methylcrotonyl-CoA). When IVD is deficient, isovaleryl-CoA and isovaleric acid accumulate. Free isovaleric acid is responsible for the distinctive "sweaty feet" (or "cheese-like") odour – a key clinical hallmark. Isovalerylcarnitine (C5-acylcarnitine) accumulates in plasma, detectable on newborn screening. Neonates present with vomiting, lethargy, high anion gap metabolic acidosis, hyperammonaemia, neutropenia, and thrombocytopaenia. Treatment: low-leucine diet + glycine supplementation (conjugates isovaleric acid forming isovalerylglycine, reducing toxic free acid) + carnitine supplementation.

Distractors: Propionyl-CoA carboxylase deficiency = propionic acidaemia (odd-chain FA / Val / Ile / Met / Thr / Tyr); methylmalonyl-CoA mutase = methylmalonic acidaemia; glutaryl-CoA dehydrogenase = glutaric aciduria type 1 (lysine/tryptophan catabolism, dystonia).

Final Answer: Isovaleryl-CoA dehydrogenase; leucine catabolism. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q3

Q4.

Solution

Concept – PDC activation by insulin: Pyruvate dehydrogenase complex (PDC) activity is regulated by phosphorylation/dephosphorylation of the E1α (pyruvate decarboxylase) subunit. **PDC kinase (PDK)** phosphorylates E1α $\rightarrow$ **inactivation**. **Protein phosphatase 2A (PDP)** dephosphorylates E1α $\rightarrow$ **activation**. Insulin (in liver and adipose tissue) activates **protein phosphatase 2A**, which dephosphorylates and thereby **activates PDC**, promoting glucose oxidation and lipogenesis from acetyl-CoA. In muscle and heart, Ca^{2+} (released during contraction) also activates PDP, activating PDC for oxidative glucose metabolism during exercise. PDK is activated by high ratios of Acetyl-CoA/CoA and NADH/NAD^+ (signals of energy excess: fatty acid oxidation, starvation).

Distractors: A (insulin phosphorylates PDC) is incorrect – phosphorylation inactivates PDC. B (insulin activates PDK) is the opposite of the truth. D (NAD^+/NADH ratio) is related to PDK regulation, not direct insulin action.

Final Answer: Insulin activates protein phosphatase 2A $\rightarrow$ dephosphorylates and activates PDC. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q4

Q5.

Solution

Concept – Tocopherols vs. Tocotrienols (Vitamin E family): Vitamin E comprises eight naturally occurring compounds: four **tocopherols** ($\alpha, \beta, \gamma, \delta$) and four **tocotrienols** ($\alpha, \beta, \gamma, \delta$). Both share a chromanol ring head group (which carries the antioxidant phenolic -OH group); they differ in their phytyl tail: **Tocopherols** have a **saturated** (fully reduced) phytyl side chain. **Tocotrienols** have an **unsaturated isoprenoid** side chain with **three double bonds** (at positions 3', 7', and 11'). The sub-types ($\alpha, \beta, \gamma, \delta$) within each class differ in the number and position of methyl groups on the chromanol ring. α-Tocopherol has the highest biological activity (greatest affinity for α-TTP, the tocopherol transfer protein in liver that determines bioavailability). Tocotrienols have additional anti-inflammatory, neuroprotective, and anti-cancer properties.

Final Answer: Tocopherols – saturated phytyl tail; tocotrienols – three double bonds in isoprenoid tail. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q5

Q6.

Solution

Concept – CPS-I vs. CPS-II: Two distinct carbamoyl phosphate synthetases exist in mammalian cells, with fundamentally different properties. **CPS-I** (mitochondrial): part of the urea cycle; uses **NH_3** (free ammonia, not glutamine) as nitrogen donor; absolutely requires **N-acetylglutamate (NAG)** as an allosteric activator; product: carbamoyl phosphate for urea cycle. **CPS-II** (cytoplasmic): part of the CAD trifunctional enzyme (CPS-II + aspartate transcarbamylase + dihydroorotase); uses **glutamine** as nitrogen donor (amide nitrogen); does **not** require NAG; activated by ATP and PRPP; inhibited by UTP (end-product inhibition); product: carbamoyl phosphate for pyrimidine synthesis. The distinction is clinically relevant because OTC deficiency (vs. CPS-I deficiency) can be distinguished by orotic acid in urine.

Final Answer: CPS-II uses glutamine, no NAG required; CPS-I uses NH_3, requires NAG. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q6

Q7.

Solution

Concept – Initiator methionine removal (methionine aminopeptidase): In eukaryotes, all proteins begin translation with methionine (AUG codon). However, approximately 50–70% of mature eukaryotic proteins lack the initiator methionine. **Methionine aminopeptidase (MAP)** cleaves the N-terminal methionine co-translationally when the **second residue (position 2) is small** – specifically Gly, Ala, Ser, Cys, Thr, Pro, or Val (amino acids with small side chains that do not sterically hinder the MAP active site). If position 2 has a bulky side chain (Lys, Arg, Phe, Tyr, Trp, Leu, Ile, Met), the initiator Met is retained. This processing is important for determining protein half-life (N-end rule): destabilising N-terminal residues target proteins for ubiquitin-mediated degradation. In bacteria, the initiator is fMet, removed first by deformylase then by MAP.

Distractors: Signal peptide presence (B) is unrelated to initiator Met removal. Formylated fMet (C) is bacterial. Proteasomal targeting (D) relates to ubiquitination, not Met removal.

Final Answer: The second residue is small (Gly, Ala, Ser, Cys, Thr, Pro, Val). $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q7

Q8.

Solution

Concept – HDL subclasses (HDL3 vs. HDL2): HDL particles are heterogeneous and undergo maturation. **Nascent (pre-β) HDL**: discoidal, lipid-poor, secreted by liver/intestine and formed from ApoA-I. It acquires free cholesterol from peripheral cells via the ABCA1 transporter. **HDL3**: small, dense, relatively protein-rich, less cholesterol – the immature form. **HDL2**: large, less dense, cholesterol ester-rich, considered the "mature" cardioprotective form formed as HDL3 matures. The key enzyme in maturation is **LCAT (lecithin-cholesterol acyltransferase)**, which esterifies free cholesterol on HDL (using phosphatidylcholine as acyl donor), converting it to cholesterol esters that move to the HDL core, causing the particle to enlarge from HDL3 to HDL2. HDL2 carries cholesterol back to the liver for disposal (reverse cholesterol transport). Low HDL2 is associated with increased cardiovascular risk.

Final Answer: HDL2 (large, cholesterol ester-rich, less dense – the mature cardio-

protective form). $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q8

Q9.

Solution

Concept – Substrate-level vs. Oxidative phosphorylation: These two mechanisms of ATP synthesis are fundamentally distinct. **Substrate-level phosphorylation (SLP):** ATP is synthesised directly from a high-energy phosphorylated intermediate by a kinase, without the need for a proton gradient or electron transport chain. Examples: (1) Phosphoglycerate kinase: 1,3-BPG + ADP $\rightarrow$ 3-PG + ATP; (2) Pyruvate kinase: PEP + ADP $\rightarrow$ pyruvate + ATP; (3) Succinyl-CoA synthetase: succinyl-CoA + GDP(ADP) $\rightarrow$ succinate + GTP(ATP). SLP can occur in the **absence of O_2** (fully anaerobic). **Oxidative phosphorylation (OxPhos):** Requires the ETC to create a proton electrochemical gradient across the inner mitochondrial membrane, which drives ATP synthase (Complex V). Requires O_2 as the final electron acceptor (Complex IV). The two processes are not interchangeable for membrane requirements or oxygen dependence.

Final Answer: Substrate-level does not require membrane gradient or O_2; oxidative phosphorylation requires ETC, proton gradient, and ATP synthase. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q9

Q10.

Solution

Concept – Brown Adipose Tissue (BAT): The tissue described is classic **brown adipose tissue (BAT)**, characterised by: (1) **multilocular** adipocytes with many small lipid droplets (vs. unilocular white fat with one large droplet); (2) extremely high mitochondrial density (the mitochondria and their cytochromes give BAT its brown colour); (3) high expression of **UCP1 (uncoupling protein 1)** – also called thermogenin – which creates a proton leak across the inner mitochondrial membrane, uncoupling electron transport from ATP synthesis and dissipating energy as heat (**non-shivering thermogenesis**); (4) rich sympathetic innervation (noradrenaline via β_3-adrenergic receptors stimulates lipolysis and UCP1 activity); (5) present in newborns (interscapular, perirenal, axillary) and in adult humans (cervical, supraclavicular depots detected by FDG-PET). Regulated by PGC-1α (master regulator of mitochondrial biogenesis).

Distractors: White adipose tissue (A) is unilocular; beige adipocytes (B) are in-

duced in adult WAT by cold/exercise; ectopic fat (C) describes lipid in non-adipose organs.

Final Answer: Brown adipose tissue (BAT) – multilocular, thermogenic, UCP1-rich. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q10

Q11.

Solution

Concept – Haemoglobin developmental switch (HbF to HbA): Haemoglobin undergoes two major developmental switches: (1) Embryonic to fetal: HbF ($\alpha_2\gamma_2$) replaces embryonic haemoglobins by 12 weeks gestation. (2) Fetal to adult: the **γ-to-β globin switch** begins before birth (around 32–36 weeks gestation) and is completed by approximately **6 months of age**. At birth, HbF comprises ~60–90% of total Hb; by 6 months, HbA ($\alpha_2\beta_2$) predominates (>95%). The switch is regulated by transcription factors, particularly **BCL11A** and **ZBTB7A (LRF)**, which silence the γ-globin genes. HbF is clinically significant: (a) HbF has higher O_2 affinity (shifts curve left) to extract O_2 from maternal HbA across the placenta; (b) HbF does not sickle – reactivating HbF with hydroxyurea ameliorates sickle cell disease and β-thalassaemia.

Final Answer: By approximately 6 months of age. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q11

Q12.

Solution

Concept – Lactoferrin (dual functions): Lactoferrin is an 80-kDa iron-binding glycoprotein (member of the transferrin superfamily) present in high concentrations in human colostrum and breast milk, and also in neutrophil secondary granules, saliva, tears, and other secretions. It binds two Fe^{3+} ions per molecule with very high affinity. **Two key functions in breast-fed infants:** (1) **Iron provision:** Lactoferrin delivers bioavailable iron to the infant – it is resistant to intestinal proteolysis and releases iron at the intestinal brush border (lower pH). (2) **Antimicrobial:** By sequestering iron, lactoferrin deprives bacteria of an essential growth factor (bacteriostatic effect – "nutritional immunity"). It also directly disrupts bacterial and fungal membranes (lactoferricin peptide), neutralises lipopolysaccharide (LPS), has antiviral and antifungal properties, and modulates the inflammatory response. Lactoferrin does not contain IgG or catalyse lipid digestion (those are other milk components).

Final Answer: Binds Fe^{3+} (iron provision) AND antimicrobial activity by iron sequestration. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q12

Q13.

Solution

Concept – RFLP (Restriction Fragment Length Polymorphism): RFLP was the first type of DNA marker used in forensic identification, paternity testing, and disease gene mapping. The technique detects **differences in restriction enzyme recognition sequences between individuals**: if a base change creates or destroys a restriction site, the pattern of fragment sizes after restriction digestion will differ. Southern blotting (transfer of restriction fragments to membrane + hybridisation with labelled probe) detects these fragment patterns. Each individual has a unique combination of RFLP alleles, producing a "DNA fingerprint." RFLP was largely superseded by **STR (short tandem repeat/microsatellite) analysis** (faster, requires less DNA, more polymorphic) and ultimately by SNP arrays and WGS. RFLP analysis is also used for direct detection of specific mutations (e.g., sickle cell Hb destroys an MstII restriction site at the β-globin codon 6).

Final Answer: Restriction fragment length polymorphism (RFLP). $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q13

Q14.

Solution

Concept – Interpretation of fasting plasma glucose: Current ADA (American Diabetes Association) diagnostic criteria for plasma glucose (after minimum 8-hour fast): **Normal:** 70–99 mg/dL ($<$100 mg/dL). **Impaired fasting glucose (IFG / pre-diabetes):** 100–125 mg/dL. **Diabetes mellitus:** $\geq$126 mg/dL on two separate occasions. Additional diagnostic criteria: random glucose $\geq$200 mg/dL with symptoms; 2-hour 75g OGTT glucose $\geq$200 mg/dL; HbA1c $\geq$6.5%. The patient's fasting glucose of 92 mg/dL falls within the **normal reference range (70–100 mg/dL)** and requires no specific intervention other than lifestyle maintenance.

Distractors: 126+ meets diabetes criterion; 100–125 is IFG/pre-diabetes; below 70 is hypoglycaemia.

Final Answer: Normal fasting plasma glucose (70–100 mg/dL). $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q14

Q15.

Solution

Concept – Ceramide structure (sphingolipid backbone): Ceramide is the fundamental building block of all sphingolipids. Its structure: **Sphingosine** (an 18-carbon amino alcohol with a trans-double bond between C4 and C5) + a **long-chain fatty acid** (usually C16–C24) linked via an **amide bond** (N-acyl linkage) at the C2 amino group of sphingosine. Critically: ceramide contains **no phosphate group** (that distinguishes it from sphingomyelin, which has phosphocholine). Ceramide biosynthesis: serine + palmitoyl-CoA $\rightarrow$ 3-ketosphingosine (serine palmitoyltransferase, rate-limiting) $\rightarrow$ sphinganine (dihydrosphingosine) $\rightarrow$ dihydroceramide $\rightarrow$ ceramide (oxidation by dihydroceramide desaturase). Ceramide is a bioactive second messenger: promotes **apoptosis**, cell cycle arrest, and differentiation. Ceramide + phosphocholine (from PC) $\rightarrow$ sphingomyelin (via sphingomyelin synthase). Ceramide + glucose $\rightarrow$ glucoceramide (first step in glycosphingolipid synthesis).

Final Answer: Sphingosine + fatty acid via amide bond; no phosphate; universal sphingolipid backbone. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q15

Q16.

Solution

Concept – Ascorbic acid (Vitamin C) and adrenal steroidogenesis: The adrenal gland (particularly the adrenal cortex) contains the **highest concentration of ascorbic acid (vitamin C) in the body**. Ascorbic acid serves multiple roles in steroidogenesis: (1) It acts as a co-factor supporting **cytochrome P450 (CYP) enzyme activity**, including **CYP11B1** (11β-hydroxylase, which converts 11-deoxycortisol $\rightarrow$ cortisol) and other adrenocortical P450s, facilitating their electron transfer chemistry. (2) It also participates in catecholamine synthesis: **dopamine β-hydroxylase** (converts dopamine $\rightarrow$ noradrenaline in adrenal medulla) requires ascorbate as electron donor. (3) **ACTH** stimulates steroidogenesis AND triggers the release of ascorbic acid from the adrenal cortex into the circulation ("ascorbic acid depletion" assay). In scurvy, impaired adrenal function can contribute to symptoms. Ascorbic acid is not a direct substrate for StAR (that is cholesterol) and does not regulate PKA directly.

Final Answer: Ascorbic acid supports P450 enzyme activity (including CYP11B1) for glucocorticoid synthesis; ACTH releases ascorbate from adrenal cortex. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q16

Q17.

Solution

Concept – Non-oxidative PPP: Transketolase and Transaldolase: The pentose phosphate pathway (PPP) has two phases. The **oxidative phase** (irreversible) generates NADPH and ribulose-5-phosphate. The **non-oxidative phase** (reversible) interconverts various sugar phosphates. Two key enzymes: (1) **Transketolase** (cofactor: **TPP – thiamine pyrophosphate, i.e., vitamin B1**): transfers a **2-carbon** unit (glycolaldehyde) between sugars. Reaction: Xylulose-5-P + Ribose-5-P $\rightarrow$ Sedoheptulose-7-P + Glyceraldehyde-3-P. (2) **Transaldolase**: transfers a **3-carbon** unit (dihydroxyacetone). Reaction: Sedoheptulose-7-P + G3P $\rightarrow$ Fructose-6-P + Erythrose-4-P. Together these reactions allow ribose-5-phosphate (in excess when NADPH is primarily needed) to be converted back into glycolytic intermediates F6P and G3P. Transketolase activity is used as a functional test for thiamine status (erythrocyte transketolase activation assay).

Final Answer: Transketolase (2-C transfer, requires TPP/Vitamin B1) and Transaldolase (3-C transfer). $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q17

Q18.

Solution

Concept – Methaemoglobin and Fe^{3+} iron: Haemoglobin's haem iron must be in the **Fe^{2+} (ferrous, reduced)** state to reversibly bind oxygen. When iron is oxidised to **Fe^{3+} (ferric)**, the resulting compound is **methaemoglobin (MetHb)**, which **cannot bind oxygen** (the ferric iron forms a stable water adduct instead). MetHb appears **chocolate-brown** (vs. the bright red of oxyHb or dark red of deoxyHb). In MetHb, the remaining normal haem groups show increased O_2 affinity (left shift of dissociation curve) – so even less O_2 is delivered to tissues. Causes: oxidant drugs (dapsone, nitrites, benzocaine, phenacetin, primaquine), congenital MetHb reductase (cytochrome b5 reductase) deficiency. The reducing system: NADH-MetHb reductase (primary, 95–99% of MetHb reduction) + ascorbic acid + GSH. Treatment: methylene blue (requires NADPH from G6PD – hence contraindicated in G6PD deficiency).

Final Answer: Fe^{3+} (ferric iron) – cannot reversibly bind O_2; blood is chocolate-brown. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q18

Q19.

Solution

Concept – OTC deficiency and orotic aciduria: The urea cycle disorders can be distinguished biochemically. **Ornithine transcarbamylase (OTC) deficiency:** X-linked (most common urea cycle disorder); affects males severely, females variably. Mechanism of orotic aciduria: OTC normally condenses ornithine + carbamoyl phosphate (produced by CPS-I in mitochondria) $\rightarrow$ citrulline. When OTC is deficient, **carbamoyl phosphate cannot be consumed in the mitochondria** and leaks into the **cytoplasm**, where it enters the **pyrimidine synthesis pathway** (CPS-II is cytoplasmic, but the leaked mitochondrial carbamoyl phosphate can also feed pyrimidine synthesis). Excess pyrimidine synthesis $\rightarrow$ **orotic acid accumulates** (orotic aciduria). By contrast, in **CPS-I deficiency**, carbamoyl phosphate is not made in the first place – so there is **no orotic aciduria**. Both have hyperammonaemia; the presence of orotic acid in urine specifically points to OTC (or other post-CPS-I blocks).

Final Answer: OTC deficiency – carbamoyl phosphate leaks to cytoplasm $\rightarrow$ pyrimidine synthesis $\rightarrow$ orotic aciduria. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q19

Q20.

Solution

Concept – ACTH signalling and StAR protein: ACTH (adrenocorticotrophic hormone) binds **MC2R** (melanocortin receptor 2), a **G_s-coupled GPCR** on the adrenal cortex cell surface. The signal cascade: ACTH $\rightarrow$ MC2R $\rightarrow$ G_s $\rightarrow$ adenylyl cyclase $\rightarrow$ **cAMP** $\uparrow$ $\rightarrow$ **PKA activation** $\rightarrow$ PKA phosphorylates **StAR protein (steroidogenic acute regulatory protein)**. StAR is the **rate-limiting acute step** of steroidogenesis: it facilitates the transfer of cholesterol from the **outer to the inner mitochondrial membrane**, where CYP11A1 (cholesterol desmolase/side-chain cleavage enzyme) converts cholesterol to pregnenolone – the first committed step of steroid hormone synthesis. StAR mutations cause congenital lipoid adrenal hyperplasia. ACTH also has chronic trophic effects (upregulating CYP11A1 and other steroidogenic enzymes at the transcriptional level).

Final Answer: ACTH $\rightarrow$ MC2R $\rightarrow$ cAMP $\rightarrow$ PKA $\rightarrow$ StAR phosphorylation $\rightarrow$ cholesterol transport $\rightarrow$ steroidogenesis. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q20

Q21.

Solution

Concept – Lipin-1 deficiency (LPIN1 mutations): Lipin-1, encoded by the *LPIN1* gene, is a **phosphatidate phosphatase** (PAP1) that dephosphorylates phosphatidic acid (PA) to diacylglycerol (DAG), a critical step in phospholipid and triglyceride biosynthesis. **LPIN1 mutations** cause: (1) **Acute rhabdomyolysis** – episodic, severe, often triggered by febrile illness or prolonged fasting in childhood (mechanism: PA accumulation disrupts mitochondrial and lysosomal membrane dynamics; also impairs fatty acid oxidation); (2) **Lipodystrophy** – partial redistribution of fat; (3) Lipin-1 also functions as a **transcriptional coactivator** (interacts with PPARα/PGC-1α to regulate lipid oxidation genes). The elevated C16 and C18 acylcarnitines reflect impaired utilisation of long-chain fatty acids in muscle. Unlike CPT-I deficiency (hepatic presentation, hypoketotic hypoglycaemia) or MCAD deficiency (C8 acylcarnitine peak), LPIN1 has a distinct childhood rhabdomyolysis phenotype.

Final Answer: Lipin-1 deficiency with acute childhood rhabdomyolysis and partial lipodystrophy. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q21

Q22.

Solution

Concept – HIF-1α regulation in normoxia vs. hypoxia: HIF-1α (hypoxia-inducible factor 1α) is the master transcriptional activator of the hypoxic response. Under **normoxia (normal O_2): PHD (prolyl hydroxylase domain)** enzymes (PHD1, 2, 3) use O_2 and α-ketoglutarate as substrates to hydroxylate Pro-402 and Pro-564 of HIF-1α. This creates a binding site for the **VHL (von Hippel-Lindau) E3 ubiquitin ligase complex**, which polyubiquitinates HIF-1α, targeting it for **proteasomal degradation**. Additionally, asparaginyl hydroxylase (FIH) hydroxylates Asn-803, blocking HIF-1α interaction with coactivators. In **hypoxia:** PHDs are inactive (no O_2 substrate) $\rightarrow$ HIF-1α is not hydroxylated $\rightarrow$ VHL cannot bind $\rightarrow$ HIF-1α accumulates $\rightarrow$ dimerises with HIF-1β (ARNT, constitutively expressed) $\rightarrow$ transcribes target genes: VEGF, EPO, GLUT1/3, glycolytic enzymes (HK2, LDHA, PFKL), PDK1. VHL loss (renal cell carcinoma) $\rightarrow$ constitutive HIF-1α activation even in normoxia.

Final Answer: PHD enzymes hydroxylate HIF-1α $\rightarrow$ VHL E3 ligase $\rightarrow$ ubiquitin-proteasomal degradation. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q22

Q23.

Solution

Concept – α-helix hydrogen bonding pattern: The right-handed α-helix is stabilised by **intramolecular hydrogen bonds** between the **carbonyl oxygen (C=O)** of residue n and the **amide hydrogen (N-H)** of residue $n+4$. Structural parameters: **3.6 residues per turn**, rise of 1.5 Å per residue, pitch (distance per full turn) of 5.4 Å. The H-bonds run nearly **parallel to the helix axis**. **Side chains project outward** from the helix backbone (radially, away from the axis). Proline disrupts α-helices because: (a) proline's nitrogen has no H-bond donor (it is in a cyclic ring with no N-H group), and (b) the rigid pyrrolidine ring constrains the ϕ backbone angle. In a 3-10 helix, the H-bond pattern is n to $n+3$ (3 residues per turn, less common). Side chains are **not** involved in stabilising the backbone α-helix – that is the domain of H-bonds between main-chain groups.

Final Answer: C=O of residue n H-bonds to N-H of residue $n+4$; 3.6 residues per turn; side chains project outward. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q23

Q24.

Solution

Concept – Vitamin D toxicity (hypervitaminosis D): Unlike vitamin D from sunlight (where the skin self-limits synthesis), **oral/supplemental vitamin D can accumulate to toxic levels**. Excess vitamin D $\rightarrow$ excess **1,25-(OH)$_2$D (calcitriol)** $\rightarrow$: (1) Massive upregulation of **intestinal calcium absorption** (TRPV6 channel, calbindin-D) far exceeding normal; (2) Enhanced **osteoclast activity** $\rightarrow$ bone calcium resorption; (3) Together: **hypercalcaemia** (the primary toxic manifestation). Consequences of hypercalcaemia: "stones, bones, groans, psychic moans" – **nephrocalcinosis** (calcium phosphate precipitation in kidneys), polyuria, polydipsia, anorexia, vomiting, constipation, confusion, cardiac arrhythmias. Soft tissue calcification (blood vessels, lungs, heart). Note: hypervitaminosis D does **not** work through PTH (PTH is suppressed); it directly upregulates calcitriol-responsive genes via VDR (vitamin D receptor). Calcitonin inhibition and PTH competition are not the primary mechanisms.

Final Answer: Excess calcitriol $\rightarrow$ massively increased intestinal Ca^{2+} absorption + bone resorption $\rightarrow$ hypercalcaemia + nephrocalcinosis. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q24

Q25.

Solution

Concept – PCSK9 inhibitors (evolocumab, alirocumab): PCSK9 (proprotein convertase subtilisin/kexin type 9) is a serine protease secreted by hepatocytes. After LDL binds the LDL receptor (LDLR) and the complex is endocytosed, PCSK9 binds LDLR in the endosome, **preventing receptor recycling** back to the cell surface and directing LDLR for lysosomal degradation. When PCSK9 is inhibited by monoclonal antibodies (evolocumab, alirocumab – both fully human mAbs), LDLR is recycled to the hepatocyte surface multiple times, dramatically **increasing LDL clearance from plasma** (reduces LDL-C by 50–60% additional, on top of statins). Evolocumab and alirocumab are injected subcutaneously every 2 or 4 weeks. Indicated in: familial hypercholesterolaemia (FH), high-CV-risk patients on max statin therapy. Statins inhibit HMG-CoA reductase; ezetimibe inhibits NPC1L1; niacin raises HDL.

Final Answer: Inhibits PCSK9 $\rightarrow$ prevents LDLR degradation $\rightarrow$ more LDL receptors recycled to surface $\rightarrow$ 50-60% additional LDL lowering. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q25

Q26.

Solution

Concept – Oxytocin structure: Oxytocin is a **nonapeptide** (9 amino acids) neurohypophyseal hormone synthesised in the paraventricular nucleus (PVN) of the hypothalamus. Key structural features: (1) **Disulfide bridge** between **Cys^{1} and Cys^{6}** creates a 6-amino-acid ring with a 3-amino-acid C-terminal "tail." (2) The C-terminus of **Gly^{9} is amidated** (Gly-NH_2) – essential for biological activity. (3) The sequence: Cys-Tyr-**Ile**-Gln-Asn-Cys-Pro-Leu-Gly(NH_2). Note position 3 is **isoleucine (Ile)** in oxytocin. Vasopressin/ADH differs at positions 3 (Phe instead of Ile) and 8 (Arg instead of Leu) – hence it is called arginine vasopressin (AVP). Both are 9-amino-acid cyclic neuropeptides made in the hypothalamus and stored/released from the posterior pituitary. Oxytocin is not a linear peptide (A, D), not a decapeptide (C), and does not contain arginine at position 8 (that is vasopressin).

Final Answer: Cyclic nonapeptide; disulfide Cys^{1}–Cys^{6}; C-terminus amidated Gly; Ile at position 3. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q26

Q27.

Solution

Concept – Macroautophagy mechanism: Macroautophagy (commonly called autophagy) proceeds through sequential, well-defined stages: (1) **Initiation:** ULK1/2 complex is activated by **AMPK** (energy depletion, low ATP/AMP ratio) and inhibited by **mTORC1** (nutrient sufficiency, high mTOR activity suppresses autophagy). (2) **Nucleation:** The **beclin-1/PI3K class III (VPS34) complex** generates PI3P on the phagophore assembly site (PAS), nucleating the **phagophore** (isolation membrane). (3) **Elongation:** Two ubiquitin-like conjugation systems (ATG5-ATG12; LC3/ATG8 lipidation to LC3-II) extend and close the phagophore around cytoplasmic cargo → **autophagosome**. (4) **Fusion:** Autophagosome fuses with a **lysosome** → **autolysosome**. (5) **Degradation:** Lysosomal hydrolases (proteases, lipases, nucleases) degrade cargo; macromolecules recycled. Note: chaperone-mediated autophagy (CMA) uses LAMP2A, not bulk macroautophagy.

Final Answer: ULK1/2 → beclin-1/PI3K phagophore → ATG/LC3-II elongation → autophagosome-lysosome fusion → lysosomal hydrolysis. ⇒ $\boxed{D}$

Answer: (D) Go Back to Q27

Q28.

Solution

Concept – Insulin PI3K-Akt (PKB) signalling: Insulin binds the **insulin receptor** (a transmembrane receptor tyrosine kinase, RTK) → receptor autophosphorylation → recruitment and tyrosine phosphorylation of **IRS (insulin receptor substrate) proteins** → IRS recruits and activates **PI3K (class I, PI3Kα)** → PI3K generates **PIP3** (phosphatidylinositol 3,4,5-trisphosphate) from PIP2 at the plasma membrane → PIP3 recruits **PDK1 (phosphoinositide-dependent kinase 1)** and Akt → PDK1 phosphorylates and **activates Akt (PKB)** → Akt phosphorylates multiple downstream targets: (a) **FOXO transcription factors** → nuclear exclusion → suppresses gluconeogenic genes (G6Pase, PEPCK); (b) **GSK-3** → inhibition → glycogen synthase dephosphorylated/activated → glycogen synthesis; (c) **mTORC1** activation → protein synthesis; (d) **AS160 (TBC1D4)** phosphorylation → GLUT4 vesicle exocytosis.

Final Answer: Insulin receptor → IRS → PI3K → PIP3 → PDK1 → Akt → GLUT4, GSK-3 inhibition, FOXO inhibition, mTOR activation. ⇒ $\boxed{A}$

Answer: (A) Go Back to Q28

Q29.

Solution

Concept – Ammonia detoxification in the brain (glutamine synthetase): Unlike the liver, the **brain lacks a functional urea cycle**. The primary mechanism for ammonia removal in the brain is: **Glutamine synthetase (GS)** (predominantly in **astrocytes**): catalyses **glutamate + NH_3 + ATP $\rightarrow$ glutamine + ADP + P_i**. Glutamine is non-toxic and can leave astrocytes to enter the blood/CSF for disposal in liver and kidney. However, in hepatic encephalopathy (HE), markedly elevated blood ammonia drives excess glutamine production in astrocytes $\rightarrow$ **osmotic swelling of astrocytes** (Alzheimer type II astrocytosis – swollen astrocytes with large nuclei) because glutamine accumulation increases intracellular osmolality. Astrocyte swelling $\rightarrow$ cerebral oedema $\rightarrow$ raised intracranial pressure $\rightarrow$ herniation (in acute liver failure). Glutamate dehydrogenase (GDH) in neurons also handles small amounts, but the dominant pathway for surplus NH_3 in brain is astrocytic GS.

Final Answer: Glutamine synthetase in astrocytes; excess glutamine causes astrocyte osmotic swelling in hepatic encephalopathy. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q29

Q30.

Solution

Concept – Fibronectin (ECM glycoprotein): Fibronectin is a large ($\sim$440 kDa) dimeric glycoprotein (two subunits linked by C-terminal disulfide bonds) of the extracellular matrix and plasma. Key properties: (1) Contains the **RGD (Arg-Gly-Asp)** tripeptide integrin-binding motif, recognised by $\alpha_5\beta_1$ (fibronectin receptor) and other integrins on cell surfaces $\rightarrow$ cell adhesion, spreading, and migration; (2) Modular structure with binding domains for **collagen** (types I, II, III), **fibrin**, **heparan sulfate** proteoglycans (e.g., syndecan), and **bacteria**; (3) **Plasma fibronectin** (soluble form) acts as an **opsonin** in wound healing, promoting phagocytosis of debris; (4) **Cellular fibronectin** is incorporated into fibrils in the ECM, regulating basement membrane assembly, cell polarity, and organogenesis. Loss of fibronectin fibril assembly is associated with cancer invasion. Laminin (A) is the major basement membrane glycoprotein (not RGD-based); vitronectin (B) binds PAI-1; tenascin (D) has anti-adhesive properties.

Final Answer: Fibronectin – RGD motif, binds $\alpha_5\beta_1$ integrins, collagen, fibrin; plasma form is wound-healing opsonin. $\Rightarrow \boxed{C}$

Answer: (C) Go Back to Q30

Q31.

Solution

Concept – Telomere biology and cancer: **Telomeres** are repetitive DNA sequences (TTAGGG in humans, up to 10-15 kb) at chromosome ends that prevent chromosome degradation and end-joining. **Normal somatic cells:** Do **not** express telomerase; each cell division, DNA polymerase cannot replicate the very 3' end of the lagging strand ("end replication problem"), so telomeres shorten by ∼**50–200 bp per division**. After ∼50 divisions (Hayflick limit), critically short telomeres trigger **replicative senescence** (p53/Rb pathway) or apoptosis. **Cancer cells:** Reactivate **telomerase (hTERT – the catalytic reverse transcriptase subunit)** to maintain telomere length, achieving unlimited replicative potential (hallmark of cancer). Telomerase is also active in germ cells, stem cells, and activated lymphocytes. Therapeutic targeting: telomerase inhibitors (e.g., imetelstat) are in clinical trials for haematological malignancies.

Final Answer: Normal somatic cells – progressive telomere shortening → replicative senescence; cancer cells reactivate telomerase → unlimited proliferation. ⇒ $\boxed{D}$

Answer: (D) Go Back to Q31

Q32.

Solution

Concept – Folate trap hypothesis (B12 deficiency): In circulation, the predominant form of folate is **5-methyl-THF** (5-methyltetrahydrofolate). To re-enter cells and be used for purine and thymidylate synthesis, the methyl group must be **removed from 5-methyl-THF** – this is done exclusively by **methionine synthase (5-methyltetrahydrofolate-homocysteine methyltransferase)**, which transfers the methyl group to **homocysteine** → methionine. Methionine synthase requires **vitamin B12 (methylcobalamin)** as a cofactor. In B12 deficiency: methionine synthase is inactive → the methyl group cannot be removed from 5-methyl-THF → folate is **trapped as 5-methyl-THF** (the "methyl-folate trap") → **THF** cannot be regenerated → functional deficiency of THF despite normal/high serum folate → impaired DNA synthesis (purine and thymidylate synthesis) → megaloblastic anaemia identical to true folate deficiency. This explains why B12 deficiency causes megaloblastic anaemia even with normal serum folate.

Final Answer: B12 traps folate as 5-methyl-THF; without B12, methionine synthase cannot regenerate THF → functional folate deficiency despite normal serum folate. ⇒ $\boxed{C}$

Answer: (C) Go Back to Q32

Q33.

Solution

Concept – Hartnup disorder (SLC6A19 deficiency): Hartnup disorder is an autosomal recessive disorder affecting the **SLC6A19 (B^0AT1)** transporter, which mediates **sodium-dependent** absorption of **neutral amino acids** (particularly tryptophan, alanine, serine, phenylalanine, histidine, leucine, isoleucine) in the **intestinal brush border** and **renal proximal tubule**. Failure to absorb tryptophan from the intestine leads to: (1) Reduced tryptophan $\rightarrow$ reduced niacin synthesis $\rightarrow$ pellagra-like **photosensitive rash** (nicotinamide supplementation treats this); (2) Excess tryptophan reaching the colon is converted to indole derivatives by bacteria $\rightarrow$ **indicanuria**. Cerebellar ataxia results from tryptophan/serotonin deficiency affecting cerebellar function. Urine shows massive neutral aminoaciduria. Blood neutral amino acids are low/normal. Contrasted with **cystinuria** (SLC3A1/SLC7A9 – cationic amino acid transporter defect: cystine, ornithine, lysine, arginine – COLA stones) and **iminoglycinuria** (proline/glycine transport).

Final Answer: SLC6A19 (B^0AT1) – sodium-dependent neutral amino acid transporter. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q33

Q34.

Solution

Concept – Phosphocreatine ATP buffering and creatine kinase: Phosphocreatine (PCr / creatine phosphate) serves as the immediate ATP buffer in skeletal muscle, cardiac muscle, and brain. The enzyme **creatine kinase (CK)** catalyses the reversible reaction: **creatine phosphate + ADP $\rightleftharpoons$ creatine + ATP**. During explosive activity, PCr donates its phosphate to ADP, regenerating ATP within milliseconds (before glycolysis or OxPhos can be upregulated). PCr stores are typically exhausted within **10–15 seconds** of maximal effort. CK isoenzymes: **CK-MM** (skeletal muscle), **CK-MB** (cardiac muscle, used as MI marker – first to rise $\sim$4h, peaks at 12-24h), **CK-BB** (brain). **Elevated serum CK** occurs in: myocardial infarction (CK-MB), skeletal muscle myopathy (CK-MM), rhabdomyolysis (total CK massively elevated), muscular dystrophy, hypothyroidism. Adenylate kinase also buffers ATP (2ADP $\rightarrow$ ATP + AMP) but CK is the primary phosphocreatine-based buffer.

Final Answer: Creatine kinase (CK): creatine phosphate + ADP $\rightleftharpoons$ creatine + ATP; elevated in MI, myopathy, rhabdomyolysis. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q34

Q35.

Solution

Concept – Acetaldehyde-protein adducts in alcoholic liver disease: Ethanol metabolism: alcohol dehydrogenase (ADH) converts ethanol $\rightarrow$ **acetaldehyde**; aldehyde dehydrogenase (ALDH, mainly ALDH2) converts acetaldehyde $\rightarrow$ acetate. Acetaldehyde is a highly reactive electrophile. Its toxic mechanisms include: (1) **Covalent adduct formation with proteins** at cysteine, lysine, and histidine residues – impairing mitochondrial function (acetaldehyde-mitochondrial protein adducts), albumin synthesis, and cytoskeletal integrity. (2) **Mallory-Denk bodies (MDBs):** inclusion bodies visible on H&E in alcoholic hepatitis; composed of **cytokeratin 8/18 filaments cross-linked by acetaldehyde adducts** + heat shock proteins + p62/ubiquitin. (3) **Immune activation:** antibodies against acetaldehyde-modified proteins trigger immune-mediated hepatocyte injury. (4) **Stellate cell activation:** acetaldehyde directly stimulates hepatic stellate cells to produce collagen (pro-fibrogenic). (5) DNA adducts contribute to hepatocarcinogenesis. Acetaldehyde does **not** activate PPAR-α (that would promote FA oxidation – the opposite of what occurs); it does not inhibit CYP2E1 (CYP2E1 is actually induced by alcohol and generates ROS).

Final Answer: Acetaldehyde forms protein adducts $\rightarrow$ Mallory-Denk bodies (cytokeratin adducts); immune activation; stellate cell collagen synthesis $\rightarrow$ fibrosis. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q35

Q36.

Solution

Concept – Peroxisomal β-oxidation (VLCFAs and Zellweger syndrome): Mitochondrial β-oxidation handles short-, medium-, and long-chain fatty acids (via carnitine shuttle). **Very-long-chain fatty acids (VLCFAs, C>22)** and **branched-chain fatty acids** (phytanic acid via α-oxidation + β-oxidation) are handled **exclusively in peroxisomes**. Key differences of **peroxisomal β-oxidation**: (1) First step: acyl-CoA oxidase transfers electrons directly to $\mathbf{O_2} \rightarrow \mathbf{H_2O_2}$ (not to FAD-linked ETC as in mitochondria) – H_2O_2 is then decomposed by **catalase** within the peroxisome $\rightarrow$ heat, not ATP. (2) Energy yield: less efficient (no Complex I

coupling for the first oxidation step). (3) Products: shortened acyl-CoAs (C8/C6) + acetyl-CoA are transferred out of peroxisomes → mitochondria via carnitine for complete oxidation. **Zellweger syndrome** (absent peroxisomes due to PEX gene mutations) → VLCFA accumulation (diagnostic) → neuronal migration defects, liver failure, dysmorphic features, and early death.

Final Answer: Peroxisomal β-oxidation: VLCFAs and branched-chain FAs; H_2O_2 (not $FADH_2$-ATP); catalase degrades H_2O_2; products transferred to mitochondria. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q36

Q37.

Solution

Concept – Cholesterol as a biosynthetic precursor: Cholesterol serves as the precursor for three major classes of biologically essential molecules: (1) **Steroid hormones:** All five classes (glucocorticoids, mineralocorticoids, androgens, oestrogens, progestogens) are derived from cholesterol via **pregnenolone** (the immediate product of CYP11A1/P450scc, the "cholesterol desmolase" or "side-chain cleavage enzyme" in inner mitochondrial membrane of adrenal cortex, gonads, placenta). The rate-limiting steps are: **StAR protein** (cholesterol transport into mitochondria – acute regulation) and **CYP11A1** (first enzymatic step – committed step). (2) **Bile acids:** Cholic acid and chenodeoxycholic acid (primary bile acids) are synthesised in liver via multiple hydroxylation steps; rate-limiting enzyme: **CYP7A1** (cholesterol 7α-hydroxylase). (3) **Vitamin D:** Cholesterol → **7-dehydrocholesterol** (provitamin D3) in skin → UV light (290-315 nm) converts it to **cholecalciferol (D3)** → hepatic 25-hydroxylation → renal 1α-hydroxylation → **1,25-(OH)$_2$D$_3$ (calcitriol)**. Catecholamines are derived from tyrosine; eicosanoids from arachidonic acid; retinol is a separate pathway from dietary provitamins.

Final Answer: Cholesterol → steroid hormones (via pregnenolone/CYP11A1), bile acids, and vitamin D (via 7-dehydrocholesterol + UV). $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q37

Q38.

Solution

Concept – NADPH oxidase (NOX2) and chronic granulomatous disease (CGD): NOX2 (gp91^{phox}) is the catalytic subunit of the phagocyte NADPH oxidase complex (also includes p22^{phox}, p47^{phox}, p67^{phox}, p40^{phox}, and Rac2). During the **respiratory/oxidative burst** (triggered by phagocytosis): NADPH + $2O_2$ →

$NADP^+$ + $2O_2^{\bullet -}$ (superoxide). Superoxide is then converted to: (a) **H_2O_2** (by SOD); (b) **HOCl** (hypochlorous acid, "bleach") via **myeloperoxidase (MPO)** using H_2O_2 + Cl^-; (c) hydroxyl radical (•OH) via Fenton/Haber-Weiss. **X-linked CGD** (most common, 70%): $gp91^{phox}$ (NOX2) mutation. Why **catalase-positive** organisms are most virulent in CGD: Normal bacteria produce H_2O_2 during their own metabolism – if they **lack catalase**, their H_2O_2 accumulates and fuels the MPO pathway in the CGD neutrophil, killing the bacteria. **Catalase-positive organisms** (Staphylococcus aureus, Aspergillus, Nocardia, Serratia, Burkholderia) **decompose their own H_2O_2**, providing nothing for the MPO pathway in the non-functional CGD neutrophil.

Final Answer: NOX2 generates $O_2^{\bullet -} \rightarrow H_2O_2 \rightarrow$ HOCl (MPO); catalase-positive organisms destroy their own H_2O_2, preventing CGD neutrophil killing. $\Rightarrow \boxed{A}$

Answer: (A) Go Back to Q38

Q39.

Solution

Concept – Ubiquitin attachment mechanism and E1-E2-E3 cascade: Ubiquitin is a 76-amino-acid protein conserved from yeast to humans. It is attached to target proteins through an enzymatic cascade and a specific chemical linkage: (1) **E1 (ubiquitin-activating enzyme):** Forms a high-energy thioester bond with ubiquitin C-terminus (Gly76) using ATP. (2) **E2 (ubiquitin-conjugating enzyme, UBC):** Accepts ubiquitin from E1 via transthioesterification. (3) **E3 (ubiquitin ligase):** Transfers ubiquitin from E2 to the **ε-amino group of a lysine** residue on the target protein, forming an **isopeptide bond** (between Gly76 C-terminus of ubiquitin and the lysine ε-NH_2 of the substrate). E3 ligases confer substrate specificity (hundreds exist). **Polyubiquitin chain linkages: K48-linked** chains (Lys48 of one ubiquitin linked to Gly76 of the next) $\rightarrow$ **proteasomal degradation**. **K63-linked** chains $\rightarrow$ DNA damage signalling, endosomal sorting, NF-κB activation. **K11-linked** chains $\rightarrow$ cell cycle regulation.

Final Answer: Ubiquitin Gly76 $\rightarrow$ isopeptide bond to ε-amino of target Lys; E1 (activating), E2 (conjugating), E3 (ligase); K48 $\rightarrow$ proteasomal degradation; K63 $\rightarrow$ signalling. $\Rightarrow \boxed{D}$

Answer: (D) Go Back to Q39

Q40.

Solution

Concept – Pernicious anaemia (autoimmune gastritis): Pernicious anaemia is caused by **autoimmune destruction of gastric parietal cells** (type A autoimmune gastritis – affects the body/fundus of the stomach). Parietal cells normally produce: (a) **Intrinsic factor (IF)** – a $\sim$60 kDa glycoprotein that binds vitamin B12 in the stomach and protects it through the intestine until absorption at the **terminal ileum** via the **cubilin receptor**; (b) **Hydrochloric acid (HCl)** – required to release protein-bound B12 from food. In pernicious anaemia: anti-parietal cell antibodies (**anti-H^+/K^+-ATPase antibodies**) destroy parietal cells $\rightarrow$ loss of both IF and HCl $\rightarrow$ achlorhydria $\rightarrow$ hypergastrinaemia (loss of HCl removes the negative feedback on G-cells in the antrum $\rightarrow$ gastrin rises dramatically). Anti-IF antibodies (anti-IF type I: block B12 binding; anti-IF type II: block cubilin receptor binding) directly impair IF function. Oral B12 cannot be absorbed without IF, so **parenteral B12 (IM/SC)** is required. Strong association with other autoimmune diseases (thyroiditis, vitiligo, Addison's disease).

Final Answer: Autoimmune gastritis $\rightarrow$ parietal cell destruction $\rightarrow$ loss of IF + HCl $\rightarrow$ B12 malabsorption; anti-parietal cell and anti-IF antibodies; secondary hypergastrinaemia. $\Rightarrow \boxed{B}$

Answer: (B) Go Back to Q40

Answer Key – FMGE Biochemistry Sample Paper 10

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