NEET PG Pathology Sample Paper-6

Duration: 20 Minutes **Maximum Marks: 100**

Instructions

- This paper contains **25** Multiple Choice Questions.
- Each correct answer carries **+4** mark. Incorrect answer: **−1** marks. Only **one** correct option.
- Unattempted questions carry **0** marks.
- Use of mobile phones, smartwatches, or any electronic gadgets is strictly prohibited.

Q1. A 45-year-old male presenting with chronic limb ischemia undergoes revascularization. Within hours of reperfusion, he develops severe local tissue edema and a profound systemic inflammatory response. Molecular analysis reveals accelerated cell death driven by iron-dependent lipid peroxidation, independent of caspase activation or executioner proteins like MLKL. Which of the following biochemical alterations directly orchestrates this specific mode of cell death?

(A) Inhibition of Glutathione Peroxidase 4 (GPX4)

(B) Activation of Poly(ADP-ribose) Polymerase 1 (PARP-1)

(C) Oligomerization of BAX and BAK pores

(D) Phosphorylation of RIPK3 by RIPK1

Q2. During a research study into chronic neurodegenerative proteinopathies, an investigator identifies a peptide misfolding pathway where a soluble monomeric alpha-helical protein transitions into insoluble cross-beta sheet rich fibrils. Kinetic monitoring demonstrates a protracted lag phase followed by an exponential elongation phase. Which thermodynamic or kinetic phenomenon best describes this rate-limiting mechanism of amyloid nucleation?

(A) High-affinity interaction with glycosaminoglycans

(B) Critical concentration-dependent homogenous nucleation

(C) Ubiquitin-proteasome system saturation threshold

(D) Serum amyloid P component chaperone inhibition

Q3. A homozygous loss-of-function mutation in the gene encoding the BH3-only protein BIM is identified in a lineage of experimental mice. When these mice are subjected to systemic stressors that induce intracellular calcium overload and endoplasmic reticulum stress, which of the following cellular outcomes is most likely to be observed in their lymphocytes compared to wild-type controls?

(A) Accelerated cytochrome c release from mitochondria

(B) Impaired activation of the death receptors Fas and TNFR1

(C) Resistance to stress-induced intrinsic pathway apoptosis

(D) Enhanced activation of Caspase-8 and Caspase-3

Q4. A 28-year-old female presents with persistent, recurrent soft tissue infections. Functional testing of her neutrophils reveals normal phagocytic ingestion and intact oxidative burst capacity. However, the neutrophils completely fail to form extracellular fibrillary traps containing chromatin and granule proteins to immobilize large fungal hyphae. This clinical phenotype is most likely driven by a genetic deficiency in which of the following enzymes?

(A) Myeloperoxidase (MPO)

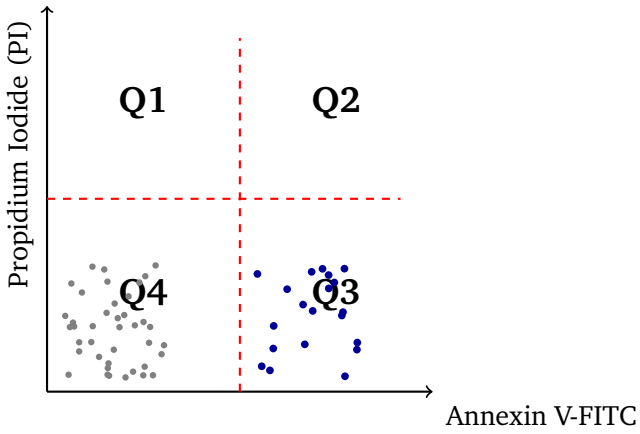
(B) NADPH Oxidase (gp91phox)

(C) Peptidylarginine Deiminase 4 (PAD4)

(D) Leukotriene B4 Receptor 1 (BLT1)

Q5. An immunopathology facility utilizes dual-parameter flow cytometry to assess a novel chemotherapeutic agent's cytotoxic kinetics on lymphoma cells. The cells are dual-stained with Annexin V-FITC and Propidium Iodide (PI). Based on the dynamic scatter distribution profiles illustrated in the quadrant plot

below, identify the specific cell population corresponding to quadrant **Q3 (Bottom-Right)**:



(A) Viable, non-apoptotic cells

(B) Necrotic or late apoptotic cells

(C) Early apoptotic cells with intact membrane asymmetry

(D) Mechanical artifacts / cellular debris only

Q6. A 4-year-old child presents with microcytic hypochromic anemia, profound hepatosplenomegaly, and skeletal changes showing a "crew-cut" appearance on cranial radiography. High-Performance Liquid Chromatography (HPLC) confirms complete absence of HbA, markedly elevated HbF, and variable HbA2 levels. Molecular analysis isolates a point mutation within the first intron of the beta-globin gene that alters a consensus splice donor site. Which molecular pathology term precisely describes the absolute mechanistic basis of this phenotype?

(A) β^0 Thalassemia allele transcription arrest

(B) Aberrant pre-mRNA splicing with unstable transcript decay

(C) Non-conservative missense substitution at codon 6

(D) Quantitative alpha-globin locus deletion events

Q7. A 62-year-old female presents with fatigue and easy bruising. Bone marrow biopsy confirms Acute Myeloid Leukemia (AML). Cytogenetic analysis reveals a specific $t(8;21)(q22;q22)$ translocation. Molecular screening for

co-existing mutations is performed to guide prognosis. Which of the following concurrent molecular alterations is associated with a significantly worsened prognosis in an otherwise cytogenetically favorable $t(8;21)$ AML?

(A) NPM1 mutation

(B) KIT tyrosine kinase mutation

(C) CEBPA double mutation

(D) RUNX1-RUNX1T1 fusion silencing

Q8. A 24-year-old pregnant female develops acute deep vein thrombosis. Laboratory investigation reveals resistance to activated protein C (APC). Genetic sequencing isolates a single point mutation ($G \rightarrow A$ substitution at nucleotide position 1691) in the Gene encoding Factor V. What structural/functional alteration in the mutated Factor V protein accounts for this hypercoagulable state?

(A) Loss of the primary Arg506 proteolytic cleavage site

(B) Hyper-responsiveness to Tissue Factor Pathway Inhibitor

(C) Constitutional inactivation of the B-domain cleavage loop

(D) Defective assembly of the functional intrinsic tenase complex

Q9. A 65-year-old male evaluated for normocytic anemia displays a markedly elevated serum ferritin, reduced total iron-binding capacity (TIBC), and decreased serum iron concentration. Bone marrow iron staining shows abundant storage iron in macrophages but minimal iron within erythroid precursors. Sustained hepatic production of which of the following acute-phase reactants is directly driving this internal iron sequestration mechanism?

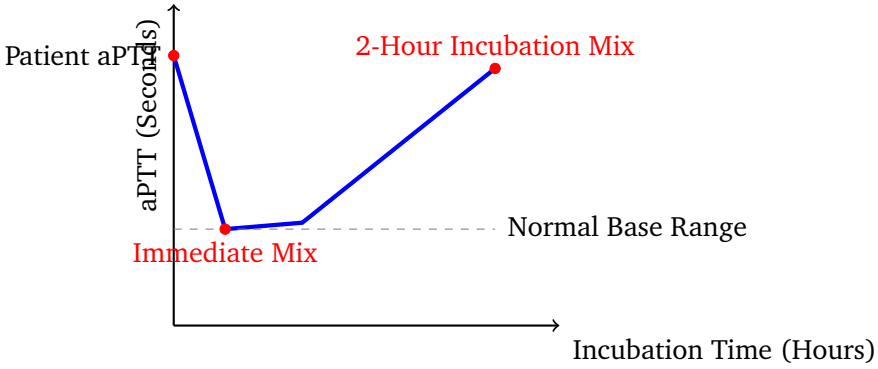
(A) Ferroportin-1 down-regulator (Hepcidin)

(B) Soluble Transferrin Receptor (sTfR)

(C) Erythroferrone (ERFE)

(D) Transferrin saturation factor

Q10. A 34-year-old male presenting with an isolated prolonged Activated Partial Thromboplastin Time (aPTT) undergoes plasma mixing studies. An immediate 1:1 mix with normal pooled plasma corrects the aPTT to baseline. However, upon incubation of the 1:1 mix at 37°C for two hours, the aPTT prolongs significantly again, as shown in the kinetic tracking graph below. This specific pattern is characteristic of which underlying pathology?



(A) Factor VIII deficiency (Hemophilia A)

(B) Factor XII deficiency (Hageman trait)

(C) Time- and temperature-dependent Factor VIII specific inhibitor

(D) Lupus Anticoagulant (antiphospholipid antibodies)

Q11. A genomic profile of a poorly differentiated colorectal adenocarcinoma reveals a homozygous mutation that alters the loop-sheet-helix motif of the p53 core domain. As a consequence, the transcription of p53 downstream target genes is completely halted. Which specific cell cycle regulator fails to be induced, directly causing a loss of the G1/S phase checkpoint inhibition?

(A) p21 (WAF1/CIP1)

(B) Cyclin D1

(C) p16 (INK4a)

(D) MDM2 oncogene

Q12. An infant presenting with profound hypotonia, feeding difficulties, and distinctive facial features is diagnosed with Prader-Willi Syndrome. Genetic

mapping demonstrates a microdeletion on the paternal chromosome 15q11-q13 region. Since the maternal copy of this specific locus is functionally inactive due to physiological epigenetic silencing, what molecular term defines this tissue-specific expression mechanism?

(A) Homologous recombination

(B) Genomic Imprinting via differential DNA methylation

(C) Histone acetylation-mediated transcript hyperactivation

(D) Random X-chromosome lyonization events

Q13. A 23-year-old female experiences acute systemic anaphylaxis within minutes of receiving an intravenous beta-lactam antibiotic. The systemic shock state is initiated when multivalent antigen cross-links specific surface receptors on mast cells and basophils. What is the precise molecular designation of these high-affinity receptors that engage the Fc region of IgE molecules?

(A) FcγRIIIa (CD16)

(B) FcϵRI

(C) FcαRI (CD89)

(D) C5a anaphylatoxin receptor

Q14. An experimental therapeutic agent is designed to halt the progression of advanced fibroatheromatous plaques in rabbits. The drug selectively inhibits the matrix metalloproteinases (MMPs) synthesized and secreted by activated macrophages within the necrotic core. Successfully blocking these specific interstitial collagenases directly prevents which pathological complication of atherosclerosis?

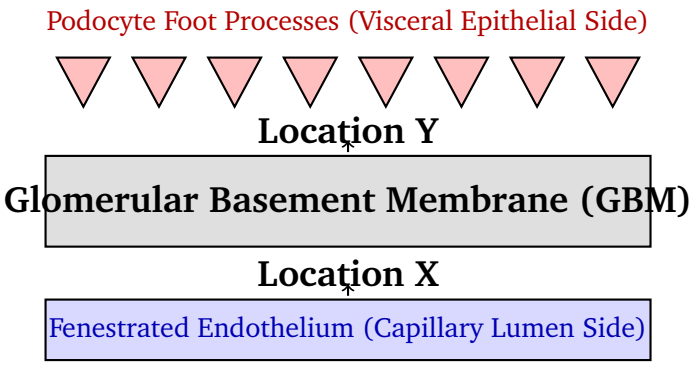
(A) Fibrous cap thinning and acute plaque rupture

(B) Endothelial cell expression of VCAM-1 molecules

(C) Scavenger receptor-mediated LDL internalization

(D) Foam cell emigration back into the blood vessel lumen

Q15. A 9-year-old boy presents with hematuria, periorbital edema, and hypertension two weeks after a streptococcal pharyngitis infection. Kidney biopsy and electron microscopy reveal characteristic electron-dense immune complex deposits. Based on the glomerular filtration barrier shown below, which option correctly identifies the location of the classic *subepithelial humps* seen in post-streptococcal glomerulonephritis (PSGN)?



(A) Location X, representing subendothelial linear deposition

(B) Location Y, representing subepithelial discrete dome-shaped humps

(C) Within the GBM core, representing intramembranous ribbon-like deposits

(D) Randomly distributed within the fenestrated endothelial cytoplasm

Q16. A 32-year-old female presents with severe generalized anasarca and a 24-hour urinary protein excretion of 8.2 grams. Renal biopsy demonstrates diffuse effacement of podocyte foot processes on electron microscopy, but no immune deposits on immunofluorescence. Genetic mapping of a familial variant of this condition reveals a mutated structural component of the slit diaphragm complex. Which target transmembrane protein is critically altered in this patient's slit diaphragm layout?

(A) Podocin (NPHS2)

(B) Nephrin (NPHS1)

(C) α-actinin-4

(D) Laminin $\beta 2$ chain

Q17. A 55-year-old male with a history of heavy smoking presents with a hard, fixed mass in the right upper pulmonary lobe. Biopsy reveals sheets of malignant epithelial cells demonstrating intracellular keratinization and prominent intercellular bridges. Molecular profiling isolates a strong upstream hyperactivation pattern. Which chromosomal alteration or driver oncogene amplification is most frequently associated with this specific histological subtype of lung carcinoma?

(A) EML4-ALK tyrosine kinase inversion fusions

(B) EGFR exon 19 deletions or L858R point mutations

(C) FGFR1 gene amplification or TP53 inactivation

(D) RET proto-oncogene structural translocations

Q18. A 44-year-old male undergoes a surveillance colonoscopy, during which an 8mm sessile polyp is excised from the sigmoid colon. Histological analysis confirms a tubular adenoma with low-grade dysplasia. Molecular analysis reveals an early somatic loss of heterozygosity in a crucial tumor suppressor gene that normally acts as a negative regulator of the Wnt/β-catenin signaling pathway. Which gene is affected at this initial stage of the adenoma-carcinoma sequence?

(A) KRAS proto-oncogene

(B) TP53 gene

(C) SMAD4 gene

(D) APC (Adenomatous Polyposis Coli) gene

Q19. A 58-year-old male with long-standing decompensated cirrhosis due to chronic Hepatitis C virus infection presents with worsening ascites and encephalopathy. Pathological analysis of a liver explant demonstrates regenerative nodules encircled by dense fibrous bands. Which cell type, residing within the Space of Disse, underwent transdifferentiation from a vitamin A-storing quiescent phenotype into a contractile myofibroblast to drive this extensive fibrogenesis?

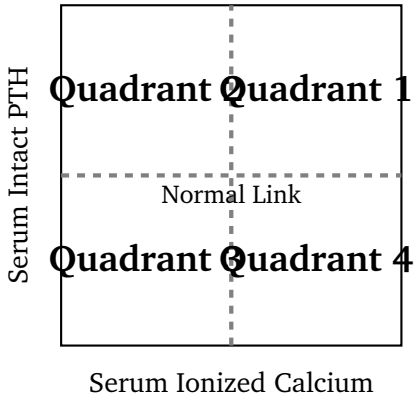
(A) Kupffer cells

(B) Hepatic Stellate Cells (Ito cells)

(C) Sinusoidal Endothelial Cells

(D) Cholangiocytes

Q20. An endocrinology unit creates an analytical mapping chart to categorize metabolic calcium anomalies based on simultaneous evaluations of Serum Intact Parathyroid Hormone (PTH) and Serum Ionized Calcium levels. A 48-year-old female presenting with recurrent nephrolithiasis, osteopenia, and a mild cognitive dampening shows biochemical values falling squarely within **Quadrant 1** of the diagnostic map below. What is the definitive pathological diagnosis?



(A) Primary Hypoparathyroidism

(B) Primary Hyperparathyroidism (e.g., Parathyroid Adenoma)

(C) Malignancy-associated Hypercalcemia (PTH independent)

(D) Secondary Hyperparathyroidism due to Vitamin D deficiency

Q21. A 26-year-old male presents with severe peptic ulceration refractory to proton pump inhibitors, paired with recurrent episodes of nephrolithiasis. Further workup confirms a pancreatic gastrinoma alongside primary hyperparathyroidism due to multiglandular parathyroid hyperplasia. Genetic screening reveals a germline mutation in a gene encoding a nuclear scaffold protein involved in transcriptional regulation and cell cycle suppression. Which specific tumor suppressor gene is mutated?

(A) RET proto-oncogene

(B) MEN1 (Menin)

(C) CASR (Calcium-Sensing Receptor)

(D) VHL (von Hippel-Lindau)

Q22. A 72-year-old female presents with progressive cognitive decline characterized by profound short-term memory deficits followed by apraxia and aphasia. Neuropathological autopsy examination reveals diffuse cortical atrophy with widening of sulci. Microscopic examination displays flame-shaped intracellular inclusions within cortical neurons. These specific neurofibrillary tangles are composed of hyperphosphorylated forms of which structural protein?

(A) Alpha-synuclein

(B) Amyloid-beta peptide ($A\beta_{42}$)

(C) Tau protein

(D) Prion Protein (PrP^{Sc})

Q23. A 52-year-old female undergoes a modified radical mastectomy for a 3.5 cm breast mass. Histopathological examination demonstrates an invasive ductal carcinoma. Immunohistochemical (IHC) assay shows complete absence of Estrogen Receptor (ER) and Progesterone Receptor (PR) staining, alongside a 1+ score for HER2/neu expression. Fluorescent In Situ Hybridization (FISH) confirms a HER2/neu gene-to-chromosome 17 centromere ratio of 1.4. This molecular profile is best categorized into which intrinsic molecular subtype of breast cancer?

(A) Luminal A subtype

(B) HER2-enriched subtype

(C) Basal-like / Triple-Negative subtype

(D) Luminal B subtype

Q24. A 29-year-old male presents with a painless, firm enlargement of the right testis. Serum tumor markers demonstrate markedly elevated levels of Alpha-Fetoprotein (AFP) and mildly elevated Beta-hCG. Histopathological evaluation reveals a primitive-appearing tumor arranged in sheets, cords, and

glandular structures, interspersed with distinct schiller-Duval bodies. What is the correct histopathological diagnosis?

(A) Pure Seminoma

(B) Choriocarcinoma

(C) Yolk Sac Tumor (Endodermal Sinus Tumor)

(D) Leydig Cell Tumor

Q25. A 62-year-old male presents with an elevated hemoglobin level of 19.8 g/dL, thrombocytosis, and leukocytosis. His serum erythropoietin (EPO) level is subnormal. Bone marrow biopsy confirms panmyelosis. Molecular analysis demonstrates a somatic point mutation within pseudo-kinase domain (JH2) of the Janus Kinase 2 gene (*JAK*2 V617F). What precise functional alteration occurs in the JAK2 signaling cascade due to this specific mutation?

(A) Loss of autoinhibitory control leading to constitutive tyrosine kinase activation

(B) Complete disruption of downstream STAT transcription factor binding

(C) Enhanced degradation of JAK2 via the ubiquitin-proteasome pathway

(D) Constitutional inactivation of the erythropoietin receptor intracellular loop

Detailed Solutions

Q1.

Solution

Concept: Ischemia-reperfusion injury can trigger a non-apoptotic, iron-dependent form of regulated cell death known as ferroptosis. This pathway is biochemically defined by the accumulation of lethal lipid peroxides, independent of caspases or necroptotic executioners like MLKL.

Solution:

Let's analyze the biochemical defenses against lipid peroxidation:

(a) Glutathione Peroxidase 4 (GPX4) is the primary protective enzyme that neutralizes lipid hydroperoxides within cellular membranes, reducing them to non-toxic lipid alcohols by utilizing reduced glutathione (GSH).

(b) Reperfusion introduces a surge of oxygen and free radicals that react with polyunsaturated fatty acids (PUFAs). If GPX4 activity is compromised or overwhelmed, iron acts as a catalyst via Fenton chemistry to drive uncontrolled lipid radical generation.

(c) Therefore, the **Inhibition of Glutathione Peroxidase 4 (GPX4)** directly orchestrates this lipid peroxidation cascade, causing membrane structural breakdown and cell death.

Final Answer: Inhibition of Glutathione Peroxidase 4 (GPX4)

Answer: (A)

Go Back to Question 1

Q2.

Solution

Concept: Amyloid formation in proteinopathies follows a nucleation-dependent polymerization model. This process describes why misfolded proteins remain soluble for extended periods before rapidly forming insoluble cross-beta sheet aggregates.

Solution:

Let's break down the kinetics of amyloid fibril assembly:

(a) The early phase of amyloid formation requires monomeric, unstable protein intermediates to interact and form a stable, ordered oligomeric nucleus.

(b) This process is called **Critical concentration-dependent homogenous nucleation**. It acts as a major thermodynamic barrier, creating a protracted "lag phase" because the assembly of these initial oligomeric seeds is highly unfavorable.

(c) Once the critical local concentration is reached and a stable nucleus forms, the reaction shifts into an exponential elongation phase. During this stage, soluble monomers add rapidly to the pre-formed ends of the fibrils.

Final Answer: Critical concentration-dependent homogenous nucleation

Answer: (B)

Go Back to Question 2

Q3.

Solution

Concept: The intrinsic (mitochondrial) pathway of apoptosis relies on BH3-only proteins to sense cellular stress and trigger downstream executioner steps.

Solution:

Let's look at how the lack of a BH3-only sensor alters cell death signaling:

(a) BIM is a prominent pro-apoptotic BH3-only protein that senses severe cellular stresses, including endoplasmic reticulum (ER) stress and intracellular calcium overload.

(b) Under stress conditions, BIM normally activates BAX and BAK, while neutralizing anti-apoptotic proteins like BCL-2. This permits outer mitochondrial membrane permeabilization and the release of cytochrome c.

(c) Lymphocytes lacking functional BIM cannot transmit these intracellular stress signals to the mitochondria. Consequently, they display marked **Resistance to stress-induced intrinsic pathway apoptosis**, failing to activate the downstream caspase cascade.

Final Answer: Resistance to stress-induced intrinsic pathway apoptosis

Answer: (C)

Go Back to Question 3

Q4.

Solution

Concept: Neutrophil Extracellular Traps (NETs) are networks of extracellular chromatin and antimicrobial proteins deployed by neutrophils to capture and eliminate large or invasive pathogens, such as fungal hyphae.

Solution:

Let's analyze the enzymatic requirements for NETosis (NET formation):

(a) This patient's neutrophils possess intact phagocytosis and oxidative burst capacities (ruling out classic NADPH oxidase or chronic granulomatous disease defects), yet fail to form NETs.

(b) NET formation requires chromatin decondensation, allowing nuclear DNA to expand and unfold into the cytoplasm before being expelled from the cell.

(c) The critical enzyme driving this chromatin remodeling is **Peptidylarginine Deiminase 4 (PAD4)**. PAD4 catalyzes the conversion of arginine residues on histones to citrulline (histone citrullination). This process strips histones of their positive charge, neutralizing their affinity for DNA and causing the chromatin architecture to unfold.

Final Answer: Peptidylarginine Deiminase 4 (PAD4)

Answer: (C)

Go Back to Question 4

Q5.

Solution

Concept: Annexin V binds with high affinity to phosphatidylserine (PS), a phospholipid normally restricted to the inner leaflet of the plasma membrane. Propidium Iodide (PI) is an impermeable dye that only stains DNA when the plasma membrane loses its physical structural integrity.

Solution:

Let's evaluate the cell population distribution across the flow cytometry quadrant map:

(a) Viable cells (Q4, bottom-left) exclude PI and do not bind Annexin V, because their membranes remain intact and asymmetric.

(b) During the early stages of apoptosis, cells flip phosphatidylserine to the outer leaflet, making them Annexin V-positive. However, they keep their plasma membrane structurally intact, allowing them to exclude PI.

(c) This makes the population in **Quadrant Q3 (Bottom-Right)** Annexin V-positive and PI-negative, which corresponds specifically to **Early apoptotic cells with intact membrane asymmetry**. Late apoptotic or necrotic cells (Q2, top-right) would stain positive for both markers.

Final Answer: Early apoptotic cells with intact membrane asymmetry

Answer: (C)

Go Back to Question 5

Q6.

Solution

Concept: β-Thalassemia major is characterized by a severe reduction or total absence of β-globin chain synthesis, leading to uncoupled, excess α-globin chains that precipitate and damage erythroid precursors.

Solution:

Let's analyze the molecular mechanism behind this splicing mutation:

(a) The point mutation alters a consensus splice donor site within the first intron of the β-globin gene, leading to **Aberrant pre-mRNA splicing with unstable transcript decay**.

(b) This splicing defect prevents the generation of functional β-globin mRNA. The resulting abnormal transcripts are targeted for degradation via nonsense-mediated decay pathways, leading to a complete absence of adult hemoglobin (HbA, $\alpha_2\beta_2$).

(c) This absolute lack of functional transcripts creates a β^0 thalassemia phenotype. To compensate, the body shifts toward persistent fetal hemoglobin synthesis (HbF, $\alpha_2\gamma_2$) and drives massive extramedullary hematopoiesis, which causes the classic bone remodeling ("crew-cut" skull) and hepatosplenomegaly.

Final Answer: Aberrant pre-mRNA splicing with unstable transcript decay

Answer: (B)

Go Back to Question 6

Q7.

Solution

Concept: Acute Myeloid Leukemia (AML) with a $t(8;21)(q22;q22)$ translocation forms a *RUNX1-RUNX1T1* (*AML1-ETO*) fusion gene. While generally considered a favorable cytogenetic subgroup, secondary molecular alterations can alter its clinical course.

Solution:

Let's analyze how co-existing mutations change the prognosis of $t(8;21)$ AML:

(a) The $t(8;21)$ translocation disrupts the core binding factor complex, a crucial transcriptional regulator of normal myeloid differentiation.

(b) When a somatic, activating **KIT tyrosine kinase mutation** occurs alongside this translocation, it introduces continuous, ligand-independent proliferation and survival signals.

(c) This concurrent *KIT* mutation overrides the favorable properties of the $t(8;21)$ subgroup, increasing the risk of relapse and significantly worsening overall survival.

Final Answer: KIT tyrosine kinase mutation

Answer: (B)

Go Back to Question 7

Q8.

Solution

Concept: Factor V Leiden is the most common inherited cause of hypercoagulability (thrombophilia) in Caucasian populations, significantly increasing the risk of venous thromboembolism.

Solution:

Let's look at how the point mutation affects the biochemistry of coagulation inactivation:

(a) Normal Activated Protein C (APC) limits clot formation by cleaving and inactivating activated Factor V (Va) and activated Factor VIII (VIIIa).

(b) The Factor V Leiden mutation ($1691G \rightarrow A$) alters the protein structure by substituting a glutamine for an arginine at position 506.

(c) This alteration results in the **Loss of the primary Arg506 proteolytic cleavage site**. Because APC cannot cleave this mutated site efficiently, Factor Va resists inactivation and persists in the circulation. This drives uninhibited thrombin generation, creating a hypercoagulable state.

Final Answer: Loss of the primary Arg506 proteolytic cleavage site

Answer: (A)

Go Back to Question 8

Q9.

Solution

Concept: Anemia of Chronic Disease (Anemia of Inflammation) is driven by inflammatory cytokines that disrupt systemic iron homeostasis, trapping iron inside storage compartments and withholding it from developing erythroid cells.

Solution:

Let's evaluate the role of the primary regulatory acute-phase reactant:

(a) In settings of chronic inflammation, cytokines (specifically IL-6) stimulate the liver to continuously synthesize and secrete **Hepcidin**, a key acute-phase reactant.

(b) Hepcidin acts as a direct **Ferroportin-1 down-regulator**. It binds to ferroportin channels on the surface of macrophages and enterocytes, triggering their internalization and lysosomal degradation.

(c) With ferroportin destroyed, macrophages cannot export recycled iron into the plasma. This causes iron to become trapped inside macrophages (elevating serum ferritin), while serum iron drops, starving erythroid precursors of the iron needed for hemoglobin synthesis.

Final Answer: Ferroportin-1 down-regulator (Hepcidin)

Answer: (A)

Go Back to Question 9

Q10.

Solution

Concept: Plasma mixing studies help differentiate between a simple coagulation factor deficiency and the presence of a circulating pathological coagulation inhibitor or antibody.

Solution:

Let's interpret the kinetic tracking graph of this mixing study:

(a) The patient's baseline aPTT is prolonged. When mixed 1:1 with normal pooled plasma, the aPTT corrects immediately back into the normal range. This indicates that the normal plasma provided enough functional clotting factors to overcome any simple deficiency.

(b) However, incubating the mixture at 37°C for two hours causes the aPTT to prolong significantly again. This recurrence demonstrates the presence of a **Time- and temperature-dependent Factor VIII specific inhibitor** (neutralizing autoantibodies).

(c) Unlike lupus anticoagulants—which typically show a prolonged aPTT immediately upon mixing—Factor VIII inhibitors act progressively. They require time and physiological warmth to bind, neutralize Factor VIII, and prolong the clotting time once more.

Final Answer: Time- and temperature-dependent Factor VIII specific inhibitor

Answer: (C)

Go Back to Question 10

Q11.

Solution

Concept: The p53 tumor suppressor protein acts as the "guardian of the genome." When DNA damage occurs, it functions as a transcription factor to halt cell cycle progression or initiate apoptosis.

Solution:

Let's look at the downstream target that executes p53-mediated G1/S arrest:

(a) Homozygous mutations in the p53 DNA-binding core domain prevent p53 from binding to promoters and initiating the transcription of downstream target genes.

(b) Under normal conditions, p53 halts the cell cycle at the G1/S transition by directly upregulating **p21 (WAF1/CIP1)**.

(c) **p21** functions as a potent cyclin-dependent kinase inhibitor (CDKi). It binds to and inhibits Cyclin E-CDK2 and Cyclin D-CDK4/6 complexes, keeping the retinoblastoma (Rb) protein hypophosphorylated. This prevents the release of E2F transcription factors, stopping entry into the S phase. A loss of p21 induction removes this checkpoint, allowing damaged cells to replicate uncontrollably.

Final Answer: p21 (WAF1/CIP1)

Answer: (A)

Go Back to Question 11

Q12.

Solution

Concept: Genomic imprinting is an epigenetic process where certain genes are expressed in a parent-of-origin-specific manner. This expression pattern is regulated by differential DNA methylation during gametogenesis.

Solution:

Let's examine how genomic imprinting underlies Prader-Willi Syndrome:

(a) In the 15q11-q13 chromosomal region, the maternal copy of specific genes is normally silenced via physiological DNA methylation, meaning only the paternal alleles are transcriptionally active.

(b) If a microdeletion occurs on the paternal chromosome 15q11-q13, the child loses their only active copies of these genes, because the maternal alleles remain silenced.

(c) This tissue-specific gene silencing based on parental origin is the definition of **Genomic Imprinting via differential DNA methylation**.

Final Answer: Genomic Imprinting via differential DNA methylation

Answer: (B)

Go Back to Question 12

Q13.

Solution

Concept: Systemic anaphylaxis is a severe, life-threatening Type I hypersensitivity reaction. It is triggered when IgE antibodies bound to high-affinity receptors on mast cells and basophils become cross-linked by a multivalent antigen.

Solution:

Let's identify the specific receptor involved in this IgE-mediated response:

(a) During initial exposure to an allergen (like a beta-lactam antibiotic), B-cells switch to IgE production. This IgE binds to high-affinity receptors on the surface of mast cells and basophils.

(b) The high-affinity receptor specific for the heavy chain constant region of IgE is designated **FcϵRI**.

(c) When the patient is re-exposed to the drug, the multivalent antigen cross-links these pre-bound **FcϵRI** receptor complexes. This triggers an intracellular calcium influx, causing rapid degranulation and the systemic release of mediators like histamine and leukotrienes, which drive anaphylactic shock.

Final Answer: FcϵRI

Answer: (B)

Go Back to Question 13

Q14.

Solution

Concept: The mechanical stability of an atheromatous plaque determines its resistance to rupture and subsequent thrombosis. This structural integrity depends heavily on the thickness and composition of its fibrous cap.

Solution:

Let's look at how matrix metalloproteinases impact plaque architecture:

(a) The fibrous cap of an atheromatous plaque is made of structural extracellular matrix components, primarily interstitial collagen synthesized by vascular smooth muscle cells.

(b) Activated macrophages within the necrotic core secrete matrix metalloproteinases (MMPs), such as collagenases and gelatinases, which degrade this structural collagen framework.

(c) Successfully blocking these MMPs stops this matrix degradation, preventing **Fibrous cap thinning and acute plaque rupture**. This keeps the plaque stable and prevents the core from exposing tissue factor to the bloodstream, reducing the risk of acute thrombotic occlusion.

Final Answer: Fibrous cap thinning and acute plaque rupture

Answer: (A)

Go Back to Question 14

Q15.

Solution

Concept: Post-Streptococcal Glomerulonephritis (PSGN) is an immune complex-mediated disease (Type III hypersensitivity) that presents clinically with a nephritic syndrome following a streptococcal infection.

Solution:

Let's analyze the spatial layout shown in the glomerular diagram:

(a) In PSGN, circulating streptococcal antigens and antibodies form immune complexes that cross the glomerular basement membrane (GBM).

(b) These complexes accumulate between the outer surface of the GBM and the overlying podocyte foot processes, a region labeled as **Location Y**.

(c) On electron microscopy, these deposits appear as discrete, dome-like **subepithelial humps**. Location X, by contrast, sits on the inside of the GBM (subendothelial side), which is characteristic of conditions like Membranoproliferative Glomerulonephritis.

Final Answer: Location Y, representing subepithelial discrete dome-like humps

Answer: (B)

Go Back to Question 15

Q16.

Solution

Concept: The glomerular filtration barrier prevents plasma proteins from leaking into the urine. The slit diaphragm complex, which bridges adjacent podocyte foot processes, acts as the final size and charge barrier.

Solution:

Let's isolate the primary structural transmembrane protein of the slit diaphragm:

(a) This patient presents with nephrotic-range proteinuria and a biopsy showing diffuse foot process effacement without immune complexes, a pattern classic for Minimal Change Disease or Focal Segmental Glomerulosclerosis (FSGS).

(b) In familial variants of these conditions, mutations often affect **Nephrin (NPHS1)**, the primary transmembrane protein that forms the structural meshwork of the slit diaphragm.

(c) **Nephrin** molecules extend from opposite podocyte foot processes and interact homophilically in the center of the slit space. Mutations in the *NPHS1* gene disrupt this structural bridge, causing podocyte destabilization, foot process effacement, and massive protein leakage.

Final Answer: Nephrin (NPHS1)

Answer: (B)

Go Back to Question 16

Q17.

Solution

Concept: Lung carcinomas are divided into distinct histological subtypes, each showing a strong correlation with specific smoking histories and driving oncogenic pathways.

Solution:

Let's align the biopsy features with the corresponding molecular drivers of lung cancer:

(a) The biopsy reveals sheets of malignant epithelial cells with intracellular keratinization (squamous pearls) and intercellular bridges (desmosomes). This profile is diagnostic for **Squamous Cell Carcinoma** of the lung.

(b) Squamous cell carcinoma occurs almost exclusively in heavy smokers, arises centrally, and is molecularly characterized by **FGFR1 gene amplification** or *TP53* inactivation.

(c) *EGFR* mutations and *EML4-ALK* fusions, by contrast, are typically associated with lung adenocarcinomas, which develop more frequently in non-smokers or light smokers and present as peripheral masses.

Final Answer: FGFR1 gene amplification or TP53 inactivation

Answer: (C)

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Q18.

Solution

Concept: The adenoma-carcinoma sequence describes the stepwise accumulation of genetic mutations that drive the transformation of normal colonic mucosa into invasive colorectal adenocarcinoma.

Solution:

Let's trace the chronological order of mutations in this oncogenic cascade:

(a) The very first event in the classic adenoma-carcinoma pathway involves a somatic or germline loss-of-function mutation in the **APC (Adenomatous Polyposis Coli)** tumor suppressor gene.

(b) The APC protein forms part of a destruction complex that degrades free cytoplasmic β-catenin. When APC is inactivated, β-catenin escapes degradation, accumulates, and translocates to the nucleus. There, it activates Wnt-target genes that drive epithelial hyperproliferation and adenoma formation.

(c) Subsequent mutations in other genes, such as *KRAS* (promoting adenoma growth), *SMAD4* (mediating clonal expansion), and *TP53* (driving malignant transformation), occur later in the sequence.

Final Answer: APC (Adenomatous Polyposis Coli) gene

Answer: (D)

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Q19.

Solution

Concept: Hepatic fibrosis and cirrhosis develop when chronic parenchymal injury triggers sustained cellular signaling cascades that alter the extracellular matrix.

Solution:

Let's track the cellular transdifferentiation that occurs during liver fibrogenesis:

(a) Chronic injury from Hepatitis C virus promotes inflammation, releasing cytokines like TGF-β from damaged hepatocytes and Kupffer cells.

(b) These cytokines target the **Hepatic Stellate Cells (Ito cells)**, which reside within the subendothelial Space of Disse and normally function to store Vitamin A.

(c) In response to chronic stress, stellate cells lose their vitamin A lipid droplets and transdifferentiate into contractile, proliferative **myofibroblasts**. These activated myofibroblasts secrete massive amounts of collagen (mainly Types I and III), restructuring the hepatic architecture into regenerative nodules encircled by fibrous bands.

Final Answer: Hepatic Stellate Cells (Ito cells)

Answer: (B)

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Q20.

Solution

Concept: Evaluating serum intact parathyroid hormone (PTH) and ionized calcium levels simultaneously helps differentiate between various disorders of calcium metabolism.

Solution:

Let's interpret the diagnostic quadrant map layout:

(a) The patient has symptoms of hypercalcemia (nephrolithiasis, osteopenia, cognitive dampening). Her laboratory values place her inside **Quadrant 1**, which indicates a high serum ionized calcium accompanied by a high (or inappropriately normal) serum intact PTH level.

(b) Under normal physiological conditions, hypercalcemia activates calcium-sensing receptors on parathyroid cells to suppress PTH secretion.

(c) A high PTH level in the setting of hypercalcemia indicates autonomous, uninhibited PTH secretion that resists negative feedback. This pattern is diagnostic of **Primary Hyperparathyroidism**, most commonly caused by a solitary parathyroid adenoma. Malignancy-associated hypercalcemia would fall into Quadrant 4 (high calcium, suppressed PTH).

Final Answer: Primary Hyperparathyroidism (e.g., Parathyroid Adenoma)

Answer: (B)

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Q21.

Solution

Concept: Multiple Endocrine Neoplasia Type 1 (MEN1, Wermer Syndrome) is an autosomal dominant disorder characterized by combinations of tumors involving the "3 Ps": Parathyroid glands, Pancreatic islets, and the Pituitary gland.

Solution:

Let's identify the specific tumor suppressor gene associated with this presentation:

(a) This patient presents with primary hyperparathyroidism due to parathyroid hyperplasia and a pancreatic gastrinoma (Zollinger-Ellison syndrome), a classic clinical picture for MEN1.

(b) The condition is driven by an inactivating germline mutation in the **MEN1** tumor suppressor gene located on chromosome 11q13.

(c) The *MEN1* gene encodes **menin**, a nuclear scaffold protein. Menin interacts with transcription factors and chromatin-modifying complexes to regulate gene expression and suppress uninhibited cell cycle progression. Mutations in the *RET* proto-oncogene, by contrast, are linked to MEN2.

Final Answer: MEN1 (Menin)

Answer: (B)

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Q22.

Solution

Concept: Alzheimer's Disease is characterized by two distinct neuropathological hallmarks: extracellular amyloid-beta plaques and intracellular neurofibrillary tangles.

Solution:

Let's isolate the structural protein that forms these intracellular inclusions:

(a) The patient's clinical presentation of progressive cognitive decline and short-term memory loss matches the profile of Alzheimer's Disease. Autopsy findings reveal cortical atrophy and flame-shaped intracellular neurofibrillary tangles (NFTs).

(b) Neurofibrillary tangles are composed of hyperphosphorylated forms of the **Tau protein**.

(c) Under normal physiological conditions, Tau binds to and stabilizes microtubules within neuronal axons. When Tau becomes hyperphosphorylated, it loses its affinity for microtubules and aggregates into insoluble helical filaments within the neuronal soma. This disrupts axonal transport and contributes to neuronal death.

Final Answer: Tau protein

Answer: (C)

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Q23.

Solution

Concept: Breast cancers are classified into intrinsic molecular subtypes based on the presence or absence of estrogen receptors (ER), progesterone receptors (PR), and Human Epidermal Growth Factor Receptor 2 (HER2) expression.

Solution:

Let's categorize this breast cancer profile using the immunohistochemical and FISH criteria:

(a) The tumor is negative for both hormone receptors (ER- and PR-).

(b) The HER2/neu immunohistochemistry score is 1+ (negative/equivocal), and subsequent FISH analysis shows a HER2/CEP17 ratio of 1.4 (non-amplified, as a ratio ≥ 2.0 defines amplification).

(c) Because the tumor lacks ER, PR, and HER2 gene amplification, it is clinically classified as a triple-negative breast cancer. This corresponds to the **Basal-like / Triple-Negative subtype** of breast cancer, which typically expresses markers characteristic of basal epithelial cells.

Final Answer: Basal-like / Triple-Negative subtype

Answer: (C)

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Q24.

Solution

Concept: Testicular germ cell tumors are divided into seminomatous and non-seminomatous lineages. Non-seminomatous tumors frequently secrete specific serum markers that reflect their embryonic differentiation pathway.

Solution:

Let's evaluate the histopathological and serological features of this testicular mass:

(a) The patient has a non-seminomatous germ cell tumor characterized by markedly elevated serum Alpha-Fetoprotein (AFP) levels.

(b) On histological evaluation, the presence of **Schiller-Duval bodies**—structures that resemble primitive glomeruli with a central blood vessel surrounded by tumor cells inside a lined space—is pathognomonic.

(c) Both elevated AFP levels and Schiller-Duval bodies are classic hallmarks of a **Yolk Sac Tumor (Endodermal Sinus Tumor)**. Pure seminomas do not secrete AFP and lack these specialized primitive architectures.

Final Answer: Yolk Sac Tumor (Endodermal Sinus Tumor)

Answer: (C)

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Q25.

Solution

Concept: The *JAK*2 V617F mutation is a driving somatic mutation found in myeloproliferative neoplasms, particularly Polycythemia Vera, Essential Thrombocythemia, and Primary Myelofibrosis.

Solution:

Let's look at how the point mutation affects the biochemistry of the JAK2 kinase:

(a) The *JAK*2 V617F mutation occurs within the pseudokinase domain (JH2) of the Janus Kinase 2 protein, substituting a valine for a phenylalanine at position 617.

(b) Under physiological conditions, the JH2 pseudokinase domain acts as a negative regulator that inhibits the activity of the adjacent catalytic kinase domain (JH1).

(c) The V617F substitution causes a **Loss of autoinhibitory control leading to constitutive tyrosine kinase activation**. As a result, the JAK2 kinase remains continuously active, sending downstream proliferative signals through the STAT pathway independent of erythropoietin binding. This drives autonomous panmyelosis and suppresses endogenous EPO production.

Final Answer: Loss of autoinhibitory control leading to constitutive tyrosine kinase activation

Answer: (A)

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Answer Key

Q	Ans	Q	Ans	Q	Ans	Q	Ans	Q	Ans
1	A	2	B	3	C	4	C	5	C
6	B	7	B	8	A	9	A	10	C
11	A	12	B	13	B	14	A	15	B
16	B	17	C	18	D	19	B	20	B
21	B	22	C	23	C	24	C	25	A