

1. A sample of double-stranded DNA contains 30% G. What is its content of A?
 - A. 20%
 - B. 30%
 - C. 50%
 - D. 80%
 - E. insufficient information

2. DNA replication requires all of the following EXCEPT
 - A. 5' → 3' exonuclease activity
 - B. an RNA primer
 - C. energy in the form of ATP
 - D. a free 5' OH
 - E. DNA ligase

3. Some of the enzymes utilized in DNA replication are (1) DNA polymerase III, (2) unwinding proteins (helicases), (3) DNA polymerase I, (4) a DNA-dependent RNA polymerase, and (5) DNA ligase. What is the correct sequence of their use during DNA replication?
 - A. 2,4,3,1,5
 - B. 2,3,4,1,5
 - C. 2,4,1,3,5
 - D. 4,2,1,3,5
 - E. 4,2,1,5,3

4. Repair of cytosine deamination in DNA involves
 - A. 5' -> 3' single-strand specific exonuclease activity
 - B. 3' -> 5' single-strand specific exonuclease activity
 - C. uracil-DNA glycosidase
 - D. DNA polymerase III
 - E. uracil aminase

5. Intron sequences are
 - A. found only in DNA, not RNA
 - B. spliced out of DNA
 - C. translated during protein synthesis
 - D. found in the nucleus but not the cytoplasm
 - E. sites for missense mutations

6. Most mRNA molecules of eucaryotes undergo which of the following?
 - A. The formation of a large precursor RNA is followed by exon rearrangement to yield the mature mRNA.
 - B. Nuclear processing mechanisms modify both the 5' and 3' ends.
 - C. Transport out of the nucleus for intron removal.
 - D. Cytoplasmic processing of the 5' and 3' ends.
 - E. Removal of the poly(A) tail following completion of translation.

7. The CAP structure of eucaryotic mRNA
- A. consists of poly(A) sequences.
 - B. contains a 5' -> 5' link between ribose residues mediated by phosphate ester bridges..
 - C. is transcribed directly from DNA sequences.
 - D. is of no significance for the activity of mRNA in translation.
 - E. is directly adjacent to the AUG initiator codon in mRNA.
8. In a cell-free protein synthesizing system containing aminoacyl tRNA synthetases and tRNA from *E. coli*, initiation and elongation factors from *B. megaterium*, ribosomes from *B. stearothermophilus* and mRNA from phage Qbeta, the proteins made would be representative of
- A. *E. coli*
 - B. *B. megaterium*
 - C. *B. stearothermophilus*
 - D. phage Qbeta
 - E. none of the above
9. During protein synthesis, the formation of each peptide bond requires the equivalent of four high-energy phosphate bonds. Consumption of a high-energy phosphate bond is required in all the following steps EXCEPT
- A. formation of peptide bond catalyzed by peptidyl transferase.
 - B. binding of aminoacyl tRNA to the A site.
 - C. translocation.
 - D. activation of amino acids.
 - E. binding of fmet-tRNA to the initiation codon.

Choose the single best answer for the following questions.

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10. An integral membrane protein with its C terminus in the lumen of the ER and its N terminus on the cytosolic side will end up in the plasma membrane with

- A. a new C terminus formed by signal peptidase action
- B. its C terminus on the cytosolic side of the plasma membrane
- C. its C terminus randomly distributed between the outside and cytosolic sides of the plasma membrane
- D. its C terminus on the outside of the plasma membrane
- E. its N terminus randomly distributed between the outside and cytosolic sides

11. In I-cell disease, enzymes normally found in lysosomes are instead present in high levels in the blood and urine. This indicates a defect in

- A. the formation of ER signal peptide.
- B. SRP receptors.
- C. signal peptidase.
- D. the formation of mannose 6-phosphate.
- E. polyubiquitinylation.

12. When proteins are transported by a vesicular transport mechanism,
- A. the transport occurs through a membrane.
 - B. the transported proteins do not cross a membrane.
 - C. the proteins must be unfolded.
 - D. the transport occurs between topologically different compartments.
 - E. the transport occurs through aqueous channels.
13. A mutation in the *i* gene of the lac operon can result in the operon being on all the time, even in the absence of lactose. This can happen if
- A. R is altered and has lost its affinity for the inducer
 - B. R is altered and has lost its affinity for the operator
 - C. the structural genes are altered
 - D. R is altered and has lost its affinity for the promoter
 - E. R is altered and binds more tightly to the promoter
14. In the presence of glucose and lactose, *E. coli* will
- A. decrease levels of galactoside permease
 - B. increase levels of cAMP
 - C. induce β -galactosidase synthesis
 - D. increase levels of the lac repressor
 - E. all of the above

15. Synthesis of tryptophan in *E. coli* is inhibited by
- A. aporepressor binding of tryptophan
 - B. reduced levels of trp-tRNA
 - C. increased levels of cAMP
 - D. low levels of tryptophan
 - E. all of the above
16. The sequence heterogeneity of the variable region of immunoglobulins is due to
- A. transposon mediated rearrangements of the immunoglobulin genes
 - B. site specific integration of λ phage DNA in the immunoglobulin genes
 - C. homologous recombination between the genes encoding the variable region of immunoglobulins located on the paternal and maternal chromosome
 - D. site specific recombination between V and J (or V,D and J) genes
 - E. "heptamer_spacer_nonamer" mediated recombination between C genes
17. Formation of the Holliday Junction requires the action of which enzyme?
- A. integrase
 - B. DNA polymerase II
 - C. RecA
 - D. TFIIH
 - E. telomerase

18. Which of the following statements is *false*?
- A. The insertion of a transposable element can produce a decrease or increase of the expression of certain genes depending on the site of insertion
 - B. The insertion of a transposable element can produce a duplication of the insertion site
 - C. Complex transposons carry genes in addition to those required for transposition
 - D. “retrovirus type” transposons (retro-transposons) move via an RNA intermediate
 - E. transposases (integrases) possess a 5' → 3' nuclease activity and a 3' → 5' polynucleotidyl transferase activity
19. Taq polymerase is
- A. An RNA polymerase of type III
 - B. A proteolytic fragment of DNA polymerase I, also called “Klenow”
 - C. A restriction enzyme that under special conditions can have polymerase activity
 - D. A thermostable DNA polymerase used in the PCR reaction
 - E. None of the above

20. Which of the following statements about restriction enzymes and ligases is *incorrect*?

- A. Restriction enzymes cleave DNA leaving either blunt or sticky ends
- B. Restriction enzymes bind to DNA at specific nucleotide sequences but it is not possible to predict at which specific nucleotide they will cut inside the recognition sequence
- C. The blunt ends of two DNA fragments can always be ligated even if they were not generated by the same enzyme
- D. The overhanging ends of two DNA fragments generated by two different restriction enzymes can still be ligated if the ends are complementary
- E. The non complementary ends of two DNA fragments can always be ligated after “filling in” or “chewing” the overhangs

21. cDNA libraries are

- A. Libraries of DNA molecules derived only from circular chromosomes.
- B. Libraries of DNA sequences complementary to mRNA's
- C. Collections of chromosomal fragments commonly used for cloning individual genes
- D. Libraries of genes encoding only cytoplasmic proteins
- E. None of the above

22. Which of the following statements about Sanger DNA sequencing technique is *incorrect*?

- A. Anyone of the four dideoxynucleotides (ddATP, ddTTP, ddCTP, ddGTP) can be incorporated into a synthesized strand each time a thymine is encountered by the polymerase
- B. Dideoxynucleotides (ddNTP) cannot form a phosphodiester bond with the next incoming dNTP and therefore stop further synthesis of the strand
- C. Information on the nucleotide sequence of a DNA fragment can be obtained only if an oligonucleotide (primer) is available complementary to some region of the DNA fragment or to one of its flanking regions.
- D. A full sequence ladder can be obtained only if each one of the four ddNTP are used in four separate sets of sequencing reactions
- E. Sanger sequencing can be adapted to sequence RNA if an RNA dependent DNA polymerase (reverse transcriptase) is used instead of a DNA dependent DNA polymerase

23. Which of the following statements regarding the introduction of foreign genes in mammalian cells is *incorrect*?

- A. A foreign gene can be expressed by inserting the gene into a plasmid vector containing a strong promoter (e.g. CMV or T7 promoter)
- B. High level expression of a foreign gene carried by a plasmid vector can be obtained if the vector carries the DHFR marker and cells are cultured in increasing concentrations of methotrexate
- C. A foreign gene can be expressed by inserting it into an adenoviral vector
- D. A foreign gene can be integrated in the chromosome if it is carried by a retroviral vector
- E. A foreign gene can be integrated in the chromosome only if it carries a selectable marker (e.g. APH, DHFR, TK, etc)

24. Which of the following statements regarding the positive-negative selection methods for the disruption of chromosomal genes of mammalian cells is *incorrect*?

A. Insertion of the foreign DNA in the recipient chromosome is associated with the acquisition of resistance to G418

B. Insertion of the foreign DNA in the recipient chromosome may take place either by homologous or non-homologous recombination

C. Successful disruption of the chromosomal gene is heralded by the acquisition of resistance to both G418 and gancyclovir

D. Homologous recombination of the foreign DNA with the recipient chromosome provides only G418 resistance

E. Non-homologous recombination of the foreign DNA with the recipient chromosome provides only G418 resistance

25. The inhibition of gene expression via “antisense genes” is based on

A. Introduction in the cell of an inactive mutant (also called “antisense mutant”) allele of the gene whose expression needs to be inhibited

B. Disruption of the chromosomal gene with an “antisense” gene (a gene that starts coding at the termination codon [e.g. TAA] and stops at the initiation codon [ATG])

C. Introduction in the cell of a gene coding for an “antisense” protein (a protein whose sequence is the inverse of that of the sense protein [e.g.: Sense protein = MAGWYLT ; Antisense protein = TLYWGAM])

D. Introduction in the cell of a vector in which a strong promoter drives the synthesis of a mRNA (antisense) complementary to the mRNA (sense) derived from a chromosomal gene

E. None of the above

26. ES cells are
- A. Differentiated cells carrying a transgene in association with a marker gene
 - B. Blastocyst undifferentiated cells
 - C. Tumor cells that carry a stably integrated portion of the SV40 virus genome and therefore express the large T antigen
 - D. Embryonic stem cells always originating from a dark coat mouse
 - E. None of the above
27. Which of the following statements about telomerases is *incorrect*?
- A. Telomerase is never expressed in germline cells
 - B. Telomerase activity is usually not detected in resting (non-dividing) somatic cells
 - C. The number of replication cycles of a cell is dependent on the number of telomeric units
 - D. Telomerase is a reverse transcriptase
 - E. Telomerase carries its own RNA template to extend the 3' end of a DNA strand

28. Which of the following statements about gene regulation is *correct*?

A. All transcription factors recognize specific patterns of hydrogen bond donors and acceptors in the DNA minor groove

B. The interaction of all DNA binding proteins with DNA is mediated by “homeodomains” that have a characteristic helix-turn-helix motif

C. The interaction of all DNA binding proteins with DNA is mediated by “zinc-fingers domains”

D. “Zinc fingers domains” are characterized by a β sheet and a helix held together by a zinc atom

E. A “Leucine zipper” domain is characterized by two β sheets that interact via hydrophobic interactions (usually provided by leucine residues)

29. Which of the following transcription factors binds at the “TATA box” consensus sequence?

A. E2F

B. TFIIH

C. p53

D. *c-myc*

E. TFIID

30. Which of the following statements about the regulation of gene expression is *incorrect*?

- A. The expression of genes can be inhibited by DNA methylation (primarily at the C5 of cytosines)
- B. DNA methylation is the primary cause of “genetic imprinting”
- C. Silencers and enhancers are located downstream of the genes they regulate and act by inhibiting or stimulating the formation of the transcription initiation complex
- D. Gene expression can be inhibited by a condensed state of the chromatin with high packing into nucleosomes
- E. Multiple silencers and enhancers can regulate the level of expression of a gene

31. Cell cycle division (CDC) yeast *ts* mutants are often used to study cell cycle in eukaryotic cells. These mutant strains can be easily recognized because

- A. They grow only at the non-permissive temperature
- B. Different cells of the cell population show a synchronous arrest of growth when the culture is transferred to the permissive temperature
- C. Different cells of the cell population show an asynchronous arrest of growth when the culture is transferred to the permissive temperature
- D. Different cells of the cell population show a synchronous arrest of growth when the culture is transferred to the non-permissive temperature
- E. They continue growing when transferred to the non-permissive temperature, but the growth rate is significantly slower

32. G1 Cyclins (e.g. Cyclin E or D1) of mammalian cells are
- A. General activators of the function of pRb
 - B. Proteins that form complexes with kinases, which in turn phosphorylate pRb
 - C. Transcription factors that cyclically (at each division) turn on the S-phase genes
 - D. Activated by the binding of several proteins (e.g. p21, p27, p16, p15)
 - E. None of the above because cyclins are only involved in the regulation of the G2-M transitions (thereby named "mitotic" cyclins)
33. Which of the following statements about the action of p53 is *incorrect*?
- A. p53 levels or activity are decreased by proteins that sense DNA damage (e.g. DNAPK, PARP, ATM)
 - B. The amount of p53 is decreased by binding of the MDM2 oncogene product
 - C. The pro-apoptotic activity of p53 is inhibited by Bcl2 and by the adenoviral E1B
 - D. p53 inhibits the phosphorylation of pRb
 - E. p53 inhibits the release of the transcription factor E2F

34. Which of the following pathways for the activation of apoptosis is most likely to involve the activity of p53?

- A. Activation of sphingomyelinase by binding of Vit-D3 to surface receptors
- B. Binding of tumor necrosis factor to surface receptors
- C. Granzyme B (Cytotoxic lymphocytes) mediated activation of caspases
- D. γ irradiation
- E. none of the above

35. The members of the Bcl2 family of oncogenes are

- A. Proteases with specificity for cutting after an aspartic acid
- B. Kinases
- C. Cyclins
- D. Membrane proteins with ion channel and docking activities
- E. Transcription factors

36. Which one of the following events is *not* associated directly with the opening of the “Permeability Transition Channel” (PTC) during the Effector phase of Program Cell Death?

- A. Collapse of the mitochondrial $\Delta\psi$
- B. Degradation of nuclear envelope proteins (e.g. Lamins) and of cytoskeletal proteins (e.g. Actin, Fodrin)
- C. Uncoupling of respiration from phosphorylation
- D. Production of reactive oxygen species
- E. ATP depletion

37. The decision to progress into the cell cycle or to take the path of apoptosis is dependent on the balance between the action of p53 and pRb. Apoptosis will take place if

- A. pRb is mostly phosphorylated and the level of p53 is low
- B. pRb is mostly non-phosphorylated and the level of p53 is low
- C. The transcription factor E2F is released from the complex with pRb and the level of p53 is high
- D. The level of non-phosphorylated pRb is much higher than the level of E2F
- E. Something else happens: indeed, the premise of this question is wrong because progress into the cell cycle at the G1-S transition is exclusively dependent on the levels of various Cdk activities and not on pRb or p53 levels

38. Which one of the following steps (not listed in sequential order) is *not* part of a “typical” hormone dependent G-protein cycle?

- A. Adenylate cyclase catalyzes the synthesis of cAMP
- B. The activated receptor binds the G-protein complex (e.g. $\alpha\beta\gamma$) and stimulates the release of GTP and the binding of GDP to the α subunit
- C. The activated $G\alpha$ dissociates from the hormone receptor and activates the membrane bound adenylate cyclase
- D. Hormone binds to the membrane receptor
- E. GTP bound to the α subunit of the G protein is hydrolyzed

39. Which of the following statements is *incorrect*?
- A. The Human Hereditary Retinoblastoma is due to the inheritance of a homozygotic defect in the RB1 gene, which produces the cancer phenotype early in life when the p53 protein becomes non-functional
 - B. The Human Hereditary Retinoblastoma is due to the inheritance of a heterozygotic recessive defect in the RB1 gene, which produces the cancer phenotype early in life when Loss of Heterozygosity (LOH) occurs
 - C. With the exception of the Human Hereditary Retinoblastoma, most tumors with defective pRb also carry a defective p53
 - D. The p53 pathway of tumor suppression includes a heterogeneous array of proteins which act either upstream (e.g. ATM, BLM gene products) or downstream (p21WAF, pRb) of p53
 - E. Several acute childhood leukemias are due to abnormal function of transcription factors that regulate the expression of human homeotic genes
40. Which of the following statements about oncogenic viruses is *incorrect*?
- A. Oncogenic viruses can produce late onset tumorigenesis
 - B. Oncogenic viruses of the retroviral type can carry a viral version of a cellular oncogene
 - C. The SV40 large T antigen (Tag) sequesters both pRb and p53
 - D. Oncogenic retroviruses integrate into the host genome via a double stranded DNA intermediate
 - E. None of the above, i.e. all are correct

41. The energy metabolism of tumor cells is usually characterized by
- A. Increased production of ATP via respiration in order to satisfy the increased energy load produced by continued cell division
 - B. Increased aerobic glycolysis and glutaminolysis with consequent increased production of lactate
 - C. Increased aerobic glycolysis and glutaminolysis with consequent decreased production of lactate
 - D. Increased mitochondrial acetyl-CoA oxidation due to increased levels of aconitase and isocitrate dehydrogenase
 - E. None of the above. Cancer is a disease with roots into genetic alterations of cell cycle regulation and tumor cells do not show metabolic abnormalities
42. Which of the following statements about Spongiform Encephalopathies (SE) is *incorrect*?
- A. SE can be produced by the injection of infectious prions from other members of the same species
 - B. SE can be produced by inherited mutations which increase the probability of conversion of a pre-prion into an infectious prion
 - C. SE can be produced by somatic mutations which increase the probability of conversion of a pre-prion into an infectious prion
 - D. SE can be produced by spontaneous conversion of a wild-type pre-prion into an infectious prion
 - E. The probability of inter-species transfer of SE is solely determined by the degree of amino acid sequence homology between the wild-type pre-prions of the various species

In each group, for each numbered question select the best lettered answer. Each lettered answer may be selected once, more than once, or not at all.

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43. A metabolic derivative of 5-fluorouracil is useful as an anti-tumor agent because it inhibits

44. Allopurinol is used to treat gout because it inhibits

45. Severe combined immune deficiency can result from a defect in

46. The enzyme deficiency seen in patients with Lesch-Nyhan syndrome is

A. dihydrofolate reductase

B. thymidine kinase

C. thymidylate synthase

D. adenosine deaminase

E. xanthine oxidase

F. ribonucleotide reductase

G. nucleoside diphosphate kinase

H. hypoxanthine-guanine phosphoribosyltransferase

I. PRPP synthetase

J. ATCase

In each group, for each numbered question select the best lettered answer. Each lettered answer may be selected once, more than once, or not at all.

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E. coli was grown for several generations in ^{15}N media to completely label its DNA, then transferred for varying times into ^{14}N media. Its DNA was isolated and characterized by density gradient centrifugation as heavy (all ^{15}N), light (all ^{14}N) and/or intermediate (equally ^{14}N and ^{15}N).

47. After two generations in ^{14}N media, its DNA was characterized as
48. After three generations in ^{14}N media, its DNA was characterized as
- A. heavy
 - B. light
 - C. intermediate
 - D. both heavy and intermediate
 - E. both light and intermediate