

Note that Two possible answers have been allowed for three questions that were confusing

SECTION I

Decide which is the **best** answer and blacken the corresponding brackets.

1. Which list is made up of only nucleosides? [E]
 - A. inosine, uridine, adenosine, cytosine
 - B. inosinate, uracyl, adenine, cytosine
 - C. inosine, uracyl, adenine, cytidine
 - D. hypoxanthine, uridylate, adenine, cytidine
 - E. inosine, uridine, adenosine, cytidine

2. Ribonucleotide reductase converts (where N is any base): [C]
 - A. dNMP to NMP
 - B. NTP to dNTP
 - C. NDP to dNDP
 - D. dNDP to NDP
 - E. NMP to dNMP

3. The enzyme(s) responsible for generating nucleotide triphosphates is/are: [C]
 - A. specific for each base type but non-specific for ribose/deoxyribose.
 - B. called diphosphonucleosidases.
 - C. called diphosphonucleoside kinase.
 - D. responsible for maintaining a low NTP/NDP ratio in the cell.
 - E. are specific for ribose/deoxyribose forms.

4. Orotic aciduria can result from: [E]
 - A. an excess of cytosolic carbamoyl phosphate synthetase activity.
 - B. insufficient aspartate transcarbamoylase (ATCase) activity.
 - C. an excess of orotatephosphoribosyltransferase activity.
 - D. an excess of UTP (inhibiting carbamoyl phosphate synthetase II).
 - E. insufficient OMP carboxylase activity.

5. The Shine-Dalgarno sequence is [1]
 - 1) Purine rich
 - 2) Complementary to 18S rRNA
 - 3) Functions in eukaryotes and prokaryotes
 - 4) Located 3' to the initiator AUG
 - 5) Approximately 20 nucleotides long

6. Shut-off of host protein synthesis by poliovirus occurs by [2]
 - 1) phosphorylation of eIF-2
 - 2) cleavage of eIF-4G
 - 3) phosphorylation of eIF-4E
 - 4) de-phosphorylation of eIF-4E
 - 5) de-phosphorylation of eIF-2

7. A mutation that inhibits eIF-2B (GEF) function in yeast should [1]
 - 1) stimulate GCN4 translation
 - 2) increase phosphorylation of eIF-4B
 - 3) inhibit GCN4 translation
 - 4) decrease phosphorylation of eIF-2
 - 5) increase phosphorylation of eIF-4E

8. A mitochondrial matrix targeting signal (MTS) is fused to the mature enzyme form of glycosidase X, which normally resides in lysosomes. You discover that this protein is not imported by mitochondria. Why? [3]
 - i) The MTS is not dominant over the lysosome sorting signal of glycosidase X.
 - ii) The MTS is not dominant over the signal sequence of glycosidase X.
 - iii) Glycosidase X may be difficult to unfold.
 - iv) The MTS is removed by a lysosomal protease.
 - v) Cytosolic chaperones do not recognize lysosomal proteins.

SECTION I - Continued

Decide which is the best answer and blacken the corresponding brackets.

9. Which of the following statements is incorrect. [3]
- i) Protein translocation into the secretory pathway occurs at the endoplasmic reticulum.
 - ii) The default destination in the lumen of the secretory pathway is the outside of the cell.
 - iii) Targeting of secretory proteins to the secretory pathway requires interaction between the signal sequence and an endoplasmic reticulum associated receptor.
 - iv) SRP is a quality control factor that prevents mislocalization of secretory proteins to the cytosol.
 - v) The ribosome contributes to unidirectionality of protein translocation into the secretory pathway.
10. Which of the following is not required for polypeptide insertion into the plasma membrane. [5]
- i) ATP
 - ii) GTP
 - iii) Sec 61 complex
 - iv) SRP receptor
 - v) Hsp 70
11. Which of the following statements is incorrect. [4]
- i) ATP is required for protein degradation by the 26S proteasome complex.
 - ii) ATP is required for protein ubiquitination.
 - iii) Ubiquitinated proteins are unfolded by the 26S proteasome complex.
 - iv) Hsp 70 is usually involved in degradation by the 26S proteasome complex.
 - v) Protein degradation by the 26S proteasome complex occurs within the interior of the complex.
12. Which of the following is associated with necrotic cell death. [3]
- i) Chromatin condensation.
 - ii) Formation of oligonucleosomal chromatin fragments.
 - iii) Inflammation.
 - iv) Inactivation of poly (ADP Ribosyl) polymerase, also known as PARP.
 - v) Cell shrinkage.
13. During development, many neurons die because [4]
- i) They do not have caspase-3
 - ii) They do not have Bcl-2
 - iii) They receive a death signal.
 - iv) They do not receive a survival signal.
 - v) They receive a survival signal which is suppressed by Bax.
14. A knock out of the Ced-4 gene in *C. elegans* would result in [5] or [1]
- i) Inappropriate cell survival.
 - ii) Activation of Ced-3.
 - iii) Inability of Ced-9 to associate with Ced-3.
 - iv) i and ii are correct
 - v) i and iii are correct.
15. Caspase-8 recognizes and cleaves the tetrapeptide sequence ala-ala-val-asp in the protein Bap31, which is part of a complex that recruits procaspase-8. Which amino acid(s) in this sequence would you predict could be substituted with an unrelated amino acid without affecting cleavage of Bap31. [5]
- i) Asp
 - ii) Val
 - iii) P3-Ala
 - iv) P4-Ala
 - v) ii or iii
16. Which of the following statements is incorrect [3] or [4]
- i) Bcl-2 prevents the release of cytochrome c from mitochondria.
 - ii) Bcl-2 blocks activation of caspase-8 by the oncogene E1A.
 - iii) Bcl-2 blocks activation of caspase-8 by Fas ligand.
 - iv) i and ii are incorrect
 - v) i and iii are correct

SECTION I - Continued

Decide which is the best answer and blacken the corresponding brackets.

16. Which of the following statement(s) are correct [i]
- i) Bcl-2 prevents the release of cytochrome c from mitochondria. Correct
 - ii) Bcl-2 blocks activation of caspase-8 by the oncogene EIA. Not correct
 - iii) Bcl-2 blocks activation of caspase-8 by Fas ligand. Not correct
 - iv) i and ii are correct
 - v) i and iii are correct

SECTION II

For each of the statements below ONE or MORE are correct. Decide which combination of statements is correct and blacken the brackets with:

- 1) If A, B and C are correct
 - 2) If A and C are correct
 - 3) If B and D are correct
 - 4) If D is correct
 - 5) If all are correct
17. Attenuation within the tryptophan operon *in vivo* could be affected one way or another by the following manipulations. Assuming that all amino acids are present in high amounts, indicate which of the following manipulations will cause an increase in readthrough transcription (less attenuation). [2]
- (A) deletion of the entire leader region between the transcription start site and the *trpE* gene
 - (B) replacement of all the tryptophan codons with alanine codons in the leader coding region.
 - (C) deletion of the sequence "1" in the leader region.
 - (D) introducing mutations that increases the stability of the 3:4 hairpin.
18. In prokaryotes, a rho-independent termination site may include the following elements: [1] or [5]
- (A) a G/C rich region
 - (B) a region capable of forming a stem and loop structure
 - (C) a stretch of adenines in the DNA coding strand that will give rise to a stretch of U's in the transcribed RNA
 - (D) an open reading frame
19. In the case of a gene that is imprinted, [2]
- (A) expression of a particular allele depends on whether it is inherited from the mother or the father.
 - (B) deletion of one allele invariably leads to the expression of the mutated phenotype.
 - (C) maintenance of the imprint pattern in somatic cells requires the action of the cytosine methyl-transferase (CMT).
 - (D) the pattern of methylation is similar on both alleles.
20. In prokaryotes, the process of transcription can involve the following events: [5]
- (A) The formation of a closed promoter complex.
 - (B) The unwinding and rewinding of DNA.
 - (C) The formation of an RNA-DNA hybrid.
 - (D) The synthesis of very short RNA molecules.
21. Transcription in prokaryotes: indicate which of the following statements are correct. [2]
- (A) The change in σ (Greek letter "sigma") factor can change the DNA binding specificity of RNA polymerase.
 - (B) Binding sites for activators interacting with the α (Greek letter alpha) factor must be located in the immediate vicinity of the -35 element.
 - (C) The carboxy-terminal domain of the α (Greek letter alpha) makes specific protein-DNA contact with the UP element.
 - (D) The core RNA polymerase binds to the promoter to form the "closed complex".
22. The regulation of a bacterial promoters involves several elements. Indicate which of the following statements are correct. [5]
- (A) A binding site which overlaps the -35 or -10 promoter elements can function as an operator.
 - (B) Some bacterial proteins can act as either activators or repressors.
 - (C) Ligands can affect gene expression by preventing or helping transcriptional factors to bind to DNA.
 - (D) To effect activation, a transcriptional activator must be able to interact with one of the subunits of RNA polymerase.

SECTION II - Continued

For each of the statements below ONE or MORE are correct. Decide which combination of statements is correct and blacken the brackets with:

- 1) If A, B and C are correct
- 2) If A and C are correct
- 3) If B and D are correct
- 4) If D is correct
- 5) If all are correct

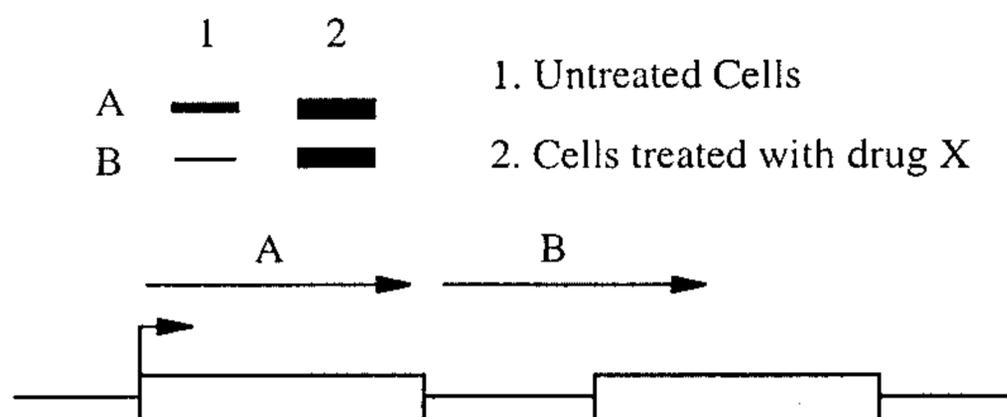
23. Transcription in eukaryotes: indicate which of the following statements are correct. [1]
- (A) The stimulation of transcription by TFIIA may involve antirepression and activation.
 - (B) The interaction between TFIIIB and RNAPII is critical in determining the transcription start site.
 - (C) TFIIIB can bind to RNA polymerase II, to the TBP-DNA complex and to some trans-activators.
 - (D) TFIIIF is involved in the assembly of the pre-initiation complex but does not affect transcript elongation.
24. Transcription in eukaryotes: indicate which of the following statements are correct. [3]
- (A) Transcription initiation *in vitro* does not require the presence of TFIIIB and TFIIH provided that the DNA template is negatively supercoiled.
 - (B) The kinase that is responsible for the phosphorylation of RNA polymerase II is a cyclin-dependent kinase.
 - (C) The kinase activity that is responsible for the phosphorylation of RNA polymerase II is provided by TFIIIF.
 - (D) TFIIH provides DNA-dependent ATPase and DNA helicase activities.
25. Transcription in eukaryotes: indicate which of the following statements are correct. [1]
- (A) Transcriptional trans-activators are required for the effect of enhancers on gene expression.
 - (B) Molecular targets for transcriptional trans-activators include TFIIH, TAFs, TFIIIB or a histone acetyltransferase.
 - (C) Transcriptional trans-activators may contain a specific DNA binding domain and a domain allowing interactions with one of the general transcription factors.
 - (D) Some sub-units of TFIIIF are also involved in DNA repair.
26. Transcription in eukaryotes: indicate which of the following statements are correct. [3]
- (A) DNA methylation is not required for normal development in mammals.
 - (B) In somatic cells, the methylation pattern is maintained from cell to cell, but with a fidelity of only ~95%.
 - (C) When tested *in vitro*, histone H1 was found to bind preferentially to unmethylated DNA.
 - (D) DNA methylation may vary with the species, the tissue, and the position along a chromosome.
27. Nucleosome assembly during DNA replication involves some of the following events. Indicate which of the following statements are correct. [1]
- (A) Histones from the parental nucleosomes are transferred directly and reassembled into nucleosomes onto either of the two DNA daughter strands.
 - (B) DNA replication is not required for the deposition of new nucleosomes on DNA by the chromatin assembly factor 1 (CAF-1).
 - (C) Chromatin assembly factor 1 (CAF-1) utilizes only acetylated histones.
 - (D) Chromatin assembly factor 1 (CAF-1) forms a protein complex consisting of three subunits, one of which interacts with histones H2A and H2B.
28. More complicated types of genetic switches can be constructed by combining positive and negative controls. Indicate which of the following statements are correct. [2]
- (A) A mutation within the coding sequence for the lactose repressor may be trans-dominant.
 - (B) Following addition of lactose to the medium, the lactose repressor protein binds to the operator of the lactose operon.
 - (C) Operator-constitutive mutations are cis-dominant.
 - (D) The catabolite activator protein (CAP) enables bacteria to use alternative carbon sources in the presence of glucose.
29. Transcription in eukaryotes: indicate which of the following statements are correct. [5]
- (A) Steps that can be activated by trans-activators include formation of a closed complex, promoter clearance and a conformational change within TFIIIB.
 - (B) Some trans-activators may bind to more than one general transcription factors.
 - (C) A repressor that prevents DNA binding by an activator does not necessarily contain a DNA binding domain.
 - (D) Some repressors function by recruiting a histone deacetylase to the promoter.

SECTION II - Continued

For each of the statements below ONE or MORE are correct. Decide which combination of statements is correct and blacken the brackets with:

- 1) If A, B and C are correct
- 2) If A and C are correct
- 3) If B and D are correct
- 4) If D is correct
- 5) If all are correct

30. Interpretation of a nuclear run-on transcription assay. Indicate which conclusions can be drawn from the results of this experiment. [1]



- (A) In untreated cells, there is a block to elongation of transcription.
- (B) Following treatment with drug X, transcription elongation is stimulated.
- (C) Following treatment with drug X, transcription initiation is increased.
- (D) Following treatment with drug X, the stability of the mature mRNA is increased.

31. Phosphorylation of eIF2 leads to [3]

- A) Degradation of viral and cellular mRNA
- B) trapping of eIF2B in a complex with eIF2
- C) Induction of oligoadenylate synthase
- D) Prevention of eIF2 GTP Met-tRNA ternary complex formation

32. Interferon triggers the following events. [2]

- A) Degradation of mRNA
- B) Phosphorylation of GEF
- C) Phosphorylation of eIF2 subunit
- D) phosphorylation of eIF4E

33. The nucleotide ppGpp: [4]

- A) Binds to the 30S ribosomal subunit
- B) Is a component of the GCN4 response
- C) Accumulates in yeast starved of amino acids
- D) Is synthesized by the rel protein

34. ATP is required in eukaryotic protein synthesis for: [4]

- A) Formation of a ternary complex
- B) Dissociation of the 74S inactive couple
- C) Release of initiation factors upon joining of the 60S subunit
- D) Binding of the 40S ribosome complex to mRNA

35. The polyadenylate tail: [1]

- A) is synthesized in the nucleus
- B) its size varies during the mRNA life cycle
- C) is synthesized by PAP
- D) is added before cleavage of the pre-mRNA

SECTION III

For each of the statements below ONE or MORE are correct. Decide which combination of statements is correct and blacken the corresponding brackets.

36. You believe that your protein is a tyrosine specific kinase. You label it in an *in vitro* kinase reaction with [³²P-γATP]. How would you prove that it phosphorylates tyrosine residues and identify which tyrosine(s) are phosphorylated (you know the sequence of your protein and you have more than one Tyr in your protein). You may use multiple experimental approaches. [D]
- 1) Subject your protein to partial alkali hydrolysis and separate amino acids by chromatography.
 - 2) Subject your protein to acid hydrolysis and separate amino acids by chromatography.
 - 3) Subject your protein to high temperatures and separate amino acids by chromatography
 - 4) Cleave your protein with a protease, separate and sequence radioactive peptides.
 - 5) Immunoblot with anti-phosphotyrosine antibodies.
- a) 1 and 5
b) 2 and 5
c) 1, 3 and 5
d) 1, 2, 4 and 5
e) 1 and 4
37. From the 3 D structure of a serine/threonine kinase (A kinase) and a tyrosine kinase (Insulin receptor). Which of the following are true. [C]
- 1) In the inactive conformation the kinases are bound to ATP
 - 2) Activation of the kinase is stabilized by phosphorylation of a Tyrosine, Serine or Threonine residue that lies within the kinase domain.
 - 3) Activation of the kinase requires a conformational change
 - 4) The 3D structure of a serine/threonine kinase is significantly different from that of a tyrosine kinase.
- a) 2
b) 1 and 2
c) 2 and 3
d) 3
e) 1 and 4
38. Which of the following are true for STAT (signal transducers and activators of transcription) factors. [5]
- 1) Unphosphorylated STAT factors are localized in the cytoplasm and do not access their target sequences.
 - 2) Activation of STAT factors requires phosphorylation of an inhibitor protein associated with STATs.
 - 3) STAT factors are bound to DNA in the nonphosphorylated state and phosphorylation activates their transactivation domain.
 - 4) Phosphorylation of STAT factors on tyrosine residues releases an inhibitory protein and they translocate to the nucleus.
- a) none of the above
b) 1 and 2
c) 3
d) 2 and 4
e) 1

SECTION IV

For the following questions, choose the TWO statements that are correct and blacken the brackets with:

- 1) If A and B are correct
- 2) If A and C are correct
- 3) If A and D are correct
- 4) If B and C are correct
- 5) If B and D are correct

39. The activated forms of sialic acid that act as donors for glycosylation of proteins is:

- A. GMP-sialic acid
- B. CMP-N-acetylneuraminic acid
- C. CMP-sialic acid
- D. UMP-sialic acid

40. Targeting of most lysosomal enzymes to the lysosomes:

- A. require the activity of GlcNAc-1-phosphotransferase
- B. require N-linked complex oligosaccharides
- C. sorting in the cis-Golgi
- D. require mannose-6-P

41. Lipid intermediates containing dolichol are required for protein glycosylation:

- A. in the lumen of the endoplasmic reticulum
- B. only for N-linked oligosaccharides formed in the endoplasmic reticulum
- C. in the transport of nucleotide sugars in the Golgi
- D. for the addition of glucose to the oligosaccharide precursor in the endoplasmic reticulum

42. The carbohydrate structure responsible for the A blood group antigenic determinant:

- A. occurs only on type 1 oligosaccharide chains
- B. contains α 1,2-linked fucose residues
- C. contains α 1,3-linked fucose residues
- D. contains terminal α 1,3-linked GalNAc

43. Glycosaminoglycan chains:

- A. always contain glucuronate
- B. always contain sulfate, with the exception of hyaluronate
- C. always contain both N-acetylglucosamine and N-acetylgalactosamine in the same oligosaccharide chain
- D. are attached to protein through a core region of Gal-Gal-Xyl