SECTION I

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

1. Hydrogen bonds

(1) are strongest when the three atoms involved make an angle of 90°
*(2) occur when a hydrogen atom is shared between two electronegative atoms
(2) have distances of 0.4nm (4.0 Ängstroms)
(3) have strengths of 80kcal/mole in water.
(4) are found in alpha helices between the carbonyl carbon atom of residue *i* and the main chain nitrogen atom of residue i+6.

2. The peptide bonds within a protein structure

*1) have a planar character due to resonance stabilization.
2) are found mainly in the cis conformation
3) have bond lengths which are longer than the regular N-Ca bond.
4) are the main structural feature of the polypeptide chain which determine the three dimensional fold of the protein
5) none of the above

3. Helical structures

1) are formed by twisting the polypeptide unit by the same amount about each nitrogen atom in the main chain.
*2) can be defined by the pitch of the helix and the number of peptide units per helical turn.
3) are found mainly as 3_{10} helices in protein structures
4) are only found as right handed structures in proteins
5) all of the above

4. The dipole moment of an a-helix

1) is a result of the fact that peptide bonds exhibit different polarities for the NH and the CO groups
2) results in a net positive charge at the amino termini of the helix and a net negative charge at the carboxyl termini.
3) is utilized by proteins to attract opposite charged ligands, such as phosphate groups, at the amino termini of the helix.
4) is aided by the fact that the peptide units are all aligned in the same orientation along the helical axis.
*5) all of the above.

5. Beta sheet structures are found within many proteins

1) in only an antiparallel orientation
2) and always exhibit psi angles of -90° to -120°.
3) and adopt a left handed twist when viewed along their strands
*4) and most often form the central core of globular protein structures
5) and show a distinct hydrogen bonding pattern within the strands of the sheet.

6. Loop regions found in protein structures **(2 ANSWERS CORRECT)**

1) are most often buried in the internal core of the molecule
2) are always rich in hydrophobic residues
*3) are the most common locations for amino acid insertions and deletions amongst homologous proteins
*4) often cause abrupt changes in chain direction between secondary structure elements.
5) none of the above

7. Ras proteins are a large superfamily of monomeric GTPases which act as signal transduction units. The structures of p21-ras have been determined for the GDP-bound and the GTP-bound form and for various mutants.

*1) Differences between the GTP-bound and GDP found forms are limited primarily to two loops of the protein.
2) All of the activating mutants are located in the core of the protein structure.
3) The structure suggests a helix is involved in interaction with the effector molecule, GAP.
4) All of the above.
5) None of the above.

8. Which of the following features is NOT characteristic of some epithelial cells?

1) line the inner and outer surface of the body
2) existence of hair-like microvilli on absorptive cells
*3) fill spaces between organs and tissues
4) epithelia of the upper respiratory tract can contain cilia
5) secretory cells release products into ducts or directly into the blood stream

9. The organelle that contains the largest % of total cell membranes is:

1) the plasma membrane
2) the inner nuclear membrane

*3) the inner mitochondrial membrane
4) the Golgi
5) smooth endoplasmic reticulum

10. Which of the following statements is FALSE?

*1) 5S rRNA is synthesized in the nucleolus
2) the 45S rRNA precursor is cleaved to form the 18 and 28S rRNAs in eukaryotes
3) the small and large ribosomal subunits mature in the nucleus
4) the mature 40S and 60S ribosomal subunits mature in the cytoplasm
5) ribosomal processing proteins are recycled

11. In cells labeled by 3H-uridine, which if the following intracellular locations is UNLIKELY to show incorporation of radioactivity?

1) the nucleolus
2) mitochondria
3) euchromatin
4) facultative heterochromatin
*5) constitutive heterochromatin

12. Which of the following statements is FALSE?

1) Histones are highly basically charged.
*2) Histones bind to DNA and regulate gene expression.
3) Eukaryotes contain five major classes of histones, H1, H2A, H2B, H3 and H4.
4) The central core of nucleosomes is comprised largely of histones H2A, H2B, H3 and H4.
5) The core of nucleosomes is made up of a histone octomer.

13. The major role of histone H1 is to:

1) Form part of the octomer core.
*2) Promote packing of nucleosomes.
3) Prevent disruption of nucleosome structure by high salt.
4) All of answers 1-3.
5) None of answers 1-3.

14. Which of the following is NOT typical of cancer cells growing in culture?

*1) increased dependence on contact with the substratum
2) disoriented cell growth
3) growth to higher saturation densities
4) lower serum requirements
5) shortened cell cycle transit time

15. Which of the following scenarios is INCORRECT following fusion of mammalian cells?

1) G2 x M - the M cell nucleus continues mitosis and the G2 nucleus goes into mitosis.
*2) G1 x M - the M cell nucleus continues mitosis and the G1 nucleus first synthesizes DNA and then goes into mitosis.
3) G1 x S - the S-phase nucleus continues DNA synthesis and the G1 nucleus starts DNA synthesis.
4) G2 x S - the S-phase nucleus continues DNA synthesis and the G2 nucleus remains in G2.
5) G1 x G2 - the G1 nucleus proceeds through G1 and into S whereas the G2 proceeds through G2.

16. Which of the following plays NO role in preventing re-replication of DNA in a single cell cycle?

1) a G2 protein kinase
2) the composition of the initiation complex
*3) the presence of growth factors
4) nuclear membrane breakdown
5) phosphorylation of minichromosome maintenance protein (MCM)

17. Which of the following DOES NOT regulate the yeast cell cycle?

1) the concentration of mating factors
2) the amount of nutrients
3) cell size
*4) the concentration of cdc2/cdc28
5) the levels of Cln1, Cln2 and Cln3

18. What kinds of phenotypes are mutations in cdc2/cdc28 likely to produce?

1) arrest in G2
2) arrest in G1
3) lethality

*4) all of answers 1-3
5) none of answers 1-3

19. What is the key regulatory event which ends mitosis?

1) activation of cdc2 kinase
*2) degradation of cyclin B
3) phosphorylation of cdc2
4) all of the above
5) none of the above

20. Which of the following is NOT a substrate for mammalian MPF?

1) histone H1
2) regulator of mitotic spindle assembly (RMSA-1)
*3) lamin B
4) microfilamental protein myosin
5) cyclin B protease

21. Activation of E2F results from which of the following?

1) increase in D cyclin levels
2) binding of cyclin D/Cdk4 to Rb
3) phosphorylation of Rb
*4) all of the above
5) none of the above

22. Which is the correct order of events in mating factor signaling?

A. degradation of G1 cyclins
B. activation of a kinase cascade
C. binding of mating factor to receptor
D. activation of a G protein

1) A to B to C to D
2) D to C to A to B
3) C to D to A to B
4) C to B to D to A
*5) none of the above

23. Which of the following processes is known NOT to be regulated by a G protein?

1) yeast mating
2) yeast adenylate cyclase activity
*3) dimerization of transmembrane tyrosine kinase receptors
4) yeast sporulation
5) MAP kinase activation

24. Which of the following is NOT a typical property of most cancer cells?

1) unrestrained cell division
2) failure to differentiate
*3) increased attachment to the substratum
4) high metabolic rate
5) chromosomal abnormalities

25. Order the following steps in the identification of human oncogenes using the mouse 3T3 cell assay.

A. isolation of DNA from human tumours
B. introduction of transformed cell DNA into bacteriophage library and transformation of 3T3 cells
C. identification of clones containing human Alu repeat sequences
D. transfection of mouse 3T3 cells
E. isolation of transformed cell clones

1) AEDCB
*2) ADEBC
3) ABEDC
4) ABCDE
5) ADCBE

26. Which of the following would NOT be considered a potential transforming oncogene?

1) MAP kinase

2) ras
3) fos/jun (AP-1)
*4) p27
5) myc

27. What kind of mutations in Rb would be the LEAST LIKELY ever to yield cancer cells?

1) point mutations
2) deletions
*3) amplification
4) translocations
5) none of the above

28. Which of the following functions has p300/CBP NOT been associated with?

1) modulation of promoter activity
2) regulation of transcription factor activity
3) histone acetylation
4) binding to viral oncogene products
*5) interaction with growth factors

29. Which one of these transcription factors can be bound by a truncated c-Jun protein.

1) c-Myc
2) Gal4
3) GCN4
4) TFIID
*5) c-fos

30. Based on the following mRNA structure/sequence how many amino acids will comprise the protein normally translated by this message.

(Cap)-----UCCUCCAUGCCCGAUGCGGUAUGCAAACCUGAAUAUUGACUCACCGG------AAUAAA------AAAAA

1) 8
2) 3
*3) 10
4) 12
5) 7

31. What is ribosome readthrough?

1) The event of an mRNA passing through a ribosome without being translated.
2) Initiation of translation at either of two AUGs
3) The event of a ribosome jumping from the 3' polyA tail to the 5' cap structure.
*4) The event of a ribosome complex translating through a termination codon.
5) None of the above

32. During splicing which snRNA is responsible for binding the donor site.

*1) U1
2) U2
3) U4
4) U5
5) U6

33. Which one of these statements is FALSE.

A lariat:

1) contains a 2'-5' linkage
2) includes the "branch point" of the intron
3) is composed of intron sequences only
4) contains the conserved GU and AG bases of the intron/exon borderies.
*5) none of the above

34. In which of the following stages of translation, is GTP not required.

1) in the formation of the initiation ternary complex that include eIF2.
2) in the removal of the free tRNA from the P site during elongation.
3) in the termination of translation by the releasing factor.
*4) in the formation of the eIF4F comlex
5) None of the above

35. In Drosophila, the protein Sxl controls which gender will result from the embryonic development because

1) it controls the speed of the translation machinery which is faster in the female fly.
*2) it binds and protects one of its own acceptor sites, forcing the splicing machinery to recognize downstream splicing acceptor sites.
3) it binds to the RNA binding protein Tra-2 which represses male differentiation genes.
4) it associates with the spliceosome to provide specificity on the snRNAs.
5) none of the above

36. The transcription factor GAL4 promotes transcription by:

1) scavenging the free galactose in the cytoplasm.
2) by trapping the GAL 80 repressor.
3) by replacing the TFIID factor on the TATAA motif
4) by forming a complex with GAL80 and free galactose.
*5) none of the above

37. Which one of the following statements best describes U7 snRNA function in hnRNA processing.

1) U7 binds to the U2 snRNA and allows splicing of hnRNA.
2) U7 interacts with the 3' end of histone hnRNA to allow polyadenylation
3) U7 remains in the spliceosome to allow degradation of the lariat.
*4) U7 binds to the 3' end of histone pre-mRNA to direct its proper cleavage.
5) none of the above

38. Which one of these statements best describes the successive steps occurring during most mRNA processing.

1) capping, poly -Adenylation, cleavage, splicing
2) poly-Adenylation, splicing, cleavage and capping
3) splicing, cleavage, capping and poly-Adenylation
4) cleavage, capping, poly-Adenylation, splicing
*5) capping, cleavage, poly-Adenylation, splicing

39. Which one of these structures does not affect the strength of translation

1) a secondary structure in the 5' noncoding sequences
2) an upstream binding site for initiation factors
*3) an overlapping open reading frame in the gene
4) a conserved Kozak sequence in front of the AUG
5) a small open reading frame in the 5' noncoding sequences

40. What is the process that describes the enzymatic modification of cytosine to uridine in mature mRNA.

1) RNA capping
2) RNA splicing
3) post-translational processing
*4) RNA editing
5) Gene activation

41. What is the role of RNA polyadenylation?

*1) to increase messenger RNA stability and prevent RNA degradation.
2) to promote splicing
3) to allow transportation through nuclear pores
4) to promote translation of messenger RNA
5) none of the above

42. If a growth factor released by one cell acts on cells in close proximity, this results in

a) Exocrine growth stimulation
b) Juxtacrine growth stimulation
c) Autocrine growth stimulation
d) Endocrine growth stimulation
*e) Paracrine growth stimulation

43. Members of the receptor tyrosine kinase family

a) have no enzymatic activity
b) act to directly regulate gene expression
c) are cytoplasmic proteins
*d) are transmembrane proteins containing one transmembrane domain
e) none of the above

44. Activation of G-protein linked receptors following binding of ligand can lead to-

a) formation of a complex between the receptor and phosphatidyl inositol 3 kinase (PI3kinase).
b) activation of the intrinsic GTPase activity of the receptor.
*c) activation of protein kinase A.
d) activation of the Ras GTPase.
e) formation of a complex with adenylate cyclase

45. Members of the steroid receptor gene family

a) are transmembrane proteins.
b) activate a kinase cascade
c) have intrinsic enzymatic activity
d) are extracellular proteins
*e) bind hydrophobic ligands

46. Binding of a growth factor to a receptor tyrosine kinase, promotes receptor dimerization, activates the receptor and leads to -

a) activation of protein kinase A
b) phosphorylation of the receptor on tyrosine and serine residues
*c) association of the receptor with SH2 domain containing proteins
d) activation of adenylate cyclase
e) association of the receptor with trimeric G proteins

47. Signal transduction requires a series of protein:protein interactions. Proteins containing an SH3 domain interact with proteins containing

a) phosphotyrosine residues
*b) proline rich domains
c) SH2 domains
d) SH3 domains
e) kinase domains

48. Activation of MAP kinase-

a) is mediated only by receptor tyrosine kinases.
b) is mediated by G-protein linked receptors through protein kinase A.
*c) is mediated by activation of the Raf serine kinase.
d) always requires activation of Ras.
e) none of the above.

49. Protein tyrosine phosphatases

a) hydrolyse the gamma phosphate of ATP
b) are always cytoplasmic proteins
c) require a metal ion for activity
*d) form a phosphoryl intermediate
e) none of the above

SECTION II

50. All answers are correct EXCEPT:

Upon stimulation of a nerve cell:

a) Transport through the voltage gated Na+ channel is always passive.
b) The membrane potential reaches the Na+ equilibrium potential stopping further net entry of Na+
c) Na+ channels are inactivated and do not reopen until restoration of the original resting potential.
d) The voltage gradient across the cell membrane changes and causes conformational changes in voltage gated channels.
*e) The resting membrane potential is altered as a consequence of the action of the Na+-K+ pump.

51. All answers are correct EXCEPT:

a) Channel proteins transport ions much faster than carrier proteins.
b) ATP supplies the energy for the Na+-K+ pump by way of phosphorylation.
*c) The Na+-K+ pump is primarily responsible for the resting membrane potential due to the excess of negative charges remaining inside the cell.
d) Conformational changes associated with ATP dependent energy transfer drive the Na+-K+ pump
e) The Na+-K+ pump consumes a third of the cell's total ATP supply.

52. All answers are correct EXCEPT:

a) Ligand gated channels open in response to neurotransmitters.
b) Ligand gated channels are insensitive to the membrane potential
*c) Ligand gated channels generate an action potential
d) Nerve cells release a ligand which activates a channel on an innervated skeletal muscle cell.
e) The chemical synapse is where signal transmission between nerve cells and target cells takes place.

53. All answers are correct EXCEPT:

a) Sugars are transported into intestinal cells by inward symport of Na+ ions and sugar molecules.
b) Vertebrate cells contain a Na+-H+ exchange carrier which regulates intracellular pH.
c) The electrochemical gradient for a charged solute is constituted by the membrane potential and the concentration gradient for that solute.
d) Potassium leak channels are responsible for the voltage across the cell membrane.
*e) The action potential is a transient self propagation depolarization of the membrane carried out by transmitter gated ion channels.

54. All answers are correct EXCEPT:

a) Phospholipids and proteins are the classes of molecules which make up cellular membranes.
b) The outer surface of a lipid bilayer is hydrophilic.
c) Integral membrane proteins penetrate the lipid bilayer.
*d) Vesicular formation is accompanied by an exchange of the inner and outer side of the membrane.
e) Integral membrane proteins drift laterally in the membrane.

55. All answers are correct EXCEPT:

In an activated neuromuscular junction, the nerve impulse leads to the following five events:

a) Transient depolarization of voltage gated Ca2+ channels at the nerve terminal.
b) Release of acetylcholine from the nerve terminal.
*c) Binding to acetylcholine receptors which are voltage gated Na+ channels in the muscle cell plasma membrane.
d) Depolarization of the muscle cell plasma membrane which activates voltage gated Ca2+ channels.
e) Opening Ca2+ release channels leading to muscle cell contraction

56. All answers are correct EXCEPT:

*a) Channel linked receptors are cell surface proteins involved in protein kinase signalling between electrically excitable cells.
b) Catalytic receptors when activated by their ligand function directly as enzymes.
c) G-protein linked receptors indirectly activate or inactivate a separate membrane bound enzyme or ion-channel.
d) Certain extracellular signalling molecules stimulate the phosphorylation of phosphatidyl inositol.
e) The Ca2+ dependent enzyme activated by diacylglycerol is called protein kinase C.

57. All answers are correct EXCEPT:

A model to explain membrane fusion has been developed from studies of the influenza virus fusion protein in which:

a) Low pH induces a conformational change in the influenza fusion protein.
b) The resultant exposure of hydrophobic fusion peptides brings together adjacent membranes.
*c) The membrane anchor of the influenza fusion protein catalyzes the fusion of the outer leaflets of the adjacent membranes.
d) The inner two leaflets subsequently fuse.
e) This leads to the exposure of the cell cytosol to the luminal interior of the membrane containing the influenza fusion protein.

58. All answers are correct EXCEPT:

The SNARE hypothesis:

a) was developed as a consequence of a molecular understanding of the association of synaptic vesicles with the nerve terminal.
b) led to the identification of synaptobrevin of the synaptic vesicle as a v- SNARE.
c) led to the model whereby the cytosolic molecules NSF and SNAPS gather v- and t-SNARES together.
d) allows for GTP binding proteins known as Rabs to guide the docking of transport vesicles with target membranes.
*e) was developed independently by a consideration of influenza virus mediated membrane fusion.

59. All answers are correct EXCEPT:

Current models of membrane vesiculation events:

a) invoke membrane deformation events
b) invoke the participation of proteinaceous ‘coats'.
*c) invoke clathrin coats for the fusion of synaptic vesicles with the synaptic junction.
d) invoke COP-I containing coats for specific intracellular transport events within the secretory pathway.
e) invoke the GTP binding protein ARF in the recruitment of COP-I coats.

60. All answers are correct EXCEPT:

GTP binding proteins such as ARFs and Rabs are modified covalently by lipid modifications:

*a) Such modifications ensure that the attached proteins are permanently associated with membranes
b) The lipids can either be fatty acid derivatives or derivatives of the cholesterol biosynthetic pathway.
c) The lipids allow for targeting to cytosolic surfaces of membranes.
d) Lipid modifications can be either at the N-terminus or C-terminus of GTP binding proteins.
e) GTP dependent conformational changes in Rabs and ARFs allow for interactions with other proteins involved in vesicular transport.

61. Only one is correct:

Which of the following 20 amino acid sequences is the most likely candidate for a transmembrane sequence.

*a) ITLIYFGVMAGVIGTILLIS
b) ITPIYFGPMAGVIGTPLLIS
c) ITEIYFGRMAGVIGTDLLIS
d) ITDIYFGKMAGVIGSELLIS
e) ITKIYFGSMAGVIGKKLLIS

62. All answers are correct EXCEPT:

The following arrangements of membrane associated proteins have been identified:

a) Single pass transmembrane proteins with covalently attached N-linked oligosaccharides facing the extracellular space.
b) Proteins associated with cytosolically oriented domains of multispanning membrane proteins.
c) Proteins associated with the phospholipid bilayer due to covalent lipid modifications.
d) Membrane proteins with covalently attached carbohydrate linked to the membrane by a glycosylphosphatidyl inositol moiety.
*e) Single pass transmembrane proteins with covalently attached N-linked oligosaccharides facing the cytoplasm.

63. All answers are correct EXCEPT:

For N-linked glycosylation in the endoplasmic reticulum:

*a) The transfer of oligosaccharides occurs onto the amido group of glutamine in a secretory glycoprotein.
b) N-linked oligosaccharides are biosynthesized form nucleotide sugar substrates.
c) The lipid dolichol serves as an intermediate in oligosaccharide assembly.
d) The synthesis of the oligosaccharide starts on the cytosolic side of the membrane and continues on the luminal face.
e) The enzyme oligosaccharyl transferase carries out protein glycosylation.

64. All answers are correct EXCEPT:

The sodium pump:

a) is a transmembrane carrier protein
b) pumps Na+ out of the cell
c) pumps K+ into the cell
*d) regulates membrane potential
e) uses energy derived from ATP hydrolysis

65. All answers are correct EXCEPT:

The following are phospholipids:

a) phosphatidyl serine
b) phosphatidyl choline
c) phosphatidyl inositol
d) sphingomyelin
*e) GM1 ganglioside

66. All answers are correct EXCEPT:

The following polar amino acids are uncharged at neutral pH:

a) N
b) Q
c) Y
*d) M
e)