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**UNIVERSITY OF GHANA MEDICAL SCHOOL**
**COLLEGE OF HEALTH SCIENCES**

**BIOC 204: IA #2** **Thursday May 9, 2013; 8:00 – 9:00am**

**ATTEMPT ALL QUESTIONS**

1. What is the correct order of the following steps in protein synthesis?

1. A peptide bond is formed.
2. The small ribosomal subunit is loaded with initiation factors, messenger RNA, and initiation aminoacyl–transfer RNA.
3. The intact ribosome slides forward three bases to read a new codon.
4. The primed small ribosomal subunit binds with the large ribosomal subunit.
5. Elongation factors deliver aminoacyl-tRNA to bind to the A site.

a. 1, 2, 5, 4, 3
b. 2, 3, 4, 5, 1
c. 4, 5, 1, 2, 3
d. 3, 2, 4, 5, 1
e. 2, 4, 5, 1, 3

2. The first 17 nucleotides from an mRNA molecule are

5' GAAUGGCCACUUAGCAA... 3'

Using the genetic code, write out the first 3 amino acids encoded by this sequence during translation:

A. N-Glu-Trp-Pro-C
B. N-Asn-Gly-Pro-C
C. N-Trp-Pro-Leu-C
D. N-Met-Ala-Pro-C
E. N-Met-Ala-Thr-C

3. The peptidyl transferase reaction:

A. is catalyzed by aminoacyl-tRNA synthetase
B. is catalyzed by translocase
C. is catalyzed by the small ribosomal subunit
D. requires the involvement of the protein composition of the ribosomes
E. is catalyzed by the large ribosomal subunit

4. Polycistronic mRNAs are common in prokaryotes, but extremely rare in eukaryotes. What key differences in protein synthesis underlie this observation?

A. Aminoacylation of the tRNAs.
B. Recognition of the start codons during initiation of protein synthesis.
C. Translocation of the ribosomes during protein synthesis.
D. Lack of GTPase translation factors in eukaryotic protein synthesis.
E. Lack of release factors in eukaryotic translation.

5. Respiratory tract infections caused by *Pseudomonas aeruginosa* are associated with secretion of exotoxin A by this organism. This toxin targets the translocation step of protein synthesis in eukaryotes. Which of the following is the most possible target of exotoxin A?

A.eIF-3 B. eEF-1α C. eEF-2 D. eIF-6 E. eIF-5

6. Accumulation of heme in reticulocytes can regulate globin synthesis by indirectly inactivating eIF-2. Which of the following steps is most directly affected by this mechanism?

A. Attachment of spliceosomes to pre-mRNA
B. Attachment of the ribosome to the endoplasmic reticulum
C. Met-tRNA$^{met}$ binding to the P-site
D. Translocation of mRNA on the ribosome
E. Attachment of RNA polymerase II to the promoter.

7. Wobble base pairing occurs between:
A. The first position in the codon and the third position in the anticodon.
B. The first position in the anticodon and the third position in the codon.
C. The second position in the codon and the second position in the anticodon.
D. The first position in the codon and the first position in the anticodon.
E. All of the above.

8. Which feature of the genetic code plays a role in reducing errors in translation and reduces the influence of mutations?
A. The first two nucleotides in codons. B. Its degeneracy C. Its triplet nature

D. Its universality. E. Its non-overlapping

9. Hydrolysis of GTP to GDP provides energy and conformational changes in the process of protein synthesis which require precision both in prokaryotes as well as in eukaryotes. Which of the following GTPase activity results in the positioning of the aminoacyl-tRNA at the A site in prokaryotes other than the P site?
A. IF-1 B. IF-2 C. EF-G D. EF-Tu E. EF-Ts

10. Which of the following tRNA structural features is always involved in interaction with aminoacyl-tRNA synthetases?
A. acceptor stem B. TψC arm C. variable loop
D. anticodon loop E. D arm

11. The ribosome is involved in all of the following EXCEPT
a. peptide bond formation
b. aminoacylation
c. binding of protein factors during elongation
d. binding of aminoacyl tRNA to mRNA
e. binding of mRNA at an initiation codon.

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12. A nasopharyngeal swab obtained from a 4-month-old infant with rhinitis and paroxysmal coughing tested positive upon culture for *Bordetella pertussis*. He was admitted to KBTH for therapy with an antibiotic that inhibits the translocation of peptidyl-tRNA on 70S ribosome. This patient was most likely treated with
A. erythromycin B. Cycloheximide C. rifamycin
D. chloramphenicol E. tetracycline.

13. In a reticulocyte lysate the polynucleotide 5'-AUGCCCCCCCCC-3' directs the synthesis of Met-Pro-Pro-Pro. In the presence of farsomycin, a new antibiotic perfected by Dzidzor Pharmaceuticals, this polymer directs synthesis of Met-Pro only. From this information, which of the following deductions could you make about farsomycin?
A. It prevents formation of the 80S initiation complex, which contains the initiator tRNA and both ribosomal subunits.
B. It inhibits binding of aminoacyl-tRNAs to the A-site in the ribosome.
C. It inactivates peptidyl transferase activity of the large ribosomal subunit.
D. It blocks translocation of peptidyl-tRNA from the A-site to the P-site of the ribosome.
E. It interferes with chain termination and release of the peptide.

14. In a bacteria cell, a mutation in an aminoacyl tRNA synthetase leads to charging of the entire $tRNA^{ser}$ population with alanine. Which of the following describes the result of using these aminoacyl tRNAs for protein synthesis in the cell?
A. The alanyl-$tRNA^{ser}$ will not function in protein synthesis
B. Proteins synthesized using the alanyl-$tRNA^{ser}$ will contain neither alanine nor serine.
C. Proteins synthesized using the alanyl-$tRNA^{ser}$ will contain only alanine where serine would normally occur.
D. Proteins synthesized using the alanyl-$tRNA^{ser}$ will contain only serine where alanine would normally occur.
E. Proteins synthesized using the alanyl-$tRNA^{ser}$ will randomly contain either alanine or serine where serine would normally occur.

15. The unusual property of Taq polymerase that is critical to the PCR is its:
A. ability to use RNA as template
B. thermostability
C. ability to use dNTPs as substrate
D. ability to use ddNTPs as substrate
E. high fidelity.

16. Which of the following is **not** required for a plasmid to be useful in the preparation of recombinant DNA?
A. restriction enzyme polylinker region
B. can accommodate DNA of the appropriate size
C. a gene conferring antibiotic resistance
D. the ability to alternate in the cell between linear and circular forms
E. should be small and easy to handle

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17. If the sequence (using the Sanger's dideoxy method) of an oligonucleotide, reading from the bottom to the top of a sequencing gel is **TGCAAT**, the sequence of the template from which it is synthesized is:
    A. (5') TGCAAT (3')
    B. (3') TGCAAT (5')
    C. (5') ACGTTA (3')
    D. (3') ACGTTA (5')
    E. (5') ACGUUA (3')
18. Two oligonucleotides: 5'-AGGCCTGTTAAGCC-3' as the template and 5'-GGCTTAACA-3' as the primer, plus Taq polymerase are added to a reaction mixture containing the appropriate buffer plus dATP, dGTP, dCTP and dTTP. The bases incorporated into the product of the reaction would have which of the following compositions?
    A. 2C:2T:1G
    B. 2G:2T:1C
    C. 2G:2C:1T
    D. 2A:2T:2C
    E. 4G:4C:3T:3A
19. Restriction fragment length polymorphism may be produced by mutations in the sites for restriction endonucleases. For instance, a single base change in the site for the endonuclease *Sal* I produces the sequence GTGGAC, which can no longer be recognized by the enzyme. The original sequence recognized by *Sal* I was:
    A. GTAGAC
    B. GCGGAC
    C. CTGGAC
    D. GTCGAC
    E. GTGTAC
20. All of the following are properties of restriction endonucleases EXCEPT:
    A. they do not degrade the host cell's DNA because the recognition site is Methylated
    B. they cleave only supercoiled DNA
    C. they recognize specific palindromic sequences in DNA
    D. they cleave both strands of DNA at specific sites
    E. they are produced by bacteria to protect against transformation by foreign DNA

21. The polymerase chain reaction (PCR):
    A. annealing of primers to single-stranded DNA is achieved by heating
    B. primers are usually synthetic oligopeptides
    C. each cycle doubles the amount of DNA in the sample
    D. the DNA polymerase synthesis DNA discontinuously
    E. the polymerase denatures in every cycle of the reaction
22. The most important step in defining the molecular basis for a human disease is to:
    A. carry out a karyotype analysis to find abnormal chromosomes in affected individuals
    B. study relatives of the affected individual to determine the pattern of inheritance of the condition

C. amplify and perform restriction mapping of the gene
D. clone and sequence the gene responsible for the diseased condition
E. isolate the protein mutated in the disease state and prepare monoclonal antibodies.

23. Preparation of recombinant DNA always requires:
A. restriction endonuclease that cut in a staggered fashion.
B. Poly (dT)
C. cDNA
D. DNA ligase
E. Restriction endonucleases that cleave to yield blunt-ended fragments.

24. During initiation of protein synthesis in eukaryotes:
A. eIF-2 is phosphorylated.
B. a complex consisting of mRNA, the 60S ribosomal subunit, and certain initiation factors is formed.
C. methyl-tRNA appears at the A site of the 80S initiation complex
D. eIF-3 and the 40S ribosomal subunit participate in forming a preinitiation complex.
E. eukaryotic releasing factor binds to its stop codon.

25. Requirement for eukaryotic protein synthesis include all of the following EXCEPT:
A. ribosome B. mRNA C. GTP.
D. fMet-tRNA$_i^{Met}$ E. 20 different amino acids in the form of aminoacyl-tRNA.

26. Which of the following is **not** required for a plasmid to be useful in the preparation of recombinant DNA?
A. restriction enzyme polylinker region
B. can accommodate DNA of the appropriate size
C. a gene conferring antibiotic resistance
D. the ability to alternate in the cell between linear and circular forms
E. should be small and easy to handle

27. Scientist studying a common mutation in the LDL receptor gene have inserted the defective gene into fertilized murine ova. The altered ova are implanted in a foster mother and the progeny are used to study the effects of the mutant allele. The mice produced in this procedure would be referred to as:
A. Knockout mice
B. Transgenic mice
C. Knock-in mice
D. Cloned mice
E. Somatic-cell engineered mice

28. Pharmacokinetic variability can be defined as variability:
a. with the target site of drugs
b. with signal transduction after a drug binds a receptor
c. in the amount of drug delivered to a receptor
d. in the extent of adverse effects among patients
e. in response to drugs among humans

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29. A patient who has a defective enzyme (PM) and is not able to metabolize a prodrug could end up with?
    a. toxic effects of the prodrug
    b. sub-therapeutic effect of the prodrug
    c. increased drug efficacy of the prodrug
    d. increased drug potency of the prodrug
    e. decreased potency of the prodrug

30. Omeprazole has been found to be a better candidate for phenotyping which CYP 450 enzyme polymorphism?
    a. CYP2D6
    b. CYP2C19
    c. CYP2C9
    d. CYP1A2
    e. CYP2D16

31. Polymorphism in the gene that codes for CYP2C9 was discovered:
    a. through a bimodal distribution of mephenytoin metabolism in the population
    b. by gene sequencing and detection of several SNPs
    c. by serendipity
    d. during Phase I clinical trials of the drug warfarin
    e. during Phase II clinical trials of the drug warfarin

32. What could be the clinical defect if a patient is given succinylcholine and develops prolonged apnea and paralysis?
    a. the patient has myasthenia gravis
    b. the patient has a defective CYP2D6
    c. the patient is a PM of succinylcholine
    d. the patient has an overexpressed plasma cholinesterase
    e. the patient has a defective N-acetyltransferase enzyme

33. The following are true with respect to the enzyme N-acetyltransferase EXCEPT?
    a. Two NAT genes have been identified
    b. There is greater polymorphism in NAT2 than NAT1
    c. Enzymes from both genes have a capacity to form N-acetylated metabolites
    d. Based on the level of NAT2 enzyme activity, patients can be classified into 2 phenotypes
    e. The slow-acetylator NAT2 phenotype is known to have a high risk of prostate cancer

34. A patient who has mutations in BCHE gene that results in an atypical homozygous plasma cholinesterase enzyme would have a Dibucaine Number ranging between:

a. 80 – 100
b. 0 – 8
c. 30 – 46
d. 8 – 28
e. 48 – 69

35. A patient after taking the drug azathioprine experienced myelosuppression, a likely cause of this is:

a. A defective UDP-glucuronyltransferase
b. A defective N-acetyltransferase
c. An overexpressed UDP-glucuronyltransferase
d. A defective thiopurine S-methyltransferase
e. A defective plasma cholinesterase

36. One disadvantage of phenotyping patients before drugs are administered is that:

a. it involves the ingestion of a model drug which is often obsolete
b. it is expensive
c. it delays the entire therapeutic procedure for a patient
d. it could lead to toxic consequences
e. it does not give any idea about the constitutional and environmental influences on the drug

37. The decreased duodenal expression of ABCB1 increases plasma concentration of the drug digoxin because ABCB1:

a. decreases hepatobiliary excretion of digoxin
b. decreases renal excretion of digoxin
c. decreases intestinal absorption of digoxin
d. increases hepatobiliary excretion of digoxin
e. increases intestinal absorption of digoxin

38. The following are true of ABCC1 and ABCC2 transporters EXCEPT:

a. They are called multidrug resistance-related proteins 1 and 2
b. They play an essential role in transport and excretion of organic cations
c. ABCC1 and ABCC2 have overlapping substrate specificities
d. Both ABCC1 and ABCC2 require co-transport of reduced glutathione
e. ABCC1 is located in basolateral membranes of polarized cells, whereas ABCC2 is located to the apical domain

39. A defect in the function of OCT2 transporter can result in a decreased renal clearance of metformin because:

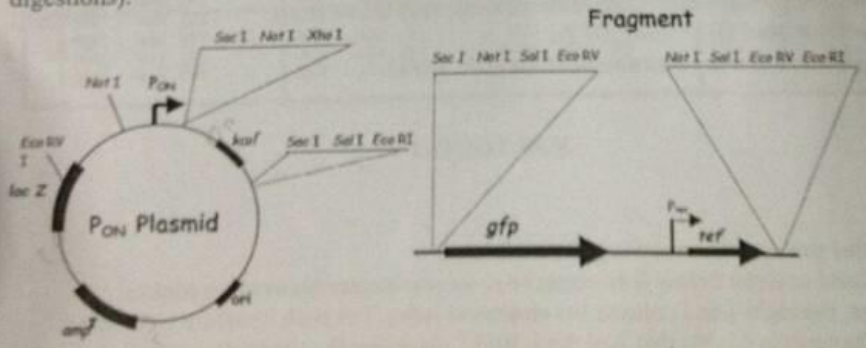
a. tubular secretion of metformin occurs via OCT2
b. tubular reabsorption of metformin occurs via OCT2
c. hepatobiliary excretion of metformin depends on OCT2 transporter
d. intestinal absorption of metformin occurs via OCT2
e. OCT2 transporter plays a vital role in metformin biotransformation

40. The following are potential problems of pharmacogenetics EXCEPT:

a. Patients who have gene variations may be prevented from using certain drugs
b. It will increase health care cost
c. It will be a disincentive for drug companies to make drugs for the "orphan genotype", especially if it is a small population
d. Lack of expertise in the field of genetics among most health care professionals
e. It will reduce the time for drug development of most pharmaceutical companies

Q41- 44.

You wish to make your pet glow in the dark so your first step is to clone gfp gene, (encoding green fluorescent protein), downstream of the "ON" promoter which is always active, expressing downstream genes. You have a vector, the $P_{ON}$ plasmid, and you've isolated a DNA fragment containing a promoter-less gfp gene as well as the $tet^r$ gene conferring resistance to tetracycline. The vector carries the lacZ gene encoding ß-Galactosidase which converts the substrate, X-gal, into a blue colored product. It also carries two antibiotic resistance genes: $kan^r$ and $amp^r$ which allow for growth on kanamycin and ampicillin, respectively. The lacZ, kan, and amp genes have their own promoters (not shown). Assume all restriction sites are unique unless shown otherwise. Assume that **only** similarly cut DNA ends can ligate with each other. You may use more than one enzyme for your cloning. Assume all digestions are complete (no partial digestions).



41. In order to clone gfp in the correct orientation downstream of Pon... , what enzymes would you cut the vector with?

A. EcoR I and EcoR V B. Not I and EcoRI C. Sac I and EcoR V

D. Sal I and EcoR I E. Sac I and EcoR I

42. What two enzymes would you cut the fragment with?

A. EcoR I and EcoR V B. Not I and EcoRI C. Sac I and EcoR V

D. Sal I and EcoR I E. Sac I and EcoR I

43. To select for the desired construct with insert you should plate the ligation on medium with?

A. Ampicillin B. Chloramphenicol C. Kanamycin

D. Tetracycline E. X-Gal

44. Bacteria transformed with original vector would grow on medium with:

A. Ampicillin and chloramphenicol B. Chloramphenicol and kanamycin

C. Kanamycin and ampicillin D. Tetracycline and ampicillin

E. Tetracycline and chloramphenicol

45. Match each of the functions on the left with the appropriate prokaryotic protein at the right.

| | |
|---|---|
| i---B---Binds fMet-tRNA and GTP. | A. IF-1 |
| ii---D---Binds aminoacyl-tRNA and GTP | B. IF-2 |
| iii---B---Hydrolyzes GTP to GDP | C. IF-3 |
| iv---D---Promotes the transfer of peptidyl-tRNA from the A site to the P site. | D. EF-Tu |
| v---C---Inhibits the interaction of the 30S and the 50S subunits. | E. EF-G. |
| vi---E---Displaces GDP from EF-Tu | F. EF-Ts |
| vii---E---Carries out the function of eukaryotic eEF-2 | |

46. **(1 point per correct answer, 10 possible)**.
The left-hand column below lists common macromolecular **Structures and/or Molecules**, the right-hand column list **characteristics**. For each structure (i-x) select ONE characteristic (A-M) that you think BEST describes the structure, and fill the space with the appropriate identifying letter. The characteristics may be used once, or never, but not twice.

| STRUCTURE/ MOLECULE | CHARACTERISTIC |
|---|---|
| i. ____ aminoacyl tRNA synthetase | A. found only in eukaryotes. |
| ii. ____ transfer RNA | B. resembles aminoacyl-tRNA |
| iii. ____ Yarus inhibitor | C. anticodon for Methionine |
| iv. ____ puromycin | D. always binds at the P-site of ribosome during translation |
| v. ____ Shine-Dalgarno sequence | E. contains an anti-codon loop |
| vi. ____ EF-G | F. contains peptidyl transferase activity |
| vii. ____ f-Met-tRNA$_i^{met}$ | G. binds to 3' end of 16S rRNA to position aminoacyl-tRNA at the P-site |
| viii. ____ Inosine | H. has GTPase activity that moves the ribosome a codon at a time |
| ix. ____ 5'-CAU-3' | I. charges tRNAs with amino acids |
| x. ____ 50S ribosome | J. recognizes and binds to termination codon |
| | K. a common anti-codon nucleotide that permits "wobble" in codon rules |
| | L. found in mitochondria and prokaryotes |
| | M. resembles tetrahedral intermediate in peptide bond formation |

The Genetic Code:

| | U | C | A | G | |
|---|---|---|---|---|---|
| U | UUU phe (F) | UCU ser (S) | UAU tyr (Y) | UGU cys (C) | U |
| | UUC phe (F) | UCC ser (S) | UAC tyr (Y) | UGC cys (C) | C |
| | UUA leu (L) | UCA ser (S) | UAA STOP | UGA STOP | A |
| | UUG leu (L) | UCG ser (S) | UAG STOP | UGG trp (W) | G |
| C | CUU leu (L) | CCU pro (P) | CAU his (H) | CGU arg (R) | U |
| | CUC leu (L) | CCC pro (P) | CAC his (H) | CGC arg (R) | C |
| | CUA leu (L) | CCA pro (P) | CAA gln (Q) | CGA arg (R) | A |
| | CUG leu (L) | CCG pro (P) | CAG gln (Q) | CGG arg (R) | G |
| A | AUU ile (I) | ACU thr (T) | AAU asn (N) | AGU ser (S) | U |
| | AUC ile (I) | ACC thr (T) | AAC asn (N) | AGC ser (S) | C |
| | AUA ile (I) | ACA thr (T) | AAA lys (K) | AGA arg (R) | A |
| | AUG met (M) | ACG thr (T) | AAG lys (K) | AGG arg (R) | G |
| G | GUU val (V) | GCU ala (A) | GAU asp (D) | GGU gly (G) | U |
| | GUC val (V) | GCC ala (A) | GAC asp (D) | GGC gly (G) | C |
| | GUA val (V) | GCA ala (A) | GAA glu (E) | GGA gly (G) | A |
| | GUG val (V) | GCG ala (A) | GAG glu (E) | GGG gly (G) | G |

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