

1.     A key component of uridine biosynthesis is
  - A. carbamoyl phosphate
  - B. thiouracil
  - C. GTP
  - D. NADP
  - E. ribose 5-phosphate
  
2.     In man, the chief catabolic product of purines is
  - A. ammonia
  - B. allantoin
  - C. hypoxanthine
  - D. urea
  - E. uric acid
  
3.     Folate analogues are useful anticancer drugs because
  - A. they inhibit thymidine kinase
  - B. they inhibit ribonucleotide reductase by increasing the production of dATP
  - C. they inhibit thymidylate synthase
  - D. they activate purine nucleoside phosphorylase, thereby inhibiting purine salvage
  - E. they inhibit dihydrofolate reductase

4. DNA polymerase I
- A. makes errors later corrected by DNA polymerase II
  - B. makes errors that it corrects after scanning completed sections of daughter DNA strands
  - C. makes errors that it corrects with its 3' exonuclease activity
  - D. makes errors that it corrects with its 5' exonuclease activity
  - E. is errorless
5. Some of the enzymes utilized in DNA replication are (1) DNA polymerase III, (2) unwinding proteins, (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. 4,3,1,2,5
  - B. 2,3,4,1,5
  - C. 4,2,1,5,3
  - D. 4,2,1,3,5
  - E. 2,4,1,3,5
6. Xeroderma pigmentosum is a genetic disease characterized by
- A. loss of melanin pigment in the skin
  - B. hyper-proliferation of dermal fibroblasts
  - C. a defect in DNA excision repair
  - D. a deficiency of DNA polymerase  $\alpha$
  - E. a defect in mismatch repair

7. If the following piece of RNA were transcribed by reverse transcriptase, what would be the resultant sequence?

AGCGG

A. TCGCC

B. CCGCT

C. UCGCC

D. CCGCU

E. TGGCT

8. For DNA-dependent RNA synthesis

A. an RNA template and a DNA primer are required

B. a DNA template and an RNA primer are required

C. a DNA template and a DNA primer are required

D. a DNA template and no primer are required

E. an RNA primer and no template are required

9. Which statement is true?

A. The capped 5' end of eucaryotic mRNA consists of poly (A) sequences

B. 28S, 18S and 5.8S rRNAs of eucaryotes are necessarily formed in equal amounts

C. all mature eucaryotic mRNAs have poly (A) tails

D. introns are removed in the cytoplasm

E. none of the above

10. Which of the following mutations would most likely cause the greatest change in the gene product?

- A. substitution of adenine for cytosine
- B. substitution of cytosine for guanine
- C. substitution of adenine for thymine
- D. insertion of one nucleotide
- E. deletion of three nucleotides

11. A feature of the lac operon in bacteria is that

- A. the operator must be to the right (downstream) of the promoter
- B. the operator must be to the left (upstream) of the promoter
- C. basal constitutive synthesis is required
- D. the *i* gene must be linked to the structural genes
- E. it is not positively regulated

12. A mutation in the *i* gene of the lac operon results in the operon being non-inducible, i.e. off even in the presence of lactose. This results because

- 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

13. *E. coli* cells grown on a mixture of glucose and lactose selectively use glucose because

- A. CAP is not present when glucose is available
- B. glucose lowers cAMP levels, which reduces the level of the cAMP-CAP complex
- C. lactose cannot enter the cells, owing to glucose-induced inhibition of the lactose transporter
- D. the synthesis of the lac repressor is elevated in the presence of glucose
- E. lactose cannot be converted to the true inducer, allolactose, in the presence of glucose

14. A soluble eucaryotic protein has a single signal directing it to the rough ER. What is its final destination?

- A. outside the cell
- B. plasma membrane
- C. cytosol
- D. ER, i.e. ER resident
- E. nucleus

15. Modification of mRNA so that a signal sequence is added to the amino terminus of a cytosolic protein results in

- A. localization of the protein in lysosomes
- B. proteolytic cleavage in the cytosol
- C. transport into the ER
- D. cytosolic localization of the protein
- E. signal recognition particle synthesis

Choose the single best answer for the following questions.

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16. That the Golgi complex plays a major role in directing protein transport in the cell is indicated by

- A. the close proximity of many small transport vesicles to the Golgi complex
- B. the knowledge of the cause of Tay-Sachs disease
- C. the increase in size of Golgi complexes in cells that are active in secretion
- D. the knowledge of the cause of I-cell disease
- E. none of the above

17. Which of the following statements about the bacteriophage lambda is FALSE?

- A. it forms “plaques” of lysed cells on a lawn of bacteria on a culture plate
- B. it encodes all the proteins required for its integration into the bacterial chromosome
- C. some of its derivatives are commonly used to construct cDNA libraries
- D. it requires the presence of specific sites to integrate into the bacterial chromosome
- E. it normally does not carry an antibiotic resistance gene

18. We have transformed a haploid yeast strain carrying a defective allele (due to a point mutation) of the nuclear URA3 gene (required for uracil synthesis) with a linear fragment of DNA containing the wild type allele and 100 nucleotides of each of the two flanking regions. The transformant has regained ura3 activity. Which of the following processes is most likely to be responsible for the regained activity?

- A. incorporation of the URA3 gene in the mitochondrial genome by site specific recombination
- B. circularization of the exogenous URA3 gene to form an autonomously replicating plasmid
- C. homologous recombination of the exogenous URA3 gene with the defective chromosomal copy
- D. integration of the exogenous URA3 gene at the site of the chromosomal allele with formation of direct repeats
- E. synthesis of mRNA directly from the linear fragment without integration into the chromosome

19. Which of the following statements about transposons is true?

- A. they can always convert into retroviruses and start an infectious cycle
- B. they do not undergo homologous recombination under any circumstances
- C. they carry one or more genes that confer antibiotic resistance
- D. they can encode the enzymes that assists the transposon duplication
- E. they always produce insertional inactivation of enhancer sequences

Choose the single best answer for the following questions.

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20. We have purified yeast adenosine deaminase and used Edman degradation to sequence its first 6 amino acids. Furthermore we have raised antibodies against the purified protein. Which of the following experimental approaches would be the most useful to clone the yeast gene for adenosine deaminase?

A. to use the polymerase chain reaction and a degenerate oligonucleotide, obtained by reverse translation of the adenosine deaminase amino acid sequence, as a primer to amplify the gene

B. to make a yeast genomic library in a non-expression vector, transform *E. coli* and assay individual transformants for adenosine deaminase activity

C. to make a yeast genomic library in a non-expression vector and screen *E. coli* transformants with the antibody to adenosine deaminase

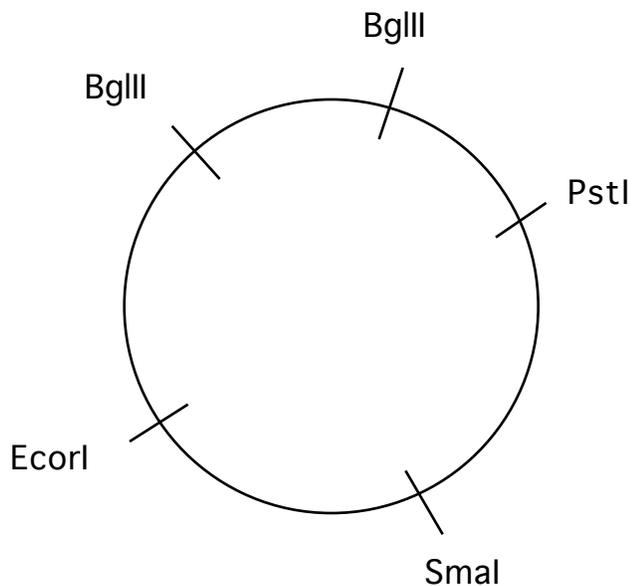
D. to make a yeast genomic library in a non-expression vector and screen *E. coli* transformants with a degenerate oligonucleotide probe obtained by reverse translation of adenosine deaminase amino acid sequence

E. none of the above. Genes can only be cloned using cDNA libraries in expression vectors

Choose the single best answer for the following questions.

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21. A plasmid has restriction endonuclease sites organized in the following circular order (distances between restriction site are not represented in correct scale) :



A digest with both BglIII and EcoRI together produces three visible bands of 4.2, 1.8 and 1.2 kb

A digest with both PstI and EcoRI together produces one visible band of 3.6 kb.

What would be the product of a digest adding together PstI and SmaI?

- A. two bands of 4.2 and 1.8 kb
- B. two bands of 5.4 and 1.8 kb
- C. one band of 1.8 kb
- D. one band of 5.4 kb
- E. the plasmid would not be cut and only one band of 7.2 kb would be visible

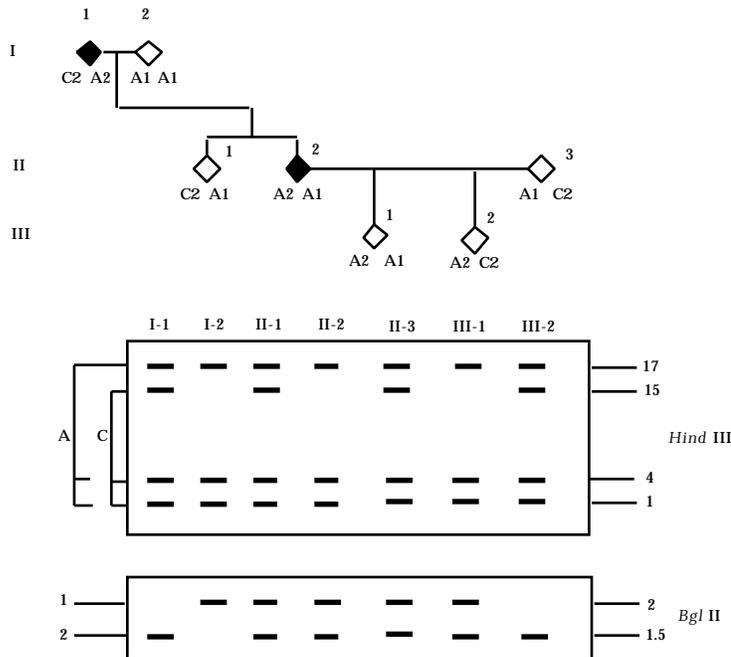
Choose the single best answer for the following questions.

10

22. Which of the following statements about site directed mutagenesis is correct?

- A. it can be done only with bacterial proteins
- B. it always requires the synthesis of at least two oligonucleotides
- C. it always requires amplification of DNA using the polymerase chain reaction
- D. it requires cloning of the gene that will be mutagenized into an expression vector
- E. none of the above

23. The youngest members (III-1 and III-2) of a family affected by a late onset disease ask about their chances of developing the disease late in their life and of transferring it to their progeny. The disease is linked to two RFLP's as shown in the figure below. Older individuals who are already affected are indicated by a full symbol:



Which of the following predictions is correct?

- A. Individual III-1 will develop the disease but will not pass it to the progeny
- B. Unfortunately both III-1 and III-2 will develop the disease and have 50% probability of transferring it to the progeny
- C. Both III-1 and III-2 (and their progeny) will stay healthy
- D. Only individual III-2 will develop the disease
- E. Analysis of the RFLP's cannot predict if the two youngest individuals will develop the disease

24. Alu sequences are
- A. DNA sequences necessary for chromosome replication
  - B. Small retroviral sequences
  - C. Highly repetitive sequences of ~300bp dispersed throughout the human genome
  - D. Alternate length units sometimes used in linkage analysis
  - E. DNA sequences homologous to ribosomal RNA
25. Which of the following statements about the mitochondrial genome is incorrect?
- A. it encodes both the tRNAs and rRNAs necessary for mitochondrial protein synthesis
  - B. it uses a slightly different genetic code from the nuclear genome
  - C. it contains U instead of T
  - D. it codes only for a small subset of mitochondrial proteins
  - E. it is a circular genome
26. Pseudogenes are
- A. genes that require splicing of the original transcript in order to generate the mature mRNA
  - B. genes no longer transcribed, which originated by duplication of a functional gene and progressive accumulation of mutations
  - C. genes that encode an inactive protein due to a single point mutation
  - D. regions of DNA that do not contain exons
  - E. none of the above

27. The promoter region of a gene is
- A. the site where histones bind to form a nucleosome
  - B. a relic of ancestral functions that have disappeared from eukaryotic genes
  - C. the site where ribosomes binds after the gene has been transcribed into mRNA
  - D. the site where the complex of RNA polymerase and the basic transcription factors assembles to begin transcription
  - E. the site where DNA replication starts when a gene is amplified in order to effectively increase its dosage in the genome
28. Which of the following statements about the regulation of gene expression is incorrect?
- A. some DNA binding proteins may regulate the activation of transcription at a promoter site, by binding to enhancer or silencer regions distant from the promoter
  - B. transcriptionally active regions of chromatin are usually hypersensitive to digestion with DNaseI
  - C. transcriptionally inactive regions of chromatin show decreased levels of methylation
  - D. post translational modifications of histones may affect the level of expression of certain genes
  - E. homeo-domains are structural domains of DNA binding proteins that regulate the development of segmented embryos

29. Three nuclear and one mitochondrial RNA polymerases are known in eukaryotic cells. Only one of the following statements about them is correct:

- A. They all bind to a Shine-Dalgarno box in the promoter region
- B. They recognize genes according to their size (e.g. Pol I the biggest genes, Pol II smaller genes, Pol III only the smallest genes, the mitochondrial polymerase only circular genes)
- C. Pol III is required for the synthesis of tRNAs and 5S RNAs
- D. Pol II is required for the synthesis of tRNAs and 5S RNA's
- E. Transcription by Pol II is stimulated only by enhancers located upstream of the promoter site

30. Which of the following statements about basal (also called general) transcription factors is correct?

- A. they are small molecular weight compounds (e.g. ATP, adenine, guanine, etc.) necessary for the synthesis of a messenger RNA
- B. they bind to enhancer sequences to increase the level of transcription
- C. they form a complex with the RNA polymerase at the promoter site
- D. they may bind to both enhancers or silencers if these elements are not methylated
- E. they can catalyze RNA synthesis by themselves in association with ATP hydrolysis

31. The increase in the level of transcription of a gene effected by enhancer sequences is explained by the fact that

- A. they encode general transcription factors
- B. they bind proteins that interact with the complex of RNA polymerase and basal transcription factors at the promoter site
- C. they undergo homologous recombination with the promoter sequences
- D. they sequester negative regulators of transcription away from the promoter site
- E. they induce amplification of a certain gene by selective duplication, thus increasing the gene dosage in the genome

32. Which of the following statements regarding the duplication of the chromosome ends by a telomerase is incorrect?

- A. the telomerase uses a mRNA as template to extend the 3'-end
- B. a DNA polymerase completes the synthesis of the 5'-end using as primer the 3' extension formed by the telomerase
- C. the telomerase contains itself a RNA molecule which is used to recognize and to extend the 3'-end of the chromosome
- D. in the absence of telomerase the synthesis of the 5'-end of the chromosome is incomplete because there is no primer for the DNA polymerase at the end of the chromosome
- E. a nuclease is required to expose the 5' and 3' ends of the chromosome after the action of the telomerase

33. Which of the following statements regarding the Polio virus is incorrect?
- A. it contains a single strand RNA with a poly(A) tail
  - B. it encodes all the proteins necessary for its life cycle
  - C. it needs a single strand DNA intermediate to replicate
  - D. it is replicated in the cytoplasm of the infected neural cells
  - E. it produces the death of the infected cells
34. Which of the following statements about retroviruses is correct?
- A. the virions contain a linear molecule of double strand DNA
  - B. their genome minimally encodes a reverse transcriptase, a capsid protein and an envelope protein
  - C. they use cellular enzymes in order to integrate their genome into the host genome
  - D. they always carry oncogenes responsible for the appearance of tumors in the host
  - E. they are not infectious because they integrate in the host genome instead of actively replicating
35. The long terminal repeats of retroviruses serve one of the following functions:
- A. they encode a reverse transcriptase
  - B. they contain sequences (like enhancers and promoters) necessary to transcribe the viral genome
  - C. they code for proteins that provide resistance to antibiotics
  - D. they anchor the viral genome to the mitotic spindle such that it can segregate to the daughter cells during mitosis
  - E. they encode a protease required for processing the product of the large viral gene pol

36. Oncogenes may code for proteins that can be characterized as
- A. kinases
  - B. membrane receptors
  - C. DNA binding proteins
  - D. growth factors
  - E. any one of the above
37. Which of the following statements about viral oncogenic transformation is incorrect?
- A. oncogenic viruses can increase the expression of cellular proto-oncogenes
  - B. oncogenic viruses can induce point mutations in cellular proto-oncogene transforming them into oncogenes
  - C. oncogenic viruses can promote the synthesis of growth factors, thus stimulating uncontrolled cell replication
  - D. oncogenic viruses can carry mutant forms of a cellular proto-oncogenes
  - E. oncogenic viruses can inhibit the activity of cellular anti-oncogenic factors
38. The progression of normal colon epithelial cells into cancer cells is most often due to
- A. a vegetarian diet
  - B. inheritance of viral oncogenes transmitted vertically as integrated retroviruses
  - C. mutations in one or more tumor suppressor genes
  - D. defects in the RB gene
  - E. none of the above

39. The nucleotide sequence of chromosome 7 in the vicinity of the cystic fibrosis locus still presents some gaps. What is the most probable cause for the missing sequences?

- A. the missing sequences are highly methylated and therefore cannot be sequenced
- B. the project was abandoned after the first reports were published
- C. no cDNA or genomic clones of the missing regions were found that would overlap with the clones already sequenced
- D. there are no restriction enzymes recognition sites in the missing regions
- E. the missing regions encode rRNAs

40. Which of the following steps is usually not included in the preparation of a cDNA library?

- A. purify mRNA's using a poly-T affinity column
- B. end label with  $^{32}\text{P}$  the 5'-OH of a poly(T) oligonucleotide to be used as primer for the synthesis of the complimentary strand by a reverse transcriptase
- C. digest the original RNA strand with Rnase H
- D. synthesize the second DNA strand with DNA polymerase
- E. add a restriction endonuclease linker to the dsDNA for cloning into a suitable vector

41. A sample of 2mg of bacterial genomic DNA is digested for 30 min. with the restriction endonuclease PstI. The DNA fragments are separated according to size on an agarose gel to determine if the digest was complete. The simplest way to visualize the fragments is

- A. to expose the gel to UV light
- B. to transfer the DNA fragment to a nitrocellulose filter (Southern blot) and then to expose the filter to UV light
- C. to transfer the DNA fragment to a nitrocellulose filter and then to hybridize the DNA bands to a radioactive highly degenerate oligonucleotide probe that will bind randomly to almost any DNA fragment
- D. to stain the gel with ethidium bromide and then to expose it to UV light
- E. It can't be done. We should have used a poly-acrylamide gel if we intended to visualize the DNA bands

42. The gene for the yeast adenosine deaminase was cloned into an E. coli expression vector carrying the ampicillin resistance gene. Analysis of the extract of E coli cells at the end of the induction period reveals that one protein is present at very high level but which has a molecular weight twice as large as that of yeast adenosine deaminase. Several tests can be done to determine why a protein with properties different from the expected ones is being expressed. Which of the following tests is likely not to be useful?

- A. determine the nucleotide sequence of the expressing plasmid at the boundary between the adenosine deaminase gene and the original vector
- B. see if antibodies against yeast adenosine deaminase recognize the protein expressed in E. coli
- C. determine if the expressed protein has adenosine deaminase activity
- D. use an antibiotic other than ampicillin to grow the E. coli cells
- E. use a strain of E coli deficient in RecA dependent recombination

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

43. After one generation in  $^{14}\text{N}$  media, its DNA was characterized as
44. After two generations in  $^{14}\text{N}$  media, its DNA was characterized as
- A. heavy
  - B. light
  - C. intermediate
  - D. both heavy and intermediate
  - E. both light and intermediate
45. Inhibits binding of amino acyl-tRNAs to bacterial ribosomes
46. Binds to the 30S ribosomal subunit
47. Inhibits translocation in procaryotes
- A. streptomycin
  - B. tetracycline
  - C. erythromycin
  - D. cycloheximide
  - E. chloramphenicol