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國立清華大學 112 學年度碩士班考試入學試題

系所班組別：生命科學暨醫學院
甲組(生物與醫學科學組)

科目代碼：0404

考試科目：分子生物學

—作答注意事項—

1. 請核對答案卷(卡)上之准考證號、科目名稱是否正確。
2. 考試開始後，請於作答前先翻閱整份試題，是否有污損或試題印刷不清，得舉手請監試人員處理，但不得要求解釋題意。
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6. 其他應考規則、違規處理及扣分方式，請自行詳閱准考證明上「國立清華大學試場規則及違規處理辦法」，無法因本試題封面作答注意事項中未列明而稱未知悉。

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*請在【答案卡】作答

單選題（共 35 題，每題 2 分，合計 70 分）

1. Restriction endonucleases are commonly used in DNA cloning. Which of the following is not true?

- A. Restriction endonucleases are main components of the bacterial restriction-modification (R-M) system.
- B. The normal function of the R-M system is to degrade DNA from invading phages.
- C. In a R-M system, phosphatases are frequently used to protect the same DNA sequences of bacteria from digestion by the restriction endonucleases.
- D. The most useful R-M systems in DNA cloning are the type II system, and the restriction activities do not need ATP as a cofactor.
- E. In the type III R-M systems, one enzyme contains two different subunits, one for DNA recognition and modification, and another for DNA cleavage.

2. Which products are made by eukaryotic RNA polymerase III?

- A. 28S and 18S rRNA
- B. 7SL RNA and 5S rRNA
- C. mRNA and tRNA
- D. tRNA and 5.8SRNA
- E. snRNA and U6snRNA

3. What is the possible outcome of a mutant cell line with reduced levels of TFIIS in transcription carried out by eukaryotic RNA polymerase II?

- A. The start site and direction of transcription will be changed.
- B. The C-terminal domain (CTD) of RNA polymerase II will not be phosphorylated.
- C. The serine residues of histones will not be modified by acetylation.
- D. The activity of transcription proofreading will be impaired.
- E. The TFIIA/TFIID/TFIIB complex will dissociate.

4. Which of the following related to eukaryotic ribosomal genes is not true?

- A. There are no repetitive sequences.
- B. They have a different base composition compared to other nuclear genes.
- C. They have a higher GC content compared to other nuclear genes.
- D. They are transcribed by RNA polymerases I and III.
- E. They are found in the nucleolus.

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5. During the activation of a eukaryotic RNA polymerase II (pol II)-dependent promoter, which of the following is the correct order of adding general transcription factors to the initiation complex?

- A. TFIIA+TFIID, TFIIE, TFIIB, TFIIF + pol II, TFIH
- B. TFIIA+TFIID, TFIIB, TFIH, TFIIF + pol II, TFIIE
- C. TFIIF + pol II, TFIIA+TFIID, TFIH, TFIIB, TFIIE
- D. TFIIA+TFIID, TFIH, TFIIB, TFIIF + pol II, TFIIE
- E. TFIIA+TFIID, TFIIB, TFIIF + pol II, TFIIE, TFIH

6. Which is not true for the following experimental techniques?

- A. DNase I footprinting assay is used to locate the specific protein-binding sites on DNA.
- B. In yeast, a temperature sensitive (*ts*) mutant can exhibit the mutant phenotype at a non-permissive temperature.
- C. Yeast one-hybrid analysis is useful for in vivo detection of physical interaction between two proteins.
- D. Gel mobility shift assay can be used for determining the ability of a protein to bind to a specific DNA fragment, and measuring the DNA binding affinity of the protein.
- E. The far-western blot analysis can be used to determine receptor-ligand interactions, and screen libraries of interacting proteins.

7. Which of the following statement related to TATA-binding protein (TBP) and its associated factors is true?

- A. TBP is not required for the TATA-less promoter.
- B. TBP-associated factors are universally required for transcription of all RNA polymerase II-activated genes
- C. TBP is a transcription factor only required for RNA polymerase I and II regulated genes
- D. For RNA polymerase II, TAF1 is responsible for recognizing Inr and DPE in the fly *hsp70* gene and its homologue in yeast contains histone acetyltransferase activity
- E. TBP can bind to the major groove of the TATA box.

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8. Sigma factors in *E. coli*. Which of the following descriptions is not correct?

- A. $\sigma 70$ (RpoD) is the primary sigma factor.
- B. $\sigma 38$ (RpoS) is the starvation/stationary phase sigma factor.
- C. $\sigma 54$ (RpoN) is the nitrogen-limitation sigma factor.
- D. $\sigma 28$ (FliA) is the extracytoplasmic/extreme heat stress sigma factor.
- E. $\sigma 32$ (RpoH) is the heat shock sigma factor.

9. Micro RNA. Which of the following descriptions is not correct?

- A. The precursor RNA molecules ("primary miRNA", pri-miRNA) fold into stem-loop structures.
- B. The double-stranded stem region of pri-miRNA is cut by Dicer to generate pre-miRNA.
- C. The pre-miRNA exits the nucleus and is finally trimmed by Dicer to form miRNA.
- D. The miRNA is bound by a protein complex, miRISC.
- E. One strand of the miRNA binds to the target mRNA.

10. Heterochromatin and euchromatin. Which of the following descriptions is not correct?

- A. Heterochromatin is usually located near the nuclear envelope of the nucleus of prokaryotes.
- B. Euchromatin is usually located in the center of the nucleus of eukaryotes.
- C. The transcription is very low near the nuclear envelope.
- D. Heterochromatin is transcriptionally inactive.
- E. The center of a nucleus has high levels of transcription taking place.

11. Nucleosome core. Which of the following histone is not a core histone?

- A. H1
- B. H2A
- C. H2B
- D. H3
- E. H4

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12. Antisense RNA and mRNA. Which of the following descriptions is not correct?

- A. mRNA is made using the non-coding strand of DNA as a template.
- B. mRNA is sense RNA.
- C. If RNA is made using the coding strand as a template, it is known as antisense RNA.
- D. The sense and antisense strands of RNA can base pair.
- E. Antisense RNA will base pair with the mRNA and enhance the translation.

13. Structure of tRNA. Which of the following descriptions is not correct?

- A. A typical tRNA has 4 base-paired stems and 3 loops.
- B. One stem is the 3' and 5' acceptor stem.
- C. One loop is the T- (or T ϕ C) loop.
- D. One loop is the D-loop.
- E. One loop is the codon loop.

14. The functions of translation initiation factor IF3 in bacteria. Which of the following descriptions is not correct?

- A. IF3 binds to free 50S subunits.
- B. IF3 prevents the 30S subunit from associating with 50S subunit. As an anti-association factor that causes a 30S subunit to remain in the pool of free subunits.
- C. IF3 controls the ability of 30S subunits to bind to mRNA. 30S must have IF3 to form initiation complexes with mRNA.
- D. IF3 must be released from the 30S-mRNA complex in order for the 50S to join.
- E. IF3 checks the accuracy of recognition of the first aminoacyl-tRNA and helps to direct it to the P site of the 30S subunit.

15. All chromatin remodeling complexes require a subunit for _____ to reorganize the nucleosomes.

- A. histone binding
- B. ATPase
- C. repressor binding
- D. DNA binding
- E. transcription factor binding

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*請在【答案卡】作答

16. When working identifying factor involved in rRNA transcription, which of the following would you expect to bind to a chromatography column made of a resin conjugated to UBF1?
- A. TFIIB
 - B. TFIIE
 - C. TFIIH
 - D. Sp1
 - E. SL1
17. What component is not included in an operon?
- A. operator
 - B. promoter
 - C. intron
 - D. both operator and promoter
 - E. both promoter and intron
18. What effects could extra acetyltransferase cause to an in vitro transcription assay?
- A. There cause a complete repression of transcription.
 - B. It will cause a tighter association of histone with DNA, resulting in reduced transcription.
 - C. It will have no effect on the interaction of DNA with histones.
 - D. It will loosen the interaction of histone with DNA.
 - E. None of the choices are correct.
19. Abnormally oligomerized yeast protein Sup35 would lead to:
- A. failure of translation to terminate.
 - B. abnormal chromosome inactivation by heterochromatin formation.
 - C. abnormal imprinting of some genes.
 - D. abnormal cytoskeletal structures.
 - E. failure of chromosomes to condense during mitosis.

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*請在【答案卡】作答

20. Histone variants are closely related to one of the core histones. They can assemble into nucleosomes, the roles of histone variants are:

- A. that are present during double-strand break repair.
- B. that are disrupted during active transcription.
- C. in centromeric regions.
- D. that compact chromatin in sperm cells.
- E. All of these are correct.

21. The effect a remodeling complex in transcription activation is:

- A. histone deacetylation.
- B. recruiting an repressor to a promoter.
- C. DNA methylation.
- D. displacing nucleosomes from a promoter.
- E. breaking apart nucleosomes.

22. Which of the following is notorious for causing covalent bonding of adjacent thymine residues in DNA?

- A. X-rays
- B. infrared radiation
- C. nucleotide analogs
- D. ultraviolet radiation
- E. microwave

23. The uptake of naked DNA from the environment is called _____.

- A. transformation
- B. transduction
- C. transfection
- D. translocation
- E. conjugation

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*請在【答案卡】作答

24. Regarding molecular cloning using restriction enzyme and ligase. Which of the following statement is correct?

- A. Blunt end is clean and thus easier to be ligated.
- B. Two sticky ends with complementary overhangs can be perfectly ligated and a restriction enzyme recognition site must be restored.
- C. Restriction enzyme more efficiently cuts at the ends of DNA fragments.
- D. Phosphatase treatment of both digested vector and digested insert reduces self-ligation so that correct ligation is enhanced.
- E. Ligase also mediates joining of sticky ends by catalyzing the formation of phosphodiester bonds.

25. DNase I protection assays or DNA footprinting is useful for _____.

- A. determining the start of transcription
- B. preventing contamination of RNA in primer extension samples
- C. determining the location of a DNA binding sequence
- D. monitoring gene expression
- E. determining DNA-protein interactions

26. A single nucleotide deletion occurred in a gene. The change is indicated below. What is the consequence of the mutation?

..... AGT CGA TTC GTT AGC CTA → AGT CGA TTG TTA GCC TA.....

- A. The mutation occurs in the third position of a codon which results in a silent mutation due to the Wobble effect.
- B. It results in premature termination of translation so a truncated polypeptide will be produced.
- C. A longer polypeptide will be made but the protein might still be functional.
- D. It leads to frameshift so the downstream amino acid sequence will alter and the protein is unlikely to be functional.
- E. It changes the single amino acid, which may or may not cause a problem.

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*請在【答案卡】作答

27. Alu is the most abundant transposon in human body. Which of the following statement is correct?

- A. It is a replicative DNA transposon.
- B. It contains LTRs
- C. It contains a poly-A tail
- D. It contains a reverse transcriptase gene
- E. It is autonomous for transposition

28. When doing PCR to amplify a DNA fragment using mouse genomic DNA as the template, which of the following primer pair is the best choice?

Forward primers:

- i. ACGTCTGCCAGGCTG, 15bp, GC content=67%, Tm=57°C
- ii. AGCTTGGGTTAATGCCAGGC, 20bp, GC content=55%, Tm=60°C
- iii. AGCCCCATTGCTATAAGGGGAG, 22bp, GC content=55%, Tm=59°C

Reverse primers:

- x. CCGTGCCAGGCAGACACGATATAA, 24bp, GC content=54%, Tm=61°C
- y. AAGGCGTCAAAGTCTAAAGCG, 21bp, GC content=48%, Tm=59°C

- A. i and x
- B. ii and x
- C. ii and y
- D. iii and x
- E. iii and y

29. The Shine-Dalgarno (SD) sequence is a ribosomal binding site in bacteria, generally contain consensus sequences as

- A. 5'-UCCUCC-3'
- B. 5'-AGGAGG-3'
- C. 5'-UAAUAA-3'
- D. 5'-GCCACC-3'
- E. 5'-ACCACC-3'

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*請在【答案卡】作答

30. Which of the following statement is **NOT** true for protein splicing?

- A. Intein is the internal segment removed from the precursor protein
- B. The splicing junction of the precursor protein is mainly a cysteine or a serine
- C. Protein splicing is sometimes associated with pre-mRNA splicing
- D. The protein splicing reactions do not require exogenous cofactors
- E. The protein splicing reaction require energy sources such as ATP

31. Which of the strategy is **NOT** used by viral genome replication with linear DNA genome?

- A. Rolling circle replication
- B. Concatemerization
- C. Create a palindromic or hairpin loop structure at the end of genome
- D. Pairing with host telomere repeat sequences
- E. Express a specific terminal protein to serve as a primer

32. General stability of messenger RNA molecules is **NOT** improved by

- A. Adding AG-rich elements in the sequence
- B. Extending the poly-A tail sequences
- C. Use of stable mRNA cap structure
- D. Use of modified nucleoside such as pseudo-uridine
- E. Addition of mRNA stabilizing agents such as actinomycin D

33. South-Western blotting is an approach used for

- A. Detect a specific DNA by a DNA probe
- B. Detect a specific RNA by a DNA probe
- C. Detect a specific protein by an antibody
- D. Detect a specific DNA by an antibody
- E. Detect a specific protein by a DNA probe

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34. Which of the following promoter is commonly used for in vitro transcription of small RNA molecules, such as microRNAs and siRNAs?

- A. T7
- B. T3
- C. SP6
- D. U6
- E. CMV

35. Which of the following mechanism can change expression level of a specific gene with hereditary effect but maintained the genome integrity of the cell?

- A. Epigenetic modulation
- B. Small interfering RNA
- C. MicroRNA
- D. Cas9-based gene editing
- E. Lentiviral transduction

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問答題（共 5 題，每題 6 分，合計 30 分）

1. For RNA polymerase II, the general transcription factor TFIIA not only can (1) stabilize TBP-TATA box binding, but also (2) stimulate TFIID-promoter binding. Please explain this mechanism of anti-repression.
2. Small subunits of the ribosome scan for translation initiation sites on eukaryotic mRNA. Column I lists initiation-related factors. Match each one in column I to the complex which it belongs to in Column II.

Column I

eIF4G, eIF4A, eIF4B, eIF1, eIF1A, eIF3

Column II

A. Cap binding complex

B. 43S pre-initiation complex

3. Please give explanations about how the following examples lead to epigenetics:
a. DNA methylation, b. HP1 and c. Prions.
4. How does DNA mismatch repair (MMR) machinery in bacteria determine which base in a mismatched base pair needs to be corrected?
5. David would like to design an expression construct that allows expressions of green fluorescent protein (GFP) and coronavirus spike (S) protein from one single RNA in 293T cells. Please draw a map of this construct and provide the rationale of the construct design, e.g., explain the function of each critical component on this map.