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並不得書寫、畫記、作答。


國立清華大學 109 學年度碩士班考試入學試題

系所班組別：生命科學院
丁組(醫學生物科技學程)

科目代碼：0704

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. 作答中如有發現試題印刷不清，得舉手請監試人員處理，但不得要求解釋題意。
3. 考生限在答案卷上標記「由此開始作答」區內作答，且不可書寫姓名、准考證號或與作答無關之其他文字或符號。
4. 答案卷用盡不得要求加頁。
5. 答案卷可用任何書寫工具作答，惟為方便閱卷辨識，請儘量使用藍色或黑色書寫；答案卡限用 2B 鉛筆畫記；如畫記不清(含未依範例畫記)致光學閱讀機無法辨識答案者，其後果一律由考生自行負責。
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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系所班組別：生命科學院甲組、丁組

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共 10 頁，第 1 頁 *請在【答案卡】作答

I. 選擇題- multiple choice questions and select **One or More Answer Choices** according to the specific question directions (80 points, 2 points for each).

Autophagy is a highly conserved catabolic process that mediates lysosomal or vacuolar degradation of cytoplasmic constituents and organelles in eukaryotes. Its activity can be regulated at transcriptional, post-transcriptional, and post-translational levels.

1. Which of the following components or events **are** involved in transcriptional gene regulation? (2 points)

- (A) RNA Polymerase II
- (B) Transcription factors
- (C) Enhancer region
- (D) Splicing
- (E) Polyadenylation

2. Which of the following components or events **are** involved in post-transcriptional gene regulation? (2 points)

- (A) Trans-regulatory elements
- (B) Cis-regulatory elements
- (C) Terminator
- (D) Capping
- (E) RNA editing

3. Which of the following components or events **are** involved in post-translational gene regulation? (2 points)

- (A) Histone acetylation and methylation
- (B) DNA methylation
- (C) Ubiquitin-mediated proteasomal degradation
- (D) Protein lipidation
- (E) MicroRNA-mediated gene downregulation

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共 10 頁，第 2 頁 *請在【答案卡】作答

Transgene expression in plants is highly variable. There is also no guarantee that primary transformants showing strong transgene expression will give rise to progeny with the same characteristics. Agrobacterium-mediated T-DNA transformation for nuclear delivery of transposable Ds elements are widely used as insertional mutagenesis and gene isolation tools in plants.

4. Which of the following statements about T-DNA are correct? (2 points)
- (A) The T-DNA is the transferred DNA of the tumor-inducing (Ti) plasmid.
 - (B) The T-DNA is bordered by 2K base-pair repeats on each end
 - (C) Transfer is initiated at the right border and terminated at the left border and requires the *vir* genes of the Ti plasmid.
 - (D) Agrobacterium *vir* genes expression results in generation of a mobile double-stranded T-DNA to be incorporated into the plant genome.
 - (E) Although T-DNA integration does appear to be random, proteins involved in chromatin modification likely play some role in integration.
5. Which of the following statements about transposon are correct? (2 points)
- (A) Transposon is a DNA sequence that can irreversibly change its position within a genome.
 - (B) Transposition often results in duplication of the same genetic material.
 - (C) The reverse transcription step of retrotransposon is catalyzed by a reverse transcriptase, which is often encoded by the transposon itself.
 - (D) Dissociation elements (Ds) is an example of an autonomous transposon, and activator element (Ac) is an example of a non-autonomous transposon. Without Ds, Ac is not able to transpose.
 - (E) Transposition of Ds was sometimes accompanied by major chromosomal rearrangements including deletions, duplications, inversions, reciprocal translocations.

Scientists have been developing methods to investigate the interaction between biomolecules from a small-scale atomic level to a large-scale interactome level, which includes genetic, biochemical, biophysical, and computational approaches.

6. Which of the following methods are biochemical technologies for testing protein-protein interactions? (2 points)
- (A) Proximity ligation assay
 - (B) Coimmunoprecipitation
 - (C) Pulldown assay
 - (D) Cross-linking
 - (E) Isothermal titration calorimetry

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共 10 頁，第 3 頁 *請在【答案卡】作答

7. Which of the following methods **are** genetic technologies for testing protein-protein interactions? (2 points)

- (A) Phage display
- (B) Yeast two-hybrid
- (C) Yeast split-ubiquitin assay
- (D) Chromatin immunoprecipitation
- (E) Split-luciferase assay

8. Which of the following methods **are** used for detecting nucleic acids-protein interactions? (2 points)

- (A) Fluorescence resonance energy transfer
- (B) Chromatin immunoprecipitation
- (C) Yeast two-hybrid
- (D) The electrophoresis mobility shift assay (EMSA)
- (E) Nuclear magnetic resonance (NMR)

9. You discover that the underlying cause of a specific type of cancer is an oncoprotein that is less stable than the non-oncogenic version of the protein. This change is most likely to be due to _____. (2 points)

- (A) a mutation within the intron of a gene
- (B) a mutation within the exon of a gene
- (C) a mutation within the promoter region of a gene
- (D) gene duplication
- (E) gene deletion

10. You find that the number of total protein species in humans (and other organisms) can vastly exceed the number of coding genes. This is largely due to _____. (2 points)

- (A) protein degradation
- (B) alternative splicing
- (C) homologous genes
- (D) mutation
- (E) horizontal transfer

11. Changes in DNA sequence from one generation to the other generation may result in offspring that are better adapted to the environment than their parents. The process of change and selection over the course of many generations is the basis of _____. (2 points)

- (A) mutation
- (B) reproduction
- (C) heredity
- (D) evolution
- (E) adaptation

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共 10 頁，第 4 頁 *請在【答案卡】作答

12. DNA double strands can be separated from each other when the temperature exceeds 95 degree Celsius. What is the principal force that holds these two strands together? (2 points)

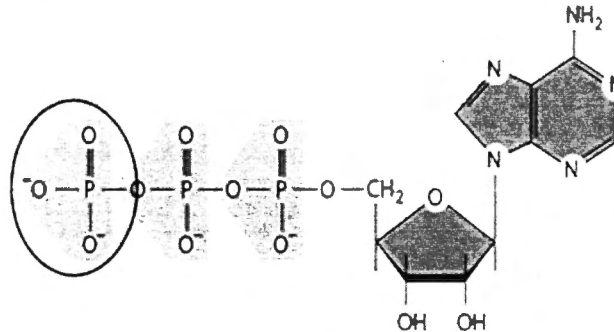
- (A) electrostatic attractions
- (B) hydrogen bonds
- (C) hydrophobic interactions
- (D) Van der Waals attractions
- (E) covalent bonds

13. We know that RNA is composed of 4 different monomer building blocks that can be used to assemble RNA polymers. Imaging a cell that has 5 different monomer building blocks that can be used to assemble RNA polymers, the number of possible sequence combinations that can be created for an RNA molecule made of 10 nucleotides will be _____. (2 points)

- (A) 5^{10}
- (B) 10^5
- (C) 5×10
- (D) $10/5$
- (E) $4^{10} \times 5$

14. What type of chemical group is circled on the nucleotide shown in the figure to the right? (2 points)

- (A) pyrophosphate
- (B) carbonyl
- (C) phosphoryl
- (D) carboxyl
- (E) hydroxyl



15. Which of the following RNA may block translation of targeted proteins? (2 points)

- (A) dsRNA
- (B) mRNA
- (C) siRNA
- (D) lnc RNA
- (E) miRNA

16. A _____ mutation has no effect on phenotype. (2 points)

- (A) frameshift
- (B) deletion
- (C) silent
- (D) nonsense
- (E) site-directed

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共 10 頁，第 5 頁

*請在【答案卡】作答

17. Minicells result from mutations that: (2 points)

- (A) prevent growth of the cell.
- (B) prevent septum formation.
- (C) prevent DNA replication.
- (D) prevent chromosome partitioning.
- (E) cause septa to be formed in the wrong place or to be formed too frequently.

18. Single-copy replication control means that: (2 points)

- (A) there can be only one origin of replication in the entire genome.
- (B) only one DNA molecule can be present in a cell at a time.
- (C) only one DNA molecule can be replicated in a cell at a time.
- (D) there can be only one origin of replication on each DNA molecule.
- (E) a DNA molecule can only be replicated once during the cell cycle.

19. The ORC in *S. cerevisiae*: (2 points)

- (A) stands for "origin replicon complex."
- (B) is associated with ARS elements throughout the cell cycle.
- (C) is a complex of eight proteins.
- (D) is similar to RNA-binding complexes in multicellular eukaryotes.
- (E) All of these are correct.

20. *E. coli* DNA polymerases IV and V are: (2 points)

- (A) RNA-dependent DNA polymerases.
- (B) for restarting replication.
- (C) for priming replication.
- (D) error-prone polymerases.
- (E) All of these are correct.

21. Although *E. coli* DNA polymerase I is not a replicase, it participates in DNA replication. What is its function? (2 points)

- (A) It synthesizes Okazaki fragments.
- (B) It synthesizes an RNA primer.
- (C) It unwinds the double helix.
- (D) It uses nick translation to replace the RNA primer with DNA.
- (E) It connects the 3' end of one Okazaki fragment with the 5' end of another.

22. Which proteins function in the resolution of Holliday junctions? (2 points)

- (A) The Ruv complex
- (B) RecA
- (C) Zip proteins
- (D) The RecBCD complex
- (E) DNA polymerase I

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共 10 頁，第 6 頁 *請在【答案卡】作答

23. The human disease xeroderma pigmentosum results from mutations in genes involved with: (2 points)

- (A) nucleotide excision repair.
- (B) photoreactivation.
- (C) base excision repair.
- (D) mismatch repair.
- (E) recombination-repair.

24. Which of the following is not true concerning immunoglobulin gene recombination signal sequences? (2 points)

- (A) There are conserved heptamers.
- (B) There are conserved nonamers.
- (C) Recombination occurs between a 12 bp signal and a 23 bp signal.
- (D) The conserved sequences are separated by a non-conserved sequence of either a 12 bp or a 23 bp sequence.
- (E) Recombination only occurs between two heptamers.

25. All of the following are proteins within the core nucleosome particle EXCEPT: (2 points)

- (A) H1
- (B) H2A
- (C) H2B
- (D) H3
- (E) H4

26. Which ones of the following descriptions about RNA editing are correct? (2 points)

- (A) trypanosome kinetoplast RNA editing occurs in both 3' 5' and 5'3' directions
- (B) mRNA must be edited before being translated
- (C) Both ADAR and CDAR could mediate nucleotide deamination
- (D) All 4 ribonucleotides (A, U, C, G) in RNA could be edited
- (E) one or more gRNAs to hybridize the edited region.

27. Which of the following splicing factors base-pair with pre-mRNA? (2 points)

- (A) U6
- (B) U5
- (C) U4
- (D) U2
- (E) U1

28. The synthesis of mRNA's that encode the proteins of eukaryotic RNA polymerase occurs in the: (2 points)

- (A) cytoplasm
- (B) nuclear envelope
- (C) nucleolus
- (D) euchromatin
- (E) heterochromatin

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共 10 頁，第 7 頁 *請在【答案卡】作答

29. Which of the following description of RNA processing events is correct? (2 points)

- (A) Cap is a modified 7-methylguanosine that 5'-3' links to the 5' terminus of RNA.
- (B) RNA polyadenylation only happens in nucleus.
- (C) RNA cap can be labeled with $[\beta, \gamma\text{-}^{32}\text{P}]\text{ATP}$ but not with $[\gamma\text{-}^{32}\text{P}]\text{ATP}$.
- (D) RNA polymerase II transcription of a gene usually stops at the polyadenylation site.
- (E) Once an mRNA loses its poly(A) tail, it is imported back into the nucleus for replenishing poly(A) tail.

30. Which of the following snRNP is mismatched with its function? (2 points)

- (A) U1: base pairs with 5' splice site of mRNA.
- (B) U2: base pairs with the conserved sequence at splicing branch point.
- (C) U4: base pairs with 3' splice site of mRNA.
- (D) U5: associates with last nucleotide in one exon and the first nucleotide in the next exon.
- (E) U6: base pairs with 5' end of the intron.

31. The functions of the mRNA cap include: (2 points)

- (A) protects the mRNA from degradation
- (B) enhances the translatability of the mRNA
- (C) enhances transport of the mRNA to the cytoplasm
- (D) enhances splicing out the first intron of the mRNA
- (E) aids transcription termination

32. Which of the following is **NOT** the possible action for miRNA? (2 points)

- (A) translation initiation blockade
- (B) translation elongation blockade
- (C) mRNA degradation
- (D) stimulate translation
- (E) targets viral DNAs

33. Which of the following sequence is responsible for the protein translation initiation in most eukaryotic mRNA transcripts? (2 points)

- (A) Kozak sequence
- (B) Shine-Dalgarno sequence
- (C) TATA Box sequence
- (D) Internal Ribosome Entry sequence
- (E) PolyA sequence

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共 10 頁，第 8 頁 *請在【答案卡】作答

34. Which of the following sequence is responsible for the eukaryotic transcription initiation? (2 points)

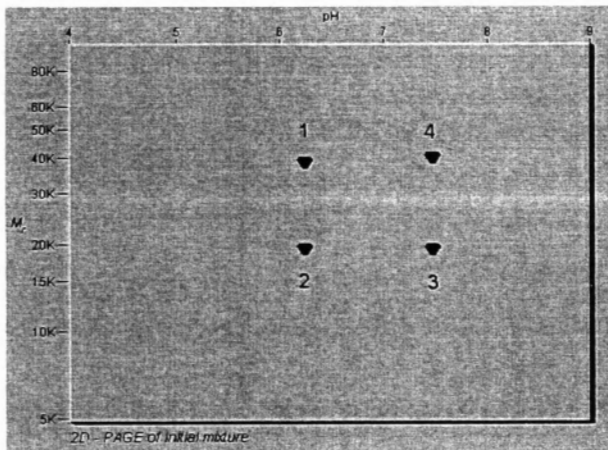
- (A) Kozak sequence
- (B) Shine-Dalgarno sequence
- (C) TATA Box sequence
- (D) Internal Ribosome Entry sequence
- (E) PolyA sequence

35. Which of the following factor is NOT a GTP binding protein involved in protein translation? (2 points)

- (A) IF-2
- (B) IF-3
- (C) EF-Tu
- (D) EF-G
- (E) RF3

36. Which of the following factor is necessary for the translocation step in protein translation in cells? (2 points)

- (A) IF-2
- (B) IF-3
- (C) EF-Tu
- (D) EF-G
- (E) RF3



You have examined a sample of the mixture by two-dimensional polyacrylamide gel electrophoresis (2D-PAGE), as shown in left figure. 2D-PAGE separates the proteins in the first dimension by isoelectric focusing followed by polyacrylamide gel electrophoresis in SDS in the second dimension. You are ready to do some protein purification experiments with the protein mixture. You have a column of DEAE-Sephadex, a positively charged slurry, to separate the proteins in the mixture.

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共 10 頁，第 9 頁 *請在【答案卡】作答

37. Following the above description, if this mixture is applied to a column of DEAE-Sephadex at pH 7.0, which proteins will bind to the column? (2 points)

- (A) All
- (B) 3, 4
- (C) 1, 4
- (D) 1, 3
- (E) 1, 2

38. Following the above description, if this mixture is applied to a column of DEAE-Sephadex at pH 8.0, which proteins will bind to the column? (2 points)

- (A) All
- (B) 3, 4
- (C) 1, 4
- (D) 1, 3
- (E) 1, 2

39. Following the above description, if you first use Sephadex G-100 gel filtration column to do the purification, what is the elution order for the four proteins (>, begin with the faster one; =, equal)? (2 points)

- (A) $3 = 4 > 1 = 2$
- (B) $2 = 3 > 1 = 4$
- (C) $2 = 4 > 1 = 3$
- (D) $1 = 4 > 2 = 3$
- (E) $1 = 2 > 3 = 4$

40. Quantitative real-time PCR (qPCR) can be used to quantify mRNA levels of genes in different samples. The cycle numbers for the measurement of mRNA expression of gene X in sample A and B are 25 and 30, respectively, and those of GAPDH (a house keeping gene) in sample A and B are 12 and 13, respectively. What is the fold-difference in gene X expression between sample A and B? The PCR efficiencies for gene X and GAPDH are closed to 100%. (2 points)

- (A) A is 4-folds higher than B.
- (B) A is 16-folds higher than B.
- (C) B is 4-folds higher than A.
- (D) B is 16-folds higher than A.
- (E) None of the above

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*請在【答案卷】作答

II. 簡答題 essay questions (20 points, 4 points for each)

41. The remarkable advances have been made by researchers to engineer DNA polymerases for their application in DNA sequencing, PCR, site-directed mutagenesis, DNA labeling, cloning, whole genome amplification, and diagnostic techniques. One of the most challenging tasks has been to engineer DNA polymerases to replicate difficult DNA sequences.

Please elaborate how to improve DNA polymerase from the four properties of the enzyme: (1) specificity, (2) thermostability, (3) fidelity and (4) processivity. (4 points)

42. New Delhi metallo-beta-lactamase 1 (NDM-1) is an enzyme that makes bacteria resistant to a broad range of beta-lactam antibiotics. NDM-1 gene was first detected in a *Klebsiella pneumoniae* (a type of bacteria). Later scientists found that the gene can spread from one strain of bacteria to another, such as *Escherichia coli*, by a mechanism known as "horizontal gene transfer". Notably, gene delivery can be seen as an artificial horizontal gene transfer, and is a form of genetic engineering. Please give an example of artificial gene delivery and explain how the gene is transferred from one to another organism. (4 points)

43. About the role of transposable P elements in hybrid dysgenesis, please describe the mechanism of P elements transposition can result in dysgenesis and why P male × M female crosses are infertile in *Drosophila*? (4 points)

44. Please briefly describe two major roles of the eukaryotic RNA Polymerase II Carboxyl-terminal domain (CTD) in gene expression. (4 points)

45. The DNA sequence (5'-CCGAGAGATCTAC-3') contains a six-base sequence that is a recognition and cutting site for a restriction enzyme. (4 points)

(a) What is this sequence? (2 points)

(b) What are "Compatible Cohesive Ends" used in the DNA cloning? (2 points)