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國立清華大學 115 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。
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. 提早交卷者不可攜出試題，請將試題連同答案卷(卡)交予監考人員，攜出將以違規論處。當節考試結束後試題將置於講台，可自行取回，本試場不負保管責任。
7. 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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共__9__頁，第__1__頁 *請在【答案卡】作答

一、Multiple-choice Questions (50%, Select the single best answer, 2 pts each):

1. Why are mitochondria and chloroplasts believed to have originated from endosymbiosis?
 - A. Because they are completely autonomous organelles that function independently of the nucleus.
 - B. Because they contain no genetic material of their own and rely entirely on the host genome.
 - C. Because their physical volume is significantly larger than that of typical prokaryotic bacteria.
 - D. Because they lack a lipid membrane and are directly exposed to the cytoplasmic environment.
 - E. Because they possess their own circular DNA and 70S ribosomes similar to those of prokaryotes.
2. In a family with an X-linked recessive disorder, if the father is unaffected and the mother is a carrier, what is the probability of the offspring being affected?
 - A. All offspring, regardless of gender, will manifest the disease phenotype.
 - B. Sons have a 50% chance of being affected, while all daughters will be phenotypically normal.
 - C. Both sons and daughters have an equal 50% probability of manifesting the disease.
 - D. Only daughters will manifest the disease, while all sons will be phenotypically normal.
 - E. All sons will manifest the disease, and all daughters will be carriers of the trait.
3. What is the functional similarity between prokaryotic Sigma factors and eukaryotic Transcription Factors?
 - A. Both possess the catalytic active site required for RNA synthesis.
 - B. Both must cross the nuclear envelope to bind DNA and regulate gene expression.
 - C. Both are primarily responsible for recognizing specific promoter sequences to recruit RNA polymerase.
 - D. Both are permanent subunits of the polymerase complex that remain bound during elongation.
 - E. Both possess helicase activity to continuously unwind the DNA double helix during transcription.

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4. The Wobble Hypothesis primarily explains which of the following biological phenomena?
- A. Each codon strictly corresponds to a unique tRNA with a fully complementary anticodon.
 - B. The start codon (AUG) allows non-standard pairing to accelerate ribosome assembly.
 - C. The ribosome undergoes a physical "wobble" conformation during translocation.
 - D. Cells can recognize all amino acid-coding codons with fewer than 61 types of tRNA.
 - E. The tRNA acceptor stem wobbles to prevent incorrect amino acid attachment.
5. Which of the following statements regarding the applications and techniques of proteomics is correct?
- A. Western blotting utilizes labeled DNA probes to detect the presence of specific protein targets.
 - B. The proteome is defined as the total number of genes encoded within an organism's complete genome.
 - C. SDS-PAGE primarily separates protein molecules based on their intrinsic charge rather than their molecular weight.
 - D. Phage display technology can be employed to investigate interactions between proteins and other molecules.
 - E. Protein microarrays are limited to detecting the purity of isolated proteins rather than their functional activities.
6. Histone acetylation is generally associated with gene activation. What is the primary molecular mechanism underlying this phenomenon?
- A. Acetylation neutralizes the positive charge on lysine residues, weakening the electrostatic attraction to the negatively charged DNA backbone and creating a more open chromatin structure.
 - B. The addition of acetyl groups increases hydrophobicity, thereby strengthening the Van der Waals forces between histones and DNA to stabilize the nucleosome.
 - C. Acetylation acts as an enzymatic cofactor that directly catalyzes the phosphorylation of RNA Polymerase II to initiate transcription elongation.
 - D. Acetyl marks specifically recruit DNA methyltransferases to promote CpG island methylation, effectively locking the gene in a silenced state.
 - E. Acetylation serves as an irreversible signal that targets histones for degradation via the ubiquitin-proteasome pathway, clearing the DNA for transcription.

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7. What is the original evolutionary function of the CRISPR-Cas9 system in bacteria?
- A. To serve as a mechanism for repairing spontaneous DNA mutations within the genome.
 - B. To regulate the expression of the bacteria's own metabolic genes during starvation.
 - C. To facilitate the conjugation process and horizontal gene transfer between bacteria.
 - D. To act as an adaptive immune system that memorizes and cleaves foreign DNA from phages.
 - E. To assist in the structural formation of endospores during extreme environmental stress.
8. If two plasmids belong to the same "Incompatibility group," what does this imply?
- A. They will inevitably fuse together via recombination to form a single large megaplasmid.
 - B. They cannot stably coexist in the same cell because they compete for the same replication or partitioning mechanisms.
 - C. They encode restriction enzymes that will specifically degrade the DNA of the opposing plasmid.
 - D. They originate from completely different bacterial species and cannot function in the current host.
 - E. They both carry identical antibiotic resistance genes, rendering one of them functionally redundant.
9. For bacteriophages, the decision to enter the "Lytic" or "Lysogenic" cycle typically involves which key factor?
- A. The metabolic state and health of the host cell.
 - B. The magnitude of temperature fluctuations in the surrounding environment.
 - C. The physical size of the viral capsid relative to the host cell's volume.
 - D. The intensity of ultraviolet light exposure present in the environment.
 - E. Whether the bacteriophage genome encodes specific antibiotic resistance genes.

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10. Beyond DNA repair, what is the primary evolutionary significance of crossing over during meiosis?
- A. It significantly reduces the overall mutation rate across the genome.
 - B. It ensures that the chromosome number is correctly doubled for the daughter cells.
 - C. It breaks the linkage between genes on the same chromosome, creating new allelic combinations.
 - D. It functions to systematically eliminate all recessive deleterious alleles from the population.
 - E. It serves to extend the length of telomeres to prevent cellular senescence.
11. Why is mitochondrial DNA (mtDNA) frequently used in evolutionary studies?
- A. It has an extremely low mutation rate, making it suitable for studying events from billions of years ago.
 - B. It shows maternal inheritance and a relatively fast mutation rate, making it suitable for studying recent evolution.
 - C. It contains the complete genetic information of the organism, replacing the need for nuclear DNA analysis.
 - D. It is highly conserved and undergoes absolutely no mutations throughout the evolutionary process.
 - E. It is universally present in all biological entities, including all known families of viruses.
12. Which statement regarding "Retrotransposons" is correct?
- A. They move within the genome using a "cut and paste" mechanism similar to DNA transposons.
 - B. Their movement does not result in any net increase in the total number of transposons in the genome.
 - C. They are found exclusively in prokaryotic organisms and are absent in eukaryotes.
 - D. They are capable of moving autonomously without requiring any host-derived or self-encoded enzymes.
 - E. Their transposition process involves an RNA intermediate and the enzyme reverse transcriptase.

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13. Which of the following is correct regarding the mechanism of RNA interference (RNAi)?

- A. RNAi is a gene silencing phenomenon triggered by single-stranded DNA (ssDNA) fragments.
- B. The Dicer enzyme is responsible for cleaving long double-stranded RNA into small siRNA fragments.
- C. The Slicer enzyme functions primarily to transport miRNA out of the nucleus into the cytoplasm.
- D. The RISC complex is primarily responsible for repairing damaged mRNA sequences in the ribosome.
- E. The RNAi phenomenon was originally discovered as an immune mechanism in bacterial cells.

14. Which statement concerning translation and the genetic code is accurate?

- A. A codon is defined as a sequence of three nucleotides located on the tRNA molecule.
- B. All types of RNA transcribed in the nucleus are eventually translated into proteins.
- C. Aminoacyl-tRNA synthetases are responsible for attaching specific amino acids to the acceptor stem of tRNA.
- D. Peptide bonds are the primary covalent bonds connecting the two strands of the DNA double helix.
- E. Release factors function by increasing the efficiency of tRNA charging during elongation.

15. Which statement regarding the human genome structure or genomic techniques is correct?

- A. Exon trapping relies on the presence of flanking splice sites to identify coding regions.
- B. Protein-coding genes constitute the vast majority (over 90%) of the human genome sequence.
- C. The bacterium *E. coli* possesses approximately 25,000 genes, similar to humans.
- D. All plant genomes are significantly smaller in size compared to the human genome.
- E. Radiation hybrids are defined as eukaryotic cells that have been infected with viral DNA.

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16. What feature is critical for rho-independent termination?
- A. Rut site
 - B. Strong rU-dA base pairs
 - C. Hairpin followed by weak rU-dA base pairs
 - D. NusA binding site
 - E. Fis sites
17. Which experimental method is commonly used to determine the binding site of a protein on DNA?
- A. Western blot
 - B. DNase I footprinting
 - C. Nitrocellulose filter-binding assay
 - D. Gel-shift (EMSA) assay
 - E. Heparin competition assay
18. Which of the following statements best describes the lac repressor (LacI)?
- A. It binds to the CAP-binding site and prevents transcription.
 - B. It binds directly to RNA polymerase to inhibit open complex formation.
 - C. It degrades lactose to allolactose.
 - D. It activates the lac promoter when glucose is absent.
 - E. It is a tetramer that binds to the operator sequence to repress transcription.
19. During λ phage infection, immediate early genes are transcribed by:
- A. Phage-encoded RNA polymerase
 - B. RNA polymerase lacking σ
 - C. RNA polymerase with $\sigma 38$
 - D. Host RNA polymerase holoenzyme
 - E. RNA polymerase bound to Q
20. What role does the alarmone ppGpp play at the molecular level in transcriptional regulation?
- A. Enhances promoter melting
 - B. Stabilizes open promoter complexes
 - C. Binds RNA polymerase and destabilizes open promoter complexes
 - D. Stimulates σ factor release
 - E. Increases elongation rate

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21. Which is incorrect for eukaryotic promoters?
- A. Class I promoters generally consists of a core element surrounding the transcription start site and an upstream promoter element (UPE).
 - B. In the 5S and 7SL RNA genes, the promoters are located entirely within the genes themselves.
 - C. For class III genes, type II promoters found in tRNA genes contain two regions, Box A and Box B, which are recognized by TFIIC.
 - D. Proximal promoter elements of class II genes act in an orientation-dependent yet position-independent manner.
 - E. In class II genes, TATA-less promoters are common in both housekeeping and developmentally regulated genes.
22. Choose a correct statement about eukaryotic RNA polymerases (RNAPs) I, II and III?
- A. Rpb5, Rpb7, Rpb9, Rpb11 and Rpb12 are common subunits for all three RNAPs.
 - B. Three loops extending from the clamp of RNAP II—the zipper, lid and rudder—are revealed by crystal structure, and the zipper initiates RNA-DNA hybrid dissociation.
 - C. RNAP containing the IIO subunit is involved in the formation of pre-initiation complex, while RNAP with the IIA subunit contributes to transcription elongation.
 - D. In RNAP, flexing of the bridge helix is crucial for translocation during transcription, while the trigger loop ensures correct nucleotide selection and positioning.
 - E. RNAP II is located in the nucleolus and is highly sensitive to alpha-amanitin, which inhibits RNAP translocation but does not block phosphodiester bond formation.
23. Which of the following is true for eukaryotic Class I and III general transcription factors, except:
- A. TFIIB and TFIIC are required for all “classical” class III genes.
 - B. TFIIC is an assembly factor that helps TFIIB to bind to a region just upstream of the transcription start site.
 - C. Human SL1 is an assembly factor that helps the UPE-binding factor of RNA polymerase I to bind to the core promoter element.
 - D. TFIIA is a zinc finger protein & is required for transcription of the 5S rRNA genes, but not the tRNA genes.
 - E. For the class I transcription, human SL1 consists of TATA-binding protein (TBP) and TBP-associated factors (TAFs), which are different from TAFs found in TFIID.

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24. Which of the following statement is correct in eukaryotic transcription?
- A. Yeast Gcn4 controls amino acid metabolism, containing a domain using the basic region to bind to DNA and helix-loop-helix to form a protein dimer.
 - B. The carboxyl-terminal domain of RNA polymerase is phosphorylated prior to the formation of the initiation complex.
 - C. By adding of excess acetyltransferase to in vitro transcription assay, it is likely lead to a tighter association of histone with DNA, resulting in reduced transcription.
 - D. TAF1 of the general transcription factor TFIID is a helicase and a histone acetyltransferase.
 - E. The high mobility group protein (HMG I(Y)) plays a role in interferon- β (IFN- β) transcription by bending the DNA, causing more activators to bind and interact with each other to enhance transcription.
25. Which of the following statement is correct related to general and gene-specific transcription factors in eukaryotes?
- A. TATA-box-binding protein (TBP) binds to the minor groove of DNA, bends the consensus TATA DNA, and is required for most members of class I, II and III genes.
 - B. For RNAP III, TBP is a component of the general transcription factor TFIIC.
 - C. The bZIP transcription factors dimerize through a basic domain and bind to target DNA through a leucine zipper.
 - D. TFIIE and TFIIH are essential for promoter clearance and transcription elongation.
 - E. The Cys₂His₂-zinc finger of TFIIIA is composed of an antiparallel beta-sheet followed by an alpha-helix, and the beta-sheet recognizes and binds to specific DNA sequences in the major groove.

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二、Short-answer Questions (50%):

1. Define the following term: Riboswitch (3 pts)
2. Draw diagrams of the *ara* operon that illustrate (and also include the explanation) (a) negative control (3 pts) and (b) positive control (4 pts) of this operon.
3. Explain the difference between type I and type II nuclear receptors and provide an example of each. (5 pts)
4. The yeast two-hybrid system is based on the concept that the DNA-binding and transcription-activation domains are independent modules. Please explain how yeast two-hybrid system works? (Draw a diagram for a clearer explanation) (5 pts)
5. In *E. coli*, even in the presence of lactose, the transcription of the lac operon remains very low if glucose is also present. Explain the molecular mechanism. (6 pts)
6. Explain the biochemical and structural constraints that make the formation of Okazaki fragments necessary during the replication of the lagging strand. (6 pts)
7. When expressing a eukaryotic protein in a bacterial host, why is it critical to use cDNA rather than genomic DNA? (4 pts)
8. In quantitative PCR (qPCR), why do we focus on the Ct value (Threshold Cycle) rather than the final amount of product at the end of the reaction? (3 pts) Briefly define what the Ct value represents. (3 pts)
9. You observe that adding DNase to a bacterial culture prevents the bacteria from acquiring a new hereditary trait. Based on this observation, which gene transfer mechanism is occurring (Transformation, Transduction, or Conjugation)? Explain your reasoning. (4 pts)
10. Why is a frameshift mutation located at the beginning of a coding region generally more detrimental to protein function than a missense mutation? Briefly explain the reason. (4 pts)