一、Multiple Choice 单选题 (70%; 2% each)

1. A nucleosome is composed of a core of ______ histone molecules and a DNA of approximately ______ bp in length.
   (a) two; 100  (b) four; 100  (c) eight; 100  (d) two; 200  (e) four; 200  (f) eight; 200

2. Which of the following statements about mRNA stability is incorrect?
   (a) The cap (a modification at the 5' end of mRNA) prevents 5'-3' exonucleases from attacking the 5' end.
   (b) The poly(A) prevents 3'-5' exonucleases from attacking the 3' end.
   (c) The most common location for destabilizing elements is within the 5' untranslated region.
   (d) Within the coding region, mutations that create termination codons trigger a surveillance system that degrades the mRNA.
   (e) Degradation of mRNA in yeast starts with removal of the poly(A) tail.

3. Which of the following methods is not used to map and/or quantify transcripts?
   (a) Northern blotting  (b) Restriction mapping  (c) S1 nuclease mapping  (d) Primer extension
   (e) RNase mapping (RNase protection assay)  (f) Run-off transcription.

4. Which of the following about DNA methylation is false?
   (a) Methylation of DNA occurs in both prokaryotes and eukaryotes but the purpose is quite different.
   (b) Methylation of DNA is often used to control gene expression during development of higher organisms.
   (c) DNA methylation in eukaryotes activates gene expression.
   (d) CpG island denotes a region of DNA containing many unmethylated CpG sequences.
   (e) Demethylases are used to remove methyl groups in higher organisms.

5. A "homebox"
   (a) is a promoter-enhancing element present in genes of many or even all eukaryotes.
   (b) is a sequence important in binding of transcriptional factors.
   (c) functions as a repressor for gene expression.
   (d) encodes a homeodomain with three α-helices important in protein-protein interaction.
   (e) is a common coding motif in homeotic genes important in controlling the developmental fate of groups of cells.

6. Which of the following about "splicing" is false?
   (a) snoRNPs participate in splicing of pre-mRNAs.
   (b) snRNAs can recognize the 5'- and 3'-splicing signals of an mRNA precursor.
   (c) The spliceosome is a complex of the snRNPs and many additional protein factors that are required for splicing.
   (d) The GU-AG motif is commonly used to predict the intron splicing sites.
   (e) The spliceosome cycle includes the assembly, splicing activity, and disassembly of the spliceosome.

7. Which of the following statements about DNA replication is false?
   (a) DNA replicates in a semiconservative manner.
   (b) DNA polymerase synthesizes the leading strand continuously in the 5'→ 3' direction.
   (c) DNA polymerase synthesizes the lagging strand discontinuously in the 5'→ 3' direction.
(d) DNA replication in bacteria involves synthesis of a short RNA primer by RNA replicase.

(e) The lagging strand is made in short sections and a new RNA primer needs to be inserted each time a new portion is made.

8. Transfection
(a) is a process in which eukaryotic cells are transformed by introducing foreign DNA into the cells.
(b) occurs when a bacterium acquires DNA from the surrounding environment.
(c) is the direct transfer of DNA from one bacterium to another.
(d) is the result of gene recombination.
(e) occurs when a phage transfers DNA from one bacterium to another.

9. Ribonuclease H (RNase H)
(a) degrades the RNA strand of an RNA-DNA hybrid.
(b) degrades single-stranded RNA at the 3' ends.
(c) degrades single-stranded RNA and DNA.
(d) degrades single-stranded RNA at the 5' ends.
(e) none of the above

10. Which of the following is not a second messenger?
(a) nitric oxide  (b) GTP  (c) diacylglycerol  (d) cAMP  (e) inositol-1,3,5-triphosphate  (f) Ca^{2+}

11. Which of the following statements about Holliday junction is incorrect?
(a) Holliday junction is generated during homologous recombination.
(b) Nicks must occur in corresponding positions in one strand of each DNA duplex.
(c) The branch in the Holliday junction undergoes “branch migration”.
(d) The Holliday junction can be resolved into one independent DNA duplexes by creating the second DNA nicks.
(e) If the same DNA strands are nicked after the Holliday junction formation, crossover recombination occurs.

12. Which of the following techniques is often used to generate ‘traditional’ (or constitutive) knockout mice?
(a) PCR-based technique  (b) gene targeting by homologous recombination  (c) enucleation of embryonic stem cell  (d) Cre-loxP system  (e) in vitro fertilization

13. Which of the following statements is false?
(a) DNA gyrase introduces negative supercoils into DNA.
(b) DNA helicase unwinds the DNA helix and single strand binding protein keeps the strands apart.
(c) Quinolone antibiotics, such as nalidixic acid, kill bacteria by inhibiting DNA gyrase and thereby preventing DNA replication.
(d) DNA ligase inserts a segment of dsDNA into another DNA molecule at a specific recognition sequence.
(e) Reverse transcriptase uses single-stranded RNA as a template for making double-stranded DNA.

14. Which of the following statements about immunoglobulin gene rearrangement is (are) true?
(a) Rearrangement of a heavy chain gene involves the joining of V, D and J segments.
(b) There are similar numbers of V and J segments in the human light chain genes.
(c) Once a productive rearrangement has occurred at one allele, the other allele also undergoes rearrangement.
(d) $V_H$ 7-12-9: 9-23-7 $J_H$ are two recombination signal sequences required for a permitted somatic recombination event in the heavy chain gene.
(e) All of the above are true.

15. A DNA segment contains a coding region of 1920 base pairs. What is the approximate calculated molecular weight of its encoded protein?
(a) 35 kDa  (b) 70 kDa  (c) 19 kDa  (d) 190 kDa  (e) none of the above

16. Anti-codon loops are found in (a) mRNA (b) rRNA (c) tRNA (d) hnRNA (e) snRNA.

17. Which of the following terms could describe a situation in which there are multiple functional alleles of a gene segregating in a population?
(a) somatic hypermutation  (b) meiotic nondisjunction  (c) loci  (d) complementation  (e) polymorphism

18. Which of the following assay cannot be used to detect protein-protein interactions?
(a) immunoprecipitation  (b) fluorescence resonance energy transfer (FRET)  (c) yeast two-hybrid  (d) Enzyme-linked immunosorbent assay (ELISA)  (e) protein footprinting

19. Which of the following dyes is most commonly used in staining DNA on an agarose gel?
(a) bromophenol blue  (b) ethidium bromide  (c) Silver stain  (d) xylene cyanol  (e) Coomassie blue

20. Which of the following methods is commonly used to determine the concentration of RNA?
(a) absorbance at 260 nm  (b) Northern blot  (c) Bradford method  (d) Lowry assay  (e) RT-PCR

21. When white gene is integrated into the genomic site close to heterochromatin, cells in which white gene is inactive give patches of white eyes, while cells in which white is active give red patches. This phenomenon in which genetically identical cells express different phenotypes is called as ___.
(a) X chromosome inactivation  (b) Genetic imprinting  (c) Genetic variation  (d) position effect variegation  (e) Gene silencing  (f) Site-directed mutagenesis

22. The transcription of eukaryotic ribosomal RNA genes, rDNAs, is performed by ___.
(a) RNA polymerase I  (b) RNA polymerase II  (c) RNA polymerase III  (d) RNA polymerase A  (e) reverse transcriptase  (f) Poly (A) RNA polymerase

23. What DNA-binding motif is used by the steroid hormone receptor to bind DNA?
(a) Cys2/Cys2 Zinc finger  (b) bHLH  (c) Lucine zipper  (d) Helix-turn-helix  (e) Cys2/His2 Zinc finger  (f) homeodomain

24. The modification of amino acid residues in the N-terminal domains of H3 and H4 histones serve as a recognition code for various transcription factors. Among these modifications, methylation of the lysine 9 of H3 serves as a repressive signal and is recognized by the ___ of HP1 protein.
(a) chromodomain  (b) Lysine-rich domain  (c) Glycine-rich domain  (d) shadow domain  (e) homeodomain  (f) bromodomain

25. The ____ enzyme catalyzes the double strand break reaction during the early stage of meiosis recombination.
(a) RecA  (b) DNA polymerase α  (c) DNA polymerase σ  (d) Ruv AB complex  (e) Spo11  (f) Topoisomerase II
26. In a particular human family, Peter and his father both have brachydactyly (BR, a very rare autosomal dominant mutation causing short fingers). His mother has Huntington disease (HD, another rare autosomal dominant mutation). Two-thirds of people who inherit the HD allele show symptoms by age 45, and Peter is 47 and has no symptoms. Brachydactyly is 90% penetrant. Both HD and BR homozygous are embryonic lethal. The following are the gene symbols for alleles of these two genes:

B: mutant brachydactyly allele; b: wildtype brachydactyly allele
H: mutant Huntington allele; h: wildtype Huntington allele

What are the genotypes of Peter’s parents for these two genes?
(a) father is bb Hh and mother is Bb hh  (b) father is bb Hh and mother is Bb HH  (c) father is BB Hh and mother Bb hh  (d) father is bb Hh and mother is BB hh  (e) mother is bb Hh and father is Bb hh  (f) both are Bb Hh

27. Following question 6, if the two loci are 20 m.u. apart, what is the possibility that Peter will carry mutant alleles of both Brachydactyly and Huntington genes?
(a) 3/10  (b) 1/4  (c) 1/6  (d) 1/2  (e) 5/8  (f) 2/3

28. Which of the following description about the activation of trp operon genes in the absence of tryptophan is correct?
(a) leader peptide is translated efficiently and trp operon is transcribed completely
(b) RNA polymerase is stalled and regions 2 and 3 of the attenuator paired
(c) leader peptide is translated efficiently and regions 1 and 2 of the attenuator paired
(d) neither leader peptide is translated efficiently nor trp operon is transcribed
(e) RNA polymerase is stalled and regions 1 and 3 of the attenuator paired
(f) RNA polymerase is stalled and regions 3 and 4 of the attenuator paired

29. The lariat product of spliced intron can be seen in the ___ complex of spliceosome during mRNA splicing.
(a) A  (b) B  (c) C  (d) D  (e) E  (f) F

30. Promoter clearance takes place ___.
(a) after homologous recombination  (b) before TBP binding to TATA box  (c) before TFF1H binding
(d) after RNA polymerase II dissociate from the enhancer  (e) after 10 bp nascent mRNA has been made
(f) before 10 bp nascent mRNA has been made

31. The catalytic center of E. coli RNA polymerase is formed by ___.
(a) αα subunits  (b) ββ subunits  (c) β′ subunits  (d) β subunits  (e) σ subunits  (f) σβ subunits

32. The products of a Dicer processed miRNA are ___.
(a) short hairpin RNA  (b) tandem repeat RNA  (c) double strand short RNA  (d) single strand RNA
(e) single strand DNA  (f) double strand short DNA

33. The destination of an un-perfectly matched siRNA/mRNA complex is ___.
(a) Cajal Body  (b) RISC  (c) RITS  (d) lysosome  (e) Dicer  (f) P body

34. Translational initiation factors eIF4E and eIF4G recognize the ___ and ___ features of the mRNA respectively to ensure the initiation of translation.
(a) Poly (A) tail/5'-7-methyl-guanine  (b) 5'-7-methyl-guanine /Poly (A) tail  (c) 5'-CAP/ribosome entry site  (d) 5'-CAP/Shine-Dalgarno sequence  (e) TATA box / Poly (A) tail  (f) Shine-Dalgarno sequence/ Poly (A) tail

35. The consensus sequence of higher eukaryotic mRNA polyadenylation signal is _____.
(a) AAUAAA  (b) AAUATT  (c) TTUAAA  (d) AATCCC  (e) ATGCAA  (f) TAGTAG

二、Essay questions (30%)
1. Please define and/or explain the following terms. (10%; 2.5% each)
(a) frameshift mutation  (b) DNA fingerprinting  (c) palindrome  (d) short interfering RNA
2. Please describe the organization of nucleosomes in a 30 nm chromatin fiber. (4%)
3. Please describe the transcriptional regulation circuits that initiate and maintain lambda phage latency. (6%)
4. A student likes to make a fusion protein of EGFP and p53 so he can trace the dynamic subcellular localization of p53 before and after the cells have been assaulted with UV radiation. So far, he has pEGFP-C1 and pEGFP-N1 vectors carrying the CDS of EGFP gene for inserting p53 CDS into its C-terminal and N-terminal sites respectively. He also has a pCDNA3.1 vector carrying p53 CDS. Unfortunately, the cutting sites in these 3 mammalian expression vectors are incompatible for making p53-EGFP and EFGP-p53 proteins.
(a) What will you do to make these two fusion proteins with these vectors? (3%)
(b) How can you introduce these new expression vectors into mammalian cells? (3%)
(c) He found that GFP-p53 protein accumulated rapidly and abundantly in the nucleus upon UV assault but was detected very weakly in both nucleus and cytoplasm under normal condition. He also found that the mRNA level of GFP-p53 remained constant during this period. What can be the causes of this phenomenon? (4%)