※注意：作答時，請於答案卷上標明作答之大題及其題號。

（一）單選題 (16%)

1. What phenomenon is referred to as the C-value paradox?
   A. The eukaryotic genome is larger than the bacterial genome.
   B. The DNA in eukaryotic chromosomes is a linear molecule and is a circular molecule in the bacterial genome.
   C. There is a lack of a consistent relationship between the amount of DNA and the genetic complexity of an organism.
   D. Most bacterial genes lack introns, whereas most genes of multicellular organisms contain introns.
2. DNA damage causes arrest of the cell cycle at
   A. G_1 only
   B. G_1 and G_2
   C. S phase
   D. S and M phases
3. Splice sites in pre-mRNA are marked by two universally conserved sequences contained:
   A. in the middle of the intron
   B. at the ends of the exons
   C. at the ends of the introns
   D. at the ends of transcripts
4. Drs. Sydney Brenner, H. Robert Horvitz and John E. Sulston won 2002 Nobel Prize in Physiology or Medicine for their discoveries concerning genetic regulation of organ development and programmed cell death. Their wonderful work was performed in which of the following model organisms?
   A. *Saccharomyces cerevisiae* (yeast)
   B. *Dictyostelium discoideum* (slime mold)
   C. *C. elegans* (nematode)
   D. *Drosophila melanogaster* (fruitfly)
   E. *Xenopus laevis* (frog)

（二）多選題 (每題全對才給分) (28 %)

1. Which of the following molecules can recognize specific mRNA sequence during bacterial translation?
   A. release factor
   B. aminoacyl-tRNA synthetase
   C. ribosomal protein
   D. 16S ribosomal RNA
   E. charged aminoacyl-tRNA
   F. free aminoacyl-tRNA
2. Which of the following elements can act to position RNA polymerase II for eukaryotic transcription initiation?
   A. an enhancer
   B. a promoter
   C. TATA box
   D. ribosome binding site
   E. an operator

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3. Which of the following is TRUE?
   A. The EST sequence is obtained from the end sequences (尾端序列) of genomic library clones.
   B. A Southern blot can be probed with radioactive DNA or RNA.
   C. The transcriptional start site of an mRNA can be determined by primer extension assay.
   D. High-density DNA microarrays can be used to analyze genome-wide expression at the transcriptional level but not translational level.
   E. PCR can be used to amplify DNA fragment using degenerate olionucleotide as primers.

4. Which of the following are TRUE about cis- and trans-acting elements?
   A. A repressor binds to an operator to regulate gene expression. The repressor is trans, and the operator is cis.
   B. snRNA acts in mRNA splicing. The splicing sites are trans, and snRNA is cis.
   C. The mobilization of transposon element requires the activity of transposase. The transposon is trans, and transposase is cis.
   D. A transcription factor binds to a regulatory element in a DNA sequence to modulate transcription. The regulatory element is trans, and the transcription factor is cis.
   E. A protein binds to mRNA 3' untranslated region to control translation. The protein is trans, and the 3' untranslated region is cis.

5. Which of the following statement(s) about the Maxam-Gilbert and the Sanger methods of DNA sequencing is right?
   A. In the Maxam-Gilbert method, chemicals are used to cleave bases and followed by DNA polymerase to replicate the cleaved DNA fragments.
   B. In the Maxam-Gilbert method, the DNA can be labeled at 5' end, and the resulting sequence will be read from 5' end from the bottom of the gel (各別的).
   C. To use Sanger method, one needs to know at least a small portion of the DNA sequence before sequencing in order to design a primer.
   D. In Sanger method, more dideoxynucleotides are used than nucleotides.
   E. The current dye-terminator method, which is commonly used in commercial DNA sequencing, is modified from the Maxam-Gilbert method.

6. Which of the following about antibiotics in protein translation are TURE?
   A. Puromycin mimics aminoacyl-tRNA and causes premature termination of protein synthesis
   B. Kirromycin inhibits the release of EF-Tu-GDP from ribosome during translocation.
   C. Fusidic acid inhibits the release of EF-G-GDP from ribosome during translocation
   D. Diphtheria toxin uses NAD as a cofactor to transfer an ADPR moiety on to the eEF-2 to inactivate protein synthesis.
   E. Ampicilin inhibits peptide termination.

7. If you are interested in studying the promoter region of a rat brain gene, which of the following libraries will NOT be used to isolate this promoter region?
   A. a rat liver genomic library
   B. a rat brain cDNA library
   C. a rat muscle cDNA library
   D. a rat brain expression library

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（三）簡答題 (56%)

1. Where relevant, refer to the following DNA sequences, which are coding strand (sense strand) sequences derived from genes within the nuclear mouse genome: (8 %)

I . CTCTTGCAAGACA

II . ATTGTTGCAGGATT

III . TTATTTTACAGGAC

A. Using Table 1 below, determine which of the above sequences has the potential to encode the following protein sequence: Leu-Leu-Gln-Asp (請寫代號 I, II and/or III).

B. In bacterial *E. coli*, would translation of sequence II yield a novel (新的) polypeptide compared with mouse ? (請寫 yes 或 no)

Table1.The genetic code : (RNA to amino acid)

		Second base			
		U	C	A	G
First base	U	UUU Phe	UCU Ser	UAU Tyr	UGU Cys
		UUC Phe	UCC Ser	UAC Tyr	UGC Cys
		UUA Leu	UCA Ser	UAA(ochre)	UGA(opal)
		UUG Leu	UCG Ser	UAG(amber)	UGG Trp
	C	CUU Leu	CCU Pro	CAU His	CGU Arg
		CUC Leu	CCC Pro	CAC His	CGC Arg
		CUA Leu	CCA Pro	CAA Gln	CGA Arg
		CUG Leu	CCG Pro	CAG Gln	CGG Arg
	A	AUU Ile	ACU Thr	AAU Asn	AGU Ser
		AUC Ile	ACC Thr	AAC Asn	AGC Ser
		AUA Ile	ACA Thr	AAA Lys	AGA Arg
		AUG Met	ACG Thr	AAG Lys	AGG Arg
	G	GUU Val	GCU Ala	GAU Asp	GGU Gly
		GUC Val	GCC Ala	GAC Asp	GGC Gly
		GUA Val	GCA Ala	GAA Glu	GGA Gly
		GUG Val	GCG Ala	GAG Glu	GGG Gly

2. Nonsense suppressor tRNAs are generated by mutations in the anticodon. You find an amber suppressor in the Ser tRNA (that recognizes the codon UCG). (8%)

A. Write down the anticodon sequence (label 5' and 3') of the suppressor tRNA and circle the mutant base. Use Table 1, if necessary.

B. What molecules are expected to compete for the binding to amber codons during protein synthesis in the bacterial strain that carries an amber suppressor?

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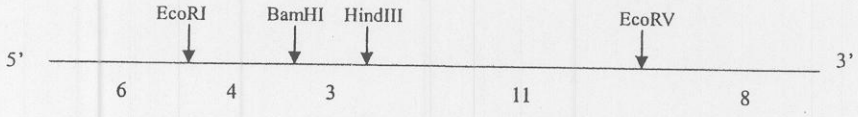
3. You have available the genome of a eukaryotic dsDNA virus and cloned restriction fragments representing all portions(部分)of this genome. A map of the genome is shown below with the distances between sites given in kbp. (8 %)



A. You believe that a particular gene is located within the 4 kbp EcoRI-BamHI fragment. When you use this fragment as probe, a positive reaction is seen with an mRNA of 3.5 kb on a northern blot. How would you explain this observation?

B. What experiment would you do to confirm this hypothesis?

4. What is the protein that converts the core polymerase from a distributive enzyme to a processive enzyme during DNA replication in *E. coli*? (4%)
Note: A distributive enzyme falls off the template after synthesizing only 10-50 nucleotides, but the processive enzyme can synthesize up to $5X10^5$ nucleotides before falling off.

5. What is the role of licensing factors in eukaryotic DNA replication during cell cycle? (4%)

6. Is DNA in the physiological condition positive-supercoiled, negative-supercoiled or relaxed? (4%) What is its biological significance(意義)? (4%)

7. The genotype of a specific diploid yeast strain is A/a. The genotypes of all four meiotic spores from a single yeast cell can be scored. You analyze 10000 spores from 2500 yeast cells and find that almost all spores are segregated in the 2A:2a ratios. But abnormal 3A:1a or 3a:1A ratios are found in some spores. You are sure that this is not caused by mutation from other parallel analysis. (8%)

A. What is the event that generates abnormal segregation ratios called?

B. If you are to explain this event, will you propose DNA breakage and DNA synthesis in your model? Please write down yes or no for DNA breakage and DNA synthesis, respectively(請各別對 DNA breakage 與 DNA synthesis 寫 yes 或 no)

8. The expression of the *trp* operon in *E. coli* is controlled by a number of genetic elements including an attenuator, an operator and a promoter. You have three different *E. coli* strains that are defective in an attenuator (strain A), an operator (strain B) and a promoter (strain C). You measure and compare the amounts of *trp* leader mRNA and full-length *trp* transcripts in mutant and wild-type strains under varying tryptophan conditions. On the basis of your data, how do you distinguish strains A, B, C and wild-type? (8 %)