**請依題號順序於答案卷上作答，未依題序作答不予計分。**

**I. Essay question** (question 1-11)

1. The novel plasmid cloning vector pNCKU-1(see Fig 1A) is cleaved with the restriction endonuclease Alu I. An isolated DNA fragment from an ekaryotic genome (also a product by Alu I cleavage) is added to the prepared vector and ligated. The mixture of ligated DNAs is then used to transform bacteria, and plasmid-containing bacteria are selected by growth in the presence of ampicllin.

   a. In addition to the desired recombinant plasmid, what other types of plasmids might be found among the transformed bacteria that are ampicllin resistant? How can they be distinguished?(5 points)

   b. The cloned DNA fragment is 1000bp in length and has an EcoR I site 250 bp from one end. Three different recombinant plasmids are cleaved with EcoR I and analyzed by gel electrophoresis, giving the pattern shown. (Fig 1B, lanes A,B,C). What dose each pattern say about the cloned RNA? Note that pNCKU-1, the AluI and EcoR I restriction sites are aboit 750bp apart. The entire plasmid with no cloned insert is 4300 kb. Size mark in lane D have the number of nucleotides notes.(5 points)

Fig 1A

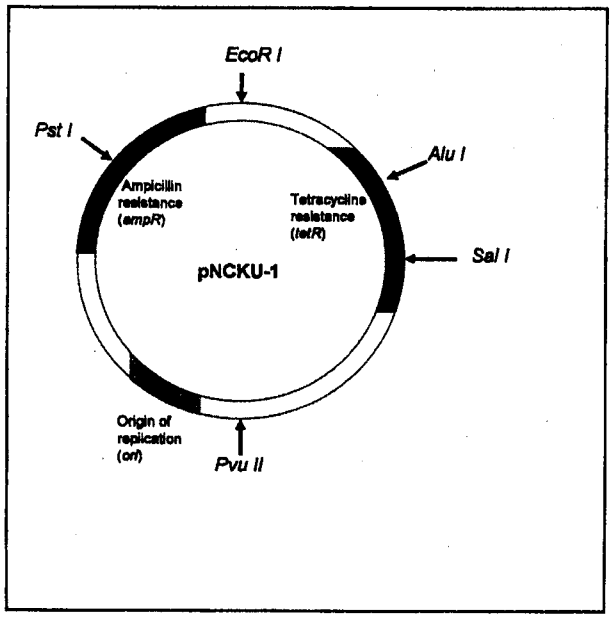
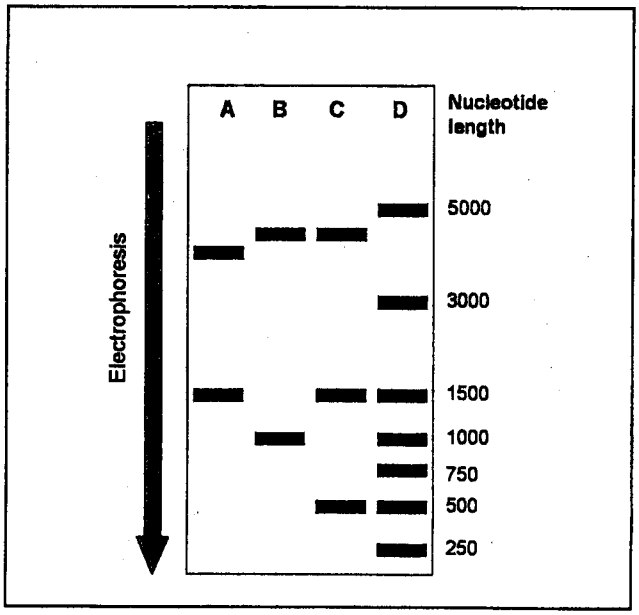



Fig 1B




（背面仍有題目,請繼續作答）

2. What is epigenomics? (5 points)

3. Please describe the advantages and disadvantages of expressing recombinant protein in *E.coli* versus mammalian cells. (5 points)

4. What is RNAi (RNA interference)? (3points)

   How does it affect gene expression? (7 points)

5. Describe how knockout mice are used as models for human disease. (10 points)

6. If you have just isolated a novel gene and would like to study how this gene is regulated, how would you ensue the experiments (e.g., analyses on promoter, transcription factors, signal transduction, etc.)? (10 points)

7. Please list two method you know to study protein-DNA interactions, and give a brief description. (10 points)

8. What is the function of micro RNA? Please give examples how microRNA is associated with diseases. (10 points)

9. Overexpression of TNF-$\alpha$ is the pathogenesis of rheumatoid arthritis. Please give three strategies to develop the drugs against the disease. (10 points)

10. Computer analysis predicted a 300 bp exon sequence from HTG (highthroughput genome ) database. You used this 300bp to search in EST database, but failed to find this 300bp in EST database. Please give all possible reasons. (10 points)

11. Using a pair of primers in PCR to amplify a full-length cDNA clone, you amplify 3 specific fragments with different sizes. Please give all possible reasons and the mechanism to generate 3 fragments. (10 points)