1. A novel pathogen X is recently proven to cause SARS. Please describe your strategy on how to understand the genomic sequences of pathogen X. (10%)

2. A recently identified gene #10001 is proposed to be associated with cancer X. Please propose one possible mechanism involved in mutation of gene #10001 and development of cancer X.　How would you prove this working hypothesis? (10%)

3. 細菌性的信息傳遞通常以 Two-component regulatory system 來描述，請解釋並簡述什麼是細菌的 Two-component regulatory system？(10%)

4. 在金黃色葡萄球菌的細菌研究上有突破性發表，有一位研究者發現一個 "X 蛋白是此菌最重要的致病因子，請問他需提供何種證據才足以令人心服？ (10%)

5. 請由下列四者之中，擇一題回答。技術部分請同時加以說明。(四者擇一作答。若回答一題以上，則閱卷者將擲銅板擇一評分而完全忽略其他答題，請勿浪費時間)。請只要選擇一題作答 (10%)。

1) 試述 RT-PCR 在臨床診斷方面的應用。

2) 試述 SSCP 在臨床診斷方面的應用。

3) 試述 real-time PCR 在臨床診斷方面的可能應用。

4) 試述 HUMARA test 在臨床診斷方面的可能應用。

6. 1) In higher eukaryotic transcripts, there is a conserved pattern of nucleotides around functional initiator codons. Such a pattern is called: A) Kozak consensus, B) Shine-Dalgarno consensus, C) Okazaki consensus, and D) Liem consensus. (1%)

2) Please write down the consensus sequence __ __ __ A T G __ (one nucleotide in each position) according to the following information. (5%)

It had been shown by point mutations that positions -3 (three nucleotides upstream from the AUG initiator codon) and $+4$ (immediately following the AUG codon) have the strongest influence on translation efficiency. A purine at position -3 is most critical; when a pyrimidine replaces the purine at position -3, translation becomes more sensitive to nucleotide changes at positions -1, -2, and $+4$. Of 699 vertebrate mRNA functional initiation codons whose contexts were examined, 175 have a combination of A/G at the $-3/+4$ position, 130 are G/G, 114 are A/A, only 8 are T/G, and none are T/C, T/T, or T/A (see table 1). The distribution in positions -1 and -2 is listed in table 2.

Table 1:

-3	A	A	A	A	G	G	G	G	C	C	C	T	T	T
$+4$	G	A	C	T	G	A	C	T	G	A	Y	G	A	Y
number	175	114	63	73	130	47	47	27	9	2	4	8	0	0

Table 2:

	A	C	G	T
-1	15%	55%	21%	9%
-2	27%	49%	13%	11%

（背面仍有題目,請繼續作答）

3) A diligent graduate student finds that the above consensus sequence contains an Nco I and an Nla III restriction sites. Please write down the recognition sequences of Nco I and Nla III. Nco I is estimated to have one recognition site per 4096 bp. Nla III is estimated to have one recognition site per 256 bp. (4%)

7. The most fascinating proteins that associate with the cytoskeleton are called motor proteins. Dozens of different motor proteins coexist in every eukaryotic cell.　1) Please list three specific features to distinguish them from one another.　2) Please list two major types of motor proteins including their associated features, molecular structures, and cellular roles.　Be sure to provide one example for each type to make your point (10%).

8. Please 1) define the central dogma of modern molecular biology including their function to the cell, then 2) provide two biological processes, which break this dogma, and the key protein components involving each process. (10%)

9. What is the principle of allele specific oligonucleotide (ASO)? The following experiment may help you to understand it. One researcher has designed the oligomers (a. GACCGCGGCCCGCTTCTG b.CAGAGGCGGGCCGAGGTc) for the ASO hybridization experiment to detect two different alleles which differ at amino acid motif EQKRAAV and EQRRAEV, respectively. Can you explain why he designed these oligomers in this manners.(You may consult the amino acid codon table to figure out why.) (10%)

a. GACCGCGGCCCGCTTCTG for Glu-Gln-Lys-Arg-Ala-Ala-Val

b. CAGAGGCGGGCCGAGGTC for Glu-Gln-Arg-Arg-Ala-Glu-Val

TABLE 4-3　The Genetic Code (RNA to Amino Acids)*

First Position (5' end)		Second Position				Third Position (3' end)
		U	C	A	G	
U		Phe	Ser	Tyr	Cys	U
		Phe	Ser	Tyr	Cys	C
		Leu	Ser	Stop (och)	Stop	A
		Leu	Ser	Stop (amb)	Trp	G
C		Leu	Pro	His	Arg	U
		Leu	Pro	His	Arg	C
		Leu	Pro	Gln	Arg	A
		Leu	Pro	Gln	Arg	G
A		Ile	Thr	Asn	Ser	U
		Ile	Thr	Asn	Ser	C
		Ile	Thr	Lys	Arg	A
		Met (start)	Thr	Lys	Arg	G
G		Val	Ala	Asp	Gly	U
		Val	Ala	Asp	Gly	C
		Val	Ala	Glu	Gly	A
		Val (Met)	Ala	Glu	Gly	G

10. From what we have learned in the past from genetic diseases, the molecular genetic mechanisms responsible for these diseases have been investigated thoroughly. Please describe from the aspects of gene structure the types and positions of mutations occurring in these diseases. (10%)