1. We now know that 30,000 to 40,000 genes possibly encode the book of a human life. Although we human beings are much more complex than fruit flies in every aspect, the total number of our genes are only 2 times of that encoded by fly genome (i.e., 19,000 genes in fruit fly genome). Please specifically propose two possible molecular mechanisms to speculate the discrepancy between complexity and gene number. (10%)

2. Two groups of genes have been implicated in tumorigenesis. Please (A) name these two groups, (B) give one example for each group then (C) illustrate their roles in normal cells (10%).

3. Virus infection has been now found to associate with a great number of pathologies including cancer. Viruses can be broadly divided into two types based on their genome type. Please (A) name these two types then (B) give an example for each type of virus and its affiliation with diseases. Finally, (C) please propose two possible mechanism how a virus can cause human diseases (10%).

4. A human diploid genome consisted of 6×10^9 nucleotides can be as long as 68 cm long if uncoiled as single molecule (0.034 cm per 106 nucleotides) whereas the diameter of a nucleus containing the genome is only in the range of several micrometers (μm). As a result, how one meter long of naked DNA molecules can be compacted into a nucleus? Please (A) propose a detailed DNA packaging mechanism and (B) describe all components involved in this packing process (10%).

5. Cell migration is an important factor for cancer metastasis. Please draw a diagram or carton to describe your model of the molecular events that happen during cell migration (10%).

6. Several techniques have been established to identify genes that are important in certain diseases or abnomalities. For example, the use of DNA micro-arrays to screen genes that differentially expressed in normal and diseased tissues. Please describe briefly two other methods for new gene identification and how they work. (10%)

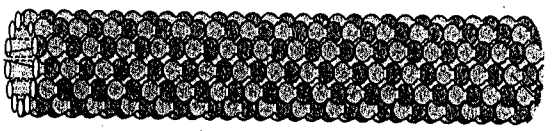
7. An autopsy was made from a victim of an unknown disease, the X-disease. Under routine pathological examination (H&E stain), the only finding is that certain type of "aggregated round cells" being found in the biopsy tissues of the lung. Start from what you have- the frozen and paraffin embedded biopsies and your knowledge in molecular medicine, what will you do to isolate and identify the nature of these round cells? How could you prove that they are the cause of X-disease? (note: the round cells may be infectious origin or neoplastic or immune origin. Do not limit your mind, make your own model and solutions as completed and reasonable as possible. (10%)

(背面仍有題目,請繼續作答)

8. (10%)

(a)

(b)



(c)

圖(a)(b)(c)代表三種 cytoskeleton 的結構。

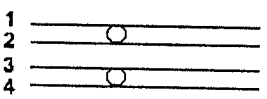
問題一 (3 分)：請問(a)(b)(c)各是哪種 cytoskeleton？

問題二 (2 分)：請問圖(b)這種 cytoskeleton，其 polymerization 的 dynamics 有何特色，與(a)(c)有何不同？

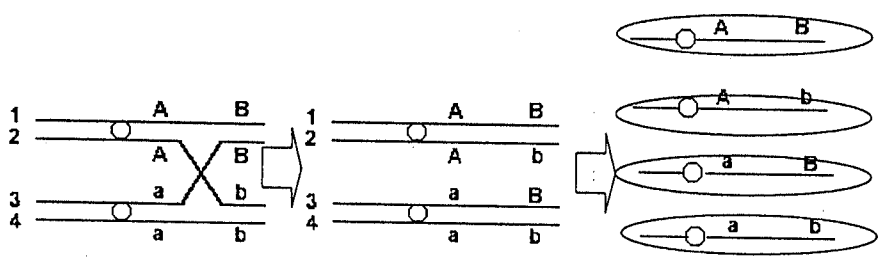
問題三 (5 分)：請問圖(b)這種 cytoskeleton 在細胞中有哪些功能？

9. 現在有許多方法可以比較兩種細胞之間的差別，例如肝癌細胞與正常肝細胞間基因表現的差異。試舉出兩種方法，並比較之間的優缺點。(原理爲主，不要描述一堆操作細節)。所舉方法最好能適用於每年研究經費 200 萬元，學生兩名的實驗室。(方法各佔 3 分；比較優缺點佔 4 分)。 (10%)

10. 背景資料一：見下圖。metaphase 的 sister chromosomes 在 meiosis 的第一次細胞分裂時是 1 與 2 配、3 與 4 配地被分到 daughter cells 中；mitosis 時，則可能是 1 與 3 配、2 與 4 配，也可能是 1 與 4 被分到同一 daughter cell、2 與 3 被分到另一 daughter cell。



背景資料二：meiotic recombination 圖示。A 與 a 代表 gene A 的不同 allels；B 與 b 代表 gene B 的不同 allels。 (10%)



問題一 (4 分)：請畫出 mitotic recombination 的可能情形。Crossover 的地方請如背景資料二一般，畫在 gene A 與 gene B 之間。(注意！請畫在答案卷上！千萬不要畫在這張試題上！)

問題二 (3 分)：mitotic recombination 如何造成 LOH (loss of heterozygosity)？請在你所畫的圖上，指出發生 LOH 的地方。

問題三 (3 分)：試述 LOH 與 cancer(癌症)的關係。