BC 378 **Problem Set #6**

1. Many members of an isolated group of humans are subject to a fatal genetic disorder known as muscular maniosis (MM). A person with this disease is subject to periodic fits of uncontrolled and violent muscle contractions of the entire body accompanied by mental delirium. It is rare for people with this disease to live more than 35 years because they usually die from fatal injuries sustained during these fits of madness. It is not known what gene is defective in individuals with muscular maniosis. It is known, however, that the disease is inherited within families as an autosomal recessive disorder.

A world-renowned group of researchers headed by the illustrious biochemist Jules Mealcard and the celebrated biophysicist Sandy Nabob has just been given a huge research grant to identify the gene responsible for muscular maniosis.

a. Initially they will need to find out roughly where the MM gene is located in the human genome. How should they do this?

b. They have successfully narrowed down the location of the MM gene to within a 100 kbp region of chromosome 14, which they have isolated in a BAC clone. At this point they need to figure out what genes are actually present in this part of the genome and what type of proteins they encode. How could they do this?

c. After finishing the preceding analysis they have narrowed down the search to 2 genes. Both of these genes encode muscle proteins, but they can't figure out the exact function of either one. How can they figure out which gene is the MM gene?

4. Professor Ablo, whom we know from her previous work on Tasmanian devils, is now busy making a genomic library from these lovely beasts. The size of the TD genome is 1200 Mbp. In making her library, Dee has randomly broken up genomic DNA and cloned the pieces into a plasmid vector. Her average insert size is 10 kbp.

a. How many independent clones will she need to have in order to have a library with a total insert size that is equal to the size of the genome (1 genome equivalent)?

b. If Dee wants to find a single-copy gene in the TD genome, can she be assured of finding it in a library with a size of 1 genome equivalent. Why or why not?

5. Professor Ablo has also made a cDNA library from Tasmanian devil brain tissue. The library consists of 120,000 independent cDNA clones.

a. She wants to obtain a cDNA clone for the fairly abundant *QED* mRNA. This mRNA is known to make up about 0.2% of all brain mRNA. In order to save on materials (grant money is running low for this project) how many cDNA clones should she screen in order to isolate a *QED* cDNA clone?

b. If she wanted to isolate a cDNA clone for the *BOB* mRNA, which represents approximately 0.0005% of all brain mRNAs, how many clones should she screen?