Subcommittee on Genetic Modification
Orientation for Staffers
Problem Set 3: Proteins and Translation

Part of every answer (now and always) should be the reasoning that led to it.

3.1. Consider the cartoon of a newly synthesized protein to the right. Spheres are supposed to be amino acids: blue – hydrophilic; gold – hydrophobic.

1.a. What are some examples of amino acids that could be blue? Yellow? You might make use of this chart of amino acids.

1b. If this protein is in solution able to move around (but the amino acids stay attached to each other), what do you predict will be its final configuration?

3.2. Most proteins have over 100 amino acids, but there is a remarkable protein of only 13 amino acids that regulates the developmental fate of certain cells.

2.a. How many nucleotides are in the gene encoding this protein?

2.b. A DNA sequence containing the gene in its entirety (plus several more nucleotides) is shown below. Figure out what must be the amino acid sequence of the corresponding protein.

AGATTATGAAGGCAATTATGTTAGTGAATTTCTGTGATGAGCGCGGTAGTGGTAGATAGAACGA

3.3. Sickle cell anemia is the result of a mutation in the 6th amino acid of beta-globin, leading to aggregation of the protein. Here are the first several amino acids of normal beta-globin and mutant beta-globin

Normal: Val-His-Leu-Thr-Pro-**Glu**-Glu-Lys-Thr-Als
Sickle: Val-His-Leu-Thr-Pro-**Val**-Glu-Lys-Thr-Als

3.a. Using a genetic code table, figure out (to the extent possible) what is the nucleotide sequences of the normal and mutant beta-globin genes.

3.b. Why might the mutation from glutamate to valine lead to aggregation?

3.c. Hemoglobin is a multimeric protein consisting of two subunits of alpha-globin and two subunits of beta-globin. One genetic treatment for sickle cell anemia is to induce the expression of gamma-globin, which is normally expressed only in fetuses and is a component of fetal hemoglobin. Do you imagine that gamma-globin is more similar to alpha-globin or beta-globin? Why?

3.4 Huntington's disease is caused by the expansion of a series of 3-nucleotide repeats, where the normal gene (called *huntingtin*) has typically 11 to 34 copies of the repeat, while a person affected with the disease may have over 66 copies. Here is the sequence of an internal portion of the normal and affected *huntingtin* gene:

Normal: ...CCTTCCACCAGCAGC...[AGC]**20**...AGCAGCCGCC...
Affected: ...CCTTCCACCAGCAGC...[AGC]**80**...AGCAGCCGCC...

From this information describe (to the extent possible) how the protein sequence differs between those with normal and affected *huntingtin* genes.