Protein Modeling Test **KEY**
Ward Melville Science Olympiad
2014-10-15

Name _____

Multiple Choice (1 point each).

1) How many nitrogen atoms are found in the backbone of each amino acid?
   A) 1
   B) 2
   C) 3
   D) 4

2) What does a nuclease do?
   A) Degrade the nucleus of a HIV-infected cell
   B) Cleave DNA or RNA
   C) Form bonds between strands of DNA or RNA
   D) Activate transcription factor proteins

3) Which of the following amino acids contains sulfur?
   A) Tryptophan
   B) Glutamic Acid
   C) Methionine
   D) Histidine

4) If you are discussing alpha helices and beta sheets then you are talking about a protein's:
   A) primary structure
   B) secondary structure
   C) tertiary structure
   D) quaternary structure

5) If a protein is membrane bound, where would you expect to find hydrophobic amino acids?
   A) At the C terminus
   B) Buried in the center of the protein
   C) In the alpha helices of the protein
   D) On the protein's surface

6) Which of the following amino acids is involved in disulfide bonds?
   A) Cysteine
   B) Histidine
   C) Tyrosine
   D) Methionine

7) What is the primary function of a zinc finger motif?
   A) Stabilizing the tertiary structure of the protein
   B) Binding to charged residues on the surface of proteins such as CCR5
   C) Cleaving phosphodiester bonds in DNA
   D) Binding to a specific DNA sequence

8) Which of the following amino acids is charged?
   A) Lysine
   B) Cysteine
   C) Glutamine
   D) Phenylalanine

9) Which of the following is a Jmol command that would display only the parts of the FokI protein relevant to this year's event (chain A, amino acids 421-560)?
   A) display chain A aa 421-560
   B) restrict *a and 421-560
   C) show A:421-560
   D) display ~a and 421:560

10) Roughly (i.e., to the nearest order of magnitude – think Fermi Questions, even though it's sadly not an event this year) how many base pairs are there in the human genome?
   A) 100,000
   B) 10,000,000
   C) 1,000,000,000
   D) 100,000,000,000

Short Answer.

1) When studying the function of different proteins in the cell, it can be useful to introduce those proteins into cells that do not normally produce them. How do researchers go about causing a cell to produce a protein it does not normally express? **(4 points)**

- **1 pt** for mention of placing the DNA encoding that protein into the cell
- **1 pt** for mention of using vectors to place DNA into cell/explaining that just injecting the DNA directly into the nucleus doesn't work
- **1 pt** for explaining that viral vectors introduce DNA sequence directly into host cell genome
- **1 pt** for explaining that once entered into host cell genome, DNA sequence is transcribed just like any natively produced protein

2) If we want to edit a specific site in the human genome using DNA-binding proteins, we need to be able to identify the correct site with high accuracy. How long a string of DNA bases does our protein have to be able to recognize in order for us to be certain that it will bind to only that one site in the human genome? Explain your answer. **(4 points)**

- **1 pt** for mention that total # of base pairs in human genome is ~3 billion
- **1 pt** for mention that maximum # of unique sequences of length n is 4^n (or 4 x 4 x … x 4 n times)
- **1 pt** for explaining that if you have a sequence long enough that there are more possible unique sequences than there are sites in the human genome, you must be able to uniquely identify any site with a sequence of that length (or rather, it's statistically so unlikely that two identical sequences of that length would appear in your genome that it essentially never happens)
- **1 pt** for correct answer: 16 bp

3) The CCR5-Δ32 mutation, present in roughly 15% of the European Caucasian population, confers resistance to HIV infection in individuals homozygous for this mutation (and slows the progression of the infection to AIDS in individuals with one copy of the mutated gene).

a) Describe how this mutation prevents HIV from entering the cell. **(4 points)**

- **1 pt** for mention that CCR5 is an HIV co-receptor that allows HIV to enter immune cells
- **1 pt** for explaining that the Δ32 mutation causes a frameshift that introduces an early stop codon, resulting in a truncated protein
- **1 pt** for explaining that the truncated protein is not trafficked to the cell surface and thus cannot be used for entry by HIV
- **1 pt** for explaining that the mutation is non-harmful because CCR5 does not seem to have any essential purpose/its function can also be performed by other proteins so a mutation that renders it non-functional doesn't have any other apparent adverse effects

b) Describe how the effects of this mutation could be replicated with lab-engineered zinc finger nucleases. **(4 points)**

- **1 pt** for explaining that an engineered zinc finger nuclease can make double-strand cuts in the human genome at any specific site
- **1 pt** for mention that zinc finger nucleases should be targeted to the start and end sites of the Δ32 mutation (also fine if they say any other site within the 32 bp deletion)
- **1 pt** for explaining that existing cell DNA repair machinery will try to put the two ends back together, but imperfectly, inducing additional mutations
- **1 pt** for explaining that the goal is to prevent CCR5 trafficking to the cell surface